OVARIAN TUMOURS
A Morphological and Experimental Study

By

Soad G. Iskander, M.B., B.Ch., D.M.Sc., Cairo.

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"The fruits of the tree of knowledge are various;
he must be strong indeed who can digest all of them."

Mary Coleridge.

"We know accurately only when we know little;
with knowledge doubt increases."

Goethe.

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INTRODUCTION

The range of variety exhibited by neoplasms in the
ovary is not duplicated in any other organ of the body
and this range is being continually expanded by the
addition from time to time of what appears to be new
entities. Experimental production of ovarian tumours,
while confined to observations on animals, has opened up
an entirely new field for investigating some fundamental
histogenetic problems, the solutions of which for years,
have in human beings, defied the efforts of embryologists
and pathologists alike.

The discovery within this group of neoplasms, of
several members which exert a physiological influence on
their host has led to exhaustive studies of the hormone
content of these ovarian neoplasms. Biological assays
of tumour tissue, blood and urine, give a partial
knowledge of the hormonal conditions existing in many
of them. Histochemical studies on ovarian tumours are,
however, very few. The identification of specific
substances in situ, no doubt, affords valuable information
as to the type of cell implicated in their production.
As Dempsey and Wislocki (1946) state "Histochemistry
deals with the chemical characterisation of substances
in their natural locations, within cells and tissues".
In recent years, emphasis in histochemical investigations
has shifted towards the development of highly specific
reactions for individual compounds or classes of

substances. Various aspects of such a correlated study reinforce and validate each other so that by the combined weight of the various lines of evidence conclusions may be drawn when a single approach would prove to be inconclusive. The present work consists of two parts:

1. A retrospective study comprising a survey of 1376 cases of ovarian neoplasms which came to the Department of Obstetrics and Gynaecology over the last ten years (1950-1959). In this review, I have tried to correlate data which has recently accumulated on the general subject of ovarian neoplasms.

2. A histochemical study incorporating an attempt to localise the site of production of steroid hormones and their precursors in 122 cases of ovarian neoplasms (accompanied with uterine body or endometrial curettings) which came to the Department of Obstetrics and Gynaecology, during the last 2 years. In addition, their has been an attempt to demonstrate several enzymes in the fresh (unfixed) neoplasms in a small number of cases.

EMBRYOLOGY OF THE HUMAN OVARY AND ITS CONTRIBUTION TO THE HISTOGENESIS OF OVARIAN NEOPLASMS.

Of all aspects of ovarian neoplasms, their histogenesis is perhaps the most difficult to understand. Certain functioning ovarian neoplasms may resemble in their morphology the stages of the embryonic development of the gonad. However, the value of embryology in clarifying problems of the origin and nature of these neoplasms has been much discredited. There is division of opinion amounting almost to confusion concerning the origin of the constituents of the ovary. Consequently, the classification of ovarian neoplasms is constantly under review and the status of many of them is still not clear. It is believed, however, that newer approaches to embryology employing histochemical methods, surgery, hormone administration, radiation and isotopes are shedding new light on the field.

The gonad originates as a ridge-like thickening (genital ridge) on the ventral border of the mesonephros. It is composed of coelomic epithelium covering the underlying mesenchyme. As the early gonad develops, strands of epithelial-like cells (sex cords) appear beneath the coelomic epithelium, extending through the mesenchyme and enclosing germ cells. The latter are believed to migrate to the genital primordium

from the entoderm of the gut. The extragonadal origin
of the germ cells and their subsequent migration to the
developing gonad is based partly on the work of Witchi
(1948) and mainly on the histochemical work of McKay
et al (1953) and Pinkerton, McKay et al (1961).

The gonad commences to differentiate into ovary
or testis at about the seventh week. In the testis
at this time the sex cords become delineated and
eventually develop into the Sertoli cells of the
seminiferous tubules. Meanwhile, certain cells of the
intervening mesenchyme differentiate into Leydig cells.
In the case of the ovary, the sex cords remain
indistinct during the seventh week but later they
encapsulate the primitive sex cells and ultimately
differentiate into granulosa cells of the primary
follicles. The mesenchyme develops to form the
ovarian stroma and theca cells. In the ovarian
medulla, a rudimentary testis-like development of the
sex cords and mesenchyme occurs. This remains in the
adult ovary as the rete ovarii and Leydig cells of the
hilus. This testicular remnant seems the logical site
of origin of arrhenoblastoma.

There is considerable controversy as to whether
the sex cords originate in the mesenchyme or whether
they are downgrowths of the coelomic epithelium.
In other words, whether or not the granulosa and
Sertoli cells originate from the mesenchyme as do the
theca and Leydig cells. A widely accepted view is
that the sex cords develop from the mesenchyme, the

coelomic epithelium being only a covering layer.
(Fischel, 1930, Politzer, 1933, Novak, 1940 and Schiller,
1950.)

However, Gillman (1948) presented evidence that
while the theca and Leydig cells are of mesenchymal
origin, the sex cords arise from the overlying coelomic
epithelium and grow down into the mesenchyme.

In granulosa-theca cell tumours it is sometimes
impossible to tell granulosa and theca cells apart.
While this does not necessarily imply metamorphosis
from one type to the other, it suggests a close relation-
ship (Morris and Scully, 1958).   Gruenwald (1942)
expressed the view that the basement membrane separating
the coelomic epithelium and the mesenchyme disappears,
forming a uniform gonadal blastema.

Quite recently, Pinkerton, McKay et al (1961),
studied the development of the human ovary, using histo-
chemical techniques.   The results of their work can be
summarised as follows:

1) The coelomic epithelium over the medial slope
of the mesonephric ridges supplies mesenchymal cells
to the underlying gonad until at least the fifteenth
week and possibly until the last trimester when it becomes
a definitive surface epithelium with a well-marked
basement membrane separating it completely from the
cortex.

2) The granulosa cells are derived from the

mesenchyme of the mesonephric ridge.   The latter, in
the early embryos, is partially derived from the surface
cells adjacent to the coelomic cavity.

3)   The ovarian stroma seems to arise mainly from
the foetal connective tissue which accompanies the
blood vessels into the ovary from the hilus.   It is
first recognisable with certainty in the twenty-eighth
week foetus.

4)   Follicular theca cells are also first seen in
the twenty-eighth week foetus.   They develop from
stroma cells around the larger follicles which have
reached the stage of antrum formation.

PART I: SURVEY OF OVARIAN NEOPLASMS

SURVEY OF OVARIAN NEOPLASMS

A group of 1,376 cases of ovarian neoplasms has been collected and reviewed in a survey of the pathological material over the last ten years, 1950-1959 inclusive. Classification of ovarian neoplasms has been done by various authors (Schiller (1940), Meigs (1943), Taylor (1940), Selye (1945), Novak (1940), Barzilai (1943) and many others) and every pathologist seems to cherish his own classification.

In the present study individual types of ovarian neoplasms are discussed without any attempt at a new classification. Special attention has been paid to the pathologic alteration in the ovary, known as cortical stromal hyperplasia, as well as to the subject of ovarian neoplasms with functioning stroma.

Ovarian Histology

In order to describe what is meant by cortical stromal hyperplasia, it is advisable to review briefly ovarian histology. The ovary is divided into 2 portions, the outer cortex and the inner medulla, the latter comprising mainly a loose fibrous stroma with blood vessels. The cortex is composed of multipotent stromal cells derived from the genital ridge mesenchyme. In adult life these cells become modified to form cells of granulosa, theca interna, corpus luteum and finally corpus albicans. In the senile ovary the stromal cells normally undergo shrinkage.

Fibrous tissue penetrates the cortex both from the tunica albuginea and from the medulla, so that in old age the cortex is indistinguisable from old fibrous tissue elsewhere in the body.   There is considerable variation in the amount of residual stroma and the number of corpora albicantia in the senile ovary. Stromal hyperplasia may be produced in the aging ovary by imperfect diffuse recapitulation of the normal cycle of the stromal cell.

Cortical Stromal Hyperplasia

It was in 1941 that George Van S. Smith first noted ovarian stromal hyperplasia in 87% of cases of post-menopausal carcinoma of the uterus. In 1942, Johnson, Hertig and Smith reconsidered this observation and initiated a study of the aging ovary in general.   The earliest appearance of stromal hyperplasia was seen in the 45-49 year age group.   After the age of 50, it was seen with greatest frequency in cases with continued endometrial activity or outright malignancy.

In 1948, Woll, Hertig, Johnson and Smith found cortical stromal hyperplasia in 84% of surgical cases of endometrial carcinoma and in 44% of autopsy control cases of comparable age.   The greatest incidence in the controls was at the age of 50-59 years.   Two subsequent series (Novak and Mohler, 1953, and Schneider and Bechtel, 1956), comparing the ovaries of surgically treated cases of endometrial carcinoma with

those of autopsy controls have confirmed an increased
incidence of stromal hyperplasia in the former groups.
More recently, however, two contradictory reports appeared
(Roddich and Greene, 1957, and Bigelow, 1958). The
ovaries from patients with endometrial carcinoma were
compared with those from control patients of comparable
age. No significant differences were found in the
ovarian cortical stroma of the two groups.

Woll et al (1948) described the earliest evidence
of stromal hyperplasia as a wide, dense stroma (Photo 1 and
2) showing spherical masses or whorls in contrast to the
linear pattern of inactive stroma. Microscopically,
the stromal cells are large and plump and grouped into
more whorls. (Photo 53.) The nucleus is enlarged and
contains coarse chromatin granules. It is oval and
blunt instead of spindle-shaped. Reticular fibres are
increased and collagen is scant.

As the process advances, some of the stromal cells
along capillaries in these whorls become large,
epithelial-like polyhedral and fat-containing. They
have distinct cell margins and look like cells of theca
interna. These cells are seen singly or in groups.
They bear no relation to atretic follicles or their scars.
To this appearance the term thecomatosis has been given.
(Photos 19 and 40.)

When a large number of such cells form a nucleus
there tends to be some infiltration with lymphocytes and

macrophages associated at times with cholesterol-like
slits.   Sometimes foreign body giant cells make their
appearance.   To these focal collections the term
cortical granulomas has been given. (Photo 12 and 14.)
The origin of giant cells is not yet known with certainty,
that is, whether the theca-like cells are transformed into
foreign body giant cells or whether the former degenerate
and lead to giant cell response. However, Corner (1932)
observed that lutein cells can transform themselves
into macrophages.   Consequently, cortical granuloma
has been regarded as a retrogressive stage of thecomatosis.

As both thecomatosis and cortical granulomas pass
the peak of their activity, collagen is laid down and
finally only a nest of whorled, hyalinised fibrous
tissue remains.

All the above described stromal changes except
cortical granuloma are seen in the natural history of the
follicle, corpus luteum and corpus albicans.

The frequent association of these lesions with
hyperplastic bleeding endometrium suggests that there
may be more than co-incidental relationship between the
fat-containing theca-like cells and oestrogen production.

McManus and Sommers (1952) found ovarian cortical
stromal hyperplasia in 72% of cases with breast cancer
which is an oestrogen-dependent tumour.   They also found
that the postcastration survival in cases with ovarian
hyperplasia was four times the survival of others without

the finding.

Oestrogen production by the post-menopausal ovary
is indicated by the work of Parkes (1926) who reported
that oestrus persisted in mice following sterilising
doses of irradiation.   The ovaries so treated showed
no follicles or follicle derivatives at autopsy or
surgical removal, but showed large lipid-containing
cells in the cortex.   The irradiated animals with
persistent oestrus which were subjected to oophorectomy
had subsequent disappearance of oestrus.   However, the
most direct evidence that hyperplastic ovarian stroma
may be responsible for post-menopausal oestrogen derives
from Smith and Emerson's study (1954) of 7 post-menopausal
instances of breast carcinoma.   Urines were assayed for
oestrogens in two fractions.   The active oestrogen
fraction (T_o) and the inactive oestrogen fraction (T_{zn})
considered by the authors to represent oestrogen
oxidation products or precursors arising from the adrenals.
Five of their patients had had x-ray castration.   All
five, however, showed elevated T_o and T_{zn} urinary
oestrogen fractions.   Oophorectomy performed on two
of these patients resulted in a disappearance of urinary
T_o oestrogen while the T_{zn} oestrogen excretion remained
elevated and, in fact, rose as the disease advanced.
The ovaries from both patients showed cortical stromal
hyperplasia.   The authors postulated that cortical stroma
of the post-menopausal ovary may either produce active

oestrogen directly or may affect adrenal oestrogen so that it is converted into active form.

It seems that increased oestrogen activity is an effect rather than a cause and that higher level pituitary over-activity may be the common denominator. Cortical stromal hyperplasia might represent a compensatory effort of the stroma to respond to hypophyseal stimulation as the ova and follicles are depleted. The gonadotrophic luteinising hormone is normally much decreased after the menopause. Smith and Smith (1946) found that products of tissue protein catabolism stimulate the pituitary secretion of gonadotrophic luteinising hormone which might initiate abnormal stromal activity. Burt (1954) found that severe grades of ovarian stromal hyperplasia are characterised by a high count of amphophile cells in the anterior lobe of pituitary. In a series of patients with breast carcinoma Burt and Castleman (1953) showed elevated counts of hypertrophic amphophils and basophils in the pituitary as compared with controls, plus increased adrenal weight and a high incidence of ovarian stromal hyperplasia. Furth and Butterworth (1936) used generalised irradiation of mice and reported hyperplasia of anterior pituitary lobe in addition to the partially luteinised granulosa cell tumours and endometrial hyperplasia. Protein catabolism from tissue damage by the radiation might have been a factor in stimulating the pituitary.

Novak (1953) found other manifestations of pituitary over-activity in patients with ovarian stromal hyperplasia (obesity in most of them, hypertension in 48% and diabetes in 18%). Way (1954) stated that the tendency for pituitary over-activity is inherited but all its manifestations need not be evident in the same individual. To these manifestations ovarian stromal hyperplasia can be added.

Grades of Hyperplasia:

As the appearance of the stroma often varies from one region of an ovary to another, the interpretation is usually quantitative. Burt (1954) classified the degree of hyperplasia into 4 grades.

Grade 0 - little or no hyperplasia either in the cortex or medulla (Photo 3).

Grade I - hyperplasia of most of the cortex but no involvement of the medulla (Photo 4).

Grade II - hyperplasia of most of the cortex with partial medullary invasion (Photo 5).

Grade III - most of the cortex and medulla are hyperplastic(Photo 6).

OVARIAN NEOPLASMS WITH FUNCTIONING STROMA

Numerous authors have reported the occasional association of cystadenomas, Brenner cell tumours and ovarian carcinomas with endocrine manifestations. Post-operative follow-up on a number of these cases has suggested strongly a cause and effect relationship between

tumours and endocrine change. Cystadenomas and Brenner tumours have in common a stroma which may resemble the cortical stroma of the ovary, an ovarian fibroma or a thecoma. Since these neoplasms are not associated with apparent endocrine effect in the great majority of cases, many authorities believe that they are never functional. The occasional association of any endocrine change has been excluded as mere coincidence.

However, Morris and Scully (1958) reported a case of a small Brenner tumour in the wall of a large pseudomucinous cystadenoma. They also reported 4 other cases (2 Brenners and 2 primary ovarian adenocarcinomas). In 4 of them, including the first, there was evidence of oestrogen production by the neoplasm, while in the fifth (a Brenner tumour) the possibility of androgen production was suggested due to masculinisation with normal 17-ketosteroids in urine. In all 5 cases, the stroma had an appearance similar to that of a thecoma. In the first case, histochemical studies for cells producing steroid hormones also gave positive results.

Brown, Kellar and Matthew (1959) reported a case of pseudomucinous cystadenoma (Case I under the pseudomucinous group of the present review) with a history of post-menopausal bleeding and cystic hyperplasia of the endometrium. Oestrogen excretion in urine was high but fell to normal level after removal of the neoplasm and oestrogen production was therefore attributed to its

functioning stroma.

Turunen (1955) reported 2 cases of Krukenberg tumours with theca-like stroma and associated with cystic hyperplasia of the endometrium.

However, it is possible, as Teilum has pointed out, that oestrogen may not be the only hormone secreted by theca cells. Some neoplasms may be associated with either a progesterone or an androgen effect. The close relationship of the various steroid hormones is such that compounds formed during their metabolism may have quite different effects than the original substances. For example, there is evidence that both testosterone and progesterone may be precursors of oestrogen.

However, the recognition of theca cells in the stroma of ovarian neoplasms can be an evidence that these neoplasms are functioning.

OVARIAN FIBROMAS

Coe (1882) was the first to study the histogenesis of ovarian fibromas. His view that they represent an overgrowth from the ovarian connective tissue stroma is now generally accepted. As Dockerty and Masson comment (1944), it is almost impossible, in many cases, to say where normal cortex ends and tumour begins. Moreover, the tumours preserve in fair degree the feather-stitch pattern of the normal ovarian architecture.

Brother's hypothesis that fibromas are in the nature of a keloid response to the haemorrhage attendant upon ovulation, has not gained much support. Dockerty and Masson in a further study following the possibility of such an origin searched for haemosiderin in a group of 283 fibromas. They found it in 23 cases only. However, they state that evidence of old haemorrhage often is not seen in corpora albicantia even though one may be sure that haemorrhage was present in the corpora lutea of origin. The haemorrhage associated with endometriosis practically also disappears. However, endometrial-like glands were found in 25 cases and this was regarded as a possible stimulation for formation of fibromas. They concluded that the non-occurrence of fibromas in patients before puberty, plus the occasional finding of haemosiderin and endometrial glands, might be factors of importance, favouring Brother's view.

The incidence of fibromas in different previous series varies from 0.6 - 12.6% (Selye, 1945). In Dockerty and Masson's series, the incidence is 5%. The age incidence in that series ranges between 16-79 years with none of the patients in the pre-pubertal age.

The present series consists of 135 cases and constitutes about 10% of the total.

The age distribution ranges between 20-85 years. Ninety-five cases occur in post-menopausal patients. The endometrium is available for examination in 88 patients (68 post-menopausal and 20 pre-menopausal).

The endometrial picture is shown in Table I.

Table I: Fibroma - Endometrial examination - 88 cases.

68 Post-menopausal					20 Pre-menopausal			
Carcin-oma Corpus	Cystic Hyper-plasia	Benign Active	Senile Cystic	Senile	Persis-tent Prolif-erative	Normal Prolif-erative	Secre-tory	Menstrual
4	16	21	9	18	9	3	7	1

The tumours vary in size. Some are small nodules (few millimeters in diameter) attached to ovarian surface by an almost microscopic pedicle. Others are large 9" or more in diameter). They are usually rounded or oval, solid or solid-cystic tumours. Central cystic degeneration is frequently met with (the Goedes of Coe). The colour is whitish or greyish white. In a few instances (5 cases) in which a twist of the tumour pedicle has taken place, infarction caused a reddish colour. A yellow colour is noted in some cases and it is either due to fatty degeneration or to the presence of some intermingled (thecomatous) elements. The surface is smooth but sometimes corrugated.

Most fibromas are localised and encapsulated, but occasionally few small diffuse fibromas tend to imitate the shape of the normal ovary. Thirteen cases exhibit slit-like openings and small cysts on the cut surface. These are adeno-fibromas (Photo 8) and cystadenofibromas.

Ten patients (7%) have bilateral fibromas. This is in agreement with the figure of 10% cited by Dockerty in his review.

Microscopically, they can be classified into cellular and fibrous types in pure or mixed forms. In typical cases the basic cell appears to be the peculiar mesodermal type so characteristic of the ovarian stroma with preservation of the closely knit "featherstitch" arrangement of the normal ovary. The tumour cells are small, thin and spindle shaped with pointed cytoplasmic processes and narrow oval nuclei parallel to the long axis. Collagenous material surrounds and compresses the cells in many fields. (Photo 7)

Hyaline and myxomatous degeneration as well as calcification are common findings. Moreover, hyaline bands typical of theca cell tumours are frequently encountered. The line of demarcation between normal and neoplastic tissue is not distinct and mitotic figures are practically absent.

Marked anaplasia, mitosis, malignant giant cells and scanty collagen fibres have all been noted in a case of fibrosarcoma in a patient aged 57 years. (Photo 9)

However, the histological picture is not always so easy. The presence of hyperplastic endometrium in association with what appears to be a fibroma has led to the careful search for (thecomatous) elements. These have been found in 7 post-menopausal patients. The endometrium shows cystic hyperplasia in 6 of them and benign activity in the remaining one. Theca cells are

plump and oval in shape, with rounded nucleus and
copious cytoplasm which may be vacuolated.   Such cells
are usually present in small groups amidst the fibroblasts.
Their distribution is so variable that they can be easily
missed.

Some workers (Biggart & Macafee, 1955) regard any
fibroma showing fatty change and associated with hyper-
plastic endometrium as a thecoma.   However, it all
depends on the nature of this fat, i.e., whether it is
simply degenerative fat or active steroid precursor.
This cannot be ascertained by ordinary H. & E. or
Sudan IV stained sections.   Hence, the need for
a histochemical study.

McKay et al (1949) distinguished between active
and inactive thecoma by the presence or absence of
histochemically demonstrable steroids. He suggests that
thecoma may pass through a stage of active secretion
followed by an inactive phase, in the same way as theca
cells of a Graafian follicle which undergoes atresia.
Both inactive thecoma and fibroma contain no reactive
material.   The differentiation between the two rests on
morphological grounds which is often very difficult.

In the present study the term fibroma with
thecomatous elements has been used to designate any
fibroma in which theca cells can be seen, the plump
appearance of the true theca cells being the deciding
factor. (Photo 10)

Examination of the other non-tumour-bearing ovary for evidence of cortical stromal hyperplasia has also been carried out in the present series.

Thecomaosis and/or cortical granuloma,as well as thickened cortex,have all been found in 15 cases. (Photos 12, 14)   Thirteen of these cases are post-menopausal.   The endometrium (available in 12 cases only) is cystic hyperplastic in 5, active benign in 5, senile and senile cystic in 2.   The remaining 2 cases are actually very near the menopause (5th and 6th decade) and the endometrium shows persistent proliferative activity in both.

In 4 post-menopausal patients the tumour is a small nodule and the remaining cortex of the same ovary also shows cortical stromal hyperplasia.   The associated endometrium is cystic hyperplastic in 1, active in 2 and adenocarcinomatous in 1.

The figures for cortical stromal hyperplasia would have been much higher but for the following reasons:

1) Presence of cysts (follicular, luteal, endometriomatous, etc.) distorting the shape of the ovary and the relation of cortex to medulla.

2) Absence of the other ovary in a minority of cases.

3) Some of the neoplasms are bilateral and therefore cortical stromal hyperplasia can no longer be considered.

CASE REPORTS:

Fibroma with thecomatous elements

Case 1. (A.7567.)   (Mrs J.M., 59 years old, 10 years
                     post-menopausal.)

This patient entered the hospital with the chief
complaint of abdominal swelling for the past year. On
examination, the abdomen was distended and dilated veins
were present on both flanks. A firm, smooth and rounded
mass was felt arising from the pelvis and extending up
to 2 fingers above the umbilicus.   Shifting dullness was
elicited.

Total hysterectomy and bilateral salpingo-oophorectomy
were performed.   A huge fibroma (size of a rugby football)
was replacing the right ovary and associated with
considerable ascites. Microscopically, the tumour
consisted of the usual interlacing fibroblasts and collagen
fibres with areas of hyaline and myxomatous degeneration.
Haemorrhagic areas were also present.   A few clusters of
cells were, however, plump and had a vacuolated cytoplasm
and a rounded nucleus, i.e., theca cells. (Photo 10)
Although the patient gave no history of post-menopausal
bleeding, the endometrium was the seat of cystic endo-
metrial hyperplasia. (Photo 11)

Fibroma with cortical stromal hyperplasia of the contra-lateral ovary

Case 2. (E.310.)   (Mrs J.B., 52 years old, 8 years
                     post-menopausal.)

This patient entered the hospital with a chief

complaint of two episodes of pain in the right groin, over
the past 10 weeks.   Examination provided the diagnosis of
ovarian tumour.   This was removed, together with the
uterus and contralateral appendages. The tumour was
a large fibroma, 6" x 4" x 3", replacing the right ovary.
Its long pedicle was partially twisted.   The left ovary
was slightly enlarged and its cortex thickened and nodular.
Microscopically, the tumour was an ordinary fibroma. The
left ovary showed (grade I) cortical stromal hyperplasia
and a cortical granuloma in the process of fibrosis
(Photo 12).   The endometrium was the seat of proliferative
activity with some dilated glands. (Photo 13)

Case 3.   (E.3871.)   (Miss B.L., 51 years old, her last
                       period on 29.9.58.)

This patient entered the hospital with a chief
complaint of abdominal swelling and irregular, heavy
periods over the past year.   Examination provided the
diagnosis of an ovarian tumour.   On 15.10.58,
hysterectomy and bilateral salpingo-oophorectomy were
performed.   The left ovary was replaced by a large, hard,
irregular tumour which showed the gross and microscopic
appearances of a fibroma.   The right ovary was larger
than normal and had a thickened cortex.   Microscopically,
it showed (grade 2) stromal hyperplasia.   Thecomatosis
passing into the stage of cortical granuloma formation
was also present (Photo 14).   The endometrium showed
very active proliferation. (Photo 15)

THECA CELL TUMOURS

The first accurate description of these neoplasms was given by Loeffler and Priesel (1932). Since then, many observations have been added and these have been summarised by Banner and Dockerty (1945) as follows:

1) The theca cell tumour is an established entity.

2) The tumour often produces oestrogen.

3) The tumour probably derives its origin from certain pleuripotential mesenchymal cells of the ovarian cortex and is related on the one hand to the histologically mature fibroma and on the other hand to the comparatively de-differentiated granulosa cell tumour.

Most investigators now agree with Fischel (1930) that both theca and granulosa cell tumours spring from ovarian cortical mesenchyme. This hypothesis has been supported by the experimental work of Furth and Butterworth (1936) and of Geist, Gaines and Pollack (1939) who through the employment of roentgen rays were able, in mice, to produce both theca and granulosa cell tumours. Both types appear to have the mesenchyme as a common origin. This explains the admixture of granulosa and theca in one and the same tumour. Novak (1940) even suggests the term mesenchymoma to designate both tumours.

On the other hand, Gillman (1948) while accepting that theca cells (with their tumours) arise from the stroma cell which is ultimately a mesenchymal derivative, he thinks that granulosa cells (with their tumours) are

derived from the coelomic epithelium.

Recently, however, the histochemical work of Pinkerton, McKay, et al (1961) provides evidence that the granulosa cells are also derived from the ovarian mesenchyme.

Similarity between granulosa cell tumours and thecomas with regard to their hormonal activity has been observed by Banner and Dockerty (1945) and Mackay et al (1953). However, Shippel (1955) suggests that theca cells are the source of androgen in the ovary. He attributes the hirsutism and other masculine features of the ovarian polycystic disease to the associated hyperthecosis. However, in 40 patients with polycystic disease of the ovaries, Evans and Riley (1961) found no relationship between the degree of hyperthecosis and hirsutism. Du Toit (1951) has also indicated that hirsutism may occur in the absence of theca cell hyperplasia. Evans and Riley presented also a case of thecoma with co-existent polycystic disease in the other ovary in a pre-menopausal patient, thirty-two years old. There was no evidence of masculinisation. Ovulation and menstruation resumed following excision of the thecoma and wedge resection of the opposite ovary. They suggest that hyperthecosis may be a contributing factor to the development of the neoplasm. The ovarian endocrine environment in such cases resembles that associated with the experimental production of granulosa and theca cell tumours in rats

and mice.   An abnormal gonadotrophic stimulation
resulting in theca cell hyperplasia and neoplasia has
been postulated by them.

According to Dockerty (1940) 80 per cent of theca
cell tumours occur after the menopause and are rare
before thirty-five years of age.   On the other hand,
Gordon and Marvin (1951) reported a case of thecoma
in a child of one year.   In Banner and Dockerty's series
(1945) the incidence of thecomas was about 3 per cent
of solid ovarian neoplasms and one third that of
granulosa cell tumours.

The present series consists of 15 cases and
constitutes about one per cent of the total. With one
exception, all are post-menopausal patients ranging
in age from 52 to 86 years.   The only pre-menopausal
patient (33 years old) had a twisted tumour which was
removed separately, leaving the uterus and other
appendages behind.   One cases shows small bilateral
tumours, all the others being unilateral.

In thirteen cases, the uterus is available for
examination.   The endometrial picture is shown in
Table II.

Table II: Thecoma — Endometrial examination — 13 cases.

Cystic hyperplasia	Carcinoma corpus	Post-menopausal active benign
7	5	1

The tumours vary in size from ½" to 7" in diameter.
They are encapsulated, solid tumours, generally
presenting the appearances of a fibroma, but frequently
showing a yellowish colour.   On cut section, the tumour
is composed of islands of yellow tissue separated by
bands of connective tissue. Occasionally, cystic areas
exist.

Microscopically, a thecoma is made up of
interlacing bands of spindle epithelioid cells,
irregularly distributed and separated by strands of
connective tissue containing hyaline plaques.
Vacuolization of the cytoplasm can often be recognised
but its extent and distribution are variable.   The
nuclei are oval or rounded with an occasional mitotic
figure present.   However, all cases are benign.
Sudan IV frozen sections reveal that the cytoplasmic
vacuoles are filled with fatty material.   Frank
luteinization is rare.

Silver stains reveal an intimate peri-cellular
network of reticular fibres (Traut and Marchetti, 1940).
This is a very important method to differentiate
between theca and granulosa cell tumours.   The granulosa
cells exist usually in large groups, each cell being
in intimate contact with its neighbouring granulosa
cell.   The complete island is surrounded but not
penetrated by the reticulum.   Granulosa cells also
contain many argentophilic granules, whereas the

cytoplasm of thecal cells has almost none. (Photos 18 and 23)

There is considerable variation from one area of the neoplasm to another as regards the amount of collagen. On the whole, collagen is scanty but occasionally it forms hyaline broad bands (Photo 16) which may fuse into a structure resembling a corpus albicans. McKay, Robinson and Hertig (1949) consider fully hyalinised tumours as inactive thecomas. They presented three such cases containing no histochemically reactive steroids and having no endocrine function. However, the distinction between fibrosed thecomas and fibromas is often impossible. Gillman (1948) states that, as such, a theca cell is capable of forming masses of fibrous tissue in the normal ovary, as is seen in the corpus albicans. Actually, some of the fibrous nodules encountered in the ovary may be abortive theca cell tumours. Burslem et al (1954) agree with Willis that "many, if not all, fibromas of the ovary are really fibrous theca-cell tumours". In the present series, all tumours consist mainly of typical theca cells.

The association of uterine cancer with theca cell tumours has been recognised for some time. Dockerty and Mussey (1951) found that twenty-seven per cent of post-menopausal women with feminising tumours had endometrial adenocarcinoma. In Biggart's series (1955)

the incidence of uterine cancer in association with thecoma in patients over 50 years of age, is 27.9%. Banner and Dockerty (1945) found that 33% of patients with thecomas over the age of 50 years had endometrial carcinoma.

In the series under review, the incidence of uterine cancer, in patients over 50 years of age, is 36%.

Highly active cortical stromal hyperplasia of the opposite uninvolved ovary has been found in seven out of nine cases (about 80%).

In the case of the bilateral tumours as well as in two other cases, the tumours are small and the remaining cortex of the same ovary shows marked stromal hyperplasia.

In three cases, the other ovary is the seat of papillary serous cystadenoma, primary adenocarcinoma and metastatic adenocarcinoma from a primary in the uterus.

Cortical stromal hyperplasia has been considered as the soil in which theca cell tumours are likely to develop. McKay, Hertig and Hickey (1953) believe that theca cell tumours have their origin in cortical stromal hyperplasia. Their evidence is that:

1) The histologic pattern of both tissues is identical, including the presence of hyaline plaques.

2) Transitional stages between cortical stromal hyperplasia and thecomas are seen.

3) Patients with theca cell tumours of one ovary

almost invariably have cortical stromal hyperplasia
of the other ovary.

4) Both conditions occur primarily in post-
menopausal patients.   This sounds reasonable, especially
if we remember that both theca cells and ovarian stroma
are derived from the primary ovarian mesenchyme and that
pituitary hyperfunction is a common factor in the
causation of cortical stromal hyperplasia and the
experimental production of theca cell tumours.

CASE REPORT:

(D.7582.)   (Miss E.H., 80 years old, 31 years post-
menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding on and off for the past
10 weeks.   On examination, no pelvic abnormality was
detected.   A diagnostic curettage produced bulky
scrapings which proved microscopically to be adeno-
carcinomatous.   Hysterectomy and bilateral salpingo-
oophorectomy were performed.   One ovary was slightly
enlarged and on cut section it was found to harbour
a small circumscribed yellowish tumour about 1"
in diameter.   The other ovary showed a thickened
cortex.   The uterine wall was invaded by greyish-white
friable and necrotic tissue which also filled the
uterine cavity.

Microscopically, the endometrium was the seat of
an advanced, well-differentiated adenocarcinoma (Photo 21)
which was invading the fibro-muscular wall of the uterus.

The small ovarian tumour was a thecoma (Photo 17).
Thecomatosis was detected in the remaining cortex of
the tumour-bearing ovary (Photo 19).   The other ovary
showed 2 cortical granulomas with giant cell formation
(Photo 20).

GRANULOSA CELL TUMOURS

Von Kahlden (1895) gave the first unmistable
description of a Granulosa cell tumour and named it
"Graafian follicle adenoma".   However, it was not until
1914 that Von Werdt introduced the more common name
"granulosa cell tumour".   Lecene (1910) and Moulonguet
(1932) described a special category of tumour known as
folliculome lipidique.   Novak, however, considers this
type of tumour to be an example of a luteinized granulosa
cell tumour.

The histogenesis of these neoplasms is not well under-
stood.   The frequent intermingling in the same neoplasm
of granulosa tissue with a thecal type of tissue has been
commented on by many authors. Because of this, Selye
classifies theca cell tumours with granulosa cell tumours.
Willis (1948) similarly classified them together but
distinguishes them for descriptive purposes as predominantly
granulosa cell, predominantly theca cell, or with the two
types in equal proportion.   Burslem, Langley and Woodcock
(1954) state that "On the basis of morphology and endo-
crinology there is an essential unity between tubular
androblastoma, granulosa cell tumours, thecomas and
fibromas, and that these various types of tumours
form continuous series poorly separated into

groups".

As already mentioned under thecomas the experimental production, in mice, of the neoplasm by Roentgen rays, tends to support the thesis of Fischel, namely that both tumours are derived from the primary ovarian mesenchyme. The results reported by Biskind and Biskind (1949) as well as Li and Gardner (1947) are, even more provokating. After castration of mice they transplanted one of the ovaries to the spleen where the ovarian oestrogen can be inactivated by the liver. Granulosa cell tumours were produced in the transplanted ovary presumably because of the unopposed effect of pituitary gonadotrophins upon that ovary. Interestingly, the injection of gonadal hormones in mice bearing intra-splenic ovarian grafts prevented the development of ovarian tumours. Granting that some of these experimental tumours may represent merely hyperplasia, Burslem (1954) points out that increased pituitary gonadotrophic function during the menopause may stimulate latent competencies in the ovary to neoplasia. However, Gillman (1948) accepts Meyer's hypothesis of origin from remnants of granulosa cells which are not associated with oogonia "granulosaballen". On embryological grounds he considers that theca and granulosa cells arise independently and do not develop the one from the other or from a common stem. He suggests that the thecomatous parts of granulosa cell tumours constitute a reaction of the theca cells to the granulosa cells,

especially when the latter are degenerating as in atretic follicles in the normal ovary. "Later all granulosa cells may disappear with only theca cells and the parent stroma cells surviving. In these circumstances, there may be a great increase in fibrous tissue intermingled with patches of theca cells. Fibrous tissue may ultimately replace all cellular elements persisting as the burnt out remains of the original granulosa cell tumour."

Recently, McKay, Hertig and Hicky (1953) have postulated that granulosa cell tumours of the human ovary arise in atretic follicles which contain persistent granulosa cells. They supported their claims with illustrations of a small granulosa cell tumour of microscopic size arising in an atretic follicle, and examples of granulosa cell tumours producing structures resembling atretic follicles. However, in spite of the extensive work which has been done on the histogenesis of this group of tumours, there is no final proof as to their origin.

The tumour has been known to be feminizing. Israel and Mutch (1957) state that two thirds of granulosa cell tumours are hormonally active, being oestrogenic in effect, even when extensively luteinized. Quantitative chemical analysis of lipid content of the tumour tissue has demonstrated high values for cholesterol and its esters, the building

stones of the oestrogen molecule (Hodgson, Dockerty
and Mussey, 1945).   On the contrary, the content of
phospholipid has been very low.   Bio-assays of blood
and urine proved the presence of circulating
oestrogenic hormone in measurable amounts.   Recently,
on the basis of a histochemical analysis of a series
of granulosa and theca cell tumours, McKay, Robinson
and Hertig (1949) concluded that reactive steroid
material occurs only in theca and theca-like cells.
They emphasize that it is to their theca cell component
no matter how slight, that functioning granulosa cell
tumours owe their biologic activity.   However,
Shippel and others believe that theca cells produce
androgen, while granulosa cells produce oestrogen.
Teilum also suggests the homology of Sertoli and
granulosa cells as well as theca and Leydig cells.

The incidence of granulosa cell tumours is usually
higher than that of thecomas.   In Hodgson's series
of 3,800 ovarian tumours, 62 cases were of the
granulosa cell type (1.6%).   61.3% of them occurred
in the post-menopausal period. Hertig (1954) gives
an incidence rate of about 2% for either theca or
granulosa cell tumours.   In the present review, there
are 36 granulosa cell tumours (about 2.6% of the total).
With one exception, these tumours occur in patients
ranging in age from 23 - 77 years, the exception being
a patient aged 15 years.   Twenty-five patients
(about 70%) are post-menopausal.   The endometrium is

available for examination in 22 cases (20 post-
menopausal, one? menopausal (48 years old) and one
pre-menopausal).

Table III: Granulosa - Endometrial Examination -

20 Post-menopausal				1? Meno-pausal	1 Pre-menopausal
Carcin-oma Corpus	Cystic Hyper-Plasia	Benign Active	Senile with some activity	Cystic Hyper-Plasia	Persistent Prolifer-ative
4	12	2	2	1	1

The tumour varies in size from ¼" to 7½" in
diameter.   The colour ranges from yellowish grey to
brown.   Most of the tumours are solid throughout, some
show central areas of softening and a few are definitely
cystic.   In large tumours necrosis and haemorrhage are
frequent.   The majority of tumours are encapsulated
although adhesions are present in some of them (espec-
ially the malignant cases).

Rupture of a cystic tumour has been the presenting
feature in the 15 years old patient.

Microscopically, the cells are very similar
to normal granulosa cells being polygonal or round with
fairly abundant, faintly acidophillic cytoplasm and
frequently ill-defined cell boundaries.   The nuclei
are either dense or vesicular.   The cells are
arranged in well recognised patterns: follicular (both
microcystic and macrocystic) trabecular, cylindromatous,
and diffuse.

In the microfolliculoid type, there are micro-
follicles or rosette-like structures, corresponding
to the Call-Exner bodies described by Kahlden. These
are frequently filled with some secretion. The
macrofolliculloid pattern shows large cystic cavities
which are essentially liquifactive areas in islands of
granulosa cells. In the trabecular pattern, the cells
are arranged in ribbons of one, two or several cells, thick-
ness, set in a connective tissue matrix. When the ribbons
are fine and the matrix is scanty, the pattern is known as
moiré silk, or gyriform. The cylindromatous type is
a variant of the trabecular pattern in which the
connective tissue shows hyaline change. The diffuse
group has been much mistaken in the past for a sarcoma.
All these varieties are frequently encountered in
different areas of the same tumour. On examination of
Sudan IV stained sections, minute fat droplets are
present in some of the granulosa cells. Richer fat
content, however, is usually seen in theca cells of the
surrounding stroma. In the few cases where luteinization
has taken place, the tumour cells are almost completely
filled with fat.

In 6 post-menopausal cases of the present series,
theca cells can easily be recognised in the stroma,
though not sufficient to warrant a diagnosis of
granulosa-theca cell tumour (Photo 22). Silver stains
reveal reticular fibres surrounding masses of granulosa

cells but never between them.   Argentophillic granules are also present in their cytoplasm (Photo 23).

Six cases (16.6%) are malignant.   The cells are irregular and arranged diffusely.   The nuclei vary in size and shape and show considerable mitotic activity (Photo 25).   Haemorrhage and necrosis are extensive. One of these cases has been found as a solid intra-cystic papilla in the wall of a papillary serous cyst in a patient aged 65 years.   Two cases (43 and 47 years old) are actually recurrences 4 and 6 years after removal of the primary neoplasms.   The 4th case occurs in a patient 38 years old and is accompanied with peritoneal metastases.   The remaining 2 cases occur in patients 28 and 68 years old.

As in thecomas, there is evidence of hormonal activity, four cases showing endometrial carcinoma, i.e., about 11% and if taken as a percentage of only these cases with available endometrium, the figure rises to about 18% (compared with 33% and 38% in thecomas).   Hertig in a personal communication to Meigs (1945) estimated that 18-20% of granulosa cell tumours are associated with uterine cancer.   Ingram and Novak (1951) in reviewing 50 cases of feminising tumours combined with endometrial carcinoma, state that this association is much greater with thecomas than with granulosa cell tumours.   This supports Biskind and Biskind (1949) and McKay et al (1949) who suggest that

the thecal and not the granulosa cells are the source of oestrogen. Based on histological structure, a thecoma may possibly be considered as a more slowly growing tumour, hence it subjects the endometrium to a more protracted oestrogen stimulation with a resultant increase in the development of malignancy (Biggart and MacAfee, 1955).

Cortical stromal hyperplasia of the ovary ovary is present in eight out of twenty post-menopausal patients (where that ovary is available and fit for such examination), i.e., 40%. In one case the opposite ovary is the seat of a primary adenocarcinoma.

CASE REPORT:

(A.5304.)   (Miss A.C., 64 years old, 19 years post-menopausal.)

This patient entered the hospital with a chief complaint of abdominal pain and swelling for the past 4 months. Abdominal palpation revealed the presence of an irregular mass arising from the pelvis and reaching the xiphisternum. The mass was hard in places and cystic in others. Per vaginam, two hard nodules were palpable in the pouch of Douglas. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The right ovary was replaced by a large tumour which was adherent to the pelvic wall. On cut section, it consisted of yellowish-brown, soft tissue with many areas of haemorrhage and necrosis. The uterus and left ovary showed no gross abnormality.

Microscopically, the tumour consisted of typical granulosa cells arranged mainly in the micro-folliculoid and gyriform patterns. Theca cells were abundant in the stroma (Photo 22). The left ovary was the seat of Grade O cortical stromal hyperplasia, as well as thecomatosis (Photo 24). The endometrium showed cystic hyperplasia.

GRANULOSA THECA CELL TUMOURS

This group includes nine patients whose ages range from 29 to 77 years. Five of them are post-menopausal and their endometria show cystic hyperplastic activity. The endometrium is also available in two pre-menopausal patients and shows persistent proliferative activity in one and secretory changes in the other.

All tumours are unilateral.

Table IV: Granulosa Theca - Endometrial Examination - 7 cases.

Cystic Hyperplasia	Persistent Proliferative	Secretory
5	1	1

The tumour varies in size from $\frac{1}{2}$" - $7\frac{1}{2}$" in diameter. The gross appearance is very similar to granulosa cell tumours. However, in a 77 years' old patient, the tumour shows an area of calcification.

Microscopically, the picture is that of a granulosa cell tumour in which the stroma is much exaggerated and made up almost exclusively of theca cells. In other

instances, it may be described as a theca cell tumour
with scattered islands of granulosa.   In a patient,
29 years' old, the granulosa element appears to be of the
diffuse type but with a pattern suggesting spreading
infiltration rather than the usual circumscribed areas.
On higher power examination, there is variation in size
and shape of these granulosa-like cells with some
mitotic figures suggesting malignancy.   Reticulum stains
clearly show the 2 components of these tumours.

Endocrine function is manifest by the presence of
cystic hyperplastic activity of the endometrium in all
post-menopausal cases.   Secretory changes of the
endometrium in a 37 years' old patient could be the
result of a degenerating corpus luteum which has been
recognised in one of the sections.   They might as well
be due to a more recent corpus luteum in the other
unremoved ovary.   Luteinisation of the tumour granulosa
cells was absent.

Mansell and Hertig (1955) divided the granulosa-theca
cell tumours into active, inactive and equivocal depending
on the histologic evaluation of thecal activity.   This
was decided from the presence of mitoses, plump or
fusiform theca cells, with or without luteinization,
but lacking collagen deposition.   In the non-active
tumours, there is extensive collagen deposition and
no mitotic activity.   In the active cases, 81% of the
endometria were influenced, whereas in the inactive or

equivocal cases only 44% were influenced. They con-
cluded that there is some correlation between the
histologic appearance and the presumed oestrogenic
activity of these tumours. Using the same criteria,
tumours of the present group can all be considered
active.

Cortical stromal hyperplasia has been found in
2 out of 5 cases with available opposite ovary (40%).
This may also account for endometrial activity.

BRENNER CELL TUMOURS

Brenner (1907) was the first to attempt to form
a special group for the neoplasms which to-day bear
his name.

Meyer (1932) pointed out the difference between
Brenner tumours and Granulosa cell tumours. He also
pointed out the association of Brenner tumours and
pseudomucinous cysts. Dockerty (1945) states that
about 33 per cent of Brenner tumours are associated
with pseudomucinous cysts.

Diverse views have been expressed regarding the
origin of Brenner tumours. Brenner himself interprets
the epithelial structures as follicles producing ova
and thinks their origin must be the primordial follicle.

The most widely accepted theory, however,
is that these tumours originate from Walthard cell
nests (Meyer, 1932). Walthard (1903) described
these nests as closely packed epithelial cells
connected with the surface epithelium and lying just

below it or deep in the stroma. He believed that they were congenital anlage developed from the surrounding stroma. Meyer (1903) had already observed these nests on the tubal serosa, mesovarium and broad ligament but he thought that they originated from the coelomic epithelium.

Recently, Reagan (1950) demonstrated continuity between superficial Walthard nests and the tumour. The cells of these nests are morphologically indistinguishable from those of Brenner epithelium. Both show infolding of the nuclear membrane, resulting in a coffee-bean-shaped nucleus. However, such nuclei have been found in many other tissues, including uterine cervix and granulosa cell tumours (Greene 1952). The main obstacle to the general acceptance of Meyers hypothesis arises from the frequency of Walthard nests underneath the serosa of Fallopian tube and the absence of Brenner tumours arising from this location (Dockerty 1945).

Origin from the coelomic epithelium has been suggested by many workers. Plaut (1943) and Arey (1944) have shown stalk-like continuity between the epithelium of a Brenner tumour and the surface epithelium. Very recently Arey (1961) presented a total reconstruction of 2 Brenner tumours by using magnified cardboard models. He found that the epithelial component of the tumour is a unit complex composed of

systems of branching cords. All such systems diverge from a slender stalk that arises directly from the surface epithelium of the ovary. He interprets Walthard nests as off-shoots from a main branch of tumour that grows towards the surface and expands against the surface epithelium.

Schiller (1934) suggests an origin from Wolffian elements in the rete ovarii. However, as Dockerty comments (1945) this concept still faces the fact that anatomic connection between Muellerian and Wolffian systems (within the ovarian boundaries at least) has not been satisfactorily proved as yet.

Dockerty and McCarty (1939) suggest a teratomatous origin because of the association of Brenner tumour and pseudomucinous cystadenoma which is itself regarded as being a teratoma. Novak and Meyer, however, state that the mucinous portion of these cysts develop from the Brenner elements.

Greene (1952) concedes a multiple origin for the Brenner tumour and adds a new source, namely the ovarian stroma. This concept was based on the findings of some reticular fibres invading the smaller Brenner cell masses which appeared to blend into the stromal tissue. However, Arey (1961) interprets such cases as regressive, rather than developing stages of Brenner tumours.

There is little evidence to support one of these theories against another. In this connection,

Novak (1952) says: "The ovary is a hotbed of differentiating potency, almost anything can happen in this respect and it often does".

The incidence of Brenner cell tumours has been estimated by Dockerty (1950) as 1.5 - 2% of all ovarian tumours.

The present series encloses 31 examples of Brenner tumour (about 2 per cent of the total). With two exceptions, all cases occur in patients over 40 years of age (41 to 72 years), the exceptions being 22 and 39 years old. This corresponds with the age distribution in fourteen cases mentioned by Novak (1952) and in fifteen cases mentioned by Biggart and Macaffee (1955). In Novak's series, only three patients were over 50 years. In Biggart's series, however, nine patients (60 per cent) were over that age.

In the present series, seventeen patients (55 per cent) are over 50 years. Twenty-one cases occur in post-menopausal patients. The endometrium is available for examination in nineteen cases. The endometrial picture is shown in Table V.

Table V: Brenner Cell Tumour - Endometrial examination - 19 cases.

14 Postmenopausal				5 Premenstrual		
Carcinoma Corpus	Cystic Hyper-Plasia	Post-Menopausal Active	Senile with some Proliferation	Persistent Proliferative	Normal Proliferative	Menstrual
5	5	3	1	1	3	1

In seven cases, (22.5 per cent) the Brenner tissue
has been found as a solid fibromatous mass in the wall
of pseudomucinous cysts.   Of these cases, one is
bilateral and six occur in post-menopausal patients.
The remaining 24 cases are solid tumours which on cross
section can easily be confused with fibromas or thecomas.
The size varies from a microscopic finding (a lower power
field) to four inches in diameter (a cystadenoma case).
They are greyish-white in colour, often lobulated and
in the solid variety densely hard.   On section, a gritty
sensation is occasionally present owing to calcium
deposits.   The cut surface shows interlacing whorls
and bands of fibrous tissue and occasionally distinct
lobulations are produced.   Numerous very small cystic
cavities are frequently seen.

Microscopically, the tumour consists of abundant
connective tissue stroma in which are embedded small
nests of compact polyhedral squamous-like epithelial
cells.   The centres of the nests are often cystic,
the cysts being lined by columnar or cuboidal cells and
contain mucous and cellular debris.   These cysts with
their contents superficially resemble ova.   Under high
power, the nuclei are large, rounded or oval and deeply
stained.   Longitudinal grooving due to folding of
the nucleus is responsible for the characteristic
coffee-bean appearance (Photo 29).   This is present
in a few cases.   Brenner tumours contained glycogen
(Photo 27 and 28) which is lacking in granulosa cell tumours.

The stroma, however, presents a variety of appearances.
In some tumours it is simply fibrous, in others it is
hyalinised, bearing a resemblance to fibrosed thecomas and
corpora albicantia.   In others, it is more cellular
though this may be seen only around the epithelial
islands.

Active stroma containing clusters of rounded
vacuolated theca-like cells has been encountered in
three post-menopausal cystadenoma cases.   The
associated endometrium shows cystic hyperplasia in two
and senile changes with some proliferation in one.
Unfortunately, the gross specimens are no longer
available and fat-stained frozen sections cannot be
obtained.

On the whole, in this group of Brenner tumours,
with available endometrium, about 25 per cent show
adenocarcinoma, 25 per cent show cystic hyperplasia
and 20 per cent post-menopausal proliferative activity.
These hormonal changes in post-menopausal patients may
be attributed to secretion by theca-like stroma.   The
presence of fat in the stromal tissue around epithelial
cells has been described by Reagan (1950) who
interpreted this finding as an indication of degeneration.
Teoh (1953) recorded three cases of post-menopausal
bleeding in association with Brenner tumours, all showing
fat in the stroma.   Biggart and Macaffee (1955) reported
fifteen cases of Brenner tumours, of which three were
associated with uterine bleeding.   Two of these were in

post-menopausal patients with endometrial hyperplasia.
The authors ascribed the hyperplasia to the tumour's
thecoma-like stroma.   They stated further that in the
cases unassociated with bleeding no fat was found in the
stroma.

In the present series, examination of the opposite
ovary has also revealed the presence of cortical stromal
hyperplasia in six out of 20 cases where that ovary is
available (30 per cent).   Five of these cases occur
in post-menopausal women.   The associated endometrium
shows adenocarcinoma in three, benign post-menopausal
activity in two and persistent proliferation in one
(a 41 years old patient).   Cortical stromal hyper-
plasia of the same ovary has also been found in
association with five small Brenner cell tumours.
Four of them are present in post-menopausal patients.
The associated endometrium shows adenocarcinoma in two,
benign post-menopausal activity in two and proliferative
changes in one (a 48 years old patient).

CASE REPORTS:

Case 1.   (C.5429)   (Mrs M. R., 63 years old, 13 years
                        post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding for the past week.
Hysterectomy and bilateral salpingo-oophorectomy were
performed.   The left ovary was replaced by a thin-walled
bluish-white cyst, measuring four inches in diameter.
On cut section, it was multilocular and filled with

thin pseudomucin. There was a small, solid area, in its wall, near the pedicle. The uterus and right ovary showed no gross abnormality. Microscopically, sections from the solid area and adjoining parts of the cyst wall showed the characteristic Brenner cells arranged in cords and islands which were mostly cystic. Transition of the epithelium into the pseudomucinous type could be traced in some areas (Photo 26).

The stroma was very cellular and consisted of plump fibroblasts and theca-like cells. (Photo 30.) The endometrium showed proliferative activity (Photo 31). The right ovary showed regressive cortical stromal hyperplasia in the form of cortical granuloma.

Case 2. (B.982.) (Mrs J.B., 66 years old, 20 years post-menopausal.)

This patient complained of increased frequency of micturition, together with incontinence of urine. Examination revealed an overflow incontinence. At laparotomy, an ovarian tumour was lying behind the uterus, and pressing it forwards so that normal emptying of the bladder was impeded. Total hysterectomy, with bilateral salpingo-oophorectomy, were performed. The tumour was three inches in diameter, cystic, but showed a small semi-solid area in its wall. Microscopically, the cyst was lined by typical pseudomucinous epithelium. Sections of the semi-solid area showed a Brenner cell tumour. The stroma showed hyaline plaques similar to those found in a thecoma (Photo 32). The endometrium was the seat of cystic hyperplasia (Photo 34). The other ovary showed grade I hyperplasia, together with thecomatosis (Photo 33).

DYSGERMINOMA

Chenot (1911) first called attention to a tumour
of the ovary which he called seminoma because of its
similarity to the already known testicular seminoma and
because he thought it to be derived from the anlage of the
seminiferous tubules. Meyer stated that the occurrence
of dysgerminoma in otherwise normal women is against
the view of Chenot. However, Seegar (1938) states that
"since each female gonad passes through a stage
corresponding to that of the male, thus making every female
temporarily a potential hermophrodite it is impossible
to say that somewhere in the ovaries of apparently
normal women there is not a small focus of male anlage
remaining, which gives origin to dysgerminoma. Moreover,
the fact that the tumour is about three times as common
in the testis as in the ovary seems to favour such an
origin."

Pick (1912) described such a tumour as chorio-
epithelioma ectodermale; a teratoid tumour derived from
the cells of the chorionic villi.

However, Meyer (1931) was the first to propose the
term dysgerminoma. He observed the close resemblance
of the cellular structures of these tumours to that
of the foetal gonad before the stage of sexual
differentiation. Hence his concept of origin from
dysgerminal cells which date back to the undifferentiated
stage of gonadal development before its cells have become

stamped with either female or male qualities or as Novak and Gray (1938) put it "Before the spark of sex has been applied". They add "Just what this spark is cannot be stated with certainty, though many biologists believe that in the human being,as in some of the lower animals, it is the enterance of the germ cells into the gonadal area after migration from a much earlier situs".

Meyers hypothesis is additionally supported by the following facts (Dockerty, 1945):

1. The tumour occurs in both sexes (seminoma testis is identical with dysgerminoma ovarii in all major pathological details.) In this respect Novak and Gray comment that this "would be expected if the origin is from cells which stray away from the germinal stream in gonads which may later develop into either testes or ovaries".

2. The neoplasm is the commonest tumour of the gonads of pseudo-hermaphrodites.

3. It has a relatively high incidence in mal-developed and misplaced gonads, especially in undescended testes.

4. Females suffering from the condition,if not actually hermaphroditis, frequently demonstrate lack of development of their sexual organs (infantile condition of the uterus and so forth). Novak, however, emphasizes that in such cases the tumour has nothing to do with the development of the sex anomaly which will persist even after removal of the tumour. This is quite different from granulosa-theca cell tumours and arrhenoblastoma

which occur in normal individuals who later respond to
the sex hormones produced by these tumours.   In such
cases removal of the ovarian tumour is followed by
regression of the feminizing or masculinizing phenomena.

In reviewing 79 cases assembled from the
literature, as well as 19 cases of his own series,
Seegar (1938) observed a predilection of the tumour for
the right ovary.   Embryologically, the right ovary
develops more slowly and to a lesser degree than does
the left ovary.   It is also known that in birds the
right ovary remains under-developed throughout life.
It is thus understandable that the probability of
occurrence of undifferentiated tissue in the right ovary
is greater than in the left.   Hence, the tumour which
is derived from such embryonic tissue, occurs more
frequently in the right ovary.

No determinations have been made to indicate that
the tumour itself secretes an endocrine substance.
Dockerty (1945) states that any evidence of hormonal
imbalance may not be directly attributable to the tumour
so much as to the sexually imbalanced status on which
the dysgerminoma is superimposed.

However, Scully (1953) reported 2 cases which he
designates as gonadoblastoma.   He suggests that they
contain cells of sexcord - mesenchyme origin as well as
cells of germ-cell type.   Both cases showed evidence
of androgen excess which he attributes to the stromal
(Leydig) cells.

On the other hand, gonadotropic hormones are
sometimes present in the urine of some cases of ovarian
dysgerminoma (as well as in testicular seminoma). This
was sometimes attributed to a co-existing chorio-carcinoma.
Others like Pedowitz (1951) suggest that the originating
cell might well be considered as totipotent. Seegar
concluded that such assays should be carried out in all
cases of suspected ovarian tumour as only in this way
will sufficient data be obtained to determine the
significance of this test.

No conclusions can be drawn concerning the
incidence of this type of tumour.

Klaften estimated the incidence at about 3% of all
malignant ovarian tumours. Novak states that they
are a little less than one third as frequent as granulosa
cell tumours.

The tumours were formerly stressed as occurring
nearly always during the first 2 decades of life.

Recently, however, they have been reported as
affecting women in the 3rd, 4th and 5th decades.
Schiller (quoted by Seegar) reported a case in a patient
aged 65 years. In Novak and Gray's group of 17 cases,
the youngest patient was 6 and the oldest was 38.
In Seegar's group of 19 cases, the corresponding
figures were 12 and 39 (a male pseudo-hermaphrodite).
Seegar states that seminoma of testis is most frequent
after the age of 30. Similarly, in hermaphrodites
dysgerminoma seems to occur in older patients.

Grossly, the tumour is usually large, lobulated and semi-solid; of a fleshy or elastic consistency. It is usually encapsulated but may be fungating. The cut surface is greyish or greyish-pink with yellowish areas. Haemorrhage and necrosis are always present. Bilateral involvement is present in almost one third of cases. In a case reported by Hoche in 1930, the tumour was associated with a dermoid cyst and in three cases of Seegar's series (1938) there was a combination of dysgerminoma with malignant teratoma. Two of Novak's 17 cases were also associated with a teratoma.

Microscopically, the histologic features are characteristic. The cells are large and uniform in size. In describing them, Seegar writes, "they stand out individually suggesting the appearance of Caviar, especially in the frozen section, in which phenomena of fixation play no part". The cytoplasm is granular and the nucleus is large, round and centrally placed. The pattern which the tumour cells assume varies from a cord-like arrangement to a medullary or alveolar form; the tumour cells being separated into small or large clumps by fine connective tissue septa. Lymphocytes are frequently found in the connective tissue and actual lymph follicles are occasionally seen. Giant cells resembling Langhans cells of tuberculosis (Photo 34C) are often found in dysgerminoma. These cells are usually seen in clumps of lymphocytes together with epitheloid cells simulating tubercles.

Heller (1943) restudied the giant cells and decided that they, like the lymphocytes and epithelioid cells represent a chronic inflammatory reaction to the presence of lipoid deposits derived from degenerating and necrotic tumour cells.

Most workers now agree about the malignant nature of the tumour. However, there is no correlation between the frequency of mitotic figures in the sections and the degree of malignancy of the tumour as shown by follow-up reports. Some authors, however, think that the tumours are of worse prognosis when 1) the capsule is not intact and the tumour is infiltrating, or associated with lymphatic metastases. 2)The tumour shows extreme cellularity and rarity of connective tissue. 3) The tumour exists with a teratoma.

Novak estimates the recurrence rate as 32%, Doderlein (1936) gives a figure of 25% and Foederl (1938) a figure of 68%. This latter figure supports the contention of Kirshbaun and Newman (1943) that dysgerminoma is very malignant.

The present review includes only the following case of dysgerminoma.

CASE REPORT:

(F.480.) (Mrs D.W., 59 years old, para 0 + 0, 7 years post-menopausal.)

This patient entered the hospital on 2.11.59 with the chief complaint of lower abdominal pain and nocturia for the past 10 days. Since the menopause in 1952,

she had been bleeding on and off; the last episode of
bleeding was 14 months prior to admission.

On examination, the patient did not look very well.
Abdominal palpation revealed a rounded swelling slightly
to the left side, arising from the pelvis and extending
up to 2 fingers below the umbilicus. Per vaginam,
a firm, semi-solid mass, continuous with the abdominal
swelling, was felt in the pouch of Douglas.

On 4.11.59 examination under anaesthesia and
diagnostic curettage were performed. No scrapings were
obtained and the diagnosis of a fibroid in the pouch of
Douglas was suspected.

On 11.11.59 laparotomy was performed with removal
of a left ovarian cyst, the uterus and right appendages.
On the posterior layer of peritoneum of the broad ligament
there was a small, ragged, solid growth lying immediately
above the left ureter. This was also removed. The
left ovarian cyst was partially twisted and measured
7" x 5" x 4". Its lower pole had a small solid area.
On opening, the cyst was filled with sebaceous material
and hairs.

The uterus contained a number of fibroids, the
largest measured 1½" in diameter. The right ovary
showed no gross abnormality.

Microscopically, the endometrium was senile and
inactive. The right ovary showed regressing stromal
hyperplasia. The left ovarian cyst was lined by

stratified squamous epithelium, characteristic of a dermoid cyst (Photo 34a). Sections from the semi-solid area showed clumps of discrete cells with large nuclei of varying size and affinity for stain and moderate number of mitotic figures. These were interspersed by a fibrous stroma which was in places markedly infiltrated with lymphocytes. The appearances were those of a dysgerminoma (Photo 34a and 34b). Sections from the peritoneal growth also showed dysgerminoma.

Following the removal of the tumour the patient had x-ray therapy to the pelvis. In June 1960, she developed metastasis in left cervical nodes and had a week's course of x-ray therapy. These nodes disappeared satisfactorily, but when seen on 27.7.60 there was a mass in the left upper abdomen and she felt some discomfort in this area. No pulmonary metastases, however, were detected after an x-ray film. On 6.1.61 the patient was re-admitted with the complaint of sickness and diarrhoea following radiotherapy. Palliative treatment was given and the patient died on 26.6.61.

ARRHENOBLASTOMAS

These neoplasms are relatively rare. Morris and Scully (1958) state that they are probably one-fifth to one-tenth as common as granulosa-theca cell tumours and constitute well under one per cent of all ovarian neoplasms.

Meyer (1930) was the first to use the term arrhenoblastoma. His hypothesis that the neoplasm arises from overgrowth of male directed elements within the hilus of the ovary is generally accepted. Pick's original theory (1905) of origin of the tubular adenoma in the testicular portion of an ovotestis has been discarded for lack of evidence of congenital hermaphroditism. However, such an origin obtains support from a few isolated cases in the literature. In this category one might include Novak's cases (1943) of testicular tubular adenoma in two sisters.

A teratomatous origin has been proposed by many workers. Krock and Wolfermann (1941) observed cartilage in a recurrent nodule of tumour and reviewed the whole subject of heterologous tissues which had been found in association with arrhenoblastoma. They discovered 34 per cent incidence of elements which included bone, cartilage, thyroid, mucinous and ciliated epithelium, and fat.

Some confusion has also been added to the problem of histogenesis by the cases known as gynandroblastomas in which there exists within the same tumour the paradoxical combination of granulosa and arrhenoblastoma elements. However, many of these cases appear to have been examples of granulosa cell tumours in which amenorrhoea had been interpreted as a masculinising symptom. The origin of the few remaining cases is difficult to interpret. There is evidence, however, that the male

gonadal cells (most probably Sertoli cells) are capable
of oestrogen production. Teilum suggests a sertoli
cell origin for both tubular granulosa cell tumours and
folliculome lipidique. Morris and Scully (1958)
refer to arrhenoblastomas as Sertoli-Leydig cell tumours.
Gillman (1948) suggests that both granulosa cells and
their equivalent in the male, Sertoli cells, arise from
the sex cords which are derived from the coelomic
epithelium. Burslem, Langley and Woodcock (1954)
support the identical origin of both granulosa and
Sertoli cells. They add "Histogenetically, both
types of tumours might arise from nests of the same
undifferentiated anlage or more likely from cells
stimulated to express latent competencies, in terms of
male or female morphology for oestrogen production",

Generally, in arrhenoblastomas, hormone assays on
blood and urine have not shown significant variation
from the normal. The finding of normal 17-ketosteroids
in the majority of these neoplasms is in contrast to
the elevated values usually found with the masculinization
produced by adrenal tumours of the ovary (masculinovoblas-
toma) and by hyperadreno-corticism.

Meyer deserves the credit for recognising the
less well differentiated patterns of this group of
neoplasms. In contrast to the highly differentiated
tubular adenoma, the undifferentiated variety is much
like a sarcoma. He also described an intermediate form
with anastomosing cords, pseudotubules and solid nests.

In all these varieties Leydig cells may or may not be present. The tubular adenoma may be indistinguishable from the tubular adenomas of the testis which, however, do not usually have hollow tubules as do many of the ovarian tubular adenomas.

In the undifferentiated forms it is the clinical evidence of masculisation that commonly leads to the diagnosis. This may explain the conclusion that the less differentiated forms of arrhenoblastoma are invariably masculinising while the differentiated type often produces no endocrine effect. Meyer has also emphasised that arrhenoblastomas are not always associated with masculinisation and that the androgenic effects could not always be correlated with the presence or absence of interstitial cells.

The neoplasm usually occurs in young patients (20-30 years old) and is rare beyond the menopause.

It may be very small in size (microscopic finding) in the hilar region, or large and bulky. Most of them are solid and lobulated but sometimes they are cystic. Adhesions to surrounding structures are usually absent. The colour is greyish-pink, yellow or brown, Haemorrhage and necrosis are not uncommon. Local invasion or peritoneal metastasis are unusual.

The present review discloses the following case only.

CASE REPORT:

(Mrs M. M.)

This 25-year-old married woman was admitted to hospital on 15.5.58, complaining of amenorrhoea since November 1957. She gave birth to a child on 19.1.57. Her first period after labour was in April, 1957. The next period was in June 1957. She missed the next period and her own doctor gave her tablets which produced a period in August. Then she had amenorrhoea until October. After another course of tablets, she had a period on 9.11.57. Since then the tablets had been tried without success.

In December 1957, the patient noticed excessive growth of facial hair. A month later her voice deepened. She was given penicillin tablets on the assumption that she was suffering from laryngitis. She had frontal headaches, blurring of vision and diplopia for four months, but these cleared up eventually. Marital relations were not affected.

On examination, there was excess of facial hairs, deepened voice and sagging breasts. The pubic hair was inclined to grow up to the umbilicus. Blood pressure was 150/70 and haemoglobin 100 per cent. On palpating the abdomen, a mass was felt arising from the pelvis below and to the left of the umbilicus. It was mobile and cystic. The clitoris was enlarged, the uterine body small, anteverted and pushed to the right by the large swelling in the left ovary, which was the size of a grapefruit. The 17-ketosteroid estimation in urine was 14.4 mg./24 hours (not increased).

On 27.5.58, left ovariotomy was performed and
a left-sided ovarian neoplasm, 2.5 inches in diameter,
was removed.   No adhesions were present.   The
consistency was partly solid, partly cystic.   The
more solid areas have a fibroid but haemorrhagic
appearance. Microscopically, one block showed areas of
active, fat-laden, fibroblasts which could be termed
sarcomatoid.   A more thorough search revealed an
attempt at tubule formation as well as clusters of
eosinophilic interstitial cells (Photo 35).   In view
of the clinical syndrome, the tumour had been regarded
as an arrhenoblastoma showing a mixture of an
intermediate and a sarcomatoid type.

PSEUDOMUCINOUS CYSTS

These neoplasms are composed of cells which have
no counterpart in the normal ovary.

They were, thus, thought to be derived from
extraneous elements, and various tissues have been
incriminated as a source of origin.   As pointed out
by Barzilai, the uterine cervix and the colonic
mucosa alone, in adult life, contain cells similar
to those of the pseudomucinous cystadenoma.   During
embryonic life, the Wolffian duct furnishes a third
possible cellular type.   Accordingly, Novak (1940)
and Meyer (1916) derive these neoplasms from teratomas
in which the tall entodermic epithelium has over-
ridden and replaced the other elements.   Facts in
evidence of this view are:

1) The frequent occurrence of mucinous cysts in the
walls of ovarian dermoids. (Five such cases will be
mentioned under the group of dermoid cysts.)

2) The demonstration in these tumours of intestinal
enzymes, such as invertase.

3) The occurrence in cases of peritoneal myxoma of
microscopically identical lesions in the ovary and in
the appendix.

4) The known tendency for the predominance of one tissue
type in ovarian teratomas as illustrated by "struma
ovarii".

5) The observation by Schiller (1940) that pseudo-
mucin is merely old mucin and not a substance peculiar
to ovarian tumours.

Some of the pseudomucinous cystadenomas have
in their walls solid nodules of Brenner cell tumours.
Novak and Jones (1939) feel that the Brenner portion
gives rise to the large mucinous portion. Other
investigators (Dockerty and MacCarty, 1939) reverse
the interpretation and regard the Brenner tumour as
further evidence favouring the teratomatous origin.

The Muellerian hypothesis of origin suggested
by Schiller is based on the similarity of the epithelial
lining of mucinous cysts to the lining of the cervical
canal. Barzilai, however, favours the metaplastic origin
of these cells from the germinal epithelium rather than
Muellerian rests.

The Wolffian hypothesis of origin, already discussed under the heading of Brenner tumours, cannot be readily accepted.

Pseudomucinous cystadenoma has been judged to include from 10-65% of all ovarian neoplasms, according to Giest (1942), Bell (1947) and Anderson (1948). Dockerty (1954) gives a figure of 20-30%. He states that the tumour practically never occurs before puberty and only about 10% affect women in the post-menopausal years of life.

The present series discloses 428 cases and is by far the largest group (31% of the total). Forty-nine cases have undergone malignant degeneration into a pseudomucinous cystadenocarcinoma.

Pseudomucinous Cystadenoma

This occurs in 378 patients (about 27% of the total),thus conforming with the figure cited by Dockerty. The age incidence ranges between 13-92 years. The 13 years' old patient is still in the pre-pubertal age. One hundred and ninety-nine patients (about 51%) are post-menopausal (this is much higher than Dockerty's figure). The endometrium is available for examination in 128 cases (100 post-menopausal and 28 pre-menopausal).

The endometrial picture is shown in Table VI.

Table VI: Pseudomucinous cystadenoma - Endometrial
Examination - 128 cases.

100 post-menopausal				28 pre-menopausal		
Cystic Hyperplasia	Post-Menopausal, Active	Senile Cystic	Senile	Persistent Proliferative	Normal Proliferative	Secretory
28	31	14	27	6	14	8

The tumour varies greatly in size. Small tumours
(few microscopic loculi) as well as large ones (12" or
more in diameter) are encountered. In 7 instances, the
tumours are bilateral. Some are pedunculated.

Grossly, some of the tumours are solid with
abundant intervening stroma separating small and more
or less uniform loculi as in the parvilocular type
discussed by Schiller (1943). In most cases, however,
the loculi are larger, more variable in size and separated
by thin connective tissue septa. Few cases contained
intra-cystic papillae. The tumour loculi contain
viscid transparent or translucent fluid which may be
inspissated or blood-stained.

Microscopically, the distinctive feature is the
lining epithelium, consisting of tall clear palisade cells
with dark stained crescent-shaped basal nuclei. Goblet
cells are encountered in few cases (Photo 36).
Pseudostratification of the epithelium due to tangential
section is occasionally noticed. In some cases the
epithelium is actively proliferating, dipping into the

underlying connective tissue and forming secondary daughter cysts. However, the demarcation between epithelium and connective tissue is sharp and such cases are considered frankly benign.

An accurate figure for the twisted cases cannot be stated, since most of them have lost every detail as to their nature. Out of the group of twisted cysts, however, 8 can be defined as being originally pseudomucinous.

That some of these neoplasms may be functioning has already been mentioned by many authors. Watts and Adair (1941) found oestrogens in 17.9% of the mucinous cysts that they studied. According to Table VI, 28% of the post-menopausal women with available endometria show cystic hyperplasia, 31% show benign proliferative activity and 14% show senile cystic change which is regarded as the regressive stage or the natural cure of cystic hyperplasia.

Careful search for theca and theca-lutein cells harboured in the stroma has been carried out particularly in those cases associated with endometrial activity in any of its forms. Active stroma (Photos 40 and 42) has been found in 20 such cases, all occurring in post-menopausal patients (20%). The associated endometrium shows cystic hyperplasia in 10, benign activity in 8 and senile cystic change in two.

Cortical stromal hyperplasia of the opposite ovary

is present only in 6 cases.   This is due to the same
reasons mentioned under fibroma.   The endometrium shows
cystic hyperplasia in 2, benign activity in 3 and senile
cystic change in one.

Pseudomucinous Cystadenocarcinoma

This sub-group of 49 cases includes both the border-
line and the frankly malignant cases.

The age distribution ranges between 30 and 74 years.
One patient, however, is 18 years old.   Twenty-six
patients are post-menopausal.

The endometrium is available for examination in
18 cases (12 post-menopausal and 6 pre-menopausal).
The endometrial picture is shown in Table VII.

Table VII: Pseudomucinous cystadenocarcinoma -
            Endometrial Examination - 18 cases.

	12 Post-menopausal				6 Pre-menopausal	
Carcin-oma on top of Cystic Hyper-plasia	Cystic Hyper-plasia	Post-Meno-pausal Active	Senile Cystic	Senile	Persist-ent Prolifer-ative	Normal Prolifer-ative
1	1	4	1	5	3	3

Grossly, the tumour differs from the benign form in
having intra- and extra-cystic papillae as well as
solid pieces of tissue, in its wall, which sometimes
replace the whole cyst.   Haemorrhage and necrosis are
much more frequent.   Adhesions to surrounding organs
are present in advanced cases.   Four cases are bilateral.

Microscopically, the epithelial cells are cuboidal, closely packed and many layers thick. The nuclei are hyper-chromatic, different in size and shape and show numerous mitotic figures. However, one can still see the tall columnar epithelium at one part or another (Photo 37). In the frankly malignant cases, the basement membrane is broken and invasion of the stroma is apparent.

The fact that typically benign as well as malignant regions could be found in the same section (Photos 37 and 38) was of special importance in that some of the neoplasms had been considered originally to be benign. The peristent search for malignant cytological changes in the present series may account for the higher incidence of malignant lesions. Meyer (1930) and Barzilai (1943) estimate that 5 and 6% of pseudomucinous cystadenoma become malignant. However, Dockerty (1954) gives a figure of 38.9%. In the present series the figure is 11% (including the borderline malignant cases). The possibility of overlapping with other types of ovarian adenocarcinoma is negligible since all neoplasms show distinct pseudomucinous type of epithelium. In the borderline cases this is particularly apparent; in fact, one can see transition areas from benign to malignant epithelium.

The stroma of most of these neoplasms is so actively proliferating that the recognition of theca

cells in H. & E. stained sections alone has been very difficult, if not impossible.

Cortical stromal hyperplasia of the opposite ovary has been found in one post-menopausal case.   The associated endometrium shows benign activity.

CASE REPORTS:

Case 1.   (C.8912.)   *(Mrs M.T., 56 years' old, 5 years post-menopausal.)

This patient entered the hospital with a chief complaint of vaginal bleeding for the past 6 weeks. Examination provided the diagnosis of ovarian tumour and on 16th March, 1956, this was removed, together with the uterus and contra-lateral appendages.   The specimen showed a huge, thin-walled cyst, 11" in diameter.   On cut section, it was multilocular and filled with pseudomucin. Microscopically, it was a typical pseudomucinous cystadenoma.   Out of the several blocks cut,2 showed large clusters of partially luteinised theca cells in the stroma (Photo 39).   Thecomotasis was manifest in the other ovary (Photo 40).   The endometrium showed cystic glandular hyperplasia (Photo 41).

The pre-operative urinary excretion of oestrogen was 44 Ug./24 hours.   The post-operative estimation fell down to 5.8Ug./24 hours.   (The given figures are the mean values for total oestrogens in urine per 24 hours.)

*This case has already been reported by Brown, Kellar and Matthew (1959).

Case 2. (D.4600.) (Miss S., 54 years old, 6 years
post-menopausal.)

(Unfortunately, I could not get the case notes
of this patient.) However, the theca cells are very
apparent in the stroma underneath the pseudomucinous
epithelium (Photo 42). The endometrium is the seat
of cystic hyperplasia (Photo 43).

SEROUS NEOPLASMS

The histogenesis of this group of neoplasms has
been very speculative. The most accepted theory
suggests an origin from the germinal epithelium.
Transitions from early invagination of surface
epithelium with tiny papillary excrescences to the
development of a definite papillary cyst have been
observed. In fact, germinal inclusion cysts and small
surface papillomata are indistinguishable from early
states of serous cystadenoma. In the present series,
a small papillomatous out-growth on the surface of the
ovary is included. Another variation is that the
surface epithelium may invade the cortex in the form
of long branching tubules producing an adenofibroma.
Thirteen such cases have been mentioned under the
group of fibromas. The germinal epithelium, being
a derivative of mesothelium, is quite variable in
appearance. The lining cells, therefore, may be
cubical, ciliated or secretory. This led Gemma
Barzilai (1943) to suggest that serous tumours arise
from tubal epithelium, and classify them as endo-
salpingiomas.

Rete ovarii, epoophoron, paroophoron and Wolffian duct have also been suggested as possible histogenetic factors. The parovarian cyst, originating in Wolffian duct tissue may be indistinguishable from a typical papillary serus cyst. Also, the association of a papillary serous growth with a mesonephroma is not a rare finding. However, in view of the common ancestry of germinal, mullerian and mesonephric epithelium, the argument is merely an academic one (Woodruff and Novak, 1954).

The present group consists of 292 cases and constitutes about 21 per cent of the total. One hundred and eleven cases are either borderline or frankly malignant.

Serous Cystadenoma

One hundred and eighty-one examples of this neoplasm are available in the present review (about 13 per cent of the total). This conforms with Dockerty's finding (1945) that serous cystadenoma comprises 15 per cent of ovarian neoplasms. The age ranges between 17 and 81 years. One patient, however, is a child, ten and a half years old. This is contrary to the common belief that these tumours are not observed prior to puberty. Seventy-four patients are post-menopausal. The endometrium is available for examination in 73 cases (53 post-menopausal and 20 pre-menopausal).

The endometrial picture is shown in Table VIII.

Table VIII: Serous Cysts - Endometrial examination -
                                              73 cases.

53 post-menopausal					20 pre-menopausal			
Carcin-oma Corpus	Cystic Hyper-plasia	Post-menop-ausal Active	Senile Cystic	Senile	Persist-ent Prolif-erative	Normal Prolif-erative	Secre-tory	Menst-rual
1	7	15	8	22	6	6	7	1

The tumour varies in size.   Small unilocular cysts
are frequently mixed up and sometimes impossible to
differentiate from follicular cysts.   In most cases,
however, the tumour is large, lobulated and multilocular.
The cystic cavities are usually filled with thin serous
fluid.   Unlike the pseudomucinous variety, papillae
are frequently present and their significance for
diagnosis is much more important than the consistency of
the fluid.   In some cases, the tumour is quite solid
(adenofibroma).   Four twisted cysts can be defined as
being originally serous.

Selye (1945) estimated that 8 per cent of serous
cystadenomas are bilateral.   In the present series, 17
cases (about 9 per cent) are bilateral.

Microscopically, the lining epithelium is more
variable than the usually very typical epithelium
of pseudomucinous variety.   In most cases the
epithelium is cuboidal with large nucleus which almost
fills the cell body.   In others the epithelium is ciliated
and much resembles that of the Fallopian tube.   (Photo 44.)
Pseudo-stratification due to tangential section is

occasionally observed.   Tiny calcified granules
(psammoma bodies) are sometimes present in the cyst wall
(Photo 45)   They might represent degenerate and
calcified papillae.   The stroma is usually dense
and fibrous but sometimes it is oedematous and myxomatous.
In such cases the papillae may resemble chorionic villi
(Photo 46.).

According to Table VIII, 13 per cent of post-
menopausal women with available endometrium show cystic
hyperplasia, 28 per cent benign endometrial activity
and 15 per cent senile cystic change.

Careful search for theca cells in the stroma has
revealed their presence in two post-menopausal cases.
The associated endometrium shows cystic hyperplasia
in one and benign activity in the other.   Theca cells,
in spite of their presence, are not always apparent
in H. & E. stained sections alone.   They are also
so irregularly distributed that more and more sections
require to be examined.

Out of the few cases where the opposite ovary is
available and fit for examination, 3 show cortical
stromal hyperplasia, all post-menopausal.   The
associated endometrium shows adenocarcinoma in one
and cystic hyperplasia in two.

Papillary serous cystadenocarcinomas

One hundred and eleven (111) cases (about 38 per
cent of the serous group) show either borderline or

frankly malignant degeneration. Pfannenstiel (1905)
states that one half of the papillary tumours of the
ovary are malignant.

The age incidence ranges between 27 and 81 years.
Seventy-nine patients are post-menopausal. The
endometrium is available for examination in 60 cases
(43 post-menopausal and 17 pre-menopausal). The
endometrial picture is shown in Table IX.

Table IX: Papillary serous cystadenocarcinoma -
endometrial examination - 60 cases.

43 Post-menopausal				17 Pre-menopausal				
Cystic Hyperplasia	Post-menopausal Active	Senile Cystic	Senile	Cystic Hyperplasia	Persistent Proliferative	Normal Proliferative	Secretory	Menstrual
5	10	6	22	1	5	7	3	1

Grossly, the tumour is not much unlike the benign
form. External papillary outgrowths and solid areas
are more frequently found. Extensive haemorrhage and
necrosis as well as adhesions to surrounding structures
are common findings in the frankly malignant cases.
Pelvic implantation has been noted in some cases.
In the literature, figures concerning bilaterality are
subject to great variation. Some authors, however,
give figures from 40 to 50 per cent (Miller (1937),
Pemberton (1904), Kahr (1937). In the present series,
28 patients (about 25 per cent) have bilateral tumours.

This is probably due to the fact that borderline cases are included.

Microscopically, there is often a difference of opinion among pathologists as to the diagnosis of malignancy in cases of papillary serous cystadenoma. The extreme variation in cellular detail exhibited by many of these tumours makes it very common to find different degrees of activity in adjacent microscopic fields. Malignant changes can be found in one area whereas the remaining sections of the same tumour (or even the remaining fields of the same section) may represent definitely benign patterns (Photos 47, 48, 49 and 50). Psammoma bodies are present in a good number of cases, indicating the serous nature of the tumours.

In the present study, the criteria employed in evaluating malignancy are those adopted by Woodruff and Novak (1954).

These can be summarised as follows:-

1) Epithelial proliferation (more than 3-4 cell-layer thickness).

2) Markedly adenomatous changes.

3) Anaplasia and neoplasia.

4) Stromal invasion (definite evidence of a malignant nature, absent or minimal in borderline cases).

5) Extension to adjacent structures: some papillary serous tumours show only local invasive tendencies but no distant dissemination.

6) Papillae: the more papillary the external surface, the greater the malignant potentialities.

In the boderline cases, the heaping up and tufting of the epithelium as well as some degree of anaplasia are very important.

According to Table IX, 5 post-menopausal patients (11.6 per cent) show cystic endometrial hyperplasia. Ten patients (23.2 per cent) show post-menopausal active endometrium.

However, identification of theca cells in the stroma has been very tedious and fruitless. The stroma in most cases is very actively proliferating (and even sarcomatous in some). Myxomatous degeneration, haemorrhage and necrosis add to the difficulty.

PRIMARY SOLID OVARIAN CARCINOMA

Selye (1945) classified ovarian carcinomas as follows:

1) Primary solid carcinomas which may become at least partly cystic due to liquefaction necrosis.

2) Cystic carcinomas arising through carcinomatous degeneration of originally benign common cysts (serous and pseudomucinous).

3) Metastatic carcinomas, including Krukenberg tumour as well as other multiple carcinomas.

It is thus clear that the division into solid and cystic carcinomas cannot be a sharp one.

Miller in his classification (1937) refers to the second group as "secondary carcinomas" (the term

secondary is not synonymous to metastatic).

Neoplasms of the present series are supposed to
fall under the first group.

Statistics on malignant ovarian tumours vary greatly
due to different standards of what is considered malignant.
Pemberton (1940) gives a figure of 17%, Shaw (1939)
approximately 25%, while Meyer (1930) states that ovarian
cancer constitutes 14.9% of all ovarian neoplasms.

The present study includes 116 cases of primary
solid carcinoma (about 8.5% of the total).   Together
with the cystic carcinomas (serous and pseudomucinous)
they constitute 20% of the total.   The age incidence
ranges between 29 and 81 years.   Two patients, however,
are 16 and 18 years old.   Eighty-six patients are
post-menopausal.   The endometrium is available for
examination in 54 patients (43 post-menopausal and
11 pre-menopausal).   The endometrial picture is shown
in Table X.

Table X: Primary solid carcinoma - Endometrial
              Examination - 54 cases.

43 Post-menopausal				11 Pre-menopausal			
Cystic Hyper- plasia	Post- Menop- ausal Active	Senile Cystic	Senile	Cystic Hyper- plasia	Persist- ent Prolif- erative	Normal Prolif- erative	Secre- tory
12	12	7	12	1	6	3	1

Tumours vary greatly in size, but in general they are
not as voluminous as the benign growths.   This is probably

because death occurs before they attain a great size.
Most of them are mainly solid but some show large areas
of haemorrhage, necrosis and cyst formation.   Thirty
cases (26%) are bilateral.   The data concerning
bilaterality of the tumour are extremely variable. Some
investigators estimated that about half the cases of
solid ovarian cancer are bilateral. Novak, however,
states that bilaterality is not a common characteristic
except in advanced cases.

The microscopic picture is quite variable.   The
cells may be small and dark or large, clear and
completely anaplastic.   The pattern may be an adeno-
carcinoma with various grades of differentiation, or
in the form of solid masses and sheets of cells
separated by scanty stroma.   Generally the neoplasms
are cellular and the stroma is minimal.   No cases of
Schirrhous carcinoma have been encountered.

The pathogenesis of the neoplasm is not yet
established.   However, an origin from follicular
epithelium, germinal epithelium or Wolffian rests has
been considered.   The so-called mesonephroma and clear
cell carcinoma are variants of ovarian carcinoma supposed
to arise from Wolffian body or mesonephros.

According to Table IX, about 28% of the post-
menopausal women with available endometrium show cystic
hyperplasia, 28% benign active endometrium and 16% senile
cystic change.

Theca cells in the stroma have been found in 3 cases only. This is because some cases are tiny bits (biopsy specimens) and others are massively necrotic and haemorrhagic. Added to the previously mentioned difficulties, the number of cases with thecal stroma is not really correct. In these 3 cases the associated endometrium shows cystic hyperplasia in 2 post-menopausal patients and persistent proliferative activity in a thirty-eight year old patient.

Out of the few cases where the opposite ovary is available and fit for examination, one case shows cortical stromal hyperplasia. The associated endometrium shows cystic hyperplasia. The following case is an example of primary ovarian adenocarcinoma in which the stromal element has an appearance similar to that of a thecoma.

CASE REPORT:

(B.1197.) (Mrs B.C., 59 years, 16 years post-menopausal.)

This patient was admitted to hospital with a chief complaint of lower abdominal discomfort and an attack of retention of urine 12 days prior to admission. Examination revealed a firm, rounded mass in the lower abdomen. Per vaginam, the mass was not tender and moved separately from the uterus. Sub-total hysterectomy and bilateral salpingo-oophorectomy were performed. One ovary was replaced by a large cystic tumour, bound posteriorly by adhesions to omentum and pelvic structures.

Small white nodules were noted on the peritoneum
covering the gut.   Grossly the tumour measured 6" in
diameter and showed solid as well as few cystic areas
which were filled with straw-coloured fluid.   The uterus
was slightly enlarged by a small interstitial fibroid.
The other ovary showed a slightly thickened cortex.

Microscopically, the endometrium was the seat of
cystic hyperplasia (Photo 54).   The ovarian tumour
was a well-differentiated adenocarcinoma.   The stroma
showed many clusters of theca cells which were frequently
vacuolated. (Photos 51 and 52.)   The other ovary showed
grade 0 cortical stromal hyperplasia (Photo 53).

METASTATIC TUMOURS OF THE OVARY
INCLUDING KRUKENBERG TUMOURS

Of all the pelvic viscera, the ovary is notorious
for being a favourite site for malignant metastases.
Two main primary sources are responsible for these
secondary tumours, namely: 1) carcinoma arising within
the pelvis (uterine fundus, Fallopian tube and pelvic
colon) and 2) carcinoma arising within the upper part
of the gastro-intestinal tract, the gall bladder and the
pancreas.   Occasionally, mammary carcinoma, melano-
epithelioma and so forth can act as a primary origin.

Krukenberg (1896) was the first to describe the
tumour bearing his name as a special entity under the
name "fibro-sarcoma ovarii mucocellulare carcinomatodes".
In his Doctor's thesis he described them as moderately

large, bilateral, solid lobulated tumours generally
preserving the shape of the ovary.   They have a smooth
external surface with a well-formed capsule and no
tendency to become adherent.   The cut surface shows firm
as well as haemorrhagic and cystic areas.   Gelatinous
appearance is also common.   The microscopic picture is
highly characteristic and consists mainly of fibro-
myxomatous tissue with scattered signet ring cells.

Krukenberg, who eventually became an opthalmologist,
thought the tumour to be primary in the ovary, and
a sarcoma.   However, he also entertained the possibility
of a carcinoma as well.   Later, Schlagenhaufer and others
(1902) showed that these tumours are really metastatic
ovarian carcinomas notably of gastric origin.   The
signet ring cells were the key to a corrected diagnosis
of carcinoma rather than sarcoma.   They noticed that the
epithelial elements may occur as clusters of well-marked
ascini showing various degrees of mucoid change.
Sometimes the mucoid material may break through the gland
wall and permeate the surrounding stroma so that the
original gland pattern may be blotted out.   Most
investigators now favour the metastatic concept and Ewing
goes so far as to state that primary Krukenberg tumours
do not exist.

However, pathologists differ in their concepts as
to: 1) what constitutes a Krukenberg tumour, 2) how
metastatis occurs, and 3) whether a primary ovarian
carcinoma may be impossible to distinguish from
a Krukenberg tumour.

Novak and Gray (1938) limit the term to those neo-plasms, whether secondary or primary, which assume the characteristics first described by Krukenberg.   Dockerty, Leffel and Masson (1942) heartily disagree with that and include all metastatic carcinomas which contain mucus in their cells whatever their gross appearance is.   They consider the presence of mucus in the epithelial cells as the most constant finding in Krukenberg tumours and as the only difference from any other metastatic carcinoma. They even prefer the name "adenocolloid carcinoma" rather than Krukenberg tumour.   They presented a case showing a few signet ring cells in the ovarian cortex as constituting a Krukenberg tumour.   Although they admit that the prominence of signet ring cells varies greatly, they state that the latter are always found by careful examination.

Ascinar structures are almost always revealed by serial sections.   Ewing, however, suggests that lesions showing ascini should be excluded.

Although some workers (Novak and Gray) deny the presence of mucus, in some cases, in the primary growth, others (Dockerty et al) found it in all their cases. Raiford (1932) distinguishes between mucoid carcinoma arising from mucin-forming elements and adenocarcinoma with mucoid degeneration.   Novak, however, attributes the presence of mucin to hypersecretion of cells in both groups rather than that the mucoid change represents

a degenerative process. He also mentions the possibility
of developing mucoid changes only after transplantation
in the ovary.

The route by which metastasis occurs is still open
to question. The four routes of cancer dissemination
in general have been considered, namely: 1) direct
implantation on the ovarian surface of cancer cells
transported by peritoneal fluid from the primary lesion;
2) lymphatic spread; 3) blood stream metastasis;
4) extension by direct continuity from an adherent
intestinal cancer. The first method of spread was first
suggested by Bucher (1893). Dockerty (1942) and others
support this method because: 1) carcinoma cells are
frequently found in peritoneal fluid in cases of abdominal
carcinomatosis; 2) early involvement of ovarian cortex
without involvement of ovarian medulla is occasionally
seen. (They presented one such case.) However, they
state that they do not know how the germinal epithelium
is permeated, nor do they know to what depth the primary
lesion must reach in the involved wall so that carcinoma
cells may reach the peritoneal fluid.

Novak, on the other hand, criticizes this method
severely. He states that it is difficult to believe
that cells from a microscopic primary - for example,
in the pylorus - can reach the serosa where a purposeful
peristalsis carries them to the ovary without emplanting
themselves on the intestines or parietal peritoneum which

are known to be vulnerable to implantation. Moreover, the portals created by ovulation and which are presumed to render the ovarian surface more prone to implantation are very minute and quite sealed off in a short time. The presence in the tumour of a dense smooth capsule with no sign of surface growth is also against surface implantation. Novak, however, favours the lymphatic route of spread. Still, he admits that the direct evidence to support the latter route is lacking.

On the contrary, the lymphatic route is strongly suggested in the form of secondary ovarian cancer associated with uterine adenocarcinoma. In this type, small cancer nests in the lymphatics of grossly normal ovaries have been demonstrated.

However, factors in favour of spread by lymphatics are:

1) high incidence of bilateral involvement (90 per cent as reported by Novak and Gray). This suggests that cancer cells reach the ovaries from a common focus which might be the lumbar peri-aortic nodes.

2) the smooth surface and the maintenance of the shape of the normal ovary. This suggests growth from within.

3) wide spread extra-abdominal metastasis in some cases.

4) high incidence of peri-aortic lymph node

involvement. From this focus retrograde lymphatic
dissemination to the ovary is supposed to occur. On the
other hand, it may be said that the peri-aortic nodal
involvement is secondary to the ovarian lesion that
previously had arisen by some other route (Dockerty).

5) demonstrable evidence of cancer cells in
peritoneal lymphatic vessels.

6) occurrence of ovarian carcinoma secondary to
cancer of the breast. Later, Dockerty et al (1942)
have also presented a case of Krukenberg tumour showing
cancer cells in a lymphatic vessel of the ovarian cortex.

Extension by way of the blood stream is undoubted,
though again there is no real evidence. Metastases from
breast cancer can also be explained by this route.
Extension by continuity from adjacent structures to the
ovary can unquestionably occur and has been accepted by
all. Dockerty et al (1942) concluded that any one or
all the routes of spread may be involved in any case
depending on 1) the site of the lesion, 2) the depth
to which the wall of the primarily involved viscus has
been invaded, and 3) the degree of malignancy of the
primary lesion.

The secondary nature of Krukenberg tumour has been
proved in the great majority of cases. However, there is
a small group of cases in the literature which is
convincingly primary (cases of Andrews (1934), Steinberg
(1901) and Frankel (1920)). Autopsy examination of all the

organs for a primary has revealed none. At present, the most probable explanation regarding the origin of these primary neoplasms is that an entodermic type of epithelium predominates and inhibits the other elements in an originally teratomatous lesion (i.e., pseudomucinous cystadenocarcinoma). A less important possible origin is the Walthard cell nests.

Statistics as to the incidence of secondary ovarian neoplasms are worthless, since many cases of advanced carcinoma are impossible to prove as either of primary or secondary type.

However, Taylor (1950) states that approximately 1 case in 5 of malignant ovarian tumours is of secondary nature. This is in agreement with the figure quoted by Shaw (1939).

The present review discloses 49 cases of metastatic ovarian carcinoma (3.5% of the total). They also constitute about 1/5 of the primary ovarian carcinomas, (solid and cystic) thus conforming with the afore-mentioned figures.

Three cases are Krukenberg tumours occurring in two post-menopausal patients (70 and 56 years old) and a third pre-menopausal patient (47 years old). The first and the third (a bilateral case) are biopsy specimens. The second is unilateral and the associated endometrium is the seat of post-operative necrosis. All the three cases show signet ring cells, acinar structures and fibro-

myxomatous stroma (Photo 67).

The remaining 46 cases are metastatic ovarian
carcinomas. The age ranges between 29 and 73 years.
Thirty-two cases occur in post-menopausal patients. The
endometrium is available for examination in 41 cases
(32 post-menopausal and 9 pre-menopausal). The endometrial
picture is shown in Table XI.

Table XI: Metastatic Ovarian Carcinoma - endometrial
examination - 41 cases.

32 Post-menopausal	9 Pre-menopausal	
Carcinoma Corpus 32	Carcinoma Corpus 8	Normal Proliferative 1

Grossly, the tumours do not differ from primary
ovarian carcinomas, being usually solid with frequent
areas of haemorrhage and necrosis. Sixteen cases
(34 per cent) are bilateral.

Microscopically, the picture imitates the primary
tumour. Groups of cancer cells are frequently seen in
hilar lymphatics as well as on the surface of early
involved ovaries.

As Selye (1945) mentions, it is sometimes impossible
to distinguish metastases of primary ovarian carcinomas
from the ovarian metastases of extra-gonadel carcinomas.
This is especially true of those cases in which both the
primary tumour and the metastases are anaplastic and fail
to retain the typical structure of the organ from which

they are derived. The association of ovarian carcinomas with cancers of the uterus is particularly common. One or the other organ may be the seat of primary growth or both of them may be secondary to a third primary.

However, the possibility of the ovary being a primary site can be suspected by the criteria once used by Lynch and Dockerty (1945). These are:-

1) The size and degree of encapsulation of the ovarian tumour.

2) The presence of cysts and papillary projections.

3) The presence of psammoma bodies.

4) Demonstration of mucin.

Conversely, the observation of rather well-differentiated uterine glands and squamous cell elements (adenoacanthoma) (Photo 68) indicates that the uterus is the primary site, although primary ovarian adenoacanthoma on top of endometriosis has been reported. Invasion of the myometrium whether centrifugal or centripetal is of some assistance in doubtful cases.

With this knowledge at hand, the uterus has been regarded as the site of origin in the 40 cases of the present group. Invasion of the Fallopian tube and the peritubular lymphatics is occasionally seen.

Out of the remaining 6 cases, 2 are composed of oat cells and the possibility of alveolar carcinoma has been put forward (Photo 69). A third case is histologically similar to a known scirrhous mammary carcinoma (Photo 70). The fourth and fifth cases are relatively anaplastic,

show some secretory activity and are probably secondary
to gastro-intestinal cancer.   The sixth case (an adeno-
carcinoma) is a biopsy specimen from a big pelvic mass
involving the omentum and invading normal ovarian tissue.
(The metastatic nature of this case is really difficult to
prove.)

Ovarian cortical stromal hyperplasia has been noted
in 2 cases, 51 and 64 years old respectively.   In the
first case, it is present in the opposite ovary.   In the
second case,both ovaries are involved.   The endometrium
in the 2 cases is the seat of primary adenocarcinoma.

OVARIAN TERATOID TUMOURS

(DERMOID CYSTS, STRUMA OVARII AND MALIGNANT TERATOMAS)

Many hypotheses have been advanced to explain the
origin of this group of tumours.   Of these, the most
important are the following:

1)   Theory of blastomeric isolation.

Bonnet (1901) has shown that if an ovum is agitated,
a blastomere can become dislodged and result in the
formation of a potential second individual.   Also in the
process of segmentation cell elements may wander or become
displaced to develop later after a period of quiescence.
Murray (1938) transplanted the blastoderm of the chick.
He found that when the entire blastoderm was grafted, the
degree of histologic differentiation was comparable to
that found in normal chicks of an equivalent age, but when
partial grafts were used, the degree of differentiation

fell short of this and appeared similar to that of
teratomas.   It is difficult, however, to explain the
predilection of such tumours for the ovary.

2) Theory of parthenogenetic development of ovum.

Asexual reproduction of ova has been observed in
lower animals.   Pricking the ovaries of a frog with
a needle sometimes results in the development of complicated
teratomas.   This theory has more supporters than the
blastomeric theory, although both of them are unsatis-
factory.

Owing to the many transitional types between the
main classes of this group a strict classification is
impossible. However, dermoid cysts are usually benign
and characterised by predominence of ectodermal elements
although mesodermal and occasionally entodermal structures
are found.   Teratomas, on the other hand, show tissues
derived from all the three germinal layers and, with the
exception of a few cases, are usually solid and malignant.
Peterson (1956) emphasises that it is the microscopic
study and not the gross appearance that differentiates
between the benign and the malignant teratoid tumours.
The tissues are mature and well differentiated in the
former, whereas in the latter they are undifferentiated
and anaplastic.

Willis (1953), after an exhaustive study of a large
number of teratomatous neoplasms, stated that although
teratomas are a single group of neoplasms there is

a wide range in their appearance and behaviour and not all fall into the classical divisions of solid and malignant on the one hand and cystic and benign on the other.

Occurrence of thyroid tissue within ovarian dermoids has long been recognised. The thyroid element may represent merely an incidental microscopic observation or it may overshadow the associated dermoid elements. The term struma ovarii has been applied when the thyroid component has formed a significantly large part of the tumour.

Ewing (1942) estimates that dermoid cysts account for about 10 per cent of all ovarian tumours. In Dockerty and Marchetti's series the incidence is 15 - 20 per cent. Blackwell et al (1946) found that about 85 per cent of these cysts were removed from patients between the ages of 16 and 55 years, that is, the incidence is greatest during the reproductive period.

The present series includes:

186 dermoid cysts (6 of them are twisted),

5 dermoid cysts with pseudomucinous cystadenoma,

11 struma ovarii, and

6 malignant teratomas, thus making a collection of 208 cases and constituting about 14 per cent of the total. The age incidence ranges between 13 and 70 years. One hundred and sixty-four (83 per cent) of dermoid cysts occur in the child-bearing period.

The endometrium is available for examination in
57 patients (21 post-menopausal and 36 pre-menopausal).
The endometrial picture is shown in Tables XII and XIII
and XIV.

Table XII: Dermoid Cysts - Endometrial examination -

49 cases.

13 Post-menopausal				36 Pre-menopausal		
Post-meno-Pausal Active	Senile Cystic	Senile	Persistent Proliferative	Normal Proliferative	Secretory	Menstrual
4	2	7	5	18	12	1

Table XIII: Struma Ovarii - Endometrial examination -

5 cases.

5 Post-menopausal			
Cystic Hyperplasia	Carcinoma Corpus	Senile Cystic	Senile
1	1	1	2

Table XIV: Malignant Teratoma - Endometrial examination -

3 cases.

3 Post-menopausal	
Senile cystic	Senile
One case of Pseudomucinous Cystadeno-carcinoma in a dermoid cyst	Two cases of Squamous Cell Carcinoma

Grossly, most of the dermoid cysts (including the
struma ovarii cases) are rounded, unilocular and moderately
large.   Those cases associated with pseudomucinous cysts
are voluminous and multilocular.   The cysts are opaque,

white in colour and filled with greasy pultaceous
material, hairs, nails and sometimes teeth.   In a good
number of cases a raised protuberance, the mamilla, can
be seen on opening the cyst.   Twenty-four (24) cases
(13 per cent) are bilateral.   In the Blackwell et al
series of 225 dermoid cysts, 12.4 per cent are bilateral.
Six twisted cysts can be defined as being originally
dermoids.

Microscopically, the majority are lined by skin and
its appendages - that is, hair, follicles, sebaceous
and sudoriferous glands.   Adipose tissue, lymphoid tissue,
cartilage, muscle fibres and columnar epithelium are
frequently encountered.   In the cases associated with
pseudomucinous cysts transition from the squamous to the
pseudomucinous epithelium can be sometimes noted.
Thyroid tissue (Photo 55) has been identified in the 11
cases of struma ovarii (about 5 per cent of dermoid cysts).
In Blackwell's series it was found in 13 per cent.

Evidence of irritation or infection is present
in about half the cases.   Most of the wall is then
composed of granulation tissue.   Occasionally, lipoid
material is seen to penetrate the cyst wall forming
sieve-like areas and provoking a giant cell reaction.

The development of malignancy in the epithelial
elements of ovarian dermoids is very rare.   Brody (1941)
states that this occurs in 1.5 per cent.   Such trans-
formation is usually in the form of a squamous cell

carcinoma. However, Burgess and Shutter (1954) reported a case of dermoid cyst showing osteogenic sarcoma and leiomyosarcoma.

In the present group of malignant teratomas, two cases of an adenocarcinoma occurring in a dermoid cyst are included. One of them is actually a pseudomucinous cystadenocarcinoma, in a patient of 63 years (Photos 56, 57 and 58). The other is a well-differentiated adenocarcinoma and appears to have originated in the sudoriferous glands (Photo 59).

The remaining four malignant cases can be summarised as follows:

Case I. The pathological material consists of a dermoid cyst which has been removed from a patient 54 years old. Sections show a squamous cell carcinoma in the wall of the cyst which also includes in its structure tall columnar epithelium, mucous glands, muscle fibres and squamous epithelium.

Case II. This consists of an ovarian semi-solid tumour, 3" across, removed from a patient 68 years old. Sections show squamous cell carcinoma with metastatic tumour emboli in myometrial lymphatics. The endometrium is atrophic.

Case III. Consists of an ovarian cyst the size of a small melon in a patient 62 years old. Sections show a keratinising squamous cell carcinoma (Photo 60).

Case IV. Consists of a semi-solid ovarian tumour,

8 x 6 x 6 inches, removed from a patient aged thirteen.
It has a smooth greyish-white surface and on cut section
it shows multiple cystic spaces of variable sizes.   In
one of them few hairs can be identified amidst the
sebaceous material.   This gave a clue to the probability
of its being a teratoid tumour (Photo 61).   Sections show
well differentiated squamous and columnar epithelium,
hair follicles, bone, cartilage, brain and neural tissues
(Photos 62, 63, 64 and 65).   None of these is histo-
logically malignant and the tumour was regarded as benign
teratoma.   Seven months later recurrence occurred and
a second tumour was removed from the pouch of Douglas.
Two biopsies were also taken from omental and peritoneal
nodules.   Sections from the second tumour still show
well differentiated adult tissues including bone, cartilage,
squamous and mucous epithelium as before.   However,
sections from the omental and peritoneal biopsies do show
sheets and clumps of undifferentiated anaplastic embryonic
cells which have no recognisable tissue origin (Photo 66).
The tumour is therefore a malignant teratoma.

None of this group of neoplasms show active stroma
or cortical stromal hyperplasia of the other ovary
(where that ovary is available, and fit for examination).
This fits in with the endometrial picture which is mainly
senile in patients beyond the menopause.

TWISTED OVARIAN CYSTS

This group comprises   58 cases.   Eighteen cases

have been identified as pseudomucinous, serous or dermoid cysts. Accordingly, they have been included in the appropriate groups. The remaining 40 cases occur in patients ranging in age from 16 - 78 years. These tumours have all undergone complete torsion of their pedicle. Consequently, they are all haemorrhagic and reddish-brown in colour. Microscopically, the wall is completely destroyed by haemorrhage and necrosis and their nature is ill-defined.

Metastatic Sarcoma in the Ovary (secondary to sarcomatous

degeneration in a uterine fibroid).

Two such cases have been encountered in the present review. One of the patients is 55 years old and the other is 77 years. The endometrium shows senile changes in both. Grossly, the ovaries show no abnormalities. Microscopically, however, sarcomatous cells (similar to those of the uterine leiomyosarcoma) have been detected in some fields.

SUMMARY

1,376 cases of ovarian neoplasms have been reviewed. In some of them the diagnosis has been re-considered.

The various types of neoplasms tended to follow the generally accepted concepts described in the previous literature.

Examples of various neoplasms with functioning stroma have been presented.

Cortical stromal hyperplasia of the contra-lateral ovary occurred in about 80% of theca-cell tumours, 40% of granulosa and granulosa-theca-cell tumours and 30% of Brenner cell tumours. Although an accurate percentage could not be worked out in the remaining tumour types, yet, there was a definite relationship between stromal hyperplasia and most of these neoplasms.

Significant correlation was found between the presence of such stromal changes, (in the ovarian neo-plasm and/or the contra-lateral ovary) and abnormal endometrial activity particularly in patients beyond the menopause.

PART II: HISTOCHEMICAL STUDY

INTRODUCTION TO THE HISTOCHEMICAL STUDY

The recent years have brought about an increased
interest in correlating the chemical and physical
qualities of tissue cells with the physiological states.
Although histochemistry has not yet attained its ideal
goals, namely qualitative and quantitative estimation
of the various metabolic processes, yet it has the great
advantage of precise localisation of substance in tissues.
Chemical analysis may prove a low concentration of certain
substance whereas the latter may be concentrated in
discrete parts of tissue cells so that its local concen-
tration is many times the average concentration determined
by purely chemical methods.   Moreover, the results of
chemical estimation based on isolation techniques may be
deceptively low because of losses during the process of
extraction and purification. However, the methods of
chemical cytology are frequently criticised because of
their lack of specificity or because they are quantitatively
untested against a reliable chemical method. Nevertheless,
useful information can be obtained from less perfect
procedures.   In endocrinology chemical identification
of active principles would have remained impossible
without prior illuminating experiments with crude extracts.
As Dempsey (1948) comments: "For relating morphological
changes in organs and tissues with their physiological
states, chemically non-specific methods may yield valid
results".

Interest in the ovarian lipids has been greatly
stimulated by the discovery that the ovarian hormones are
fat soluble steroids. It is now also established that
cholesterol is a precursor of oestrogens (Cook, 1958).
Recently, it has been shown, in humans, that cholesterol
is converted to oestrone in vivo (Werbin et al, 1957).

However, the initial attempt to localise ketosteroids
histochemically was made by Bennett (1940). He applied to
sections of the cat's adrenal gland chemical tests already
known to be characteristic of the hormones. He realised
that the available tests would reveal both aldehydes and
ketones. However, he noticed that no aldehyde with
the solubility properties of the hormones had been
detected in adrenal cortex, so that any alcohol or
acetone-soluble reactive substance might be presumed to
be ketonic. The reactions which he used were the
phenyl-dydrazine hydrochloride test, the ammoniacal
silver hydroxide test, the digitonin reaction, the
Sudan stain, in addition to acetone solubility and
examination of unstained frozen sections under the
polarizing microscope for evidence of birefringence.
Bennett concluded that the spongy zone contained both
cholesterol and ketonic steroids.

In 1943, Dempsey and Bassett examined rat's ovary
and contributed additions and modifications to the
methods introduced by Bennett. Phenylhydrazones and
birefringent crystals were found in theca interna of
follicles, in lutein cells and in epithelioid interstitial

cells. Unstained frozen sections were also examined under the fluorescent microscope. Intense fluorescence of acetone soluble droplets was found only in the above-mentioned sites. The spectrum of this fluorescence had its peak in the green wave lengths, and as oestrogens fluoresce in this range it was suggested that the fluorescence was due to the steroid hormones. Frozen sections were also treated with concentrated sulphuric acid (Liebermann Burchardt reaction) and a display of colours appeared in the lipid droplets. Since all unsaturated steroids, including hormones give such a colour reaction this was considered as a further evidence for the presence of steroids in the droplets. Dempsey and Bassett came to the same conclusion that the reactive lipids contained a mixture of cholesterol and biologically active steroids. Like Bennett they emphasized that in some sites lipid droplets might be abundant yet relatively inactive by the tests whereas in other sites, even though sparse they showed great reactivity.

Everett (1945) used the Schultz test instead of the concentrated sulphuric acid test. The former test is more refined and more specific for cholesterol and its esters whereas the latter reveals a larger number of unsaturated polycyclic compounds.

Deane and Barker (1952) indicated that the Schultz test declines or disappears from the lipid droplets in thecae internae, interstitial cells and lutein cells of sow's ovary at those periods when there

is physiological evidence that hormone secretion is rapid
and reaccumulates when secretion subsides.

Gormori (1942) was the first to criticize the
phenylhydrazine reaction as a test for ketosteroids.
He pointed out that the reaction required treatment of
the tissues by oxidizing agents and that it gave results
identical with those of the plasmal reaction of Feulgen
and Voit (1924). This reaction consists of the
re-colourisation of Schiffs reagent, leucofuchsin, after
previous exposure of the tissues to mild oxidizing agents.
Schiffs reaction is commonly believed to be an aldehyde
reaction. Gomori considered that the carbonyl
substances in the lipid droplets were plasmal (fatty
aldehydes which are hydrolsed from acetal phosphatides,
plasmalogens, by dilute mineral acids or mercuric
chloride). Dempsey and Wislocki (1944, 1946) agreed
that both phenyl-dydrazine and the Schiff reaction
appeared superimposable. However, they disapproved that
the reaction was therefore necessarily due to aldehydes
citing Lison (1932) to the effect that certain cyclic
ketones and unsaturated compounds also recolourize
the Schiff reagent. They described a positive Schiff
reaction as well as a positive phenylhydrazine reaction
in the syncytium. Dempsey also reported that pure
desoxycorticosterone acetate recolourised the Schiffs
reagent in the test tube. Reports soon appeared which
disagreed with Dempsey's assertion of this in vitro
reaction and many workers accepted Gomori's suggestion

that both the Schiff and the hydrazine reactions were
probably indicative of plasmal.

However, Hayes (1949) and Cain (1949) both stressed
that plasmalogen (an acetal phosphatide from which
plasmal is derived) can be identified only in unfixed
frozen section and that a control section not exposed
to mercuric chloride or mineral acid must be used.
Cain indicated that the occurrence of Schiff staining
of the lipid droplets of fixed tissues was not due to
plasmal but to another substance which he called
pseudo-plasmal and which consists of epoxides, peroxides,
and aldehydes derived from unsaturated fatty acid residues
present in the lipid droplets.

Recently, the study of the reactivity of tissues to
hydrazines has been greatly facilitated by the intro-
duction of the reagent 3-hydroxy - 2-naphthoic acid
hydrazide (Ashbel and Seligmen, 1949, 1952). Most
workers now use the Ashbel and Seligman method in
preference to the older phenylhydrazine methods in
which the coloured product was much paler and there
was relatively more background staining. Using the
Ashbel and Seligman method there is lack of complete
paralellism with the Schiff reaction. Ashbel and
Seligman reported that a positive hydrazine test
still occurred in droplets of the adrenal cortex and the
testis following the differential blocking of aldehydes
by sulphonilic acid or aniline. This is particularly

significant since Boscott and Mandl (1949) found that
aniline effectively blocked all staining with phenyl
hydrazine. Moreover, the reaction with the hydrazide
was reversed rapidly by treatment with an excess of the
sodium salt of ortho-sulphobenzaldehyde which is
capable of reversing the reaction of aldehydes only slowly
but of ketones quite rapidly because of competition of
the active aldehyde group of the strongly water soluble
sulphobenzaldehyde for the hydrazide.

In an excellent review of the subject Deane and
Sligman (1953) came to the conclusion that: 1) all the
carbonyl groups of the lipid droplets, which are
reactive to leucofuschsin are derived from unsaturated
groups (probably in fatty acids) and are supposedly
aldehydic in nature, whereas, 2) additional carbonyls
are formed (even when the unsaturated groups are blocked)
which, being reactive only to the hydrazide were
presumably ketonic. That these ketones are steroidal
may be assumed since there has been no evidence for the
existence of lipid ketones other than ketosteroids.
Conclusive proof that it is ketonic steroid which is
being demonstrated may have to await the isolation and
identification of the lipid components stained by the
histochemical method.

To sum up, although any one of the tests (Sudan IV,
Birefringence, Fluorescence, Schultz test, Ashbel-Seligman
test and acetone solubility) may be given by a wide

variety of substances, their combined occurrence within
the lipoid droplets of the ovaries and (other steroid
producing glands) indicates their value in localising the
sites of steroid hormone production.

This battery of tests when positive indicates
that the reactive material is fat soluble, has a poly-
cyclic molecule with a double bond somewhere in the
molecule and a carbonyl group attached to it. Keto-
steroids and their precursors have such a structure and
give these reactions. More important is that these
tissues which fail to give the reactions are devoid of
steroid hormones. The tests so far developed are
incapable of distinguishing between the various
steroids. The group of tests also appears to have
value in determining the phase of secretory activity.
The reactive droplets are small when secretion is
rapid, whereas they are large when secretion is not
occurring, i.e., the birefringent crystals are finest
and the carbonyl reactions and fluorescence most
intense during active secretion. Again, the
birefringence and Schultz tests are considered more
indicative of precursor substances (cholesterol and its
esters) while carbonyl tests and fluorescence indicate
substances more nearly related to mature hormones.

Recently, investigations have emphasized the
relation of enzymes to the storage and release of
energy for living processes. It has been suggested that
hormones produce their actions because they regulate

enzyme action, synthesize enzymes or are themselves enzymes or co-enzymes.

Among the enzymes intimately associated with cell growth and function in the ovary are the dehydrogenases. Meyer and McShan (1950) found a high level of succinic dehydrogenase activity in the corpora lutea of the rat ovary during pregnancy. They felt that this high enzyme activity is correlated with function and growth in the corpus. Using the tertrazolium salt (neotetrazolium) as an indication of dehydrogenase activity in the ovary, Foraker et al (1953) found that the deposition of purple black formazan granules (which indicate the sites of dehydrogenase activity) was heavy in senescent ovaries showing cortical stromal hyperplasia (Photo 125). Heavy deposition of the formazan granules also occurred in active corpora lutea while corpora albicantia contained no formazan. They concluded that the pattern of dehydrogenase activity in the ovary correlated with the presumed sites of hormone production as well as with the more general evidence of cellular proliferation.

Quite recently, McKay et al (1961) in a histochemical study of the human ovary, found that, in addition to the other steroid reactions, both theca interna cells and granulosa lutein cells acquire enzyme activities (alkaline phosphatase, acid phosphatase and non-specific esterase), whereas their parent cell types (the cortical stromal cells and the granulosa cells) are initially free of enzymes and steroids. They concluded

that "the fact that these cells acquire these enzymes activities when they change from an inactive to an active state, suggests that these enzymes are in some way related to the manufacture of steroid substances. The role that each plays in this process remains to be elucidated".

MATERIAL AND METHODS

A group of histochemical tests was carried out on 122 cases of ovarian neoplasms (accompanied with uterus or endometrial curettings). These cases were obtained from the 3 Gynaecological Wards of the Royal Infirmary of Edinburgh, Chalmers Hospital Annexe, the Western General Hospital, theEastern General Hospital, Bruntsfield Hospital, Longmore Hospital, Deaconess Hospital, Dunfermline and West Fife Hospital, Bangour General Hospital and some private nursing homes.

The neoplasms comprised the following types:

Granulosa-cell tumours	8	cases
Theca-cell tumours	4	"
Fibroma with thecomatous elements	7	"
Fibroma	14	"
Brenner-cell tumours	3	"
Pseudomucinous tumours	37	"
Serous tumours	23	"
Primary solid carcinoma	15	"
Metastatic carcinoma	7	"
Dermoid cysts	4	"
Total -	122 Cases	

In most cases the tissues were already fixed in 10%
ordinary formalin before they reached the laboratory.
These were quickly washed, examined and refixed in 10%
neutral formalin for 24 hours or longer.   The contra-
lateral ovary was usually fixed in Bouin's fluid.
Several blocks (3-10) were taken from different parts
of the ovarian neoplasms and serial* sections were cut
on the freezing microtome at 15 u thickness.   In case
of cystic or friable neoplasms, gelatine embedding had
to be resorted to.

Unstained frozen sections were mounted in non-
fluorescent glycerine and examined under both the
polarizing and the fluorescent microscopes.   Other
sections were stained with the Sudan IV stain.   Sections
were also subjected to the Schultz test and the Ashbel-
Seligman ketosteroid reaction.

The digitonin test was done in some cases (either
alone or combined with Sudan IV).   As a control,
alcohol-xylol was effective in preventing all the above
reactions in sections already extracted in it for 24
hours at room temperature.

Routine H and E paraffin sections were also obtained
from the ovarian tumour, the uterus or endometrial
curettings and the contra-lateral ovary (mid-saggittal
section).

For enzyme work (alkaline phosphatase, acid phosphatase
and non-specific esterase) blocks of tumour tissue were
fixed in absolute acetone and in 10% neutral formalin

*The use of serial sections has permitted the
comparison of the same sites showing positive results with
the different tests.

immediately after their surgical removal. They were then

kept in the refrigerator at $4^{\circ}C$ for 24 hours. The acetone

fixed blocks were used for demonstrating enzyme activities

by the paraffin method, whereas the formalin fixed

blocks were used for the frozen method.

For demonstrating succinic dehydrogenase activity

in cases of cortical stromal hyperplasia of the contra-

lateral ovary, midsaggittal section was made through that

ovary, while fresh, and frozen sections, 15 u thick, were

cut and stained with Nitro B.T.

For evaluation of the functional activity of each

neoplasm, the patient's case notes were reviewed for

clinical evidence. The endometrium was examined, and

in some cases urinary oestrogen excretion was estimated

before and after removal of the ovarian neoplasm.

The contra-lateral ovary was also examined for evidence

and degree of cortical stromal hyperplasia.

METHODOLOGY

Birefringence

Light rays vibrate in all directions. Polarization

is the process of excluding all rays excepting those

vibrating in one plane. This is accomplished by the

use of 2 Nicol prisms and a rotating stage. One prism

is put below the condenser (the polarizer) and the second

in the eye piece (the analyser). Ordinary light is

polarized by passage through the polarizer, with

a vertical axis. If the analyser is oriented with its

axis parallel to that of the polarizer the beam is trans-

mitted. If the analyser is crossed, i.e., its axis is
perpendicular to the axis of the polarizer, the beam
is not passed and the field is dark.

Polaroid sheets can be used instead of prisms.
These have been found very helpful in microphotography.

Some crystalline substances, when introduced
between the Nicol prisms, i.e., on the stage of the
microscope, they break the polarization and are visible
as bright white bodies in the dark field(anisotropic or
birefringent). Substances with a single index of
refraction (isotropic) do not interfere with the
polarization and are invisible in the dark field.

Lison (1936) and Cain (1950) found that a variety
of lipids become crystalline in cold or fixed tissues,
and exhibit birefringence. Pure cholesterol appears
as rhomboid bright crystals which light up and become
extinguished alternately once in each, 90 degrees of
rotation of the stage. Both cholesterol (and its esters)
and phosphatides may occur in droplets and are seen as
bright tetrad-like spherical bodies with Maltese cross
markings, the so-called fluid crystals of Lehmann
(Photo 133). Claesson and Hillarp (1947c) demonstrated
that the crystalline birefringence in sections of fixed
ovaries disappeared if the slide was heated to $60^{\circ}C$ and
then reappeared as the slide cooled. Since many
cholesterol esters crystallize at approximately $60^{\circ}C$
this was taken as evidence that the crystals in the
droplets consisted of cholesterol esters rather than of
other less readily crystallizable lipids.

Another type of birefringence is that shown by the
ovarian connective tissue (Dempsey and Bassett, 1943).
It appears fibrillar, continuous and non-granular
(Photo 104 and 107).   Extraction in alcohol-xylol does
not affect this latter type of birefringence although
it prevents the crystalline granular type.

FLUORESCENCE

Hamperl (1934) showed that the colour and intensity
of fluorescence varied greatly in different structures.
Using fluorescence as an analytical tool, Bierry and
Gouzon (1936) showed that purified oestrogenic
substances fluoresced with characteristic emission
bands in the green, yellow and red regions of the
spectrum.   Popper and Ragins (1942) have described
a fading green fluorescence in a number of unfixed
animal tissues, a colour which they consider identical
to that of vitamin A.   In fixed ovarian tissue Dempsey
and Bassett (1943) were the first to observe a lipoid
soluble stable fluorescence in the green and yellow
regions of the spectrum which was associated with the
thecal, luteal and interstitial tissue.   Because of the
similarity in colour to that observed by Bierry and
Gouzon, and because of the anatomical localisation,
in tissues which give other reactions for steroid
substances, Dempsey and Bassett regarded the ovarian
steroids as a likely source of this fluorescence.

Recently, Rochenschaub (1952) has come to the same

conclusion and apparently independently.   Fluorescence

is absent from the lipid droplets in unfixed tissues

except for a rapidly fading green fluorescence ascribable

to Vitamin A.   Many have suggested that Dempsey and

Bassett were indeed observing the fluorescence of

Vitamin A but as re-emphasized by Nicander (1952)

the fluorescence of Vitamin A is lost after exposure of

tissue to formalin for 6-24 H.

Deane and Barker (1952) noticed that the fluorescence

of steroid producing organs appears to parallel the

carbonyl reaction, in intensity, rather than birefringence

and Schultz reaction.   In the present study, I found the

same observation true.   In no case was the fluorescence

positive while the carbonyl reaction was negative or the

reverse.

PRINCIPLE OF FLUORESCENCE MICROSCOPY
(Popper and Szanto, 1950.)

In general, under the microscope, specimens are

observed either in natural colour or after staining.

Fluorescence microscopy substitutes fluorescence in

ultra-violet light for the colour of the specimen.

Fluorescence is the emission of light by substances

under the influence of an exciting agent.   This agent

is usually light of shorter wave length than the

fluorescent light.   The wave length of the exciting

light and the wave length or colour of the fluorescent

light are both specific for a given substance and may

characterise it.   Up to the present relatively long

ultra violet light waves (wave lengths between 3,000-4,000 Å) have been applied, a light source strong in that range is easily available and absorption of the light rays by quartz, and even by glass is negligible.

Most biological material, especially animal and human, tissue is capable of auto-fluorescence which permits orientation even in an unstained section. In addition to the study of fixed tissue, living organs may be examined by fluorescent microscopy. Fluorescence microscopy differs from ultra-violet microscopy which records specific absorption of ultra-violet light by certain structures.

Apparatus

For observation with the long ultra-violet rays (3,000 - 4,000Å), a standard monoccular microscope with ordinary condenser can be used, only a special light source and a filter system are applied. The light source which was used in this study was a Mazda* mercury vapour glass lamp (A.C./D.C.) 250 watts, type ME/D, in a proper casing.

The filter system removes the entire visible light. The one used was a 2" Wratten (Kodak*) filter, type 18A quality SpL. It permits only ultra-violet and some red rays to pass. The latter were absorbed by a glass cell containing a 5% copper sulphate solution to which one drop of concentrated $H_2 SO_4$ is added. Thus, only ultra-violet rays reach the microscope mirror. Ultra-violet rays are converted by fluorescent structures in

* Manufacturers of the lamp; Associated Electrical Industries, Lamp and Lighting Company, Edinburgh.
* Filter obtained from Cooke, Troughton and Simms, Ltd., Haxby Road, York.

the specimen to visible light so that above the specimen both ultra-violet and visible rays are present.

A filter in the eye piece (Ultra-violet protective filter, Kodak)[*] absorbs the ultra-violet light to protect the eye of the examiner who therefore observes only the newly formed fluorescent light against a dark background. A quartz or aluminised mirror has been recommended by many workers to avoid significant absorption of ultra-violet rays. However, an ordinary mirror was quite satisfactory.

Neither a quartz condenser nor quartz slides were necessary, since the long ultra-violet rays (and not the short) were used. At the beginning of this study, it was noticed that the ultra-violet light was weak. The mirror was blamed for absorbing some of the rays. However, the light remained weak even after exclusion of the mirror and orienting the beam of rays directly into the condenser. At last the use of a stronger condenser (taken from a binocular microscope) produced fairly bright ultra-violet light. Great cleanliness is essential since dust particles are often strongly fluorescent. Slides or coverslips were therefore preserved in cleaning solution and rinsed with water immediately before use.

The parenchyma and connective tissue in general give a blue colour. Elastic tissue is bright yellow and neutral fat is bluish white.

[*] Filter obtained from Cooke, Troughton and Simms,Ltd., Haxby Road, York.

Much time has been spent in trying to ascertain the
exact colour of the biologically reactive lipids.   The
occurrence of the involved fluorescence in the same
sites shown to be positive by other tests, was the clue
to its recognition. It can be described as luminous
yellow light with a green tinge.   Dull green or bright
yellow were frequently met with in old degenerating
corpora lutea or degenerative fat.   This has nothing
to do with the fluorescence in study.   Unfortunately,
we have been unable to photograph the results successfully.

SUDANOPHILIA

The Sudan stains do not differentiate between
various lipid compounds, but merely mark those substances
into which they dissolve. Sudans are soluble in neutral
fats, fatty acids, cholesterol esters and other lipids.
The depth of colour of the lipid droplets stained with
Sudan cannot be related to the chemical constitution of
the fats but is attributable to the factor of physical
solubility. Not all intracellular lipids can be
demonstrated by Sudan.   Certain physical states may
inhibit solution of the dye and combination with proteins
may render fats indetectable. This method then demonstrates
only free lipid the physical state of which allows
solution of the dye.

It is of interest to know that in the adrenal gland,
Selye (1937), Sarason (1943) and Dalton et al (1944),
have all described the fat droplets as being small when
the gland is in a state of activity and much coarser and

larger during inactivity (McKay and Robinson, 1947).
In the present study the Sudan stain was sometimes the
only positive test. In these cases it was considered
to demonstrate biologically inactive (degenerative or
neutral) fat and such cases were nevertheless considered
negative.

Sudan IV Stain (Lillie, 1952).

Fixative 10% neutral formalin.

Method

1. Rinse in water and cut frozen sections 10-15 U.

2. Wash in water.

3. Rinse in 70% alcohol.

4. Stain in Herxheimer's alkaline Sudan IV in 70%
alcohol (containing 1% Na OH) for 5-10 minutes.

5. Rinse in 70% alcohol to remove excess stain.

6. Rinse in water.

7. Stain lightly with Harris' hematoxylin (diluted
1 in 4 with distilled water) for 4 minutes.

8. Differentiate with 1% glacial acetic acid or
1% Hcl (the Hcl is quicker).

9. Blue by washing in tap water or Scott's tap water
substitute followed by washing in water.

10. Mount in glycerol jelly.

Preparation of Saturated Sudan IV Solution

Weigh one gram of Sudan IV powder and dissolve in
70 ml. of absolute alcohol by immersing the flask in hot,
but not boiling, water. Help by shaking and stirring.
If not in a hurry, the powder can be left at room

temperature to dissolve overnight.   Add to the above
solution, 30 cc. distilled water in which is dissolved
1 gm. sodium hydroxide.   This gives a final solution
of 1% Na Oh.

Harris's Alum Haematoxylin (Mallory, 1938)

Haematoxylin	2.5 gm.
Absolute alcohol	25 ml.
Ammonium or Potassium Alum	50 gm.
Distilled water	500 ml.
Mercuric oxide	1.5 gm.
Glacial acetic acid	20 ml.

Preparation

Dissolve the haematoxylin in the absolute alcohol
and the alum in the water, using heat if necessary.
Mix the 2 solutions together. Heat the mixture to
boiling point and add the mercuric oxide.   Cool rapidly
by plunging the flask into cold water. The solution
is ready for staining as soon as it is cool.   Although
optional, it is preferable to add the glacial acid,
before use, as this gives more precise and selective
nuclear staining.   Harris's alum haematoxylin has the
advantage of being ready for use as it is cool.

Ripening: The addition of mercuric oxide ripens the
stain immediately.

Although this stain is said to have good durability,
the selectivity and speed of staining diminish after 2-3
months.   It is advisable, therefore, to prepare small
quantities each month rather than a large stock.

A precipitate forms during storage which may be filtered off without detriment to the stain, although this is an indication that the stain is deteriorating.

Scott's Tap Water Substitute

This is a slightly alkaline solution used for rapid blueing of haematoxylin stains.

Sodium Bicarbonate	3.5 gms.
Magnesium Sulphate	20 gms.
Thymol water	1,000 ml.

Dissolve the sodium bicarbonate and the magnesium sulphate separately in the water, then mix.

SCHULTZ TEST

This is a histochemical application of the Liebermann Burchardt reaction. Unlike the digitonin test which depends on the presence of a free hydroxyl group, the Schultz test is given not only by free cholesterol but also by most of the esters. By model tests Everett (1947) determined that a positive reaction requires that cholesterol constitute at least 10% of the lipid droplet. Reiner (1953) has obtained comparable results. Bierry and Gouzon (1936) considered this test a general reaction for unsaturated steroids. Pearse (1960) states that Schultz test can be regarded as highly specific for cholesterol and its esters although its specificity is not absolute.

There are so many methods for Schultz test. After trying one or two other methods without success the following method was adopted and it proved very satisfactory.

Technique: after Weber et al (1956).

Fixative, 10% neutral formalin for 24 hours or longer.

1. Cut frozen sections at 15-20 U.

2. Wash for 24 H in distilled water (several changes).

3. Treat with 2.5% Ferric ammonium sulphate in 0.2
    M. acetate buffer at 37°C for 7 days. It is
    recommended that the buffer should be adjusted
    to ph 3 by mixing 2 cc. of 0.2 M. sodium acetate
    with 98 cc. of 0.2 M acetic acid.   The final
    PH is about 2.

4. Wash sections for 1 hour each in 3 changes of
    acetate buffer to remove excess of iron alum.

5. Rinse in distilled water, transfer to 5% formalin
    for 10 minutes (5 cc. commercial formalin and
    95 cc. distilled water).

6. Mount sections on slides and remove excess water
    by blotting the edges.   Do not dry the sections.

7. Place one drop of a mixture of equal parts of
    concentrated sulphuric acid and acetic acids on
    a coverslip. Invert the slid and apply it to the
    coverslip.   Turn right way up and apply even
    pressure to the coverslip so as to flatten the
    section.   Grasp the coverslip at the corners
    and oscillate several times.

Result: cholesterol and its esters appear violet or red,
turning rapidly to green within a few seconds.   The
colour remains stable for 30-60 minutes, then the whole
section becomes brown. It is essential that the reagents

used for this test should be as pure as possible.

Preparation of Molar Acetic Acid

57.9 ml. of 99.5% acetic acid in 1,000 ml. of
distilled water gives a M/1 acetic acid.

Windaus Digitonin Reaction

Windaus (1910) showed that free cholesterol (but
not its esters) treated with alcoholic solutions of
digitonin, yielded a crystalline complex insoluble in
water, acetone and ether but soluble in glacial acetic
acid or pyridine.   The reaction was first used in
histochemistry by Burnswick (1922).   He used a 0.5%
solution of digitonin in 85% alcohol and examined the
sections, in this medium under a coverslip, for the
birefringent crystals of digitonin-cholesterol. Leulier
and Revol (1930) used digitonin in 35% alcohol and
distinguished the birefringence of digitonin cholesterol
from that of the cholesterol esters by subsequently stain-
ing the sections with a red sudan dye.   The esters
became coloured and lost their birefringence while the
crystals of the digitonin complex remained anisotropic
and colourless.   Bennet (1940) also employed the reaction
in his studies on cat's adrenal cortex.

Technique (Lillie, 1952)

1. Cut frozen sections and wash them in water.

2. Immerse in a 0.5% solution of digitonin in 50%
    alcohol in a small covered dish for 2 hours.

3. Rinse in 50% alcohol.

4. Extract some of the sections in acetone, rinse
    in 50% alcohol, then pass to water.

5. Counterstain some other sections by the usual
   Hx Sudan IV stain.

6. Mount all sections in glycerol jelly.

Results: examine the uncounterstained sections (not
extracted with acetone) under the polarized light.
Needles or rosettes of cholestryl digitonids are formed
(i.e., the birefringent material is increased than in
the untreated sections).   The digitonids are still seen
after acetone extraction.   In the counterstained prep-
arations the digitonids remain doubly refractile and
do not stain while the esters colour with the dye and
lose their birefringence.   However, I agree with Pearse
(1960) that, in practice, useful results are seldom
obtained.   Like him, I have found that all the lipids,
in a digitonin treated section, stain with Sudan IV
and that the cholesterides cannot be distinguished.
In the cases treated with digitonin without counter-
staining the birefringent material is supposed to
increase due to precipitation of the birefringent
cholesterol digitonide.   I found that this increase
was absent or negligible especially when the bulk of
the reactive material consisted of cholesterol esters
or ketosteroids.   However, in very few cases, sections
treated with digitonin and extracted in acetone still
showed few birefringent crystals which were apparently
due to the digitonide.

Naphthoic Acid Hydrazide Method
(Ashbel and Seligman, 1949,1952)
In order to improve the sensitivity of the

phenylhydrazine reaction, by increasing the colour value of the final compounds, reagents were synthesized which contain a hydrazine group and which react with active carbonyl groups to form nearly colourless substances which may be converted by coupling with a tetrazolium compound (tetrazotized diortho-anisidine) into an intensely blue azo dye.   The best reagent for this purpose, proved to be the hydrazide of 2-hydroxy - 3-naphthoic acid. This was found to react in vitro with 3, 11, and 20-ketosteroid, but, as was expected, not to react with 11-ketosteroid.

In 1952, Ashbel and Seligman made a modification to their technique in order to eliminate the diffuse violet or bluish stain, especially prominent in epithelial structures, which is due to the non-specific binding or absorption of 2-hydroxy -3-naphthoic acid hydrazide to proteins.   The binding material was considered to be proteinaceous because the stain could not be removed by extraction with lipid solvents which readily extract ketosteroids.   The intensity of this diffuse stain was more prominent in tissues fixed in formalin for a long time.

Technique

Fixative: 10% neutral formalin for 24 hours or longer.

Reagents required

1.   * 2-hydroxy - 3-nephthoic acid hydrazide (0.1%).

* Obtained from Light and Company, Ltd., Colnbrook, England.

1 gm. of hydrazide is dissolved in 50 cc. of hot glacial acetic acid in a volumetric flask.   To this is added 950 cc. of 50% alcohol by volume prepared just before use from aldehyde-free absolute ethanol and distilled water. The reagent may be stored at room temperature for 2 weeks.

2.   Alcohol-buffer solution.

1/15 M. Phosphate buffer (Ph 7.2 - 7.5) is mixed with an equal volume of absolute ethyl alcohol just before use.

The buffer used in this study was Sorenson's buffer (Dempsey, 1951).

Ph 7.2 - 7.5 $\left(\begin{array}{c} \\ \\ \end{array}\right.$ 1/15 M. $Na H_2 PO_4$ 28 ml.

               1/15 M. $Na_2 H PO_4$ 72 ml.

3.   Ethyl alcohol 50%.

4.   Hcl 0.5 N.

5.   Sodium Bicarbonate 1%.

6.   Tetrazotized diorthoanisidine.   50 mgm. of the powder is stirred in 50 ml. of alcohol-buffer solution containing the sections.   Addition of the powder is done at the time of coupling without prior solution in water because the diazonium compound decomposes and darkens rapidly in pure aqueous solution.

Procedure

1. Wash formalin from frozen sections in several changes of cool water for several hours.

2. Incubate sections in hydrazide solution at room temperature for two hours.   The maximum number of sections in 50 ml. reagent is 10-20.

3. Wash in several changes of 50% alcohol for 2 hours.

4. Incubate in 0.5 N Hcl at room temperature for ½ hour (optional).

5. Wash in water.

6. Rinse in 1% sodium bicarbonate.

7. Wash in water.

8. Place in alcohol buffer solution. Add tetrazotized diorthoanisidine powder and stir for 2 minutes.

9. Wash in several changes of water.

10. Rinse in 50% alcohol followed by water to dislodge gas bubbles.

11. Mount in glycerol jelly.

Results:

Ketosteroids are stained dark blue.

N.B.   The blocking experiments with lipoid solvents were more efficient in preventing the blue reaction than were attempts to remove the blue compound with acetone extraction after the sections were stained. In both cases a delicate, lipoid-insoluble blue stain was noted in the lining membranes of blood sinusoids. Occasional nerves cut longitudinally were stained a brilliant blue which was not removed by acetone or alcohol extraction.

To render alcohol aldehyde free

the following method was used (after Varley, 1958):

1. Add 4 gms. of Phenylene diamine dihydrochloride per one litre of alcohol.

2. Allow to stand in a dark bottle for one week shaking occasionally.

3. Redistil using a fractional column.

FIXATIVES, EMBEDDING AND MOUNTING MEDIA

10% Neutral Formalin (Lillie, 1952).

Solutions of formaldehyde diluted with distilled water are commonly acid due to the presence of small amounts of formic acid, either as an impurity remaining during manufacture or as a result of oxidation of part of the formaldehyde. To correct this acidity a common practice is to shake the diluted formaldehyde solution with calcium carbonate and store it over a layer of this salt. Other workers use magnesium carbonate. With either these methods the formaldehyde solution drawn from the reservoir and used for fixation very promptly becomes more acid as the tissue is fixed.

This shift in PH is avoided by using a soluble buffer in the dilute formaldehyde solution used for fixation. The following formula gives approximately PH 7.

Monohydrated Na Phosphate	4 gm.
Anhydrous disodium phosphate	6.5 gm.
40% formaldehyde	100 cc.
Distilled water	900 cc.

N.B. In the Department of Obstetrics and Gynaecology, it has been found that instead of 4 gm. monohydrated Na phosphate, the use of 4.52 gm. of ($Na\ H_2\ PO_4$, $2H_2O$ = 156.03) gives better results.

Bouins fluid (Culling, 1957).

Formula -

Picric acid, saturated aqueous solution 75 ml.
(1.2%)

Formalin (40% formaldehyde)	5 ml.
Glacial acetic acid	5 ml.

This fixative penetrates rapidly and evenly into the tissues. It has been recommended by Woll, Hertig et al (1948) for the study of ovarian cortical stromal hyperplasia as it causes little shrinkage of the cells. Fixation is usually complete in 24 hours. The excess picric acid is removed from the sections by treatment with alcohol or prolonged washing.

Glycerol Jelly (Carlton, 1943)

Refractive index, circa 1.47.

Gelatine	10 gm.
Distilled water	60 cc.
Pure glycerol	70 cc.
Phenol cryst.	0.25 gm.

Method

Dissolve the gelatine in the water in a beaker placed in a waterbath. When the gelatine has dissolved, add the glycerol and finally the phenol. Keep this medium either in a corked tube or in a thin-walled balsam bottle. To melt it, place the vessel in hot water.

Gelatin Embedding (Culling, 1957).

Used when frozen sections are required from cystic, friable or partially necrotic tissues. Following embedding the block is immersed in 10% formalin to convert the gelatin to an irreversible gel.

Technique

1. Tissue is fixed in formol saline (neutral formaline was used) and then washed in running water for 6-12 hours (usually overnight) to remove the formalin.

2. Tissue is transferred to 10% gelatin in 1% phenol (to prevent the growth of moulds) for 24 hours at $37C$.

3. Tissue is transferred to 20% phenol gelatine for 12 hours at $37C$.

4. Tissue should now be embedded in 20% gelatin, using a mould as for paraffin wax embedding (a paper mould can be used).

5. Having been allowed to set preferably in the cold room, excess gelatin should be trimmed leaving a margin of approximately 3 mm. around the specimen and as little as possible on the surface to place on the freezing microtome stage.

6. The trimmed block is then immersed in 10% (neutral formalin for 12-24 hours to harden.

7. Frozen sections can now be cut in the usual way. It is preferable to cut them thin (10-15 U) to avoid undue background staining caused by the gelatin.

SUCCINIC DEHYDROGENASE

This enzyme is located in the cytoplasmic granules related to the process of intracellular respiration and known as mitochondria. The enzyme is concerned with the oxidation of carbohydrates and in a general way with both the metabolic and proliferative functions of the cells. Tetrazolium salts as indicators of dehydrogenase activity are recent additions to histochemistry. They act as hydrogen acceptors. If an excess of succinate is

furnished as a substrate for the reaction, much of the formazan deposition is believed to be related to the presence, in the cells, of succinic dehydrogenase. Triphenyl tetrazolium chloride (TTC) was the first salt used. The difficulty of obtaining a positive reaction and the weak colour and diffusibility of the formazan produced in tissues were serious objections to its continued use. Much better results were obtained after the synthesis of the new compounds namely neotetrazolium (NT) and Blue tetrazolium (BT). Almost all histochemical work in the field of dehydrogenase histochemistry between 1950 - 1958 was carried out with either NT or BT. Recently, Nachlas et al (1957) introduced another new tetrazolium salt, nitro blue tetrazolium (nitro BT) which possesses most of properties of an ideal reagent for histochemical purposes. It permits the cytochemical visualisation of the sites of enzymic activity in thin tissue sections 2-10 U thick, under aerobic condition, after a relatively short incubation period.

Technique   (Pearse, 1960)

Using Nitro - BT (after Nachlas et al, 1957).

Cut fresh frozen, cold microtome sections and mount on cover slips.

Preparation of substrate solutions.

1. Stock buffered succinate: combine equal volumes of 0.2 M phosphate buffer (Ph 7.6) and 0.2 M sodium succinate.

2. Incubating Medium: add 10 ml. stock succinate solution to 10 ml. aqueous solution of Nitro-BT (1 mgm./ 1 ml).

Procedure:

1. Incubate sections for 5-20 minutes at 37C^{o} in air.

2. Wash in saline.

3. Fix in 10% formol saline for 10 minutes.

4. Rinse in 15% alcohol for 5 minutes.

5. Mount in glycerol jelly.

Result: Blue diformazan deposits indicate sites of succinate dehydrogenase activity.

The 0.2 M Phosphate buffer (Ph 7.6) was prepared as follows:

| 0.2 M. Na H$_2$ PO$_4$ | 16 ml. |
| 0.2 M. Na$_2$ H PO$_4$ | 84 ml. |

THE PHOSPHATASES

(Pearse, 1953, 1960).

These enzymes are divided on the basis of their optimum pH levels in vitro.   Those which work on the alkaline side of neutrality and particularly at pH 9.0 and above are called alkaline phosphatases, while those which work in the region of pH 5.0 constitute the acid phosphatases.

Two methods have been used for the demonstration of these enzymes, i.e., Gormori's method for paraffin (and frozen) sections and Coupling Azo-dye method for frozen sections.

In the frozen sections there is better localisation

and the nuclei are not stained.

In the paraffin sections the enzyme is somewhat inactivated by the process of paraffin embedding and the nuclei are stained. This nuclear staining is believed to be entirely due to artifact (Photo 114).

ALKALINE PHOSPHATASE

I. (Gomori's calcium cobalt method for demonstrating sites of alkaline phosphatase activity.)

Steps

1. Fix thin bits of tissue (2 mm. thick) in absolute acetone at $4^{o}C$, for 24 hours.

2. Transfer progressively to absolute alcohol at $\frac{1}{2}$-hourly intervals.

3. Transfer to absolute alcohol/ether (1-2 changes) 20 minutes each.

4. Then to 1% celloidin for 30 minutes.

5. Drain off the excess and harden in chloroform for 20 minutes.

6. Clear in benzene. Two changes 15 minutes each.

7. Empermeate with paraffin in vacuum embedding bath (avoiding overheat) 3 changes 15 minutes each.

8. Embed in paraffin wax of melting point $56C^{o}$.

9. Store in the refrigerator if need to wait.

10. Trim the blocks and cut sections at 6 U thickness. Mount on albuminised (or ordinary) slides using warm water for floating out the sections.

11. Dry the slides for 2-3 hours at $37C^{o}$.

12. Use at once or store in the refrigerator at 4C° for few days (if need to wait).

13. Remove wax from the slides by brief immersion in light petroleum or xylol.

14. Pass to water via absolute acetone.

15. Incubate for $\frac{1}{2}$ - 16 hours at 37C° ($2\frac{1}{2}$ hours have been found satisfactory) in the following medium (Ph 9):

    10 ml. 2% sod. B. glycerophosphate

    10 ml. 2% sod. diethyl barbiturate

    20 ml. distilled water

    2 ml. 2% calcium chloride

    1 ml. 2% magnesium sulphate.

16. Rinse in running water.

17. Treat with 2% cobalt nitrate or acetate for 3-5 minutes.

18. Rinse well in distilled water.

19. Treat with a dilute solution of yellow ammonium sulphide (2%) for 1-2 minutes.

20. Wash in water, counterstain with 1% aqueous eosin for 5 minutes if desired.

<u>Result:</u>

Various structures possessing alkaline phosphatase activity are stained black or brownish black.

II. <u>A modified coupling azo dye method for alkaline phosphatase:</u>

1. Fix thin slices of tissue in 10% neutral formalin at 4C° for 10-16 hours.

2. Cut frozen sections 10-15 U thick and mount on clean glass slides without any adhesive.

3. If the tissues are delicate or friable, gelatine embedding is indespensable.

4. Allow the sections to dry in air for 1-3 hours to ensure adherence.

5. Dissolve 10-20 mgm. *sod. α-naphthyl phosphate in 20 ml. 0.1 M veronal acetate buffer (Ph 9.2). (The Ph of the medium is lowered both by the addition of the substrate and also by the various diazotates.)

6. Stir in 20 mgm. of the stable diazotate of *4-Benzoyl-amino- 2:5 - dimethoxy-aniline.

7. Filter on to the slides sufficient to cover each section adequately and incubate at room temperature (17-22C) for 15-60 minutes. (With temperature above 22C diffusion and abnormal crystallisation effects may be noted.)

8. Wash in running water for 1-3 minutes.

9. Counterstain with Mayer's haemalum (if desired) for 4-6 minutes. Then wash in running water for 30-60 minutes.

10. Mount in glycerine jelly.

Result: sites of alkaline phosphatase activity are coloured black.

To prepare veronal acetate buffer (Ph 9.2).

Make up a veronal acetate solution as follows:

Hydrated sod. acetate   1.943 gm.

* sod. α-naphthyl phosphate and the diazonium salt were obtained from Light and Company.

| Veronal (sodium barbiturate) | 2.943 gm. |
| Distilled water up to | 100 ml. |

Then make up the buffer as follows:

Veronal acetate solution	5 ml.
M/10 hydrochloric acid	0.25 ml.
Distilled water	19.75 ml.

Mayer's haemalum (Culling, 1957)

Haematoxylin	1 gm.
Distilled water	1000 ml.
Amm. or Potassium alum	50 gm.
Sodium iodate	0.2 gm.
Citric Acid	1 gm.
Chloral hydrate	50 gm.

Dissolve the haematoxylin in the distilled water using gentle heat if necessary. Add the alum, shaking to dissolve, but again using heat if required. When the alum is dissolved add the sodium iodate followed by the citric acid and chloral hydrate. This modification by Mayer is very precise for nuclei and is one of the few haematoxylin stains still used progressively usually as a counterstain.

ACID PHOSPHATASE

Two methods were used for the investigation of acid phosphatase activity:

1. Lead phosphate method of Gomori (1950) for both paraffin and frozen sections.

2. Coupling Azo method (which is based on Burton's modification of Seligman's method) for frozen sections.

I. Lead phosphate method of Gomori (1950)

Paraffin and frozen sections were cut from the same blocks used for alkaline phosphatase.

1. Mount frozen sections on clean glass slides and leave to dry in the air for 1-3 hours.

2. Remove wax from paraffin sections and bring down to water via absolute acetone.

3. Incubate both paraffin and frozen sections in the substrate solution at 37°C for 24 hours.

Preparation of the substrate solution

M/5 acetate buffer (Ph 4.8)	12 ml.
Lead nitrate (0.1M)	10 ml.
Distilled water	74 ml.
Sodium B glycerophosphate (3.2%)	4 ml.

added in the given order.

Shake well. Heat to about 60°C for about 10 minutes; then filter. Leave the filterate overnight, then filter again and use for incubation.

4. Rinse in distilled water then in a 2-3% acetic acid.

5. Rinse again thoroughly in distilled water then immerse in 2% dilution of yellow ammonium sulphide for 1 minute.

6. Wash thoroughly in tap water.

7. Counterstain, if desired, with 1% aqueous eosin for 5 minutes.

8. Wash well and mount in glycerine jelly.   Result: The presence of acid phosphatase in the sections is indicated by a black precipitate of lead sulphide.

Preparation of acetate buffer (Ph 4.8)

M/5 acetic acid	5 cc.
M/5 sod. acetate	15 cc.

According to Walpole's table (Lillie, 1952) this gives a buffer for Ph 5.11. When the various chemicals are added to the buffer, the Ph is slightly lowered and as the buffered substrate is left overnight the final ph is again lowered to 4.8.

II. Coupling azo method of Burton

Frozen sections from the same blocks used for the above methods were used. The substrate medium is prepared as follows:

1. Add 8 mgm. sod. α-naphthyl phosphate to 40 ml. of acetate buffer ph 5.7 (Lillie, 1952). This is made as follows:

      0.1 M acetic acid   1.5 cc.

      0.1 M sod. acetate   18.5 cc.

2. Shake well and add 40 mgm. of the diazonium salt (4-Benzoylamino- 2:5 - dimethoxyaniline). The salt used by Burton was tetrazotised di-o-anisidine, but it has the disadvantage of giving a brown colour to the whole background.

3. Shake again and filter.

Incubate the sections in the substrate solution in a small covered dish at 37°C for 1 hour.

Wash in distilled water, transfer to another change of distilled water, cover and leave at room temperature overnight, to allow air bubbles to come out of the sections. Mount on clean slides as such or after counterstaining the nuclei with Grenachers alum carmine for 10 minutes, washing in water and mounting in

glycerine jelly.

Result: sites of acid phosphatase activity are coloured

black.

Grenachers alum Carmine (Mallory, 1938)

Carmine	1 gm.
Ammonium alum	2 gm.
Distilled water	50 ml.

Boil for one hour, add water to make up for the

original volume. When cool, filter and add a crystal

of thymol.

Non-specific esterase

α-Naphthyl acetate method (Pearse, 1960).

Done on both frozen and paraffin sections taken

from the same blocks used for alkaline phosphatase and

acid phosphatase. The substrate solution was prepared

as follows:

1. Add 50 mgm. of the diazonium salt (4-Benzoylamino

2:5 - diamethoxyaniline) to 50 ml. 0.1 M phosphate buffer

pH 7.4 (which is made by adding 10 ml. KH_2 phosphate to

40 ml. Na_2 H phosphate).

2. Shake well till most of the initial cloudiness

disappears.

3. Dissolve 50 mgm. α-naphthyl acetate in 0.5 ml. acetone.

4. Filter. The filterate is the buffered substrate

enough for one group of sections, either the paraffin or

the frozen ones and has to be used immediately.

The frozen sections were incubated in the substrate

solution for 15 minutes in a covered petri dish at room

temperature, while the paraffin sections after being

deparaffinised are incubated in the substrate solution
in a coplin jar for one hour, also at room temperature.

After incubation sections are washed with water
then mounted using glycerine jelly. Counterstaining
with Grenachers alum carmine can be done if desired.
Result: sites of esterase activity are represented
by a black deposit.

Gelatine Embedding for Enzyme Histochemistry (Pearse 1960)

This process is usually carried out when it is
necessary to support delicate tissues so that sections
can be cut on the freezing microtome. When sections
of delicate tissues are required for enzyme studies and
particularly for the coupling azo-dye techniques,
a modified gelatine embedding procedure, designed to
damage the enzymes as little as possible can be employed.

Method

1. Fix thin slices or portions of tissue in 10% cold
neutral formalin ($4^{\circ}C$) for 10-16 hours.

2. Wash in running water for 30 minutes.

3. Embed in gelatine for 1 hour at $37^{\circ}C$. The gelatine
is made as follows:

Gelatine	15 gm.
Glycerine	15 ml.
Distilled water	70 ml.
Thymol	a small crystal.

4. Cool and harden in formalin (40 per cent formaldehyde)
for one hour at $17-22^{\circ}C$. Wash.

5. Store at $4^{\circ}C$ until frozen sections are required.

RESULTS

GRANULOSA CELL TUMOURS

Case 1.

1343/61.   (Miss M.H., 41 years old, $1\frac{1}{2}$ years post-menopausal.)

This patient entered the hospital complaining of scant,irregular, vaginal bleeding ever since the menopause and an abdominal swelling which she hadnoticed for the past year.   Abdominal examination revealed a firm, regular mass arising from the pelvis and extending up to half-way between the umbilicus and xiphisternum.   Per vaginam: it was impossible to define the uterus and appendages separate from the mass.   Hysterectomy and bilateral salpingo-oophorectomy were performed.   The right ovary was replaced by a large, semi-solid tumour which weighed 9 lb. 13 oz. and measured 12 x 10 x 5".   It was pinkish grey in colour, smooth and well encapsulated. On section, it showed a yellowish, brain-like appearance with many small cavities filled with watery fluid.   The uterus was slightly bulky with a small seedling fibroid on its anterior surface.   The left ovary was a bit larger than normal and its cortex was thickened and nodular.

Microscopically, the endometrium was the seat of cystic hyperplastic activity (Photo 76).   The left ovary showed grade II hyperplasia with two cortical granulomas (Photo 75).   The right ovarian tumour consisted of masses and cords of granulosa cells, mainly arranged in

trabecular and gyniform patterns. Thin bands of
connective tissue penetrated in between the cords
separating them. Theca-like connective tissue cells
containing red droplets were readily revealed by Sudan
IV stain (Photo 71), although they were not recognised
in H and E sections. The whole battery of histochemical
tests (birefringence, Schultz test, Ashbel-Seligman test
and flourescence) was positive in these stromal theca-
like cells but negative in the granulosa cells (Photos 72,
73 and 74). Control sections were negative.

Case 2.

5818/60. (Mrs A.M., 73 years old, para 5 + 1, 27 years
post-menopausal.)

This patient was admitted to hospital with a chief
complaint of vaginal bleeding for the last $1\frac{1}{2}$ years.
A diagnostic dilatation and curettage done 6 months prior
to admission showed a cystic hyperplastic endometrium.
As she had not been on oestrogen therapy, the possibility
of a functioning ovarian tumour was raised. On examin-
ation, she looked younger than her age. Abdominal
examination revealed no abnormality. The vagina showed
oestrogenic effects. The uterus was anteverted and
normal in size. The appendages were normal.
*Oestrogen excretion in urine was 17.8 Ug./24 hours
(oestriol 14.4 Ug, oestrone 1.4 Ug. and oestradiol 2.0 Ug.).
Hysterectomy and bilateral salpingo-oophorectomy were

  * These values are higher than normal and are in
the range where endometrial stimulation would be expected.

performed.   The uterus was larger than would be
expected in a patient of this age and on cut section the
endometrium was thick and profuse.   The left ovary showed
a small, yellowish nodule $\frac{1}{4}$" in diameter.   Microscopically,
the uterus showed myohyperplasia and the endometrium
cystic hyperplasia (Photo 80).   The right ovary showed
grade 0 cortical stromal hyperplasia with an area of
thecomatosis.   The yellowish nodule of left ovary
consisted of thin cords of granulosa cells anastomosing
with each other (trabecular pattern).   Solid sheets
of granulosa cells were also present in some fields
(diffuse pattern).   In many areas the granulosa cells
exhibited vacuolization of their cytoplasm (luteinization)
(Photo 77).   Bands of connective tissue lay in between
the tumour cell masses and cords.   A good number of
these connective tissue cells had assumed a plump
fusiform shape similar to theca interna cells.   Sudan IV
stain revealed very fine red droplets in the granulosa
cells, the luteinized cells being almost filled with
fat (Photo 78).   A large concentration of red droplets
was also present in the stromal theca-like cells.
Birefringent crystals were present in theca cells and
in luteinized granulosa (Photo 79).   Schultz test was
positive in the same sites.

The Ashbel-Seligman and fluorescence tests gave
similar results and were mainly positive in stromal
theca cells, especially adjacent to the cords of tumour
cells.   Control sections were negative.

Case 3.

6056/61. (Mrs G. H., 55 years old, 6 years post-menopausal.)

This patient entered the hospital with a chief complaint of intermittent vaginal bleeding over the past two months.   Her general condition was good and abdominal examination revealed no abnormality. Per vaginam: the uterus was bulky and there was a solid mass lying in the pouch of Douglas behind the uterus. Total hysterectomy and bilateral salpingo-oophorectomy were performed.   The uterus showed no gross abnormality. Both ovaries were slightly enlarged and had thickened nodular cortex.   Attached to the right ovary, by a rather broad pedicle, was a solid well-encapsulated lobulated tumour (2 x 1 x 1½").   Its cut surface was greyish white, with some yellowish areas.

Microscopically, the endometrium was the seat of proliferative activity with some dilated glands. Both ovaries showed grade I cortical stromal hyperplasia. The right ovarian tumour consisted mostly of solid sheets of polygonal granulosa cells with rounded to oval nuclei. In some areas these cells seem to intermingle with spindle shaped, theca-like stromal cells so that the growth can be designated as a granulosa cell tumour with a prominent thecal component.   Sudan IV stain revealed red droplets in theca cells only.   The latter also contained birefringent crystals and gave positive results with Schultz test, Ashbel-Seligman test and showed yellowish-green fluorescence.   Control sections were negative.

Case 4.

4537/61. (Mrs F. B., 54 years old, Para 4 + 0, 15 years
post-menopausal.)

This patient was admitted to hospital because of
an attack of abdominal pain, vomiting and faintness
one day before admission.   She also had vaginal bleeding
for the past fortnight and a gradually increasing
abdominal swelling over the past year.   She gave a hist-
ory of two episodes of vaginal bleeding, of one day's
duration, 3½ and 2½ years prior to admission.

On examination, a hard, ill-defined, abdominal
mass was felt to arise from the pelvis and reach up to
the umbilicus.   Per vaginam: it was difficult to
define the uterine body.   Total hysterectomy and
bilateral salpingo-oophorectomy were performed.   Much
fresh blood was lying in the peritoneal cavity (8-9 pints).
The palpated abdominal mass was, in fact, two large
masses of organised blood clots intermingled with soft
yellowish grey pieces of friable tumour tissue.   The
right ovary was the site of a ruptured tumour, and the
ruptured ovarian vessels over its surface were thought
to be the source of intraperitoneal haemorrhage.   The
uterus was bulky and contained two cervical polypi and
several fibroids, the largest of which was interstitial
and measured 1" in diameter.   The endometrium looked
profuse.   The left ovary showed a thickened nodular
cortex.   Microscopically, the uterine fibromyomas and
the cervical polypi were benign.   The endometrium

showed cystic hyperplasia.   The left ovary showed whirly

nodules of hyperplastic cells (grade II cortical stromal

hyperplasia) and an area of thecomatosis.   The pieces of

tumour tissue showed a granulosa-cell tumour of the diffuse

pattern.   No theca cells could be recognised in the few

connective tissue bands in ordinary H and E sections.

Sudan stain, however, revealed scattered clusters of

plump connective tissue cells.   These cells contained

birefringent crystals, exhibited yellowish green

fluorescence and gave positive Schultz and Ashbel-

Seligman tests.   No reactive materials were present in

granulosa cells.   Control sections were negative.

Case 5.

4498/61.   (Mrs W. W., 25 years old, Para 1 + 0,

L.M.P.*   2 days.)

This patient entered the hospital with a chief

complaint of continuous, vaginal bleeding for the past

4 weeks.   Her periods became irregular and heavier for

the past 7 months.   Abdominal swelling was also noticed

over the last three weeks.   On examination, a cystic

abdominal mass was felt to arise from the pelvis and

reach up to the umbilicus.   Per vaginam: the uterus was

palpable behind the mass which was thought to arise from

the right ovary.   A dilatation and curettage yielded

a proliferative endometrium.   Right ovarian cystectomy

was performed.   The right ovary was replaced by a thin-

* In this study the L.M.P. was always calculated

from the date of the operation.

walled cyst of plate-like shape, measuring 9 x 8 x 3".
It was multilocular and filled with straw-coloured watery
fluid. In some areas its wall was slightly thickened by
yellowish fleshy tissue. Its capsule was intact.

The uterus, though bulky, was regular in outline.
The other ovary looked healthy and together with the
uterus they were left behind. Microscopically, the right
ovarian tumour proved to be a granulosa cell tumour of the
macrofolliculoid, tubular and trabecular patterns.
Theca cells were abundant and well shown in the stroma
in H and E sections. Sudan IV stain proved them to be
filled with red droplets. They also contained high
concentrations of birefringent crystals and yellowish
green fluorescence. Schultz test and Ashbel-
Seligman reactions were positive only in theca cells.
Control sections were negative.

Case 6.

3907/60. (Miss E.S., 58 years old, 6 years post-
menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding for the past week.
Abdominal and vaginal examination revealed no abnormality.
A diagnostic dilatation and curettage yielded a cystic
hyperplastic endometrium.

Hysterectomy and bilateral salpingo-oophorectomy
were performed. The uterus was smaller than normal
but on cut section it showed a profuse endometrium.
The right ovary was slightly enlarged and its cut
surface showed a circumscribed semisolid yellowish

tumour ($\frac{1}{2}$" in diameter). The left appendages showed
no gross abnormality. Microscopically, the endometrium
showed cystic hyperplasia and the left ovary showed
slight cortical hyperplasia (grade 0). The right
ovarian tumour consisted of compact sheets of
granulosa cells with minimal connective tissue bands
(diffuse pattern). In several areas the cells were
vacuolated and luteinized. Sudan IV stained revealed
red droplets in the luteinized granulosa cells as well
as in scanty plump fusiform connective tissue cells.
Birefringent crystals were present only in luteinized
granulosa cells and in stromal theca-like cells.
Schultz test was weakly positive in the same sites.
Fluorescence and Ashbel Seligman tests were negative.
Control sections were negative.

Case 7.

4313/60. (Mrs A.M., 54 years old, para 1, 6 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding for the past two weeks
with occasional spotting ever since the menopause.
On examination, she was healthy looking. Abdominal
examination revealed no abnormality, apart from slight
tenderness in the right iliac fossa on deep palpation.
Per vaginam: there was an enlarged left ovary (about
3" in diameter) which was firm and fixed. Total
hysterectomy and bilateral salpingo-oophorectomy were
performed. The uterus was normal in size and on cut

section three seedling fibroids were found in its wall
and a small endometrial polypus was present in its
cavity.   The left ovary was replaced by an irregular
yellowish pink semisolid tumour which measured 2 x $1\frac{1}{2}$ x
$1\frac{1}{2}$".   It was well encapsulated and showed no adhesions
to surrounding structures.   The right ovary showed
thickened irregular cortex and the right tube showed
a small hydrosalpinx. Microscopically, the endometrium
showed proliferative activity.   The right ovary showed
grade I cortical stromal hyperplasia and few cortical
granulomas.   The left ovarian tumour consisted of
masses of granulosa cells with round to oval nuclei
arranged in palisades near the periphery of the tumour
masses where they were in contact with the numerous bands
of connective tissue. Numerous Call-Exner bodies were
present in the tumour masses.   In some areas the
tumour cells were arranged in cords and acquired the
trabecular pattern.   Sudan IV stain revealed the
presence of a few fat laden theca-like cells, in the
fibrous trabeculae, which were not apparent in the H
and E stained sections.   These stromal cells contained
birefringent crystals and gave a weakly positive
Schultz reaction.   The fluorescence and Ashbel-Seligman
tests were, however, negative. No reactive materials
were present in granulosa cells.   Control sections
were negative.   The urinary oestrogen excretion of this
patient before the operation was 8.1 Ug (total oestrogens)

per 24 hours). Three-four days after the operation it was 7.5 Ug/24 hours. (The normal post-menopausal range is 3.8 Ug - 8.1 Ug./24 hours.)

MALIGNANT GRANULOSA-THECA CELL TUMOUR

Case 8.

5055/61. (Miss E.G., 78 years old, para 0 + 0, 32 years post-menopausal.)

This patient entered the hospital with the chief complaint of an episode of vaginal bleeding which lasted for the first three days of the past week. On examination, she looked fairly healthy. Abdominal palpation revealed a cystic swelling arising from the pelvis and extending up to three fingers below the umbilicus. Hysterectomy and bilateral salpingo-oophorectomy were performed. The left ovary was replaced by a large cystic tumour measuring about 6 x 4 x 4". It had a pinkish white smooth surface and a thin wall with several solid areas. On cut section, it was multilocular and contained many pieces of soft yellowish white tissue in its wall. The uterine wall was thickened and the endometrium looked quite profuse.

Microscopically, there was cystic hyperplasia of the endometrium in its full-blown picture. The right ovary showed grade I cortical stromal hyperplasia and a cortical granuloma. The ovarian tumour was composed of sheets of typical theca cells surrounding masses of malignant granulosa cells. Their nuclei were hyper-chromatic, differed in size and shape and showed marked mitotic activity. Sudan stain revealed red droplets in some of the theca cells, particularly those adjacent to the granulosa islands. The remaining tests were all positive, only in theca cells, more concentrated near the

granulosa islands.   Control sections were negative.

THECOMAS

Case 9.

83/61. (Mrs G. T., 58 years old, para 0 + 0, 12 years post-menopausal.)

This patient entered the hospital with a chief complaint of vaginal bleeding on and off for the past 4 weeks.   On examination, there was fullness in the lower abdomen.   Vaginal examination revealed bulky, irregular uterus with multiple fibroids. Hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was considerably enlarged and irregular in outline as a result of 2 subperitoneal fibroids.   The largest of these measured $1\frac{1}{2}$" across. On cut section, the uterine wall was markedly thickened and the endometrium was velvety and thick (Photo 81).   The cervix showed Nabothian follicle formation and the right ovary a thick nodular cortex.   The left ovary was slightly enlarged and on cut section it appeared to harbour a small fibroma ($\frac{1}{2}$" in diameter) and a tiny yellowish tumour ($\frac{1}{4}$" in diameter) which was partially surrounded by haemorrhage and lay adjacent to the fibroma (Photo 82). Microscopically, the uterus showed myohyperplasia and the endometrium cystic hyperplasia (Photo 88a).   The two fibromyomas were benign.   The right ovary showed Grade I stromal hyperplasia and an area of endometriosis. The left ovary contained a fibroma made of interlacing

spindle shaped fibroblasts and collagen fibres.
Clusters of plump theca-like cells were present in a
certain area near the periphery of the fibroma.   The
small yellow nodule consisted of typical theca cells
constituting a small thecoma (Photo 83) and surrounded
by an area of endometriosis.   Reticulum stain
revealed a pericellular reticular network surrounding
clear individual theca cells (Photo 84).   Sudan IV
stain showed numerous red droplets which almost
filled most of the theca cells present in the thecoma
(Photo 85) and in the periphery of the fibroma.
Steroid substances, i.e., birefringent crystals
(Photo 86) exhibiting yellowish green fluorescence, and
giving green colour with Schultz test (Photo 87), and
dark blue colour with Ashbel and Seligman test (Photo 88)
were present only in theca cells but were absent in the
fibroblasts and collagen bundles of the fibroma.   Con-
trol sections were negative.

Case 10.

3432/60. (Miss F. F., 65 years old, 16 years post-
menopausal.)

This patient entered the hospital with the chief
complaint of vaginal bleeding (she had noted staining
for the past 2-3 months and a heavy flow of bright red
blood for the past two weeks).

On examination, she looked pale.   Abdominal
examination revealed no abnormality.   The vagina was

full of clotted blood. The uterus could not be outlined
and the appendages were not felt. Total hysterectomy
and bilateral salpingo-oophorectomy were performed.
The uterus was bulky and contained several fibroids, the
largest of which ($3\frac{1}{2}$" in diameter) was subperitoneal,
pedunculated and arising from the fundus. On cut
section, the endometrium was the seat of an advanced
malignant growth which was invading the myometrium.
The uterine cavity was filled with blood clots, and
necrotic tissue. The left ovary was slightly enlarged
and on cut section showed a rounded semi-solid
yellowish tumour 1" in diameter. The right ovary
showed a thickened nodular cortex. Microscopically,
the endometrium showed a well differentiated adeno-
carcinoma which had invaded about 9/10 of the muscle
wall. The fibromyomas were benign. The right ovary
showed grade II cortical stromal hyperplasia and an
area of thecomatosis. The left ovarian tumour
consisted of islands of theca cells arranged diffusely
and separated by few bands of fibrous tissue. The
cells were mostly ovoid in shape and had a rounded
nucleus. A good number of them had a vacuolated
cytoplasm. There were no mitotic figures. Silver
stains showed a pericellular reticular network.

Sudan IV stain revealed a heavy content of red
droplets in most of the theca cells. The other histo-
chemical tests were all positive. Control sections
were negative.

Case 11.

5500/60 and 3113/61. (Mrs A.G., 50 years old, Para 1 +1, 1½ years post-menopausal.)

This patient was admitted to hospital with the complaint of loss of weight over the last 6 months, dragging sensation of the lower abdomen and tiredness for the past two months. On examination, she looked pale and anxious. Abdominal examination revealed the presence of a vague ill-defined tender swelling in the left iliac fossa. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The peritoneal cavity was filled with fragments of friable tumour-like tissue which were lying free and not attached to anything. There were no metastases in the liver or peritoneum. The left ovary was absent.

These findings were suggestive of a malignant left ovarian tumour which had undergone torsion and became detached from the primary site. The uterus was slightly smaller than usual and on cut section showed no characteristic feature. The right ovary showed no abnormality. Microscopically, the endometrium was thin but showed some degree of proliferative activity and areas of adenomyosis. The right ovary showed early cortical stromal hyperplasia (grade 0). Three blocks from the left ovarian fragmented tumour, revealed extensive haemorrhage and necrosis. The fourth block, however, showed areas of plump fibroblasts arranged

diffusely, as well as areas of rounded and ovoid vacuolated cells with round vesicular nuclei. In some fields the nuclei varied in shape and size and showed mitotic figures (Photo 89). Reticulum stain revealed the characteristic pericellular network around clear cells (Photo 90). The possibility of a malignant thecoma was therefore suggested.

Six months later, the patient was re-operated on, and ascitic fluid and loose pieces of tissue were removed. Microscopically, the tissue fragments showed the same appearances as the previous specimen.

Sudan IV stain showed the cells to be heavily loaded with red droplets (Photo 91). The cells contained numerous birefringent crystals (Photo 92) and yellowish green fluorescent droplets. The Schultz and Ashbel-Seligman tests were strongly positive (Photos 93 and 94). Control sections were negative.

Case 12.

(A predominantly theca-cell tumour, containing very few islands of granulosa.)

499/59. (Mrs L., 58 years old, para 1 + 1, 5 years post-menopausal.)

This patient entered the hospital with a chief complaint of vaginal bleeding which was first noted 15 months after the last menstrual period. A D. & C. were then performed, which yielded distinctly hyperplastic endometrium. The bleeding stopped for several months but recurred later on and had been continuous for

10 weeks prior to admission.   Abdominal examination
revealed no abnormality.   Per vaginam, the uterus showed
a small, subperitoneal posterior fibroid.   The left ovary
was enlarged to the size of a walnut.   The right
appendages showed no abnormality.   Hysterectomy and
bilateral salpingo-oophorectomy were performed.   The
uterus was slightly enlarged with subperitoneal fibroid.
On cut section, the endometrium was thick and profuse.
The right ovary showed a thickened nodular cortex.   The
left ovary was 1½" long and on cut section it showed
a semi-solid whorled yellowish white tumour (about 1" in
diameter).   Microscopically, the endometrium showed
cystic hyperplasia and adenomyosis.   The right ovary
showed grade I cortical stromal hyperplasia.   The left
ovarian tumour consisted of whorled bundles of spindle
shaped fibroblasts and plump theca like cells.   A few
islands of granulosa cells were present.   Sudanophillic
droplets were present only in theca cells which also
contained birefringent crystals.   All the other tests
were, however, negative.   The urinary oestrogen
excretion (before the operation) was 11 Ug/24 hrs.
(total oestrogens).

<div align="center">FIBROMA WITH THECOMATOUS ELEMENTS</div>

Case 13.

200/61.   (Mrs B., 52 years old.)

This patient complained of shortened menstrual
cycles for the past 18 months with occasional inter-
menstrual bleeding.   Per vaginam, the uterus was bulky.

Total hysterectomy and bilateral salpingo-oophorectomy
were performed.   The uterus was enlarged and on cut
section its wall thickened and showed few seedling
fibroids.   The endometrium was profuse.   The right
ovary looked normal exteriorly but on cut section, it
showed a thickened cortex and a small yellowish white
tumour (3 mm. in diameter) which was more or less
centrally placed (Photo 95).   The left ovary contained
a small cyst ($\frac{3}{4}$" in diameter).   Microscopically, the
endometrium showed proliferative activity with a few
cystic glands.   The left ovary showed a follicular cyst
and several atretic follicles.   The right ovary showed
grade I cortical stromal hyperplasia and thecomatosis
(Photo 97).   It harboured also a small fibroma made of
interlacing bundles of spindle shaped fibroblasts and
collagen.   Few clusters of ovoid theca-like cells
were present in some areas.   Sudan IV stain revealed
red droplets of fat in the theca-like cells but not in
the thin spindle shaped fibroblasts.   This fat was
birefringent (Photo 96), gave a weakly positive
Schultz, ashbel-Seligman and fluorescence tests.
Control sections were negative.

Case 14.

3949/60.   (Mrs I.T., 66 years old, para 3 + 0, 17 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of two episodes of vaginal bleeding within the
past 3 weeks.   Abdominal examination revealed no

abnormality.   Per vaginam, there was a small cervical
polyp coming out through the os.   The uterine body was
hard to define but seemed bulky and irregular.   The
adnexa could not be felt.   D. & C. yielded bulky
curettings which proved microscopically to be adeno-
carcinomatous.   Total hysterectomy and bilateral
salpingo-oophorectomy were performed.   The uterus was
slightly enlarged and its cut surface showed a friable
greyish white polypoidal growth which had invaded about
one half of the muscle wall.   The left ovary was
replaced by a whitish pink, well encapsulated, solid
tumour about 3" in diameter.   On section, it showed
white fibrous cut surface with streaks of yellow.
The right ovary showed a thickened cortex at one part.
Microscopically, the endometrium was the seat of
a moderately differentiated adenocarcinoma which was
invading the myometrium.   The right ovary showed
grade O cortical stroamal hyperplasia.   The left
ovarian tumour consisted of interlacing bundles and
whirls of spindle shaped fibroblasts among which were
scattered the characteristic pink hyaline masses
resembling corpora albicantia.   In many areas the
cells were plump, vacuolated and theca-like.   Sudano-
phillic droplets were present in most of the cells but not
in the hyaline masses.   Birefringent crystals were
abundant and Schultz test was positive in the theca cells
only.   Fluorescence and Ashbel-Seligman tests were only
a trace positive.   Control sections were negative.

Case 15.

869/61.   (Mrs A.M., 54 years old, para 3 + 0, 3 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding which occurred in two
episodes within the past 6 months.   Abdominal examination
revealed a palpable, hard mass coming out of the pelvis.
Per vaginam, a mass was felt in the posterior fornix.
Total hysterectomy and bilateral salpingo-oophorectomy
were performed.   The uterus was enlarged and on cut
section it showed an interstitial fibroid (4 x 4 x 3").
The endometrium was rather profuse.   A right solid
ovarian tumour was lying in the pouch of Douglas.   It
measured 4 x 3 x $2\frac{1}{2}$", was well encapsulated and had
a white smooth surface.   Its cut surface showed several
yellow streaks amidst whirls of fibrous tissue.   The
left ovary showed a thickened nodular cortex.   Micro-
scopically, the uterine fibromyoma was benign.   The
endometrium showed proliferative activity with a few
dilated glands.   The left ovary showed grade I cortical
stromal hyperplasia and few cortical granulomas.   The
right ovarian tumour consisted of spindle shaped fibro-
blasts and collagen fibres among which were scattered
few groups of plump, theca-like cells.   The latter
contained sudanophillic droplets, birefringent crystals
and gave a positive Schultz test.   The Ashbel-Seligman
and fluorescence tests were only a trace positive.
Control sections were negative.

Case 16.

3763/60.   (Mrs M.D., 51 years old, para 3 + 0, 6 years
post-menopausal.)

This patient remained free of bleeding for 1 year
after the menopause.   Then she had intermittent vaginal
bleeding for 2 years.   A diagnostic D. & C. revealed
cystic endometrial hyperplasia and the patient received
irradiation therapy,   Since then, the patient had a light
brown discharge which changed into actual blood for the
past 2 months.   Abdominal and vaginal examination
revealed no abnormality.   Total hysterectomy and left
salpingo-oophorectomy were performed (the right ovary
was removed at a previous operation).   The uterus showed
no gross abnormality.   The left ovary was slightly
enlarged and on cut section it showed a small semi-solid
yellowish-white tumour ¼" in diameter.

Microscopically, the endometrium was the seat of
cystic hyperplastic activity.   The tiny ovarian tumour
consisted of whirls and bundles of spindle shaped
fibroblasts and intermingled with clusters of theca cells.
The latter contained sudanophillic droplets, birefringent
crystals and Schultz positive material.   The Ashbel-
Seligman and fluorescence tests were a trace positive.
Control sections were negative.

Case 17.

5351/61.   (Mrs D. T., 71 years, para 2 + 0, many years
post-menopausal.)

This patient entered the hospital in November, 1961,

with a chief complaint of having 2 attacks of abdominal pain. The first in September 1961 and the second in October 1961. The pain was distributed all over the abdomen and was accompanied with nausea and vomiting. Abdominal palpation revealed a firm, irregular mass arising from the pelvis and reaching up to one third the distance between the pubis and umbilicus. It was more obvious on the right side and was not tender. Per vaginam, the uterus was retroverted and deviated to the left. An irregular, mobile mass was felt anterior to the uterus and to the right of the midline. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The right ovary was replaced by a pedunculated solid, rounded tumour, measuring $4\frac{1}{2}$ x $3\frac{1}{2}$ x 3". It was well encapsulated and had a smooth surface. On cut section, it showed interlacing fascicles of fibrous tissue, mostly masked by interstitial haemorrhage. The left ovary harboured a smaller, white, solid tumour, measuring 2 x 1 x $\frac{1}{2}$". On cut section, it showed also a fibrous appearance. The uterus showed no gross abnormality. Microscopically, there was cystic hyperplasia of the endometrium. The right ovarian tumour was a fibroma with many areas of haemorrhage due to torsion of its pedicle. The left tumour was also a fibroma made of interlacing bands of interlacing fibroblasts and collagen fibres. Sudanophillic droplets were found in a few clusters of theca-like cells in the right tumour only. These cells

contained birefringent crystals and gave positive
Schultz test. Ashbel-Seligman and fluorescence tests
were only a trace positive. Control sections were
negative.

Case 18.

4619/61. (Mrs M. R., 51 years old, para 3 + 0, 13 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding (3 episodes in the past
fortnight).

Abdominal and vaginal examination revealed no
abnormality. Examination under anaesthesia and
D. & C. were performed. The uterus was bulky and
profuse curettings were obtained which proved micro-
scopically to be malignant. However, the tissues were
so disintegrated that it was difficult to ascertain
whether they were carcinomatous or sarcomatous.
Hysterectomy and bilateral salpingo-oophorectomy were
performed. The uterus was slightly enlarged. Its
cavity was filled with a haemorrhagic friable polypoid
mass (Photo 98) which was attached to the lateral wall
of the uterus near the fundus but did not appear to
invade the musculature. The right ovary contained
a small yellowish white solid tumour ($\frac{3}{4}$" in diameter)
and its surface showed white discrete nodules, about
$\frac{1}{4}$" across (Photo 99). The left ovary showed
a slightly thickened cortex. Microscopically, the
polypoid mass was a submucous fibroid which had become

a leiomyosarcoma. Numerous malignant giant cells were present (Photo 101). The endometrial glands were quite benign and showed proliferative activity with some dilated glands. The left ovary showed grade I cortical stromal hyperplasia. The right ovary was the seat of few surface papillomata and contained a typical fibroma with several areas of theca-like cells. The latter contained sudanophillic droplets (Photo 100) and birefringent crystals. They gave a weakly positive Schultz, and a trace positive Ashbel-Seligman and fluorescence tests. Control sections were negative.

Case 19.

949/62. (Miss A.I., 59 years old, 20 years post-menopausal.)

This patient entered the hospital with a chief complaint of a gradually increasing abdominal swelling over the past 3 years. Abdominal examination revealed a firm, mobile swelling in the right lower quadrant. Per vaginam, the adnexa was not clearly defined. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The right ovary was replaced by a cystic tumour which measured 9 x 6½ x 4". It was greyish white, smooth and glistening. On cut section, it was composed of 3 loculi filled with straw-coloured watery fluid. At one part, the cyst wall was thickened and replaced by a fibromatous flattened area (about 4" in diameter). Its cut surface showed whirly fibrous tissue with fatty streaks. Other portions of the cyst wall were thin.

The uterus contained a large, fleshy, polypus ($1\frac{1}{2}$" x $\frac{1}{4}$" x $\frac{3}{4}$"). The left ovary showed a nodular cortex.

Microscopically, the endometrium and its polypus were the seat of cystic glandular hyperplasia. The left ovary showed Grade 0 cortical stromal hyperplasia. (Weakly positive succinic-dehydrogenase test.) The right ovarian tumour was a fibroma that had undergone cystic degeneration. Sudan IV stain revealed clusters of fat-laden theca cells amidst the fibroblasts in many fields. These cells contained birefringent crystals and gave positive Schultz test (Photo 102). Ashbel-Seligman and fluorescence tests were, however, negative. Enzyme work revealed absence of alkaline phosphatase in this tumour. Acid phosphatase and non-specific esterase were present in traces. Control sections were negative.

FIBROMAS

Case 20.

5252/61. (Mrs N. M., 78 years old, para 3 + 0, 28 years post-menopausal.)

This patient entered the hospital with a chief complaint of abdominal swelling for the past 8-9 months. On examination, a cystic swelling was filling almost the whole lower abdomen. Per vaginam, a firm swelling was felt in the pouch of Douglas. Hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was small and atrophic. The right ovary was replaced by a large, thin-walled cyst, with a hard irregular area at its lower pole. The cyst measured

6 x 5 x 5" and on cut sections it was unilocular and contained watery fluid.   The left ovary was atrophic. Microscopically, the endometrium was thinned out and senile.   The left ovary was completely fibrosed.   The ovarian cyst was a typical pseudomucinous cystadenoma and the solid nodule at its lower pole was a fibroma. No histochemically reactive steroid material was found in this tumour.

Case 21.

1871/61.   (Mrs E.A., 60 years old, para 8 + 0, 12 years post-menopausal.)

This patient entered the hospital with a chief complaint of feeling something coming down, and stress incontinence for the past six months.   Abdominal examination revealed no abnormality.   Per vaginam, there was a cystocele (grade 2).   A hard, irregular mass was felt in the pelvis and could not be defined as separate from the uterus.   Total hysterectomy and bilateral salpingo-oophorectomy were performed.   The left ovary was replaced by a solid, well-encapsulated pinkish white tumour (3 x 2 x 2").   On cut section, it showed a fibrous surface.   The uterus was small in size and the other ovary was atrophic.   Microscopically, the endo- metrium showed senile changes.   The left ovarian tumour was an ordinary fibroma.   The right ovary was fibrosed.   No histochemically reactive material was found in this tumour.

Case 22.

2597/60. (Mrs J. C., 57 years old, para 5 + 0, 8 years post-menopausal.)

This patient entered the hospital with a chief complaint of abdominal discomfort and a sensation of being blown up for over a year. Abdominal examination revealed a large fluctuant swelling arising from the pelvis and reaching up to 2 fingers above the umbilicus. It was dull to percussion and not tender. No ascites was detected. Total hysterectomy and bilateral salpingo-oophorectomy were performed. There was a large thin-walled ovarian cyst with a well-formed semi-solid area. On opening the cyst it contained straw-coloured fluid and its lining presented a shaggy appearance, especially that part made by the solid area. The latter was greyish white in colour and its cut surface was slightly oedematous. The uterus and other appendages showed no abnormality. Microscopically, the endometrium was atrophic. The ovarian cyst was actually a fibroma which had undergone extensive cystic degeneration. The remaining solid portion showed a typical fibroma with areas of oedema, hyaline and myxomatous degeneration. The other ovary was atrophic. Histochemical study revealed no reactive materials in this tumour.

Case 23.

6192/61. (Mrs J. O., 77 years old, para 4 + 0, 26 years post-menopausal.)

This patient entered the hospital with a chief complaint of episodes of giddiness, sickness and

sightlessness over the past 3 months. On examination, a lump was felt in the right sideof the abdomen. Per vaginam, theuterus was normal in size. Irregular, mobile masses were present in front of and on each side of theuterus. Total hysterectomy and bilateral salpingo-oophorectomy were performed. Both ovaries were replaced by hard, lobulated greyish white tumours. The left measured 5 x 4 x 3" and the right 4 x 2 x 1½". Both contained large, thin-walled, cystic cavities filled with watery fluid. On cut section, the tumour solid tissue showed the whirly fibrous appearance. The uterus was small and atrophic. Microscopically, the endometrium showed senile changes with theodd gland showing proliferative activity. Both ovarian tumours were typical fibromas with cystic degeneration. Tests for steroid material were all negative. Tests for alkaline phosphatase, acid phosphatase and non-specific esterase were also negative in both tumours.

Case 24.

5589/61. (Mrs P., 54 years old, para 3 + 0, 1½ years post-menopausal.)

This patient entered the hospital with a chief complaint of an episode of vaginal bleeding for 4 days, one month prior to admission. Abdominal examination revealed no abnormality. Per vaginam, the uterus was bulky and irregular. Total hysterectomy and left ovariotomy were performed. The left ovary was replaced

by a solid pedunculated tumour (3½" in diameter) with
prominent vessels running on its smooth surface. On
cut section, it showed whirly bundles of fibrous tissue
and large cystic spaces. The uterus was enlarged by
several fibroids, one of which was submucous and filled
the uterine cavity. Microscopically, the endometrium
showed senile changes. The fibromyomata were all
benign. The left ovarian tumour was a typical fibroma
with areas of cystic degeneration. Histochemical
tests were all negative in this tumour.

Case 25.

5337/60. (Mrs H., 56 years old, para 2 + 0, 3 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding for the past few days.
Abdominal and vaginal examination revealed no abnormality.
Total hysterectomy and bilateral salpingo-oophorectomy
were performed. The uterus was bulkier than normal and
on cut section, the endometrium showed an area suggestive
of malignancy. However, there was no invasion of the
muscle wall. The right ovary showed a thickened
nodular cortex. The left ovary was the seat of a firm
mass (1½" in diameter) with a rounded smooth glistening
surface. On section, it presented a firm greyish white
fibrous cut surface. Microscopically, the endometrium
was partially autolysed. However, there were two or
three areas near the surface where the epithelium was
actively proliferating, anaplastic and many layers thick.

Mitotic figures were numerous. The myometrium was not invaded. The appearances were, therefore, suggestive of an early adenocarcinoma. The right ovary showed grade I cortical stromal hyperplasia. The left ovarian tumour was composed of dense collagenous connective tissue bundles and was a typical fibroma. No histochemically reactive steroid material was found in this tumour.

Case 26.

1076/61. (Mrs J. H., 46 years old, para 1 + 0, L.M.P. 1 day.)

This patient entered the hospital with a chief complaint of intermenstrual bleeding and prolonged periods on and off for the past two years. Vaginal examination revealed a bulky uterus. Hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was enlarged and on cut section it showed a large submucous fibroid, 3" in diameter and few small interstitial ones. A small, white nodule, measuring $\frac{1}{2}$" x $\frac{1}{2}$" x $\frac{3}{4}$" was present on the surface of the left ovary. A similar but smaller one was also present on the right ovary.

Microscopically, the submucous uterine fibromyoma was richly cellular with hyperchromatic nuclei but its general pattern was regular and there was no definite evidence of sarcomatous change. The endometrium overlying the submucous fibromyoma was thinned out and inactive but elsewhere it was in the proliferative phase.

Both ovarian tumours were in the nature of a fibroma.
No histochemically reactive materials were found in
these tumours.

Case 27.

4062/61. (Mrs M. C., 38 years old, para 1 + 0,
L.M.P., 11 days.)

This patient was admitted to hospital with
a complaint of menorrhagia for the last 2-3 years.
Four days prior to admission she got severe flooding
and was given progesteron, with some relief.   On
examination, she was very obese.   A firm, mobile
mass was felt in the left iliac fossa.   Owing to gross
obesity of the patient, vaginal examination yielded
no information.   Total hysterectomy and left salpingo-
oophorectomy were performed.   The uterus was enlarged
to the size of 8 weeks' pregnancy.   On cut section
its wall was slightly thickened and showed a submucous
fibroid 2" in diameter.   The left ovary was the seat
of a cystic tumour, 4" in diameter.   On cut section,
it was multilocular.   Some of the loculi were filled
with gelatinous material, others contained intra-
cystic papillae.   The right ovary showed no abnormality
and so was not removed.   Microscopically, the endo-
metrium showed a well developed proliferative phase.
The left ovarian tumour was a serous cystadenofibroma.
Histochemical study revealed no reactive steroid materials
in this tumour.   The oestrogen excretion in urine was
not increased:

1 week before operation   5.5 Ug./total oestrogens.

3 days after operation   11.3 Ug./24 hr.(total
    oestrogens).

Case 28.

2208/61. (Mrs M. S., 51 years old, para 5 + 1.)

This patient entered the hospital with a chief
complaint of amenorrhoea for 4 weeks.   Her periods had
been heavy and irregular for the previous 3 months.
Per vaginam the uterus was bulky and the appendages
showed no abnormality.   Total hysterectomy and bilateral
salpingo-oophorectomy were performed.   The uterus was
much enlarged (5 x 5 x 4½").   On cut section, its
muscular wall was remarkably and symmetrically thickened
to about 2".   It showed few haemorrhagic spots and
small slit-like openings.   The endometrium, however, was
not remarkable.   One ovary was slightly enlarged and on
cut section it contained a small white solid tumour, 1"
in diameter.   The cortex of the same ovary was thickened
and nodular.   The other ovary looked normal.   Micro-
scopically, the thickened uterine wall was the seat of
diffuse adenomyosis.   The surface endometrium itself
was thin, although it showed proliferative activity.
Most of the adenomyotic islands, however, were the seat
of cystic glandular hyperplasia.   The tumour bearing
ovary showed a whirly hyperplastic cortex and an area
of thecomatosis.   The tumour itself was an adenofibroma.
The other ovary showed 1-2 hyperplastic nodules and

a small area of endometriosis.   No reactive steroid

material was found in this ovarian tumour.

Case 29.

4773/60.   (Mrs F.I., 48 years old, para 4 + 1.)

This patient entered the hospital with a chief

complaint of right subcostal pain on two occasions

within the past few months.   She had been missing periods

on and off for one year and had not had one for the past

three months.   Abdominal examination revealed a hard

swelling arising from the pelvis and reaching up to

3 fingers above the symphysis pubis.   The mass was fixed

and not tender.   Total hysterectomy and bilateral

salpingo-oophorectomy were performed.   The ovary was

replaced by a rounded cystic tumour (4" in diameter)

which was adherent to the surrounding structures. On

cut section, it was multilocular with broad fibrous

septa separating small compartments.   Few intra-cystic

papillae were present.   The uterus was bulky and on

cut section it showed multiple interstitial fibroids.

The right ovary showed a small cyst (about $\frac{1}{4}$" in

diameter).   Microscopically, the uterine fibromyomas

were benign and the endometrium showed proliferative

activity.   The right ovary showed a follicular cyst.

The left ovarian tumour consisted of dense whirls of

hyaline fibrous tissue among large cystic spaces lined

by flattened cuboidal epithelium.   The appearance was

that of a serous cystadenofibroma.   Histochemical study

revealed no reactive steroid material in this tumour.

Case 30.

3814/60. (Mrs S.D., 33 years old, para 0 + 0,
L.M.P. 7 days.)

This patient entered the hospital in 1960 with
a chief complaint of dysmenorrhoea and menorrhagia for
the past three months. Her first admission to hospital
had been in 1953 when a myomectomy, a Baldy Webster
suspension and excision of left fimbrial cyst were
performed. A mild endometriosis was also noted.
Abdominal examination revealed an irregular, firm, tender
mass arising from the pelvis and extending up to 3 fingers
below the umbilicus. Per vaginam, the uterus was
continuous with the mass. Appendages showed no abnor-
mality. Hysterectomy and left salpingo-oophorectomy
were performed. A fair amount of clear fluid was found
in the peritoneal cavity. The uterus was bulky and
irregular with multiple fibroids, including one fibroid
burrowing into each broad ligament. On cut section,
all fibroids were interstitial and the largest measured
2" in diameter. A typical adenomyoma was also present.
The left ovary was the seat of a solid white tumour
measuring 2 x 1½ x 1¼" and its cut surface showed dense
whirly fibrous bands. Microscopically, all the fibro-
myomata were benign and the endometrium was in the
proliferative phase. Adenomyosis was well demonstrated.
The left ovarian tumour consisted of interlacing fibro-
blasts and collagen fibres. There were no sudanophillic
droplets or reactive steroid substances in this tumour.

Case 31.

2622/60. (Mrs C. D., 48 years old, para 1, L.M.P. 20 days.)

This patient entered the hospital with a chief complaint of menorrhagia over the past 8 months. Abdominal examination revealed no abnormality. Per vaginam, the uterus was found bulky and its mobility was impaired. Hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus contained few seedling fibroids. One ovary contained a degenerating corpus luteum. The other ovary showed on its surface a solid pedunculated white mass ($\frac{1}{2}$" in diameter). Microscopically, the endometrium showed proliferative changes and the small ovarian tumour was a typical fibroma. There were no sudanophillic droplets or reactive steroid material in this tumour.

Case 32.

3566/61. (Mrs H. G., 39 years old, para 0 + 0, L.M.P., 18 days.)

This patient entered the hospital with a chief complaint of menorrhagia for the past 18 months. On examination, she looked pale. No masses were felt in the abdomen but there was tenderness in the right iliac fossa and suprapubic regions. Vaginal examination revealed a bulky uterus which was not well defined as well as tenderness in the right fornices. Total hysterectomy, removal of the right ovary and part of the left ovary were performed. The uterus

was slightly enlarged and on cut section, it showed
2 small interstitial fibroids, the larger of which
measured $\frac{3}{4}$" in diameter. A small polypus was seen in
the uterine cavity. The left ovary contained a corpus
luteum. The right ovary showed 2 small pedunculated
solid white masses. The larger was 1" in diamter
and the smaller about $\frac{1}{4}$". Microscopically, the uterine
fibromyomas and the fibroadenomatous polypus were
benign. The endometrium was in the late secretory phase.
The left ovary showed a degenerating corpus luteum. The
right ovarian tumours were typical fibromas. No reactive
materials were present in these tumours.

Case 33.

3668/60. (Mrs M. S., 49 years old, para 3.)

This patient had no gynaecological complaint.
A hard ovarian mass accompanied with ascites was
discovered incidentally at an operation for hiatus hernia.
Her periods were always regular and the last one was 25
days prior to admission. Abdominal examination revealed
a hard mass in the left iliac fossa. Ascites with
a fluid thrill and shifting dullness was present. The
chest was free. The hard mass was also palpable in the
left lateral vaginal fornix and was tender. Total
hysterectomy and bilateral salpingo-oophorectomy were
performed. A little free fluid was found, in the
peritoneal cavity. The uterus was slightly bulky
and on cut section it showed 2 small seedling fibroids.

The endometrium was somewhat thick.   The right ovary looked normal.   The left ovary was the seat of a solid tumour measuring 5 x 4 x 3" with a smooth glistening greyish white surface.   On section, it showed the characteristic whirly appearance of a fibroma.   Microscopically, the endometrium was in the early secretory phase, the right ovary showed two tiny follicular cysts. The left ovarian tumour was a cellular fibroma.   No reactive steroid material was found in this tumour.

BRENNER-CELL TUMOUR

Case 34.

650/60.   (Miss C.M., 66 years old, 20 years post-menopausal.)

This patient entered the hospital with a chief complaint of vaginal bleeding for the past week.   She had been feeling a lump in the lower abdomen over the past 6 months.   The patient gave a history of a previous episode of vaginal bleeding 5 years prior to admission. She did not consult her doctor, at that time, and the bleeding stopped spontaneously.   Abdominal palpation revealed a mass arising from the pelvis and occupying hypogastrium and both iliac fossae.   It was hard, nodular, mobile and not tender.   Vaginally, it was not easy to define the mass as uterine or ovarian.   A cervical polyp was easily palpable.   Total hysterectomy and bilateral salpingo-oophorectomy were performed.   The left ovary was replaced by a lobulated whitish pink solid tumour about 4" in diameter.   Its surface showed few

adhesions to omentum and its pedicle was partially
twisted.   On cut section, it showed interlacing
bands of fibrous tissue with small, slit-like openings
here and there.   Fatty streaks were present in some
areas. The uterus was not enlarged but on cut section,
it showed a profuse endometrium and a cervical polypus.
The right ovary was small in size, but its cortex was
thickened and nodular.   Microscopically, the endometrium
showed cystic hyperplastic activity (Photo 105).
The cervical polyp was benign.   The right ovary showed
grade 0 cortical stromal hyperplasia.   The left ovarian
tumour was a typical Brenner cell tumour composed of
islands of polygonal cells in a fibrous stroma.   Near
the epithelial islands, the stroma was more cellular
but, theca-like cells filled with fat droplets were only
identified by Sudan IV stain (Photo 103).   They also
contained birefringent crystals (Photo 104) and gave
a positive Schultz test.   Ashbel-Seligman and
flourescent tests were only a trace positive.

Case 35.

1524/61.   (Miss J. B., 74 years old, 20 years post-
menopausal.)

This patient was admitted to hospital, as an
emergency case, complaining of severe abdominal pain
and vomiting. On examination, she looked slightly
dehydrated.   The abdomen was obese and there was no
tenderness on palpation.   Vaginal examination revealed

a large left ovarian cyst.   Total hysterectomy and

bilateral salpingo-oophorectomy were performed.   The

left ovary was the seat of a large, thin-walled cyst

(5" in diameter) which had undergone torsion of its

pedicle and was densely adherent to loops of small

intestine.   On section, the cyst was unilocular, contained

blood-stained fluid and its wall was haemorrhagic.   The

uterus was enlarged and on cut section it contained

a submucous fibroid 3" in diameter.   Four soft, smooth

polypi (2 large and 2 small) were present in the uterine

cavity.   The right ovary was a bit larger than usual

for a patient of this age and on cut surface it showed

a small whitish grey firm nodule (4 mm. in diameter).

The ovarian cortex was somewhat thickened.

Microscopically, the endometrium being pressed

upon by the submucous fibromyoma and the uterine polypi,

was reduced to a thin layer with very few cystic glands.

The polypi were benign and showed fibro-adenomatous areas

as well as cystic hyperplastic endometrial glands (Photo

108).   The wall of the twisted cyst was completely

necrotic and its nature, though benign, could not be

identified.   The nodule of the right ovary was a Brenner

cell tumour with hyaline bands around some of the

epithelial islands.   The ovarian cortex of the same

ovary showed whirly hyperplastic nodules (grade 0) and

a cortical granuloma.   Sudan IV stain revealed the

presence of red droplets in theca like cells immediately

adjacent to Brenner islands (Photo 106). These stromal
cells contained also birefringent crystals (Photo 107),
gave a positive Schultz test and a weakly positive Ashbel-
Seligman and fluorescence tests. Control sections were
negative.

Case 36.

2700/60. (Mrs H. W., 45 years old, para 2 + 0,
L.M.P. 1 day.)

This patient entered the hospital with a chief
complaint of low backache referred to the front, for the
past week. She had been suffering from frequency and
stress incontinence over the past year. Abdominal
examination revealed no abnormality. On vaginal
examination, however, a rounded cystic swelling was
detected in the pouch of Douglas. Total hysterectomy
and bilateral salpingo-oophorectomy were performed.
The right ovary was replaced by a large unilocular
cyst (about 4" in diameter) filled with pseudomucin.
The uterus showed no abnormality. The left ovary was
slightly enlarged and on cut section showed a corpus
luteum and a small greyish white nodule $\frac{1}{4}$" in diameter.
Microscopically, the endometrium showed menstrual changes.
The right ovarian cyst was a typical pseudomucinous
cystadenoma. The left ovary showed grade 0 cortical
stromal hyperplasia and a recent corpus luteum. It
contained also a small Brenner cell tumour which was
well encapsulated. Both the right and left ovarian
tumours showed no reactive materials.

POSITIVE PSEUDOMUCINOUS CYSTADENOMAS

Case 37.

3143/61. (Miss M. A., 82 years old. Many years post-
menopausal.)

This old patient, who was rather forgetful, entered
the hospital with a chief complaint of pain in the left
iliac fossa for the past three weeks. Abdominal
examination revealed a large cystic swelling arising
from the pelvis and extending up to the umbilicus.
Total hysterectomy and bilateral salpingo-oophorectomy
were performed. The uterus was bulky and irregular
in outline. On cut section, it contained multiple
interstitial fibroids, the largest of which ($1\frac{1}{2}$" across)
was completely calcified. The uterine cavity contained
a large fleshy polypus measuring 2" in diameter. The
left ovary was replaced by a large bluish white
glistening cyst (about 6" in diameter). It was multi-
locular with broad septa and small loculi giving it
a semisolid appearance in some areas. The right ovary
showed a small cyst, about $1\frac{1}{4}$" in diameter. On cut
section it was multilocular, contained pseudomucin and
tiny intracystic papillae.

Microscopically, the uterine fibromyomata were all
benign. The endometrium and its polypus showed cystic
hyperplasia. The left ovarian cyst was lined by the
clear tall columnar epithelium characteristic of
pseudomucinous cystadenoma. In some areas the stroma
was much exaggerated, giving it the appearance of

a cystadenofibroma. In these areas the stroma cells were mostly oval and plump with rounded nuclei. Some of the cells especially those adjacent to the epithelium lining the loculi had a vacuolated cytoplasm and were very much like theca cells. These gave positive results with the whole battery of histochemical tests. No reactive materials were found in the other cellular structures of the cyst. Control sections were negative.

The right ovarian cyst was again lined by tall columnar epithelium characteristic of pseudomucinous cystadenoma (Photo 131). Some of the loculi, however, were lined by cuboidal epithelium which also lined the intracystic papillae present and the appearance was that of a[*] papillary serous cystadenoma (Photo 132). This cyst contained no reactive materials.

Case 38.

393/61. (Mrs B., 64 years old, para 2 + 0, post-menopausal.)

This patient entered the hospital with a chief complaint of frequency of micturition and stress in-continence for the past year. Examination revealed a large ovarian cyst. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus showed no abnormality. The left ovary was replaced by a large bluish-white ovarian cyst which was opened before reaching the laboratory and approximately measured 6 x 4 x 4". It was unilocular and for the most part its wall was thin and glistening. The right ovary was

[*]A similar cyst showing both pseudomucinous and serous types was reported by Dockerty (1954).

small in size. Microscopically, the endometrium showed
senile cystic change with proliferative activity and
adenomyosis. The right ovary was atrophic. The left
ovarian cyst was lined by the characteristic pseudo-
mucinous tall columnar epithelium. Some areas of
adenofibroma were seen in some of the sections. Sudan
IV stain revealed the presence of groups of oval and
rounded cells filled with red droplets and located
in the stroma of the cyst. These cells contained
birefringent crystals, gave yellowish green fluorescence
and reacted weakly to Schultz and Ashbel Seligman tests.
Control sections were negative.

Case 39.

5876/61. (Mrs H. M., 61 years, para 3 + 0, 11 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of three episodes of vaginal bleeding over
the past three months. Abdominal and vaginal
examination provided the diagnosis of a left ovarian
cyst. This was removed together with the uterus
and contralateral appendages. The cyst was thin-walled,
had a smooth outline and measured 8" in diameter. On
cut section it was multilocular with 2 firm areas where
the loculi were very small in size. It was filled with
clear watery fluid. The uterus showed no gross
abnormality. The right ovary was slightly enlarged and
showed a thickened nodular cortex. Microscopically,
the endometrium showed proliferative activity with some

adenomyosis. The right ovary was the seat of grade
2 stromal hyperplasia. This was confirmed by a positive
succinic dehydrogenase test (Photo 116). The ovarian
cyst was lined by the clear tall columnar epithelium
characteristic of a pseudomucinous cystadenoma. Reactive
steroid material giving the whole battery of reactions
has been found in some theca-like stromal cells (Photo
109). Alkaline phosphatase was abundant in the stroma
(Photos 110, 111) and absent in the epithelium. Acid
phosphatase and non-specific esterase were mainly
present in the epithelium (Photos 112, 113, 114, 115).

Case 40.

436/61. (Miss T., 72 years old, many years post-
menopausal.)

This patient entered the hospital with a chief
complaint of continuous vaginal bleeding for the past
3 weeks. A large ovarian cyst was felt in the abdomen.
On vaginal examination the pelvic organs could not be
defined. Total hysterectomy and bilateral salpingo-
oophorectomy were performed. The uterus was slightly
larger than what would be expected for the patient's
age. On cut section the endometrium was fairly profuse.
The left ovary was the seat of a smooth, thin-walled
bluish white cyst measuring 7" in diameter. It was
multi-locular and had been emptied of its contents
before reaching the laboratory. The right ovary was
slightly enlarged and showed a thickened cortex.
Microscopically, the endometrium showed proliferative

activity with few dilated glands and some degree of
adenomyosis (Photo 120).   The right ovary showed
whirly nodules of plump hyperplastic fibroblasts (grade
2 stromal hyperplasia).   Small groups of theca cells were
also seen amidst the cortical cells (Thecomatosis,
 Photo 119).

The left ovarian cyst was a typical pseudomucinous
cystadenoma.   Theca-like stromal cells containing fine
red sudanophillic droplets were present in some areas
(Photo 117).   They contained birefringent crystals and
gave green colour with Schültz test, dark blue colour
with Ashbel-Seligman test (Photo 118) and yellowish green
fluorescence.   Control sections were negative.

Case 41.

3448/61.   (Mrs I. B., 54 years old, para 2 + 0, 15
months post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding and abdominal swelling
and discomfort, over the past 5 months.

On examination, the abdomen was symmetrically
swollen and tense cystic (size of a 36 weeks pregnancy).
Per vaginam: neither the uterus nor the adnexae could
be defined.   Total hysterectomy and bilateral salpingo-
oophorectomy were performed.   The uterus was 3" long
and showed longitudinal scar on its anterior surface
indicating a previous classical Caesarean section.   On
cut section there was a tiny polypus in the uterine
cavity and a similar one in the cervical canal.   The

left ovary was the seat of a large thin-walled bluish
white cyst measuring 8 x 7 x 4" in diameter. It was
composed of one large and several small loculi which
contained thin and clear pseudomucin. The right ovary
showed slightly thickened nodular cortex. Microscopic-
ally, the myometrium showed diffuse adenomyosis especially
at the area of Caesarean scar. The endometrium showed
proliferative activity (Photo 126). Proliferation
was also noted in the endometrial glands of adenomyosis
and endometrial fibroadenomatous polypus. The left
ovarian cyst was lined by tall columnar epithelium,
characteristic of pseudomucinous cystadenoma. Out of the
many sections examined few of them showed small groups of
theca-like cells in the stroma. However, in one section
there was a fairly large collection of polygonal stromal
cells with rounded nuclei and vacuolated cytoplasm
(Photo 121). These looked like typical theca cells
and gave positive results with all the histochemical
tests (Photos 122, 123, 124). The other ovary was
sectioned while fresh and treated with nitro B.T. for
demonstrating succinic dehydrogenase activity. Marked
deposition of bluish purple granules was noticed
(Photo 125). This indicated cortical stromal hyper-
plasia (grade II). Oestrogen excretion in urine
4 days before the operation was 28.4 Ug./24 hours
(total oestrogens in urine). One week after the operation
it fell down to 5.0 Ug./24 hours (total oestrogens in
urine).

Case 42.

5999/60. (Mrs B.D., 51 years old, para 2 + 0, 4 years post-menopausal.)

This patient entered the hospital with a chief complaint of abdominal distension which was gradually increasing over the past year. On examination, there was gross distention of the abdomen with tenderness in the left hypochondrium. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus showed no gross abnormality. The left ovary was the seat of a large bluish white thin-walled cyst, measuring 11" in diameter. On section, it was multilocular and filled with pseudomucin. The right ovary showed a thickened nodular cortex. Microscopically, the endometrium showed senile cystic change with evidence of active proliferation in some areas (Photo 130). The right ovary showed whirly hyperplastic stroma (grade I). The left ovarian cyst was a typical pseudomucinous cystadenoma. Its stroma was made of ordinary spindle shaped fibroblasts. However, a few groups of oval shaped cells were scattered just beneath the epithelial lining of the cyst. These cells were shown to be active theca cells by their high content of sudanophillic droplets, birefringent crystals (Photo 127) and yellowish green fluorescence. They gave green colour with Schultz test and dark blue colour with Ashbel-Seligman test (Photos 128 & 129). Control sections were negative.

Case 43.

918/61. (Mrs M. C., 62 years old, para 3 + 1, 20 years
post-menopausal.)

This patient entered the hospital in 1960 with
a chief complaint of feeling a lump in the vagina for
the past 8-10 weeks. She gave no history of vaginal
bleeding. On examination, a tense swelling was felt
in the abdomen below the umbilicus. Per vaginam: a large
left ovarian cyst. The uterus was anteverted and moved
separately from the cyst. Total hysterectomy and
bilateral salpingo-oophorectomy were performed. The
uterus was slightly enlarged and showed a sub-peritoneal
fibroid, 1" in diameter. On cut section, the muscular
wall was almost completely infiltrated by greyish white
friable necrotic malignant tissue which also filled
the uterine cavity. The left ovarian cyst was bluish
white in colour and measured 9 x 8 x 5". It was
multilocular and filled with thin pseudomucin. The right
ovary showed no abnormality. Microscopically, the
endometrium was the seat of an advanced adenocarcinoma
with acanthomatous change. The fibromyoma was benign.
The right ovary showed slight cortical stromal hyperplasia
(grade 0). The left ovarian cyst was a typical
pseudomucinous cystadenoma. Sudan IV stain revealed
fine red droplets in a few groups of theca like cells
in the stroma (beneath the epithelial lining of the cyst).
These cells gave positive results with the remaining
histochemical tests. Control sections were negative.

Case 44.

4085/60. (Miss J. R., 40 years old, L.M.P. 15 days.)

This patient had no gynaecological complaint.
An ovarian cyst was discovered in the surgical section
where she had a right mastectomy for cancer of the breast.
Two months later she was transferred to the gynaecological
ward. On examination there was a palpable cystic
swelling arising from the pelvis and extending almost
to 3 fingers below the right costal margin. Total
hysterectomy and bilateral salpingo-oophorectomy were
performed. The uterus was normal in size and its cut
surface showed a small seedling fibroid. The right
ovary was replaced by a large bluish white cyst which
on section was multilocular and filled with thick pseudo-
mucin. The left ovary showed a well formed corpus
luteum.

Microscopically, the endometrium showed secretory
changes. The left ovary showed several atretic follicles
and a recent corpus luteum. The right ovarian cyst was
lined by tall columnar epithelium with basal nuclei,
characteristic of pseudomucinous cystadenoma. Many goblet
cell s were also present. Active stromal cells resembling
theca cells, were revealed by Sudan stain. They also
gave weakly positive results with all the other histo-
chemical tests. Control sections were negative.

Case 45.

5863/60. (Mrs M. T., 45 years old, para 1 + 0, L.M.P.

6 days.)

This patient entered the hospital with a chief
complaint of abdominal swelling and menorrhagia over
the past 5 months.   On examination, a large abdominal
swelling was felt arising from the pelvis and reaching
up to the level of the umbilicus. It was firm, smooth,
dull to percussion and not tender.   Hysterectomy and
bilateral salpingo-oophorectomy were performed. The
uterus was enlarged with several fibroids, the largest
of which was subperitoneal and measured $2\frac{1}{2}$" across.
The left ovary was replaced by large ovarian cyst
measuring 12 x 8 x 5".   It was bluish white in colour
and thin walled. On section, it was unilocular and
contained a small intra-cystic papilla.   The right
ovary was slightly enlarged and cystic.

Microscopically, the uterine fibromyomata were
benign.   The endometrium showed mainly proliferative
activity save for few areas where evidence of secretory
activity was still seen.   The right ovary contained
a haemorrhagic corpus luteum.   The ovarian cyst was
lined by clear, tall columnar epithelium and was a
pseudomucinous cystadenoma.   Sudan IV stain revealed
the presence of fat laden large oval cells beneath
the epithelial lining of the cyst at the region of the
intra-cystic papilla.   These cells contained birefringent
crystals and reacted positively to the remaining histo-
chemical tests.   Control sections were negative.

Case 46.

3491/60. (Mrs P. W., 36 years old, para 4 + 0,
L.M.P., 3 weeks.)

This patient entered the hospital with a chief
complaint of abdominal swelling and suprapubic pain of 6
weeks duration. For the past 3-4 months, her periods
had been heavy and occurred every 2 weeks instead of
every 4 weeks. The last period, however, occurred
after 4 weeks.

On examination, a large ovarian cyst was felt in
the abdomen. It was also felt, per vaginam, in the
pouch of Douglas. Total hysterectomy and bilateral
salpingo-oophorectomy were performed. Both ovaries
were replaced by bluish white thin walled cystic
tumours. The right measured 8 x 8 x 6" and the left
6 x 5 x 3¼". They had smooth surfaces and on cut
section they were multilocular and filled with
pseudomucin. The uterus showed no abnormality.
Microscopically, the endometrium showed persistent
proliferative changes. Both cysts showed few areas
of necrosis but both were benign. Plump theca like
stromal cells filled with red droplets were revealed by
Sudan IV stain. They were mostly located underneath
the epithelium. They contained birefringent crystals,
gave positive Schultz and Ashbel-Seligman tests and
showed yellowish green fluorescence. Control sections
were negative.

Case 47.

(Mrs C.C., 51 years old, para 2 + 0, L.M.P. 3 days.)

This patient entered the hospital with a chief
complaint of swelling and tightness in the abdomen.
On examination, there was fullness in the right lower
abdomen.   Vaginal examination revealed a right ovarian
cyst pushing the uterus to the left.   Total hysterectomy
and bilateral salpingo-oophorectomy were performed.
The uterus was slightly enlarged and on section showed
a thickened wall.   The right ovary was the seat of
a large smooth and thin-walled cyst, measuring 7" in
diameter.   On section, it was multilocular and was
emptied of its contents before reaching the laboratory.
The left ovary showed a small cyst $\frac{1}{2}$" across.

Microscopically, the endometrium was the seat of
cystic hyperplasia.   The left ovary contained
a follicular cyst and showed a few hyperplastic whirly
cortical nodules.   The right ovarian cyst was a typical
pseudomucinous cystadenoma.   Theca like cells containing
sudanophillic droplets and giving positive results with
the histochemical battery of tests were present under-
neath the epithelium in many fields.   Control sections
were negative.

POSITIVE MALIGNANT PSEUDOMUCINOUS CYSTS

Case 48.

2608/60.   (Mrs J. K., 46 years old, para 0 + 0,
6 months post-menopausal.)

This patient entered the hospital in May 1960

with a chief complaint of abdominal swelling which had
been first noticed towards the end of 1959. Since then,
it was increasing in size. Her periods had been irregular
since the beginning of 1959 and stopped completely in
December 1959. Her prior admission to hospital was
in 1950, when she had an actively proliferating left
pseudomucinous cystadenoma removed, and part of right
ovary showing a luteal haematoma resected. Abdominal
examination revealed a large cystic swelling with solid
areas, arising from the pelvis and extending up to 4
fingers from the xyphisternum. Total hysterectomy and
removal of the cyst were performed. A large amount of
free fluid was present in the peritoneal cavity. The cyst
was arising from right ovary, contained many irregular,
solid areas in its wall and measured 11 x 10 x 5". It
had a smooth surface and there were no adhesions to
surrounding structures. However, metastatic peritoneal
nodules were scattered in the omentum and serosal covering
of bowels. On section it was multilocular, filled with
pseudomucin and showed foci of haemorrhage and necrosis.
The uterus showed no abnormality. Microscopically, the
endometrium was senile with some proliferative activity.
The cyst was a frank psuedomucinous cystadenocarcinoma
showing invasion of the stroma as well as massive
haemorrhage and necrosis. Out of the several blocks
taken, one showed a few groups of stromal cells (usually
adjacent to the epithelium and sometimes seen to rupture
into the lumen) which contained sudanophillic granules

and reactive steroid material.   Control sections were
negative.

Case 49.

6041/60.   (Mrs J. M., 55 years old, para 2 + 0,
12 years post-menopausal.)

This patient, who gave a poor history, entered
the hospital with a complaint of pain in left iliac
fossa for one month.   Abdominal examination revealed
a cystic swelling arising from the pelvis and
reaching halfway between umbilicus and xyphisternum.
This swelling was also felt through the right vaginal
fornix.   The uterus was bulky and anteverted.   Total
hysterectomy and bilateral salpingo-oophorectomy were
performed. Uterus was slightly enlarged and on cut
section its wall was thickened.   The left ovary was
the seat of large cystic tumour pinkish grey in colour
and measuring 9 x 6 x 4".   Its surface was smooth
and on cut section it contained one large loculus filled
with straw-coloured watery fluid and several small loculi
filled with infected necrotic material.   Semi-solid
areas were also present in the cyst wall.   The right
ovary showed a thickened cortex in one part.

Microscopically, the uterine wall showed marked
degree of adenomyosis and the endometrium showed
proliferative activity.   The right ovary showed grade
0 cortical stromal hyperplasia.   The left ovarian cyst
was lined by the pseudomucinous type of epithelium which,

however, was heaped up in more than one layer, showed hyperchromatic nuclei of variable size and shape as well as markedly adenomatous patterns. There was no invasion of the underlying stroma. The tumour was therefore regarded as borderline malignant pseudomucinous cyst. Sudan stain revealed the presence of a few clusters of rounded and oval stromal cells which were filled with red droplets. These cells also contained birefringent crystals and gave positive results with the remaining histochemical tests. Control sections were negative.

Case 50.

1883/61. (Miss B., 64 years old, post-menopausal.)

This patient entered the hospital with a chief complaint of lower abdominal discomfort and increasing size of the abdomen for the past 1 or 2 months. A large ovarian cyst was detected both abdominally and vaginally. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus showed no external abnormality but on cut section it contained a small submucous fibroid (the size of a pea). The left ovary was replaced by a large, thin-walled, bluish-white, smooth cyst measuring 6" in diameter. On cut section it was multilocular and filled with pseudomucin. The right ovary was slightly enlarged and contained a small cyst about 1" in diameter.

Microscopically, the endometrium showed proliferative activity with some dilated glands and adenomyosis. The submucous fibromyoma was benign and showed hyaline change. The right ovarian cyst was lined by flattened

cubical epithelium and could be an early simple serous
cyst. The large left ovarian cyst was a typical
pseudomucinous cyst. It was mainly benign, but in
few fields the cells were multilayered the nuclei were
hyperchromatic and varied in size and shape, and the
pattern was very adenomatous. There was no invasion
of the underlying stroma and hence the tumour could be
classified as of borderline malignancy. Plump stromal
cells containing sudanophillic droplets and giving
positive results with all the other histochemical tests
were seen immediately beneath the epithelium in many
fields. Sometimes they were seen rupturing through
the epithelial lining into the lumen. Control sections
were negative.

NEGATIVE PSEUDOMUCINOUS CYSTADENOMAS

Case 51.

5424/60. (Mrs J.C., 46 years old, para 1 + 1, L.M.P.
4 days.)

This patient entered the hospital with a chief
complaint of feeling a lump in the lower abdomen and
backache for the past 6 months. Abdominal palpation
revealed a hard, rounded, smooth swelling arising from
the pelvis and reaching almost the umbilicus. It was
freely mobile and not tender.

Total hysterectomy and bilateral salpingo-
oophorectomy were performed. The right ovary was
replaced by a smooth thin-walled rounded cyst measuring
8 x 6 x 4". On cut section, it was multilocular and
contained pseudomucin. The uterus showed no abnormality.

The left ovary showed a small corpus luteum. Microscopically, the endometrium was in the proliferative phase of the cycle.   The left ovary contained a degenerating corpus luteum and a small follicular cyst.   The cystic tumour was lined by tall columnar epithelium which was flattened in many areas. It was a pseudomucinous cystadenoma. No sudanophillic droplets or reactive steroid material were found in this tumour.

Case 52.

4230/61. (Mrs C.C., 47 years old, para 0 + 3, L.M.P. 7 days.)

This patient entered the hospital with a chief complaint of occasional, heavy periods for the past year.   On examination, a mass was felt in the right iliac fossa.   Per vaginam: it was found to arise from the right appendages.   The uterus was mobile and bulky.   Total hysterectomy and bilateral salpingo-oophorectomy were performed.   The uterus was enlarged by a submucous fibroid measuring 2" in diameter.   The right ovary was replaced by thin-walled pinkish white cyst measuring 4 x 3 x 3".   On cut sections it was multilocular and contained pseudomucin. The left ovary showed no abnormality. Microscopically, the endometrium was in the proliferative phase.   The right ovarian cyst was a typical pseudomucinous cystadenoma. The left ovary showed no abnormality. Histochemical tests were all negative.

Case 53.

2944/60. (Mrs M. T., 45 years old, para 3 + 0, L.M.P.,
8 days.)

This patient entered the hospital with a chief
complaint of irregular and prolonged periods (every three
months). Abdominal examination revealed a firm abdom-
inal mass extending out of the pelvis to 2/3 the way
between umbilicus and symphysis pubis. Per vaginam:
the mass filled the pelvis and could not be distinguished
from the uterus. On examination under anaesthesia, the
mass was defined to the right and separate from the uterus.
Total hysterectomy and right ovariotomy were performed.
The right ovary was the seat of a thin-walled cyst 4"
in diameter. It was multilocular and filled with thin,
almost watery fluid. The uterus showed no abnormality
apart from being slightly bulky. The left ovary looked
normal and so it was preserved.

Microscopically, the endometrium showed prolifer-
ative changes. The ovarian cyst was lined with tall
columnar epithelium, characteristic of pseudomucinous
cystadenoma. No sudanophillic droplets or reactive
steroid material were found in this cyst.

Case 54.

6071/61. (Mrs C. F., 49 years old, para 5 + 0, L.M.P.
2 weeks.)

This patient entered the hospital in December 1961,
with a chief complaint of severe pain in the right side
of the abdomen for the past 15 hours. Her previous

admission to hospital had been in 1954 when a right oophor-
ectomy was performed for a cystic ovary.

On examination, there was generalised guarding and
tenderness, especially in right iliac fossa. A cystic
mass was felt to arise from the pelvis and reach up to the
level of the umbilicus. At operation, the mass was
a large (7" in diameter) thin-walled cyst, arising
from the left ovary. There were no adhesions or torsion
but there was free fluid in the peritoneal cavity.
A partial rupture had occurred high up on the posterior
aspect of the cyst. The uterus showed no gross abnormality
and together with the cyst, were both removed. Micro-
scopically, the endometrium was in the proliferative
phase. The ovarian cyst was a pseudomucinous cystadenoma.
No histochemically reactive materials were found in this
cyst.

Case 55.

4666/60. (Mrs M. L., 45 years old, para 2 + 0.)

This patient entered the hospital in September 1960
with a chief complaint of continuous vaginal bleeding
for the past month. Following a D. & C. in 1956, periods
were regular with a normal loss for a few months. During
1957-1959 periods lasted 7-10 days with 6-8 months
amenorrhoea in between. In January 1960, she had
vaginal bleeding for 8-9 days. Since then, she had
amenorrhoea until this last episode of bleeding. On
examination, the abdomen was obese and no masses were

felt Per vaginam: the uterus was normal sized and
a cystic swelling was felt in the left ovary.   Total
hysterectomy and bilateral salpingo-oophorectomy were
performed.   The uterus was somewhat bulky and on section
it showed a small fibroid in its anterior wall and a
profuse endometrium.   The left ovary was replaced by
a rounded smooth thin-walled cyst (4" in diameter).
On cut section, it contained numerous small loculi
filled with pseudomucin.   The right ovary showed a small
corpus luteum on its cut surface. Microscopically, the
endometrium was the seat of cystic hyperplastic activity.
The left ovary proved to contain a haemorrhagic corpus
luteum and a corpus albicans cyst with active theca
cells in its wall.   The ovarian cyst was a typical
pseudomucinous cystadenoma showing areas of calcification
in its stroma.   No sudanophillic droplets or reactive
steroid material were found in this tumour.

Case 56.

1506/61.   (Mrs E. R., 43 years old, para 3 + 1, L.M.P.
2½ months.)

This patient entered the hospital in March 1961
with a chief complaint of lower abdominal pain for the
past week. Her periods were regular till October 1960,
when she had an episode of vaginal bleeding for 6 weeks.
In December 1960, and January 1961, she had normal periods.
Since then, she had amenorrhoea. In 1958, she had had
a right adrenalectomy for a pheochromocytoma.

On examination, an abdominal mass was felt in the
right iliac fossa.   Vaginal examination revealed it to
be a right ovarian cyst.   Total hysterectomy and bilateral
salpingo-oophorectomy were performed.   The right ovarian
cyst was smooth, thin-walled and 4" in diameter.   On
cut section it was unilocular and filled with thin
pseudomucin.   The uterus contained a small interstitial
fibroid, the size of a pea and showed a profuse endo-
metrium.   The left ovary contained a small cyst.   Micro-
scopically, the endometrium showed cystic hyperplasia.
The left ovary contained a follicular cyst.   The right
ovarian cyst was a typical pseudomucinous cystadenoma.
No sudanophillic droplets or reactive steroid material
were found in this cyst.

Case 57.

981/61. (Miss I.C., 48 years old, para 0 + 0, L.M.P.,
3 days.)

This patient entered the hospital with a chief
complaint of abdominal swelling, menorrhagia and missed
periods over the past 6 months.   On examination, the
abdomen was protuberant and there was a swelling arising
from the pelvis and extending up to 1 finger below the
umbilicus.   Total hysterectomy and bilateral salpingo-
oophorectomy were performed.   The uterus was enlarged,
and irregular in outline.   On cut section, it showed
multiple, interstitial fibroids, the largest of which
measured 3" in diameter.   The left ovary was replaced

by a thin-walled smooth cyst measuring $3\frac{1}{2}$ x $2\frac{1}{2}$ x $2\frac{1}{2}$".

On cut section, it was composed of one large and

several small loculi, all filled with pseudomucin.   The

right ovary showed no gross abnormality. Microscopically,

the endometrium was the seat of cystic hyperplasia.   The

right ovary contained a haemorrhagic corpus luteum and

showed minimal stromal hyperplasia (grade 0) and an

area of thecomatosis.   The left ovarian cyst was

a typical pseudomucinous cystadenoma. No sudanophillic

droplets or reactive steroid material were found in this

cyst.

Case 58.

4563/61. (Mrs J.B., 42 years old, para 5 + 0, L.M.P.

28 days.)

This patient entered the hospital with a chief

complaint of heaviness in the lower abdomen for the past

2 months.   On examination, there was deep tenderness

in the left iliac fossa. Per vaginam, an indefinite

mass was present close to the right of the uterus.

Total hysterectomy and bilateral salpingo-

oophorectomy were performed.   The uterus contained

a fibroid which was becoming submucous and measured

$1\frac{1}{2}$" in diameter.   The right ovary was replaced by

a thin-walled cyst measuring 3 x 2 x 2". It was

unilocular and filled with thin pseudomucin.   The

left ovary was slightly enlarged and showed a thick

nodular cortex.

Microscopically, the endometrium was thinned out

but the few glands present showed proliferative activity.
There was also some degree of adenomyosis. The left ovary
showed grade 2 stromal hyperplasia. The right ovarian
cyst was lined by the tall columnar epithelium, characteristic
of pseudomucinous cystadenoma. No sudanophillic droplets
or reactive steroid material were found in this tumour.

Case 59.

4648/61. (Mrs E. P., 49 years old, para 1 + 0, L.M.P.
6 months.)

This patient entered the hospital with a chief
complaint of dull aching pain in the lower abdomen for
the past 2 days. On examination, there was a firm
abdominal swelling arising from the pelvis and reaching
to the umbilicus. Per vaginam: there was fullness
in the left fornix. Total hysterectomy and bilateral
salpingo-oophorectomy were performed. The uterus was
slightly enlarged and contained a seedling fibroid. The
left ovary was the seat of a thin-walled cyst, 7 x 6 x
4". It was reddish in colour (and contained blood-
stained fluid) due to partial torsion of the pedicle.
The right ovary was cystic.

Microscopically, the endometrium showed prolif-
erative activity and adenomyosis. The right ovary
contained follicular cysts. The left ovarian cyst was
a pseudomucinous cystadenoma, showing areas of inter-
stitial haemorrhage. No histochemically reactive
materials were found in this cyst.

Case 60.

5459/61. (Mrs M. C., 55 years old, para 3 + 2,
18 months post-menopausal.)

This patient was discovered to have an abdominal
mass during routine examination. The mass was cystic
and occupied the whole lower abdomen. Per vaginam,
the uterus was pushed over to the left. Total hysterect-
omy and bilateral salpingo-oophorectomy were performed.
The uterus showed a small, interstitial fibroid $\frac{1}{2}$" in
diameter. The right ovary was replaced by a thin-walled
multilocular cyst (6" in diameter) and filled with
pseudomucin. The left ovary contained 2 tiny cysts.
Microscopically, the endometrium showed senile changes
with some proliferative activity and few dilated glands.
The left ovary contained 2 follicular cysts. The right
ovarian cyst was a pseudomucinous cystadenoma. No histo-
chemically reactive material was found in this cyst.

Case 61.

5322/61. (Mrs S., 56 years old, para 2 + 0, 6 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of lower abdominal down-bearing and difficulty
with defaecation. Abdominal and vaginal examination
provided the diagnosis of a right ovarian cyst.
Hysterectomy and bilateral salpingo-oophorectomy were
performed. The uterus showed no abnormality. The
right ovary was replaced by a rounded thin-walled cyst
3" in diameter. On section, it was unilocular and
filled with thick mucoid material. The left ovary was

small and fibrosed.

Microscopically, the endometrium showed senile changes. The left ovary was atrophic. The right cyst was a pseudomucinous cystadenoma with areas of cystadeno-fibroma. No histochemically reactive materials were found in this cyst.

Case 62.

3741/61. (Miss M., 57 years old, 8 years post-meno-pausal.)

This patient entered the hospital with a chief complaint of abdominal swelling for 2-3 years. Abdominal examination revealed a cystic swelling arising from the pelvis and extending to xyphisternum. Total hysterectomy and bilateral salpingo-oophorectomy were performed. A big, thin-walled cyst, arising from the right ovary, was filling the whole abdomen. It measured 14 x 13 x 10" and weighed 31 lbs. Its surface was smooth and on cut section it was multilocular and contained straw-coloured watery fluid. The uterus was small and so was the left ovary.

Microscopically, the endometrium showed senile changes and the left ovary was atrophic. The right ovarian cyst was a pseudomucinous cystadenoma. No histochemically reactive materials were found in this cyst.

Case 63.

763/61. (Mrs A.G., 52 years old, para 0 + 0, 2 years post-menopausal.)

This patient was admitted to hospital with
a complaint of stress incontinence and feeling a lump in
the abdomen for the past 6 months.   Abdominal examin-
ation revealed a tense cystic ovoid mass arising from the
pelvis on the right side.   Total hysterectomy and bilat-
eral salpingo-oophorectomy were performed.   The uterus
showed no abnormality but on cut section its cavity
contained 2 tiny soft polypi.   The right ovary was the
seat of a smooth, thin-walled cystic tumour measuring
4" in diameter.   It was unilocular and filled with thick
pseudomucin.   The left ovary showed a slightly thickened
nodular cortex.

Microscopically, the endometrium with its 2 benign
fibro-adenomatous polypi were the seat of regressive
cystic hyperplasia.   The left ovary showed grade I
C.S.H. with an area of thecomatosis.   The right ovarian
cyst was lined by the typical palisade epithelium of
a pseudomucinous cystadenoma.   No sudanophillic droplets
or reactive steroid material were present in this cyst.

Case 64.

4963/61.   (Mrs J.B., 68 years old, para 2 + 0, 14 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of intermittent vaginal bleeding for the past
4 months.   On examination, the abdomen was distended
and there was some dullness in the region below the
umbilicus.   Examination under anaesthesia and D. & C.

revealed a cervical polyp which was removed.   Two months
later the patient was re-admitted because of further
bleeding.   Curettage yielded no scrapings.   She was
then started on a course of Ethinyl Oestradiol, (0.5 mgm.
daily for 21 days).   As the bleeding recurred,
hysterectomy and bilateral salpingo-oophorectomy were
performed.   The uterus was slightly bulky with irregular
outline, due to 3 interstitial fibroids, the largest
of which measured 1" in diameter.   The right ovary was
replaced by a thin-walled cyst (7 x 6 x 3").   On cut
section, it was multilocular and filled with pseudomucin.
The left ovary was small in size but its cortex was
thickened.

Microscopically, the endometrium showed senile
changes with some proliferative activity.   The left ovary
showed whirly nodules of hyperplastic fibroblasts (grade
I, cortical stromal hyperplasia).   The right ovarian cyst
was lined by tall columnar epithelium, characteristic
of pseudomucinous cystadenoma. No histochemically
reactive steroids were found in this cyst.

Case 65.

(Mrs J. M., 69 years old, para 4 + 0, 19 years post-
menopausal.)

This patient entered the hospital with a chief
complaint of abdominal pain radiating to the groin.
This occurred on one occasion, a month prior to admission.
On examination, the abdomen was protuberant and a cystic
mass arising from the pelvis and reaching to the umbilicus,

was felt.   Total hysterectomy and bilateral salpingo-
oophorectomy were performed.   The left ovary was the
seat of a large, smooth cyst 6" in diameter.   It was
multilocular and emptied of its contents before
reaching the laboratory.   The uterus was bulky and on
cut section it showed a polypoidal endometrium.   The
right ovary showed no gross abnormality.

Microscopically, the endometrium showed regressing
cystic hyperplasia.   The right ovary showed grade 0
cortical stromal hyperplasia, and 2 cortical granulomas.
The right ovarian cyst was a typical pseudomucinous
cystadenoma.   No sudanophillia or reactive steroid
material were present in the cyst.

Case 66.

(Mrs C. M., 70 years old, para 4 + 1, 24 years post-
menopausal.)

This patient entered the hospital with a chief
complaint of abdominal swelling and indigestion.
On examination, a cystic mass was felt in the abdomen.
Ascites was also present. On laparotomy, the mass was
found to arise from the right ovary.   Total hysterect-
omy and bilateral salpingo-oophorectomy were therefore
performed.   The right ovarian tumour was a smooth,
thin-walled cyst (7 x 6 x 5").   It was multilocular and
filled with pseudomucin. The uterus showed no abnormality
but on cut section the endometrium was a little more
profuse than would be expected in a patient of this age.
The left ovary was very small and atrophic. Microscopic-

ally, the endometrium showed cystic hyperplasia which
was starting to regress. The left ovary was almost
totally fibrosed. The right ovarian cyst was a typical
pseudomucinous cystadenoma showing some areas of
infection and necrosis. Ten blocks from the cyst wall
were cut and examined histochemically, but all of them
showed no sudanophillia or reactive steroid material.

Case 67.

6122/60. (Mrs J. R., 52 years old, para 5 + 0, 1 year
post-menopausal.)

This patient entered the hospital with a chief
complaint of abdominal swelling which was gradually
increasing over the past year. On examination, there
was a cystic swelling which appeared to fill the whole
abdomen. Total hysterectomy and bilateral salpingo-
oophorectomy were performed. A cystic swelling arising
from the right ovary was occupying the whole abdominal
cavity and showed few adhesions to the anterior
abdominal wall. The uterus and left ovary showed no
abnormality.

Microscopically, the endometrium showed proliferative
activity with some adenomyosis. The left ovary showed
whirly nodules of hyperplastic plump fibroblasts (grade
I hyperplasia) as well as few cortical granulomas. The
right ovarian cyst was a typical pseudomucinous cyst-
adenoma. No sudanophillic or reactive steroid material
was found in this cyst.

Case 68.

271/61. (Mrs M. M., 56 years old, para 3 + 0, 3½ years

post menopausal.)

This patient entered the hospital with a chief complaint of an episode of vaginal bleeding, lasting two days, three weeks prior to admission. Vaginal examination revealed a normal sized, retroverted uterus and a cystic left ovary. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The right ovary was replaced by a thin-walled, rounded cyst, measuring 3" in diameter. On cut section, it was composed of 2 locules filled with straw-coloured watery fluid. The left ovary showed a small cyst and a thickened nodular cortex. The uterus showed no gross abnormality.

Microscopically, the endometrium was thin, but showed some proliferative activity and adenomyosis. The left ovary showed a small follicular cyst and whirly nodules of hyperplastic stromal cells (grade II). Several cortical granulomas were also present.

The right ovarian cyst was a typical pseudomucinous cystadenoma.

No sudanophillic granules or reactive steroid material was found in this cyst.

Case 69.

5394/60. (Miss F. M., 55 years old, para 0 + 0, 2 years post-menopausal.)

This patient entered the hospital with a chief complaint of intermittent vaginal bleeding for the past 8 months. Examination under anaesthesia and curettage

were performed. An ovarian tumour was felt to the left
and behind the uterus. The scrapings were bulky, friable
and clinically malignant. This was confirmed microscop-
ically. Total hysterectomy and bilateral salpingo-
oophorectomy were performed. The left ovary was replaced
by a thin-walled cyst, measuring 3 x 2 x 2". It was
bilocular and filled with thin pseudomucin. The uterus
was bulky and its wall infiltrated with friable greyish-
white tissue which partially filled the uterine cavity.
The right ovary showed a slightly thickened nodular
cortex.

Microscopically, the endometrium was the seat of
a well-differentiated adenocarcinoma which was invading
the muscle wall. The right ovary showed grade I cortical
stromal hyperplasia and a regressing cortical granuloma.
The left ovarian cyst was a pseudomucinous cystadenoma.
No histochemically reactive materials were found in this
cyst.

Case 70.

17/61. (Mrs J.S., 70 years old, para 3 + 1, 30 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of gradually increasing abdominal swelling for
the past 6 months. On examination, the abdomen was
distended by a smooth fluctuant swelling. Per vaginam,
the uterus could not be outlined. Hysterectomy and
bilateral salpingo-oophorectomy were performed. The
left ovary was the seat of a large, thin-walled cyst

(9" in diameter). Its surface was smooth and on cut
section it was multilocular and contained about 20 pints
of straw-coloured watery fluid. The uterus showed no
gross abnormality. The right ovary showed a tiny
whitish cortical nodule.

Microscopically, the endometrium showed senile
cystic change with some proliferation. The right ovary
contained a completely hyalinised whirly cortical nodule
(indicative of regressing stromal hyperplasia). The left
ovarian cyst was a typical pseudomucinous cystadenoma.
No sudanophillic droplets or reactive steroid materials
were present in this cyst.

Case 71.

5462/61. (Miss W., 79 years old, many years post-
menopausal.)

This patient had no gynaecological complaint. An
ovarian cyst was incidentally discovered during routine
examination. It was large and filled the whole lower
abdomen. Total hysterectomy and bilateral salpingo-
oophorectomy were performed. The uterus was small in size
and showed a number of tiny subperitoneal fibroids. The
left ovary was replaced by a thin-walled multilocular cyst
(6" in diameter). The right ovary was slightly larger
than what would be expected in that age. Microscopically,
the endometrium showed proliferative activity with some
dilated glands. The right ovary showed grade I cortical
stromal hyperplasia. The left ovarian cyst was
a pseudomucinous cystadenoma. No histochemically reactive

materials were found in this cyst.

Case 72.

1623/61. (Mrs M. A., 54 years old, para 0 + 0, 3 years post-menopausal.)

This patient entered the hospital with a chief complaint of abdominal pain for the past week.

Abdominal examination revealed a large cystic swelling reaching to halfway between the umbilicus and xyphisternum. It was lobulated and tender. Vaginally, the uterus could not be felt distinctly from the mass.

On 6.4.61 total hysterectomy and right cystectomy were performed. The right ovary was the seat of a large cystic tumour (6" in diameter) which was multilocular. Many of the loculi contained pseudomucin. A large locule, however, contained sebaceous material and hairs. The left ovary was slightly enlarged and showed a thickened nodular cortex. The uterus was small and contained a small polypus in its cavity.

Microscopically, the endometrium showed senile changes with some proliferative activity. The left ovary showed grade 2 cortical stromal hyperplasia and a few cortical granulomas. The right ovarian cyst was a combination of a dermoid cyst with pseudomucinous cystadenoma. No sudanophillic droplets or reactive steroid material were found in the cyst.

Case 73.

3517/61. (Miss J. B., 54 years old, 4 years post-

menopausal.)

This patient entered the hospital with a chief complaint of vaginal bleeding for 7 days in each of the past 3 months. The bleeding was like that of a normal period with no intermenstrual bleeding.

Abdominal palpation revealed a large, cystic tumour arising from the pelvis and reaching to the level of the umbilicus. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The cyst was originating from the right ovary. It ruptured in the course of the operation and clear pseudomucinous material was discharged. It was composed of one large and several small loculi. The uterus contained 2 fibroids, the largest of which was subperitoneal and measured $\frac{3}{4}$" across. The other fibroid was interstitial. The left ovary was larger than would be expected in a post-menopausal patient and its cortex was thick and nodular. Microscopically, the endometrium showed proliferative activity with some dilated glands. The left ovary showed grade I cortical stromal hyperplasia with several foci of thecomatosis and cortical granulomas. The right ovarian cyst was a pseudomucinous cystadenoma. No sudanophillic droplets or reactive steroid material were found in this cyst.

<p style="text-align:center">SEROUS TUMOURS</p>

I. POSITIVE CASES

Simple Serous Cysts

Case 74.

4646/60. (Miss H. M., 51 years old, para 0 + 0,
L.M.P. irregular.)

This patient entered the hospital with a chief
complaint of vaginal bleeding for the past 6 weeks.
Her periods had been irregular and scanty for the past
6 years. On examination, a firm mass arising from the
pelvis was palpable in the lower abdomen.   Total
hysterectomy and bilateral salpingo-oophorectomy were
performed.   The uterine body and cervical canal appeared
to be replaced by greyish white friable malignant tissue.
At one point of the endocervix the muscle wall was almost
completely infiltrated.   The left ovary was replaced
by a thin-walled ovarian cyst, measuring 7 x 4 x 4".
On cut section it was multilocular and filled with
gelatinous fluid.   The right ovary showed 2 tiny cysts.

Microscopically, the uterus was extensively invaded
by a poorly differentiated adenocarcinoma with few foci
of squamous metaplasia.   It was not possible to determine
the origin of the neoplasm with certainty.   Most of the
malignant tissue resembled an endometrial growth but in
places the appearance was consistent with an origin from
the endocervix.   The right ovary contained 2 follicular
cysts.   The left ovarian tumour was a simple serous
cyst.   Plump theca like cells were found beneath the
epithelium.   They contained sudanophillic droplets and
birefringent droplets (Photo 133).   Schultz, Ashbel-

Seligman and fluorescence tests were weakly positive.

Control sections were negative.

Case 75.

4869/61. (Mrs M. R., 56 years old, para 1 + 0, 10 years post-menopausal.)

This patient entered the hospital with a chief complaint of scanty, irregular bleeding for the past year. Abdominal and vaginal examination revealed no abnormality. A D. & C. yielded scanty scrapings which showed senile changes with some proliferative activity. Laparotomy was performed with removal of a smooth, thin-walled left ovarian cyst (3" in diameter). On opening it contained watery fluid and showed few yellowish specks underneath the epithelium. Microscopically, the cyst wall, lined with cuboidal epithelium, was a simple serous cyst. The histochemical tests were all positive in a few islands of stromal theca-like cells near the epithelium. Control sections were negative.

Serous Papilloma

Case 76.

4125/61. (Mrs J. M., 47 years old, para 1 + 0, L.M.P. 11 days.)

This patient entered the hospital because of an abdominal mass which had been discovered during routine examination. Abdominal palpation, however, revealed a firm, irregular mass arising from the pelvis. Per vaginam, the uterus was enlarged to the size of a 20 weeks' pregnancy. Total hysterectomy and left salpingo-

oophorectomy were performed. The uterus was enlarged
and grossly distorted by multiple fibroids of varying
sizes. The largest was interstitial and measured $2\frac{1}{2}"$
in diameter. The endometrium was rather profuse.
The left ovary measured $1\frac{1}{2}"$ in its longest diameter and
had, attached to its surface, a firm papillary growth,
measuring 1" in diameter. The growth had created
a bed for itself on the surface of the ovary (Photo 134).
Microscopically, the endometrium showed a well-developed
proliferative phase. The ovarian growth consisted of
multiple papillae having a core of ovarian stroma and
covered with cuboidal epithelium, i.e., serous papilloma.
A few of the stromal cells were plump and contained
sudanophillic droplets. They also gave a trace positive
results with the remaining histochemical tests. Control
sections were negative.

Positive Papillary Serous Cyst of borderline
malignancy.

Case 77.

2326/61. (Mrs M. H., 51 years old, para 2 + 0, 3 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of lower abdominal pain and dysuria for the
past six months. On vaginal examination, the uterus
was displaced to the right by a large, cystic swelling
arising from the left appendages. Total hysterectomy
and bilateral salpingo-oophorectomy were performed.
Both ovaries were replaced by cystic tumours measuring

5 x 4½ x 3" and 6 x 5 x 4".   Both were multilocular,
filled with clear watery fluid and contained intra and
extra cystic papillae.   The uterus showed no gross
abnormality. Microscopically, the endometrium showed
proliferative activity with some degree of adenomyosis.
Sections from both cysts showed an actively growing
papillary serous cystadenoma with areas of borderline
malignancy.

Sudan IV stain revealed the presence of red droplets
in a good number of plump, stromal cells (Photo 135).
These cells contained a high concentration of birefringent
crystals (Photo 136), gave positive Schultz and Ashbel-
Seligman tests (Photo 137) and exhibited yellowish-green
fluorescence.   Control sections were negative.

Case 78.

2682/61. (Mrs A.B., 52 years old, para 2 + 0, 3 years
post-menopausal.)

This patient was admitted to hospital because of
an abdominal mass which had been discovered during
routine examination.   On examination, a large mass was
palpable in the left lower abdominal quadrant. It was
firm, irregular and appeared to arise from the pelvis.
Laparotomy was performed with removal of the uterus,
and a large ovarian cystic tumour incorporating both
ovaries and lying in the pouch of Douglas.   Adhesions
were binding it to the rectum and other pelvic structures.
The tumour measured 6 x 5 x 4", was thick-walled and
opaque-white.   On cut section, it consisted of one

large and several small loculi filled with infected
necrotic material. Intracystic papillae and yellow
semi-solid areas were present in the cyst wall. The
uterus was small in size and showed no abnormality.
Microscopically, the endometrium showed senile changes
with some proliferative activity and adenomyosis.
The ovarian tumour was a papillary serous cyst of
borderline malignancy. Sudan IV stain revealed the
presence of red droplets in several plump stromal cells,
especially those lying beneath the epithelial lining
of the cyst and sometimes rupturing through it. These
cells gave also positive results with the remaining
tests. Control sections were negative.

Positive Papillary Serous Cystadenocarcinoma.

Case 79.

5033/61. (Mrs C. S., 53 years old, para 1 + 0, 2 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of brown, offensive, vaginal discharge for
the past three months. She also had a heavy feeling
in the abdomen for 2 months. Abdominal palpation
revealed a firm nodular mass with cystic areas, arising
from the pelvis and extending up to 2 fingers below the
umbilicus. Per vaginam, the cervix was pushed up,
beneath the symphysis pubis, by the mass which filled
the pouch of Douglas. Total hysterectomy and bilateral
salpingo-oophorectomy were performed. The peritoneal

cavity was filled with a large right ovarian cyst (11"
in diameter) which was densely adherent to the pelvic
colon and caecum. It was composed of one large and
several small loculi, filled with straw-coloured fluid.
Intra- and extra-cystic papillae as well as solid
pieces of greyish-white tissue were present in the cyst
wall.   The uterus was enlarged by 3-4 fibroids, the
largest being submucous and measuring 1½" in diameter.
The left ovary showed a thickened cortex. Microscopic-
ally, the endometrium showed proliferative activity
with some dilated glands. The left ovary showed grade I
cortical stromal hyperplasia.   The right ovarian tumour
was a frankly malignant papillary serous cystadenocar-
cinoma. Histochemical study of this tumour revealed
sudanophillic droplets with reactive steroid material
in several clusters of plump stromal cells and in
necrotic tissue.   Control sections were negative.

Case 80.

5215/61. (Mrs B. M., 50 years old, para 2 + 0, 8 years
post-menopausal.)

   This patient entered the hospital with a chief
complaint of brown vaginal discharge for the past year.

   By abdominal palpation, a mass was suspected to be
felt in the lower abdomen.   Examination under anaesthesia
was carried out and the mass previously noted arising
out of the pelvis was confirmed. It was about the size
of a 3½ months' pregnancy and was continuous with the

cervix, on which a fibroid polypus, 1" in diameter, could be felt. A sound passed through the cervical canal was deviated greatly to the right and could not be passed any further than $3\frac{1}{2}$". On opening the abdomen, the mass was a big cyst located in the left broad ligament and as well replacing the left ovary. The uterus was elongated and stretched tightly over its anterior surface and the left tube passed over its summit towards the side wall of the pelvis. It was adherent to the pouch of Douglas and the posterior wall of the uterus. The cyst was removed, together with the uterus and other ovary. It was thin-walled, unilocular and filled with pus-like material. Several intra- and extra- cystic papillae were present. The right ovary showed 2 small cysts $\frac{1}{4}$" each, and several papillomatous growths on its surface. The uterus was small and elongated.

Microscopically, the endometrium showed proliferative activity with some adenomyosis. The left ovarian cyst was a typical papillary serous tumour with borderline and frankly malignant areas. The same type of growth was present in few foci in the right ovary. Histochemical study of the left tumour revealed sudanophillic droplets and reactive steroid material in several plump stromal cells. Control sections were negative.

Case 81.

60/61. (Mrs A. O., 62 years old, para 1 + 0, 6 years post-menopausal.)

This patient entered the hospital with a chief complaint of abdominal swelling noticed for the past 2 years. Three days prior to admission, she had an attack of right-sided abdominal pain. On examination, a firm fixed, tender, abdominal mass was palpated and a laparotomy was performed with removal of bilateral ovarian cysts, tubes and the uterus. There were few tumour nodules on anterior aspect of abdominal peritoneum. The uterus was irregularly enlarged by a number of small fibroids, the largest of which was sub-peritoneal and measured 1" in diameter. A small cervical polypus was also present. Both ovarian cysts (5" in diameter) contained numerous intra- and extra-cystic papillae as well as greyish-white solid pieces of tissue in their walls. Microscopically, these showed cystic hyperplasia of the endometrium. The tumours showed a picture of a papillary serous cystadenocarcinoma with some psammoma bodies. The stroma contained many plump cells which were rich in sudanophillic droplets and gave positive results with the other histochemical tests. Control sections were negative.

Case 82.

5454/60. (Mrs M. I., 58 years old, para 1 + 0, 3 years post-menopausal.)

This patient entered the hospital on 16.11.60

complaining of a lump in the abdomen which had been
noticed for the past 6 weeks. Her first admission to
hospital had been in 1957 when she entered with a com-
plaint of heavy vaginal bleeding for $3\frac{1}{2}$ months. At
that time, a D. & C., yielded a cystic hyperplastic
endometrium. No vaginal bleeding had been noticed
since then. On examination, a firm, smooth mass was
palpable in the lower abdomen, arising from the pelvis.
Vaginal examination was very difficult. Laparotomy was
performed with removal of bilateral cystic ovarian
tumours and the uterus. Both tumours were adherent to
the surrounding structures. The left tumour measured
6" in diameter, and contained intra- and extra-cystic
papillae as well as solid pieces of greyish-white tissue.
The right tumour showed similar features save for being
smaller (2.5" in diameter). Both were filled with dirty
brownish fluid. The uterus showed no gross abnormality.
Microscopically, the endometrium showed proliferative
activity and some degree of adenomyosis. Both tumours
were typical papillary serous cystadenocarcinomas.
Sudanophillic droplets and reactive steroid material
were present in some plump stromal cells and in necrotic
tissue.

Case 83.

2804/60. (Mrs S. M., 48 years old, para 0 + 0, 4 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of abdominal swelling, vomiting and discomfort

for the past 6 weeks. On examination, there was massive

ascites so that nothing could be palpated. Vaginal

examination was impossible. Laparotomy was performed

with removal of a large cystic ovarian tumour, uterus

and other ovary. The ovarian tumour, 6" in diameter,

contained numerous intracystic papillae and several

extracystic ones. It was filled with gelatinous material.

The uterus showed a small interstitial fibroid. The

other ovary contained a small cyst, filled with chocolate

material. Microscopically, there was cystic hyperplasia

of the endometrium. The other ovary was the seat of

an endometriomatous cyst. The ovarian tumour was

a typical papillary serous cystadenocarcinoma. Sudano-

phillic droplets and reactive steroid material were

present in some stromal cells and in necrotic areas.

Control sections were negative.

Case 84.

5945/61. (Mrs M. W., 54 years old, para 3 + 0, 4 years

post-menopausal.)

This patient entered the hospital with a chief

complaint of abdominal swelling for the past month.

Examination revealed a pelvic mass extending up to the

umbilicus. Per vaginam, one or two cystic masses

were distinguishable from the uterus which was normal

in size. Hysterectomy and bilateral salpingo-

oophorectomy were performed. The right ovary was

replaced by a cystic tumour, measuring 7" in diameter.

On cut section, it contained many intra-cystic papillae

and semi-solid yellow areas in its wall. The left ovary
was the seat of a smooth cyst (6" in diameter). It was
multilocular with thick septa in between the loculi.
The uterus showed no abnormality, apart from a small
polypus in its cavity. Microscopically, the endo-
metrium showed proliferative activity with some dilated
glands. The right ovarian tumour was a papillary serous
cystadenocarcinoma showing the typical psammoma bodies.
The left ovarian cyst was a benign serous one. Stromal
cells, giving positive results with the histochemical
tests for steroids, were present in the malignant tumour
only. Control sections were negative.

Case 85.

5092/61. (Mrs B. S., 37 years old, para 0 + 0,
L.M.P. 27 days)

This patient entered the hospital with a chief
complaint of abdominal pain and swelling for the past
3-4 months. Abdominal examination revealed a firm
swelling arising from the pelvis and extending up to
the umbilicus. Per vaginam, the swelling was palpable
anterior to the uterus. Hysterectomy and bilateral
salpingo-oophorectomy were performed. The left ovary
was replaced by a large cystic tumour, measuring 6"
in diameter. On cut section, it consisted of one large
locule which was nearly filled with a cauliflower
papillary mass arising from one side of the cyst wall.
The uterus showed a fairly profuse endometrium.

Microscopically, the endometrium was in the late

secretory phase. The right ovary contained a recent
corpus luteum. The right ovarian tumour was a papillary
serous cystadenocarcinoma. Some stromal cells gave
weakly positive results with the histochemical tests
for steroids. Control sections were negative.

Case 86.

2762/60. (Mrs V. B., 47 years old, para 1 + 0, L.M.P.
18 days.)

This patient entered the hospital with a chief
complaint of abdominal swelling over the past few
months. Abdominal examination revealed a mass arising
from the pelvis and extending up to the umbilicus. Per
vaginam, the uterus was outlined anteriorly to the
mass which filled the pelvis. Total hysterectomy and
bilateral salpingo-oophorectomy were performed. The
uterus was rather bulky but showed no other abnormality.
The left ovary was the seat of a cyst about 4" in diam-
eter and contained an extra-cystic papillary growth.
The right ovary was replaced by a large extra-cystic
papillomatous tumour filling the whole pelvis. Micro-
scopically, the endometrium showed secretory changes.
Both ovarian tumours showed a papillary serous
cystadenocarcinoma. A recent corpus luteum was found
in one of the tumours. Histochemical study revealed the
presence of a trace of sudanophillic and reactive steroid
material in the stroma of these tumours. Control
sections were negative.

Case 87.

3513/61. (Mrs M. G., 46 years old, para 5 + 0, L.M.P.
1 day.)

This patient entered the hospital with a complaint
of swollen right leg and lower abdominal pain for the
past 3-7 weeks. On examination, a mass was palpable above
the pelvic brim. The uterus was felt to be normal.

Hysterectomy and bilateral salpingo-oophorectomy
were performed. Both ovaries were the seat of friable
cystic tumours, 4" in diameter each. They contained
numerous extra-cystic papillae with a lot of necrotic
tumour tissue. On section, one of them showed intra-
cystic papillae, while the inside of the other cyst was
mainly semisolid. Tumour nodules were spread in the
pouch of Douglas which also contained a lot of infected
fluid. The uterus showed a thickened wall and some
tumour papillae on its peritoneal surface. The abdom-
inal peritoneum, however, showed no spread.

Microscopically, the endometrium showed proliferative
activity and adenomyosis. Invasion of the myometrium by
adenocarcinomatous tissue was evident just beneath the
peritoneum. Both ovarian tumours were serous cystadeno-
carcinomas. Sudan stain revealed the presence of red
droplets in some of the stromal cells and in necrotic
areas. The remaining histochemical tests gave positive
results in the same sites. Control sections were
negative.

II. NEGATIVE CASES.

Simple Serous Cysts

Case 88.

3696/61. (Mrs E. M., 56 years old, para 2 + 1, 8 years post-menopausal.)

This patient entered the hospital with a chief complaint of acute abdominal swelling for the past 5 days. She had been experiencing vague abdominal pain on and off over the past 2 years. On examination, the abdomen was swollen up to the size of a seven months' pregnancy by a large cystic swelling arising from the pelvis. Per vaginam, the uterus could not be defined. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The right ovary was the seat of a large thin-walled smooth cyst, measuring about 12" in diameter. On opening, it was unilocular and contained watery fluid. The left ovary showed no abnormality.   The uterus showed a tiny subperitoneal fibroid ($\frac{1}{4}$" in diameter).

Microscopically, the endometrium showed senile changes, the large ovarian cyst was lined by a simple layer of flattened cuboidal epithelium.   The left ovary was atrophic. No histochemically reactive materials were present in this cyst.

Case 89.

2734/61. (Mrs F., 54 years old, para 2 + 2, 5 years post-menopausal.)

This patient entered the hospital with a chief

complaint of dull pain in the lower abdomen for the
past 10 months. On examination, there was slight
tenderness in the left iliac fossa. Per vaginam, the
uterus was normal in size. A cystic swelling was felt
in the left appendages. Hysterectomy and bilateral
salpingo-oophorectomy were performed. The left ovary
was replaced by a thin-walled cyst about 3" in diameter.
It was unilocular and filled with straw-coloured
watery fluid. The uterus and right ovary were small
in size. Microscopically, the endometrium showed
senile changes. The right ovary was atrophic. The
left ovarian cyst was lined by cuboidal epithelium,
characteristic of simple serous cyst. No reactive
steroid material was found in this cyst.

Case 90.

5753/61. (Mrs M. W., 53 years old, para 2 + 0, 2 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of backache, especially after exertion.
Abdominal and vaginal examination yielded no information.
Hysterectomy and bilateral salpingo-oophorectomy were
performed. The left ovary was replaced by a smooth,
thin-walled cyst, 2" in diameter. It was unilocular
and contained clear watery fluid. The uterus con-
tained several fibroids, the largest of which was sub-
peritoneal and measured 1" in diameter. The right
ovary showed no abnormality. Microscopically, the

endometrium showed senile changes.   The right ovary was
atrophic.   The left cyst was of the simple serous variety.
No reactive steroid materials were present in this cyst.

Case 91.

3607/61.   (Mrs I.S., 49 years old, para 4 + 1, 3 years
post-menopausal.)

This patient entered the hospital in July 1961, with
a chief complaint of 2 episodes of vaginal bleeding
within the past 3 months.   Her previous admission to
hospital was in 1958 when a D. & C. was performed for
menorrhagia.   (The scrapings showed secretory changes).
Since then, the periods had stopped.   On examination,
there was slight lower abdominal tenderness and distension.
Per vaginam, the uterus was bulky and there was a swelling
in the pouch of Douglas. Hysterectomy and bilateral
salpingo-oophorectomy were performed.   The uterus
contained 2 fibroids, the larger of which (1" in diameter)
was submucous.   A soft endometrial polypus was also
present in the uterine cavity.   The right ovary was
replaced by a thin-walled cyst (2½ x 2 x 2").   On
section, it was unilocular and filled with clear watery
fluid.   The left ovary showed a thickened cortex.

Microscopically, the endometrium showed senile
changes with minimal proliferation.   The left ovary
showed grade I cortical stromal hyperplasia.   The
right ovarian cyst was lined by cubical epithelium
(simple serous cyst).   No reactive steroid materials
were found in the cyst.

Case 92.

2209/61. (Mrs B. N., 64 years old, para 4 + 0, 24 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of uterine prolapse and nocturnal frequency
of micturition for one year. On examination, the
anterior lip of cervix was hypertrophied and prolapsing
outside the introitus. There was little descent of
the uterus and a mass was felt in the pouch of Douglas.
Hysterectomy and bilateral salpingo-oophorectomy were
performed. The pouch of Douglas was very deep and
contained a large cystic tumour, arising from the right
ovary. It was thin-walled with a few fairly solid
areas and measured about 3 x $2\frac{1}{2}$ x $2\frac{1}{2}$". On cut section,
it was composed of several loculi filled with straw-
coloured watery fluid. The left ovary was slightly
enlarged. On cut section, minute yellowish specks were
apparent in the thickened cortex. The uterus was small
in size and showed no abnormality.

Microscopically, the endometrium was the seat of
proliferative activity and some adenomyosis. The right
ovarian cyst was lined by flattened cuboidal epithelium
and in some areas where the stroma was much exaggerated,
the appearance was that of a cystadenofibroma. The left
ovary harboured a microscopical adenofibroma. It also
showed grade II cortical stromal hyperplasia and
several foci of thecomatosis and cortical granulomas
(Photos 138, 139). Histochemical study revealed no

reactive materials in the right ovarian tumour.

Case 93.

4524/61. (Mrs M. M., 48 years old, para 5 + 1, L.M.P.,
24 days.)

This patient entered the hospital with a chief
complaint of lower abdominal pain for the past 2-3
months. Her periods were irregular for the past 6 months.
On examination, a soft swelling was felt in the suprapubic
region. Hysterectomy and bilateral salpingo-oophorect-
omy were performed. Both ovaries were replaced by smooth,
thin-walled cysts, measuring 5 x 3 x 3" and 2 x 1½ x 1½".
On cut section, they were multilocular and filled with
watery fluid (blood-stained in one of them). The uterus
showed no gross abnormality.

Microscopically, the endometrium showed proliferative
changes. Both cysts were lined by flattened cuboidal
epithelium (simple serous cysts).

No histochemically reactive steroid materials were
present in either cyst.

Negative papillary serous cystadenoma.

Case 94.

5354/60. (Mrs E.T., 77 years old, para 6 + 0, many
years post-menopausal.)

This patient entered the hospital with a chief
complaint of a gradually increasing abdominal swelling
over the past 5 months. On examination, the abdomen
was greatly distended, tense and dull all over. No masses
were felt. Rectal examination revealed a sensation of

fullness anteriorly. Laparotomy was performed. A right
ovarian cyst was found to be the cause of the swelling.
It was removed, together with the uterus and other ovary.
The cyst measured 13 x 11 x 8", was unilocular and
filled with straw-coloured watery fluid. Few intra-
cystic papillae were present. The uterus contained
a small polypus in its cavity. The left ovary was small
in size. Microscopically, the endometrium showed senile
changes. The right ovarian cyst was lined by cuboidal
epithelium with few papillae, typical of a serous cyst-
adenoma. The left ovary was atrophic.

No histochemically reactive material was found in
this cyst.

Case 95.

2083/61. (Mrs M. C., 65 years old, para 7 + 1, 18 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of abdominal pain, and stress incontinence,
for the past several months. Vaginal examination
revealed a right ovarian cyst and a smooth swelling in
the pouch of Douglas, which was thought to be the
body of the uterus or left ovarian cyst. Hysterectomy
and bilateral salpingo-oophorectomy were performed.
Both ovaries were replaced by cystic tumours. The
right cyst was 3" in diameter and unilocular. It was
filled with watery fluid and contained few low intra-
cystic papillae. The left cyst was 2" in diameter,

filled with thick gelatinous material and contained few
intra- and extra-cystic papillae. The uterus showed
no abnormality.

Microscopically, the endometrium was inactive and
atrophic. Both ovarian cysts were lined with cuboidal
epithelium and showed the appearances of a typical
papillary serous cystadenoma.

No histochemically reactive materials were found
in these cysts.

Case 96.

3167/61. (Mrs M. P., 77 years old, para 3 + 1, 23 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of a little spotting of blood for the past
1-2 days and dysuria for the past 3 months. Examination
under anaesthesia revealed a bulky uterus (size of a three
months' pregnancy). Curettage yielded scanty scrapings
which proved microscopically to be a cervical polyp.
Sub-total hysterectomy and bilateral salpingo-oophorectomy
were performed. The uterus was the seat of several
fibroids, one of the largest - which was interstitial -
measured 3" in diameter. The right ovary was replaced
by a small, thick-walled cyst 1½" in diameter. It was
unilocular and filled with sebaceous-like material. No
hair could be seen but 2 intra-cystic nodules were
present. The left ovary showed a thick nodular cortex.

Microscopically, the endometrium showed mainly
senile cystic changes, but in a few instances, the glands

showed proliferative activity.   The left ovary showed

grade I cortical stromal hyperplasia and an early

adenofibroma.   The right ovarian cyst was a papillary

serous cystadenoma.

No histochemically reactive steroid material was

found in this cyst.

<div align="center">PRIMARY SOLID CARCINOMA</div>

I. Positive Cases

Case 97.

52/61. (Mrs I. C., 53 years old, para 0 + 0, 3 years

post-menopausal.)

This patient entered the hospital with a chief

complaint of vaginal bleeding for the past month.

Abdominal palpation revealed no abnormality. Per

vaginam, the uterus was bulky, irregular and mobile.

Tttal hysterectomy and bilateral salpingo-oophorectomy

were performed. The right ovary was the seat of a lob-

ulated solid greyish-pink tumour $2\frac{1}{2}$" in diameter. The

left ovary was slightly enlarged and showed a thickened

nodular cortex. The uterus was bulky with multiple

fibroids, the largest was subperitoneal and measured

$2\frac{1}{2}$" in diameter. A small polypus was also present

in the uterine cavity. Microscopically, the endometrium

showed proliferative activity and adenomyosis. The

endometrial polypus contained cystic hyperplastic glands.

The left ovary showed grade 2 cortical stromal hyperplasia

as well as an area of thecomatosis (Photo 143) and a

cortical granuloma. The right ovarian tumour was a well

differentiated adenocarcinoma with an exaggerated stromal
component . Many clusters of stromal cells were
plump and gave positive results with the whole battery
of histochemical reactions (Photos 140, 141, 142).
Control sections were negative.

Case 98.

5039/60. (Miss H.P., 61 years old, para 0 + 0, 10 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of abdominal swelling and pain in the right
iliac fossa for the past month. On examination, a tender,
soft, mobile mass was plapable in the right iliac fossa.
Per vaginam, a mass was felt in the pouch of Douglas and
right appendages. The uterus was erect and mobile.

Total hysterectomy and bilateral salpingo-oophor-
ectomy were performed. The left ovary was replaced by
a large tumour (about 4" in diameter) which was very
adherent to bladder and bowel. It was partly solid,
partly cystic and its cut surface showed extensive
haemorrhage and necrosis. The uterus was small in size
but the endometrium was thick and there were two small
endometrial polypi in the uterine cavity. Microscopically,
the endometrium showed cystic hyperplasia. The right
ovary showed grade I cortical stromal hyperplasia and
a tiny adenofibroma. The left ovarian tumour was
a moderately differentiated adenocarcinoma. Clusters
of theca-like stromal cells gave positive results with
all the histochemical tests. Control sections were negative.

Case 99.

1951/60. (Mrs J. J., 56 years old, para 1 + 0, 2 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of an episode of vaginal bleeding which lasted
for three days, 2 months prior to admission. She also
suffered from intermittent pain in the right iliac fossa
for the past month. On palpating the abdomen, there was
a mass arising from the pelvis, and reaching up to
2-fingers above the umbilicus. Per vaginam, the mass
was filling all the fornices, especially the laterals and
the uterus seemed to be behind the mass.

Total hysterectomy and bilateral salpingo-
oophorectomy were performed. The right ovary was
replaced by a partly solid partly cystic tumour,
measuring 8" x 7" x 5". On cut section, it was com-
posed of greyish-pink solid tissue, with one cystic
cavity filled with infected necrotic tissue. A small
nodule was present on the fimbriated end of the right
Fallopian tube. The left ovary was slightly enlarged
and showed a thickened nodular cortex. The uterus was
bulky and on cut section it showed a profuse endo-
metrium. Microscopically, the endometrium showed cystic
hyperplasia. The left ovary showed grade I cortical
stromal hyperplasia. The right ovarian tumour was
a poorly differentiated adenocarcinoma. Many clusters
of stromal cells, however, were plump, and contained
sudanophillic droplets and gave positive results with

the histochemical tests (Photos 144, 145).   Control
sections were negative.

Case 100.

5920/61. (Mrs J. Y., 72 years old, para 0 + 0, many
years post-menopausal.)

This patient was admitted to hospital with retention
of urine.   She gave history of repeated attacks of
dysuria and frequency for the past 6-7 months.   Abdom-
inal examination revealed the presence of a pelvic tumour
extending to the umbilicus. Per vaginam, the pelvis
was filled by the tumour mass displacing the uterus to
the left side. Hysterectomy and bilateral salpingo-
oophorectomy were performed. The right ovary was
replaced by a large, partly cystic tumour which had
ruptured and become fragmented into greyish-white
necrotic pieces of tissue.   The tumour was adherent
to the bladder and uterus.   The latter was slightly
enlarged and contained a small polypus in its cavity.
The left ovary was not remarkable. Microscopically,
the endometrium showed proliferative activity with some
dilated glands. The outer layers of the myometrium
were invaded by a poorly differentiated adenocarcinoma.
Tumour emboli were also present in the myometrial
lymphatics. The left ovary also contained similar
tumour emboli. The tumour itself consisted of masses
and irregular ascini of malignant cells, with many
areas of haemorrhage and necrosis. Histo-chemical study
revealed the presence of stromal theca-like cells

giving positive results with the whole battery of
tests.   Control sections were negative.

Case 101.

3417/60.   (Mrs M. H., 53 years old, para 1 + 1, 1 year
post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding for the past 10 days.
The abdomen was tense and a rounded mass was felt in the
left iliac fossa and reached up to the umbilicus.

Total hysterectomy and bilateral salpingo-
oophorectomy were performed.   Both ovaries were replaced
by large cyst-like masses, about 4" in diameter each.
They were adherent to the surrounding structures and on
cut sections they were composed of greyish brown friable
tissue with many cystic areas filled with blood and
liquified necrotic tissue.   The uterus was bulky and
on cut section the endometrium was profuse and polypoidal.
A small area at the fundus was greyish white and friable.
Microscopically, most of the endometrium was benign and
showed cystic hyperplastic activity.   Only at that
suspicious area in the fundus there was a malignant
change on top of the cystic hyperplasia (Photo 148).
Both ovarian tumours showed a well-differentiated
adenocarcinoma.   Clusters of plump stromal cells
contained sudanophillic droplets and gave positive
results with the remaining histochemical tests (Photos
146, 147).   Control sections were negative.

Case 102.

5862/60. (Mrs E. C., 72 years old, para 3 + 0, 26 years post-menopausal.)

This patient entered the hospital on 27.11.60 with a chief complaint of abdominal swelling, frequency of micturition and stress incontinence for the past 2 weeks. Her previous admission to hospital was in 1956 when she entered with a chief complaint of post-menopausal bleeding for one week. The uterus was found bulky and restricted in mobility. The right ovary was enlarged, hard and freely mobile. At that time a D. & C. was performed and radium was inserted. Microscopical examination revealed a hyperplastic, benign endometrium.

On examination, the abdomen was very swollen and the umbilicus was everted. A large, abdominal mass was arising from the pelvis and extending up to the costal margin. Vaginal examination yielded no information. Laparotomy was performed with removal of the uterus, a large right ovarian tumour and the other ovary.

The tumour was partly solid, partly cystic and measured 9 x 7 x 7". On cut section it showed several cystic cavities filled with blood-stained fluid. Most of the tumour, however, consisted of greyish-white, haemorrhagic solid tissue. The uterine wall was thickened but the endometrium was thin. The left ovary showed a tiny nodule on its surface. Microscopically, the endometrium showed senile changes with proliferative activity and adenomyosis. The left ovary contained 2 germinal cysts and the nodule on its surface was an

adenofibroma.   The right ovarian tumour was a well-
differentiated adenocarcinoma with a remarkable stromal
component.   Clusters of plump stromal cells, especially
near the epithelial islands, contained sudanophillic
droplets and gave positive results with all the other
tests.   Control sections were negative.

Case 103.

6149/61.   (Mrs A. W., 58 years old, para 3 + 1, 10 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of vaginal bleeding for 4-5 weeks.   Examination
revealed a mass in the lower abdomen. It was cystic,
regular and mobile. Per vaginam, the uterus was bulky.
Total hysterectomy and right ovariotomy were performed.
The uterus was the seat of small interstitial fibroids.
The right ovary was replaced by a smooth, semi-solid
tumour (5 x 3 x 2").   On cut section, it consisted of
soft brain- like tissue.   At one pole, there was
a small cystic cavity showing few papillae and filled with
pus. The left ovary showed no abnormality and was left
behind. Microscopically, the endometrium showed
proliferative activity and some adenomyosis.   The ovarian
tumour was a well-differentiated adenocarcinoma. Histo-
chemical tests for steroid material were all positive in
many theca-like stromal cells (Photo 149). Alkaline
phosphatase, however, was almost absent (Photo 150). Acid
phosphatase and non-specific esterase were abundant but
mainly in the epithelim (Photos 151, 152). Control

sections were negative.

Case 104.

1227/62. (Miss C. R., 64 years old, 15 years post-menopausal.)

This patient entered the hospital with a chief complaint of abdominal swelling and pain for the past 2-3 months.

Abdominal examination revealed an irregular cystic mass arising from the pelvis and reaching the left hypo-chondrium.   Total hysterectomy and bilateral salpingo-oophorectomy were performed.   The left ovary was replaced by a large cystic tumour (about 10" in diameter) which was adherent to the surrounding structures. On cut section it was unilocular and filled with brownish liquified necrotic material. Its wall contained many pieces of yellowish-grey solid tissue.   The right ovary was enlarged and cystic.   On cut section it harboured also a small tumour nodule.   The uterus was small and showed no gross abnormality.

Microscopically, the superficial layers of the endometrium were the seat of a well-differentiated adenocarcinoma whereas the deeper layers showed cystic hyperplastic activity (i.e., a malignant change on top of cystic glandular hyperplasia).   The left ovarian tumour as well as the nodule of right ovary showed an adenocarcinoma with a prominent stromal element. Its pattern was quite different from the endometrial adenocarcinoma.   Numerous fat-laden theca-like stromal cells were revealed by Sudan IV stain.   They reacted positively to the whole

battery of histochemical tests. Enzyme work revealed
absence of alkaline phosphatase. However, acid phos-
phatase and non-specific esterase were abundant,
mainly in the glandular epithelium. Control sections
were negative.

Case 105.

(Positive primary medullary carcinoma in one ovary and
early metastatic adenoacanthoma in other ovary.)
4544/61. (Mrs N. B., 52 years old, para 2 + 0, 1 year
post-menopausal.)

This patient entered the hospital with a chief
complaint of severe abdominal pain, accompanied by low
backache for 10 days. She also had bloodly vaginal
discharge over the past 5 weeks. On examination, there
was tenderness and guarding in both iliac fossae.
Vaginal examination revealed a bulky uterus and tender
fornices. Total hysterectomy and bilateral salpingo-
oophorectomy were performed. The uterus was enlarged
and on section it contained a small submucous fibroid
$\frac{1}{4}$" in diameter. The right ovary was replaced by a large
semi-solid greyish-pink tumour (5" in diameter). On
cut section, it showed extensive necrosis. The left
ovary was slightly enlarged and its cut surface showed
foci of tumour tissue. Microscopically, the endometrium
was the seat of an adeno-acanthoma with a prominent
squamous element (Photo 157). The submucous fibromyoma
was partially covered with squamous epithelium and showed
invasion by adeno-acanthoma in places. The left ovary

was infiltrated by adenoacanthoma with a well-marked
acanthomatous change (Photo 152). The right ovarian
tumour consisted of sheets and masses of malignant cells,
separated by minimal stroma, was completely anaplastic
and showed extensive necrosis (Photo 153). Sudanophillic
droplets and reactive steroid material was found in many
stromal cells which gave positive results with all the
tests (Photos 154, 155, 156). Control sections were
negative. This case could be considered as a primary
medullary carcinoma of right ovary and metastatic adeno-
acanthoma of left ovary, secondary to uterine adeno-
acanthoma.

Case 106.

3496/61. (Mrs M. C., 51 years old, para 0 + 1, L.M.P.
9 days).

This patient entered the hospital with a chief
complaint of feeling a solid lump in the abdomen. For the
past 2 months her periods became irregular and more
frequent (every fortnight, with 3-4 days bleeding in
mid-cycle). Abdominal palpation revealed a firm,
irregular mass arising from the pelvis and reaching up to
the umbilicus. Per vaginam, the uterus seemed attached
to the mass. Total hysterectomy and bilateral salpingo-
oophorectomy were performed. The left ovary was replaced
by a large solid tumour (6 x 6 x 5"). It was lobulated
and brain-like in appearance. Multiple tumour nodules
were present on pelvic peritoneum. The right ovary was
the seat of a thin-walled cyst (3½" in diameter) which

was unilocular and filled with watery fluid.

The uterus was irregularly enlarged by several fibroids, the largest of which was subperitoneal, measured 2" in diameter. A small polypus was present in the uterine cavity.

Microscopically, the endometrium showed a mixed appearance of proliferative and secretory glands. The right ovarian cyst was lined by cuboidal epithelium compatible with a simple serous cyst. The left ovarian tumour showed a well-differentiated adenocarcinoma. Sudanophillic droplets and traces of reactive steroid material were present in a few stromal cells and in necrotic tissue. Control sections were negative.

Case 107.

1611/60. (Mrs M.C., 40 years old, para 3 + 0, L.M.P., 19 days.)

This patient entered the hospital with a chief complaint of swelling in the right groin and discomfort in the right iliac fossa for the past 3 months. On examination, a cystic mass arising from the pelvis was palpable in the right iliac fossa. Per vaginam, the uterus was of normal size and distinct from the cystic mass which arose from the right appendages.

Hysterectomy and bilateral salpingo-oophorectomy were performed. Both ovaries were the site of large, partly cystic, swellings, larger on the right than on the left. On cut section, they showed friable, greyish-pink tissue with several haemorrhagic cavities.

The uterine body was slightly enlarged and contained a small interstitial fibroid.

Microscopically, the endometrium showed secretory changes. Both ovarian tumours showed a poorly differentiated adenocarcinoma, composed mainly of solid sheets of malignant cells with a few irregular ascini. Histochemical study revealed a trace of sudanophillic droplets and reactive steroid material in a few stromal cells. Control sections were negative.

Case 108.

2483/61. (Mrs P.A., 37 years old, para 1 + 0, L.M.P. 2 days)

Unfortunately, the case notes of this private patient could not be obtained. However, the pathological specimen consisted of a uterus with a few seedling fibroids and a small soft polypus in its cavity. The left ovary was the seat of a partly solid, partly cystic tumour, measuring 6 x 5 x 4". Its surface was covered by adhesions and on cut section, it showed yellowish-pink friable tissue and cystic areas which were filled with brown watery fluid and necrotic material. The right ovary showed no gross abnormality. Microscopically, the endometrium was in the proliferative phase of the cycle. The left ovarian tumour was a well-differentiated adenocarcinoma with areas of haemorrhage and necrosis. The right ovary showed several foci of adenocarcinomatous invasion. Traces of sudanophillic droplets and reactive steroid material were found in

a few stromal cells in the left tumour. Control sections
were negative.

II. Negative cases of Primary Solid Carcinoma

Case 109.

6061/61. (Mrs F.W., 66 years old, para 0 + 0, 13 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of abdominal swelling and dragging pain in the
left side for the past 1-2 years. Examination revealed
a central, lower, abdominal mass. Hysterectomy and
bilateral salpingo-oophorectomy were performed. Both
ovaries were replaced by partly cystic tumours,
measuring 6 x 4 x 4" and 3 x 3 x 2". Their walls
contained large pieces of greyish-white friable tissue.
The uterus was irregularly enlarged by several fibroids,
which showed extensive calcareous degeneration.
Microscopically, the endometrium showed senile changes.
Both tumours showed a poorly differentiated adeno-
carcinoma. Histochemical study revealed no reactive
steroid materials in these tumours.

Case 110.

927/61. (Mrs A.F., 47 years old, para 2 + 0, L.M.P.
11 days.)

This patient entered the hospital with a chief
complaint of menorrhagia for the past year and abdominal
swelling for 2 months. Examination under anaesthesia
revealed a cystic mass displacing the uterus to the
right side. Numerous hard masses were also felt in

the right iliac fossa. A laparotomy was performed.
Both ovaries were the seat of large, irregular, semi-
solid tumours, measuring $5\frac{1}{2}$ x 4 x 3" and 5 x 3 x 3".
They were somewhat adherent to the surrounding structures.
Tumour nodules were present in the pouch of Douglas,
posterior vaginal wall and utero-sacral ligaments.
On cut section, both tumours consisted of semi-solid
greyish-pink tissue with numerous cystic and necrotic
areas. The uterus showed no abnormality, but on cut
section, its wall was slightly thickened.

Microscopically, the endometrium was in the
proliferative phase. Sections from both ovarian tumours
showed sheets of malignant cells with few irregular
ascini indicating a poorly differentiated adenocarcinoma
with extensive haemorrhage and necrosis. Both tumours
showed no histochemically reactive steroid materials.

Case 111.

4490/61. (Mrs M.P., 76 years old, para 0 + 0, 28 years
post-menopausal.)

This patient entered the hospital with a chief
complaint of abdominal discomfort and swelling for the
past 6-7 weeks. She gave history of an occasional
vaginal bleeding 9 months prior to admission. On
examination, there was a large, rounded swelling filling
the whole abdomen. Vaginal examination was impossible.
Hysterectomy and bilateral salpingo-oophorectomy were
performed. The uterus was enlarged and contained
a submucous fibroid ($1\frac{1}{2}$" in diameter). The left ovary

was the seat of a large cyst (9 x 8 x 4"). Its surface
was covered with adhesions and on cut section it was
composed of several loculi and semi-solid areas. The
right ovary showed a thickened cortex. Microscopically,
the endometrium showed cystic hyperplasia. The right
ovary showed (grade I) cortical stromal hyperplasia. The
left ovarian tumour was a well-differentiated adenocarcinoma.
No histochemically reactive steroid material was found in
this tumour.

METASTATIC OVARIAN CARCINOMA

I. Positive Cases.

Case 112.

5033/60. (Mrs R. H., 59 years old, para 1 + 0, 12 years
post-menopausal.)

This patient was admitted to hospital with a chief
complaint of vaginal bleeding for the past 6 weeks.
Abdominal examination revealed the presence of ascites
as well as an irregular mass in the left iliac fossa.
Per vaginam, the uterus was enlarged to the size of
6-7 weeks gestation. An ovarian tumour was felt to the
right and behind the uterus. Total hysterectomy and
bilateral salpingo-oophorectomy were performed. Both
ovaries were replaced by semi-solid tumours (about 3"
in diameter each). They were adherent to the side wall
of the pelvis and pelvic colon. Their cut surface
showed greyish-white friable tissue with extensive
necrosis and cystic cavities. The uterus was bulky and
its wall was infiltrated by greyish-white tissue which

partially filled the uterine cavity. Microscopically, the endometrium was the seat of an adenocarcinoma which was invading the myometrium. Both ovarian tumours showed the same type of tumour as the endometrium. Histochemical study revealed weak positive results in some stromal cells and in necrotic tissue.

Case 113.

3223/61.   (Mrs E. G., 57 years old, para 1 + 0, 7 years post-menopausal.)

This patient entered the hospital on 24.6.61 with a chief complaint of vaginal bleeding for the past fortnight. Her previous admission to hospital was in 1958 when she had had a cervical carcinoma. Microscopical examination of the endocervical tissue at that time showed an anaplastic carcinoma and the patient was treated by radium.

On examination, there was an abdominal mass (the size of a three months' gestation) and the uterus was not separable from it.   It was impossible to pass a sound into the uterus or to find the cervical canal. Total hysterectomy and bilateral salpingo-oophorectomy were performed.   The uterus was enlarged and cystic. On cut section its cavity was filled with necrotic material. The cervix was completely destroyed by tumour tissue which extended up through almost the entire uterine cavity and at some points had invaded the entire uterine wall.   The left ovary was replaced by a cystic tumour (2" in diameter).   On cut section, it showed obviously malignant friable tissue.   The right ovary was small

and showed no gross abnormality. Microscopically, the
endometrium, the cervix and the ovarian tumour were all
the seat of an undifferentiated carcinoma. In some areas
it showed a plexiform arrangement, in others a tendency
to acinar formation. The characteristic endocervical
epithelium was identified in a few fields. Sudanophillic
droplets were present in a few theca-like cells in the
stroma of the ovarian tumour. These cells gave all the
tests for steroid material which was also seen in necrotic
tumour tissue. The right ovary was atrophic.

Case 114.

5429/60. (Miss E. S., 61 years old, $2\frac{1}{2}$ years post-
menopausal.)

This patient entered the hospital with a chief
complaint of intermittent vaginal bleeding which began
7 months after the menopause. She also suffered from
abdominal distension and ankle oedema for the past 4 weeks.
She was originally admitted to a medical section
where no medical cause was found to explain her rapidly
accumulating ascites (after tapping). No tumour cells
were detected in the ascitic fluid. She was then
transferred to the gynaecological ward for investigation
of her post-menopausal bleeding. A. D. & C. yielded
profuse fleshy material which looked almost certainly
malignant. At the same time a left ovarian cyst was
palpated. Laparotomy was then carried out immediately
and it seemed that the ascitic fluid was escaping from
an ovarian cyst which had a hole on its surface. Total

hysterectomy and bilateral salpingo-oophorectomy were
performed.   The uterus was bulky and on cut section it
showed a friable papilliferous growth which was filling
the cavity and invading the muscle wall.   The left ovary
was replaced by a partly cystic tumour, measuring 4"
in diameter. Its surface showed adhesions and on cut
section it was composed of solid greyish white friable
tissue, as well as cystic areas filled with liquified
necrotic material. The other ovary showed no gross
abnormality.

Microscopically, the endometrium was the seat of
an invasive, well differentiated adenocarcinoma
(Photo 165).   The left ovary showed few islands of
adenocarcinomatous tissue on its surface. It also
showed a slightly hyperplastic cortex (grade 0) and
a cortical granuloma (Photo 164). The right ovarian
cyst was a duplicate of the uterine adenocarcinoma.
Sudan stain revealed plump theca-like stromal cells
filled with red droplets (Photo 159). These cells
reacted positively to the whole group of histo-
chemical tests (Photos 160, 161, 162, 163).   Control
sections were negative.

Case 115.

1668/60. (Mrs J. W., 46 years old, para 9 + 0, L.M.P.?)

This patient was operated upon on 8.4.60, when
a hysterectomy and bilateral salpingo-oophorectomy
were performed.   The uterus showed no gross abnormality.
Both ovaries were replaced by two semisolid greyish-pink

lobulated tumours.   The cut surface showed gelatinous
and necrotic areas.   Examination of the colon at the time
of operation revealed no lesion.   Microscopically, the
endometrium was in the secretory phase.   Both tumours
were composed of acinar and cystic structures of varying
size and shape lying in a connective tissue stroma.   Most
of the ascini had no epithelial lining, but were filled
with mucin-containing material.   Others had a complete or
partial lining of mucus secreting cuboidal or low
columnar cells.   A good number of the epithelial cells
had a signet ring appearance and were filled with mucin.
The appearance was that of an atypical Krukenberg tumour.

Follow-up of the patient revealed that she was
well and symptomless until 31.5.60.   On 21.6.60 she
developed some free fluid in the peritoneal cavity and
her condition, thereafter, deteriorated.   On 20.9.60
her doctor referred her to the surgeon who diagnosed
the condition as one of multiple carcinomatosis.   His
notes indicated that on abdominal examination, large
masses of tumour could be felt but that on paracentesis
little fluid was obtained.   In October 1960, the patient
died and no post-mortem was performed.

Sudan IV stained sections revealed the presence
of red droplets in a few stromal cells which also
contained some birefringent crystals and gave a trace of
positive results with the remaining tests.

Case 116.

II. Negative Cases.

6093/60. (Mrs J.H., 56 years old, para 0 + 0, 2 years post-menopausal.)

This patient entered the hospital with a chief complaint of vaginal bleeding which occurred in three episodes (a week each) over the past year. On examination, a mass was suspected to be felt above the symphysis pubis. Per vaginam, the uterus was bulky and irregular. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was enlarged, had a neoplastic feel and was bound down to the rectum posteriorly. The appendages were also adherent to the surrounding viscera. Spread had taken place to many of the pelvic lymph nodes which were hard and enlarged. On cut section, the uterine wall was thickened by a polypoidal greyish-white friable tissue which had invaded the muscle layer. Left ovary harboured a small, solid, whitish tumour ($\frac{1}{2}$" in diameter). The right ovary showed no gross abnormality.

Microscopically, the endometrium was the seat of a moderately differentiated adenocarcinoma which had invaded the whole thickness of the uterine wall. Tumour cells were frequently filling the dilated myometrial lymphatics. The right ovary showed Grade I cortical stromal hyperplasia.

The left ovarian nodule was composed of similar adenocarcinomatous tissue. No reactive materials were found in this tumour.

Case 117.

2778/61. (Mrs C.S., 48 years old, para 0 + 0, 9 years
post-menopausal; a pseudo-menopause after radium
treatment.)

This patient entered the hospital in May 1961 with
a chief complaint of vaginal bleeding for the past 2 days.
Her previous admission to hospital was in 1952 when she
had radium treatment for adenocarcinoma of the uterine
body. On examination, the abdomen was so obese and
tender that it was difficult to examine. Total
hysterectomy and bilateral salpingo-oophorectomy were
performed. There was a right large ovarian cyst
(4" in diameter). Its surface was covered with some
adhesions and on cut section it was filled with papillary
necrotic tissue and dirty fluid. The uterus was bulky and
on cut section its wall was invaded by greyish-white
friable necrotic tissue. The left ovary was almost
completely fibrosed.

Microscopically, the endometrium was the seat of
a well-differentiated adenocarcinoma invading the
myometrium. The left ovary showed massive hyaline fibrosis.
The right ovarian tumour was a duplicate of the uterine
adenocarcinoma. No histochemically reactive materials were
found in this tumour.

Case 118.
2752/61. (Mrs M. W., 46 years old, para 6 + 1, L.M.P.,
8 days.)

This patient entered the hospital on 19.4.61

because of an episode of heavy vaginal bleeding for 3 weeks in March 1961. In April and May, however, she had 2 normal periods. In April 1959 the patient had had a left mammary cancer which was treated by radical mastectomy followed by x-ray therapy.

Vaginal examination revealed a bulky uterus and mobile appendages. On 17.5.61 a diagnostic curettage was carried out and microscopical examination of the curettings revealed an undifferentiated adenocarcinoma. On 7.6.61 total hysterectomy and bilateral salpingo-oophorectomy were performed. It was a most technically difficult operation, owing to massive adhesions. The uterus was bulky, but showed no naked eye evidence of malignancy. Both ovaries were slightly enlarged and cystic. Microscopically, the endometrial stroma was the seat of an alveolar cell carcinoma which showed no relation to the endometrial glands or surface epithelium which showed proliferative changes. The myometrium was infiltrated by the same type of growth and many tumour emboli were seen inside dilated myometrial lymphatics. Both ovaries were diffusely infiltrated by the alveolar cell carcinoma.

Histochemical study of both ovarian tumours revealed no reactive steroid material.

DERMOID CYSTS

I. Positive Cases

Case 119.

5764/61. (Mrs M., 50 years old, para 1 + 0, 1½ years

post-menopausal.)

This patient entered the hospital with a chief complaint of intermittent vaginal bleeding for the past 2 months. Abdominal examination revealed no abnormality. Per vaginam, the uterus was bulkier than normal and there was indefinite swelling in the appendages. Hysterectomy and bilateral salpingo-oophorectomy were performed. The left ovary was replaced by a smooth, opaque, white cyst, about 3" in diameter. On opening it contained sebaceous material, hairs, bone and a row of 4 incisor teeth fixed on a bony structure resembling an alveolar margin. The uterus was slightly enlarged and contained a small interstitial fibroid ($\frac{3}{4}$" in diameter). The endometrium was profuse. The right ovary showed a thickened cortex.

Microscopically, the endometrium showed proliferative activity. The right ovary showed grade I cortical stromal hyperplasia. The left ovarian cyst was a benign dermoid cyst. Sudanophillic droplets and reactive steroid materials were present in many stromal cells underneath the epithelium. Control sections were negative.

Case 120.

766/61.

(Mrs M.I., 51 years old, para 4 + 1, L.M.P., 22 days.)

This patient was admitted to hospital on 11.2.61 because of heavy irregular periods over the past year. Her previous admission to hospital was on 17.8.60 when

a diagnostic curettage was performed and a cervical
mucous polyp was removed.   The curettings showed secretory
changes.   At that time she was noted to have a swelling
in the left appendages.   Following discharge, she
continued to have heavy frequent periods and was re-admitted.

Total hysterectomy and bilateral salpingo-oophorectomy
were performed.   The uterus was bulky and its wall thickened.
There was a left ovarian tumour $1\frac{3}{4}"$ in diameter.   It was
opaque-white in colour and filled with pultaceous material
containing hairs.   The right ovary contained 2 tiny
cysts and showed a thicked cortex in places.   Micro-
scopically, the endometrium showed proliferative changes
and slight adenomyosis.   The right ovary showed 2 foll-
icular cysts, a hyperplastic cortex (grade 0) and
a cortical granuloma.   The left ovarian cyst was lined
by skin and its appendages showing some inflammatory
changes and foreign body giant cells.   Sudan IV stain
revealed the presence of red droplets in many stromal
cells rupturing through the surface epithelium.   These
cells gave positive results with the whole battery of
histochemical tests.   Control sections were negative.

II. Negative Cases

Case 121.

4684/61.   (Mrs A.M., 50 years old, para 1 + 0, 3 years
post-menopausal.)

This patient entered the hospital with the chief
complaint of pain and swelling of left ankle. Abdominal
examination revealed no lumps or tenderness. Per vaginam,

there was a cystic swelling behind the uterus and to the left of it. Right appendages showed no abnormality. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The left ovary was replaced by a rounded smooth cyst measuring 4" in diameter. On section it was unilocular and contained sebaceous material and hairs. The uterus showed no abnormality. The right ovary showed a thickened prominent cortex.

Microscopically, the endometrium showed some proliferative activity. The right ovary showed grade 2 cortical stromal hyperplasia. The left ovarian cyst was lined by stratified squamous epithelium with hair follicles and sebaceous glands. No reactive materials were found in this cyst. Negative dermoid cyst.

Case 122.

3228/61. (Miss D.T., 52 years old, para 0 + 0, L.M.P. 27 days.)

This very obese patient had no complaint except backache which she felt was due to her obesity. During routine examination, her own doctor noted the presence of a mass in lower abdomen and referred her to the gynaecological out-patient clinic. On examination, a firm mass was arising out of the pelvis and extending up to the umbilicus. Hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was slightly enlarged and contained 2 interstitial fibroids, each measuring almost 1" in diameter. Two smooth and soft endometrial polypi were present in the uterine cavity.

Both ovaries were the seat of a pedunculated cystic
opaque-whitish tumours, each measuring about 5" in
diameter. They were filled with sebaceous material and
hairs. Microscopically, the endometrium showed
proliferative activity and adenomyosis. Both cysts were
lined with stratified squamous epithelium containing
hair follicles and sebaceous glands. Adipose tissue was
also present. No sudanophillic droplets or reactive
steroid materials were found in the cysts.

DISCUSSION

As already stated in Part I of this thesis the
stroma cells of the ovary are known to possess the ability
of differentiating into theca cells, granulosa cells,
lutein cells and ordinary connective tissue fibroblasts.
The factors responsible for this differentiation are not
fully known but pituitary gonadotrophins definitely play
a part.

The intensive participation of the stromal tissue
of the ovary in the formation of all ovarian neoplasms,
even those of a metastatic nature is far beyond doubt.
The connective tissue portion of these tumours could be
formed by the active hypertrophy of the stromal tissue
of the ovary itself and it is thus easily understandable
that the theca cells originating from the ovarian conn-
ective tissue are to some extent represented in the stroma
of all ovarian tumours. Therefore, these tumours might
secrete amounts of ovarian oestrogens (Turunen, 1955).

As Morris and Scully state (1958) "there is nothing

illogical about the concept of tumours with functioning

stroma. In bone, neoplasia may stimulate the osseous

mesenchyme to its specific function of bone formation.

It would not be surprising then if a similar sequence of

events took place in the ovary with stimulation of the

mesenchyme to its specific function of differentiating

into hormone producing theca or lutein-like cells".

They emphasize that "An attempt must be made in the future

to distinguish tumours which have a thecoma-like stroma

from those with a fibroma-like stroma".

In a study of the post-menopausal endometrial

hyperplasia, Novak (1956) found that 11% of cases had

ovarian neoplasms other than the granulosa theca group

and 60% had ovarian cortical stromal hyperplasia.

The part played by the theca cells in the secretion

of oestrogens has been conslusively proved by Westman

(1935) who removed the granulosa cells from the follicles

of the normal ovary by suction with a pipette and observed

that oestrogen secretion still continued.

In order to confirm the presence of oestrogen-

secreting cell types in the stroma of ovarian neoplasms

this histochemical study was undertaken.

Like Turunen, I was unable to find cell types

corresponding to granulosa cells or tissue corresponding

to a granulosa cell tumour in the stroma of any of the

ovarian neoplasms (other than the granulosa-theca group).

On the other hand, cells containing histochemically

reactive steroid materials, which were obviously theca

cells, were found in the connective tissue of many ovarian neoplasms in greater or smaller amounts.

In the 8 cases of granulosa cell tumour, the granulosa cells contained no reactive steroid material unless luteinized (cases No.2 and 6.).   Conversely, large amounts of reactive material were present in the surrounding theca-like connective tissue cells.   Vaginal bleeding was the chief complaint in all cases.   The endometrium showed changes characteristic of oestrogen stimulation even in the 2 cases showing luteinization.   This confirms the observation once made by Novak (1958) that luteinized granulosa tumours may be morphologically, but not functionally like lutein cells. He suggests the term pseudolutein to describe the cells of such tumours.

The histochemical results are also in agreement with previous studies of a similar nature.   Greenblatt et al (1939) found birefringent crystals only in stromal theca-like cells of three granulosa-cell tumours.   McKay et al (1949) studied three granulosa cell tumours histochemically. Reactive steroid materials were found only in theca-like stromal cells in 2 oestrogenic tumours.   The third tumour contained no reactive materials and was non-oestrogenic.

In Cases No.6 and 7, the stromal theca cells contained only a little steroid material (in the precursor form), as the tests for the more mature steroids (Ashbel-Seligman) and fluorescence tests) were negative. Consequently in Case 7 the endometrium showed only some

proliferative activity and the oestrogen excretion in urine was within normal post-menopausal levels. Vaginal bleeding in both cases could have been the result of oestrogen withdrawal following atrophy and fibrosis of some of the oestrogen-producing theca cells.

Varying grades of cortical stromal hyperplasia were present in all the cases where the other ovary was available. These hyperplastic changes could have also contributed to stimulate the endometrium. Their degree of activity was more or less parallel to the amount and degree of activity of theca cells in the granulosa cell tumours. For example, in case No.1, 2, 3, 4 and 8, where the tumours showed an active thecal element (giving strongly positive results with all the tests) the contra-lateral ovary showed advanced hyperplasia, cortical granulomas and sometimes thecomatosis. On the other hand, in cases No.6 and 7, where the thecal component was scanty and not so active, the contra-lateral ovary showed less marked hyperplasia. This can be easily explained by the fact that theca cell activity and cortical stromal hyperplasia are regulated by a common denominator - the pituitary.

Cases No.9 and 10 were typically active thecomas containing much larger amounts of reactive steroid material than in either of the granulosa cell tumours. This confirms the findings of Giest (1935) who found that the hormone content, of the one case of thecoma examined, was far greater in amount than reported for

granulosa cell tumours. The findings are also in agreement with the results of the histochemical study of McKay et al. The endometrium showed evidence of oestrogen stimulation in the 4 thecoma cases and vaginal bleeding was the chief complaint in three of them. In Case No.11 the patient presented by loss of weight and tiredness. The possibility of a malignant thecoma was first suspected and later confirmed by the strongly positive histochemical tests. Although the endometrium did not manifest frank hyperplasia, yet it showed proliferative activity and adenomyosis. There is the possibility that it might not have enough time to be strongly stimulated. Alternatively, one may cite Novak to the effect that "after the menopause, as before, the endometrium appears to vary in the degree of its sensitivity or its refractoriness to the oestrogenic stimulus and these variations are often seen in different parts of the same endometrium".

Case No.12 is an example where the thecal component, although prominent, was passing into the stage of inactivity and fibrosis (as proved by the tests). The urinary oestrogen excretion was in accord with the histochemical results being barely raised above the normal post-menopausal level. Cortical stromal hyperplasia of the opposite ovary was found in all cases.

Most workers do not differentiate between theca cell tumours and fibromas with thecomatous elements. However,

this was easily attained by means of the histochemical
tests.   In the 7 cases of fibroma with thecomatous
elements, reactive steroid material was much less in
amount, being present only in scattered groups of theca
cells.   In addition, the reactive material was mainly
present in the precursor form (very weakly positive or
negative Ashbel-Seligman and fluorescence tests).

In Case No.19, enzyme study revealed absence of
alkaline phosphatase, whereas acid phosphatase and non-
specific esterase were present in traces.   It seems
that these enzymes are more related to the manufacture of
mature hormones (and not their precurosrs) which were
absent in this case.   However, in all 7 cases the
endometrium showed evidence of oestrogen stimulation
and in 5 of them there was history of vaginal bleeding.
Cortical stromal hyperplasia was present in minor degrees.

In all cases of ordinary ovarian fibroma, the whole
battery of histochemical tests was negative. With one
exception in post-menopausal patients, the endometrium
showed no sign of oestrogen stimulation, being senile
and atrophic (Cases No.20-24).   The exception was a case
of uterine carcinoma (Case No.25).   Vaginal bleeding
was a chief complaint in this latter case and in case 24
(due to a large submucous fibroid.).   Cortical stromal
hyperplasia of the other ovary was practically absent
except in the case of uterine cancer.

Enzyme study was also carried out in Case No.23

which gave negative results for the three aforementioned enzymes. This conformed with the absence of reactive steroid material in this case and presented a further evidence for its inactivity.

In the group of premenopausal patients, the endometrium was quite undisturbed (cases No.26, 27, 30, 31, 32 and 33) and in Case 27 the urinary oestrogen excretion was not increased. However, cases No.28 and 29 (in the 5th and 6th decades) showed persistent proliferative endometrial activity. This was apparently due to cortical stromal hyperplasia in the former and follicular cyst in the latter. Vaginal bleeding in Cases 26 and 27 was due to submucous fibroids.

Therefore, the histochemical tests enable one to differentiate active thecoma, fibroma with thecomatous elements and ordinary fibroma.

Whilst Brenner cell tumours are not usually regarded as having endocrine function, reactive steroid materials were found in 2 out of the 3 cases examined. Both cases (Cases 34 and 35), however, contained more precursors than actual hormones (weakly positive Ashbel-Seligman and fluorescence tests). The reacting theca like cells were present in the stroma near the epithelial islands. Case No.34 showed a hyperplastic endometrium. Although a cervical polypus was present in this case, one cannot disregard the hyperplastic endometrium as a cause of the post-

menopausal bleeding. In case No.35 it was difficult
to judge the condition of the endometrium, being pressed
upon by the large endometrial polypi and the submucous
fibroid. Cystic hyperplastic glands were, however,
recognised in the endometrial polypi. Case No.35
gave negative results. The associated endometrium showed
no abnormal stimulation and the tumour was functionally
inactive. In all the three cases cortical stromal
hyperplasia of the other ovary was minimal.

The results of the histochemical study of
pseudomucinous tumours are not so easy to interpret.
However, positive cases can be divided into 2 groups:

Group I - includes 10 post-menopausal cases, in
which the stroma harboured theca-like cells which reacted
positively to the whole battery of tests (cases No.37-43
and 48-50). The endometrium showed varying degrees of
oestrogen stimulation. Only three cases, however,
presented with vaginal bleeding (Cases No.39, 40, 41).
In this context Novak says "Many of us are beginning to
feel that oestrogen production may continue in the post-
menopausal era even in the absence of any bleeding".
In Case No.40 the oestrogen excretion in urine was
increased but fell to normal levels after removal of the
tumour. With the exception of Case No.38, the opposite
ovary, when available, showed stromal hyperplastic changes.
Such changes were greatly advanced (as confirmed by the
succinic dehydrogenase test in Cases No.39 and 41).

Case No.40 illustrates a good example of thecomatosis.

Case No.39 was also investigated for the presence of enzymes. Alkaline phosphatase was abundant in the stroma (the same site where reactive steroid material was found). This is in agreement with the results of McKay et al (1961) in their histochemical study of the adult human ovary. They found alkaline phosphatase activity in theca interna and lutein cells during steroid hormone synthesis and relative inactivity in the same cells when hormone synthesis is absent or minimal. Acid phosphatase and non-specific esterase, however, were mainly present in the pseudomucinous epithelium where they might be concerned with other metabolic processes. The latter 2 enzymes have not been as thoroughly explored as alkaline phosphatase and as already mentioned "the precise role of all these enzymes in the chain of reactions leading to steroid hormone synthesis remains to be demonstrated". (McKay et al, 1961.)

Group II - includes 4 premenopausal cases which reacted rather weakly to the histochemical tests:

a) Cases 46 and 47, in which the endometrium showed evidence of oestrogen stimulation.

b) Cases No.44 and 45 in which the endometrium showed normal secretory changes and was practically undisturbed by the presence of the tumour. In these cases it is possible that the corpus luteum progesterone masked any oestrogen effect caused by the stromal theca cells in the ovarian neoplasm. Perhaps also it is

wrong to assume that thecal cell activity indicates the production of only an oestrogenic steroid (Smith, 1942).

Twenty-three cases of pseudomucinous cysts gave negative histochemical tests. They can be divided into two groups.

Group I - includes 13 post-menopausal cases:

a) Cases No.61 and 62, where the endometrium showed quiescent senile changes and the contra-lateral ovary was atrophic.

b) Cases No.63-73 where the endometrium showed varying degrees of oestrogen stimulation and the contra-lateral ovary was the seat of cortical stromal hyperplasia (and sometimes thecomatosis and cortical granuloma). In Case No.66, however, the other ovary was completely atrophic. Vaginal bleeding was present in 4 cases (64, 68, 69 and 73). In this subgroup of cases there is the possibility that the stromal theca cells might have undergone atresia (just as they do in the normal ovary) before the stimulated endometrium had time to retrogress. Also the presence of stromal hyperplastic changes in the other ovary could have contributed to endometrial activity in most of these negative cases. It must be remembered, however, that the stromal thecal elements in the ovarian neoplasms are so irregularly distributed that they can be easily missed. Although several blocks, up to 10 in some cases, were taken from different parts of these (usually large) tumours, yet, a thorough examination might require the whole tumour to be cut into

blocks and sections.   Such a process involving
thousands or even millions of sections is practically
impossible.

Group II - includes 10 negative cases mostly
premenopausal (in the 5th decade of life):

a) Cases No.51-54 in which the endometrium was in
the normal phase of the cycle although some of them had
irregular, heavy periods.

b) Cases No.55-58 in which the endometrium was
hyperactive and thecontralateral ovary showed follicular
cysts and/or some degree of stromal hyperplasia.

c) Cases No.59 and 60 showing proliferative
endometrium 6 and 18 months after the menopause. The
other ovary contained follicular cysts which might be
responsible for endometrial stimulation.

All the above-mentioned explanations can be applied
to the remaining types of tumours.

Twenty-four cases of serous neoplasms were available
for the histochemical study. Fourteen of them harboured
theca-like stromal cells which gave positive results.
They can be divided into 2 groups.

Group I - includes 10 cases (No.74, 75 and 77-84)
mostly post-menopausal and, showing varying degrees of
endometrial activity. Most of these cases were malignant
and bilateral. Therefore, cortical stromal hyperplasia
of the opposite ovary could not be considered.

Group II - includes 4 premenopausal cases (No.76,85,
86 and 87) which reacted very weakly to the histochemical

tests. The endometrium was in the normal phase of the cycle and apparently not affected by the tumour. Perhaps, also, lesser grades of thecal cell activity yield sub-threshold oestrogenic steroid for the endometrium (Smith, 1942).

Nine cases gave negative results:

Group I - (Cases No.88, 89, 90, 94, 95).

Both the endometrium and the opposite ovary showed senile atrophic changes.

Group II - Cases No.91, 92, 96. The endometrium showed some post-menopausal activity and the other ovary stromal hyperplasia. Case 93, however, was at the time of the menopause with menstrual irregularities, proliferative endometrium and bilateral simple serous tumours.

Fifteen cases of primary solid carcinoma have been studied histochemically. Twelve cases contained stromal cells which gave positive results. These fall into two groups:

Group I includes 9 post-menopausal cases (97 to 105) in which the endometrium showed strong evidence of oestrogen stimulation. Vaginal bleeding was the chief complaint in 5 of them (cases 97, 99, 101, 103, 105). As most of these tumours were bilateral, cortical stromal hyperplasia was found only in 3 cases where the other ovary was available and fit for examination (cases 97, 98, 99). Cases 103 and 104 were also studied for enzymes. In both, alkaline phosphatase was almost absent, whereas, acid phosphatase and non-specific phosphatase were abundant in

the epithelium. Thus, the correlation between reactive steroid material and alkaline phosphatase could not be considered. However, the results conform with the observations of previous workers that alkaline phosphatase is usually absent in malignant tissues whereas acid phosphatase and non-specific esterase are in excess (McKay, et al, 1956).

Group II includes three premenopausal patients which gave a trace positive histochemical tests. The endometrium was in the normal phase of the cycle (unaffected by the tumour).

Three cases gave negative histochemical tests. Cases 109, and 110 were bilateral tumours and their endometria showed normal changes according to their age. Case 111, however, showed endometrial cystic hyperplasia and grade I corticle stromal hyperplasia of the opposite ovary.

Seven cases of metastatic ovarian carcinoma were also studied histochemically. Four of them gave positive results and fell into two groups:

Group I includes 3 post-menopausal cases (112,113, 114) in which the endometrium (or endocervix in case 113) was the primary site.

Group II includes one premenopausal case (115) which gave trace positive results. The uterus was not the primary site of malignancy and the endometrium was apparently in the normal phase of the cycle.

Three negative cases were secondary to a uterine

carcinoma. Cortical stromal hyperplasia was found in Case 116. In case 117, however, the opposite ovary was completely fibrosed most probably due to a previous irradiation therapy. The third negative case (118) was secondary to a breast carcinoma. Although the endometrial stroma was invaded by cancer cells, yet the endometrial glands were apparently in the normal phase of the cycle.

Four cases of dermoid cysts were included in this study.

Two cases reacted positively to the histochemical tests. In case 119 there was history of post-menopausal bleeding and the endometrium showed proliferative activity. Cortical stromal hyperplasia of the opposite ovary was also present. Case 120 was in the menopausal period of life, had menstrual irregularities and persistently proliferative endometrium. The other ovary was the seat of two follicular cysts.

The two negative cases were post-menopausal. The endometrium showed proliferative activity in both of them. Cortical stromal hyperplasia was present in Case 121 (Case 122 being bilateral).

SUMMARY

One hundred and twenty-two consecutive cases of ovarian neoplasms have been studied histochemically for the presence and localisation of steroid hormones and their precursors. Of them, 5 cases were suitable also for investigating alkaline phosphatase, acid phosphatase and non-specific esterase activity. Succinic dehydro-

genase was also studied in a few cases.

The results have been correlated with the histo-
logical appearance of the endometriu, vaginal bleeding
and urinary oestrogen excretion (whenever available).

In general, reactive steroid material was present
in theca cells of thecomas, theca-like cells of
granulosa-cell tumours and luteinized cells. This
confirms the consensus that the thecal component of
granulosa-cell tumours, rather than the tumour cells
themselves, are concerned in hormone production.

The histochemical tests could differentiate an
active thecoma from a fibroma with thecomatous elements
and ordinary inactive fibroma.

Steroid substances were also present in stromal
theca-like cells in a good number of all the other types
of ovarian neoplasms.

A direct correlation was found between the histo-
logical state of the endometrium and the presence or
absence of reactive steroid material in the neoplasm,
particularly in the post-menopausal cases.

Cortical stromal hyperplasia of the contra-lateral
ovary explained the cause of endometrial activity in those
cases where the neoplasms gave negative results.

It was noticed that in the reproductive period
of life, the stroma of the ovarian neoplasms, other
than the granulosa-theca group, does not usually acquire
functioning activity and if it does, this is usually
not enough to disturb the endometrium. (Weakly positive
results.)

In the few cases which were suitable for enzyme study, there was a correlation between the presence or absence of reactive steroid material and alkaline phosphatase in the stroma of three benign neoplasms. However, in two cases of primary adenocarcinoma, alkaline phosphatase was absent while steroid material was present in the stroma. This is in agreement with the observations of previous workers that alkaline phosphatase is absent in malignant tissues, whereas acid phosphatase and non-specific esterase are in excess.

The significance of the presence of acid phosphatase and non-specific esterase in the pseudomucinous epithelium remains to be elucidated.

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PHOTO 1.   (660/62)

Ovarian cortical stromal hyperplasia in a patient aged 75 years, with uterine carcinoma.

Note the wide dense cortex.

PHOTO 2.   (417/62)

Thickened hyperplastic cortex in a post-menopausal patient with endometrial cystic hyperplasia.
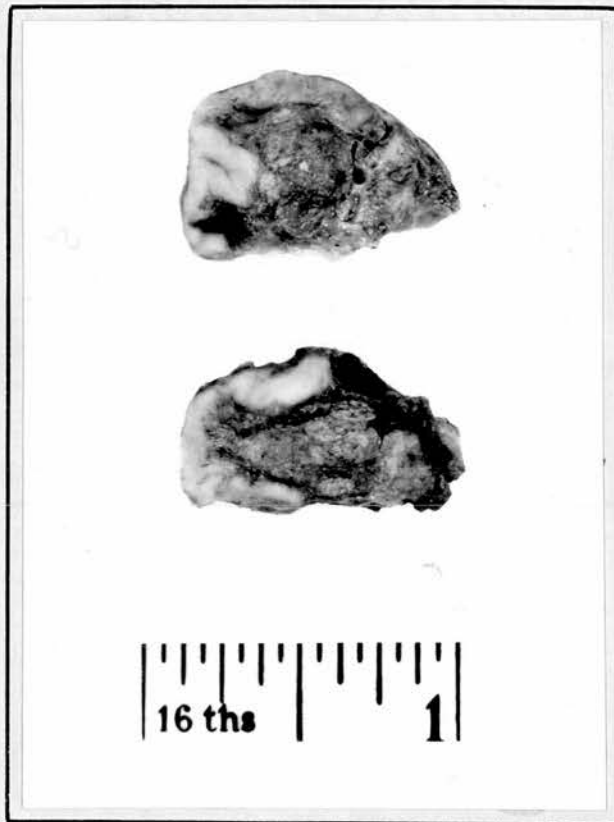
Photo 1.

Photo 2.

PHOTO 3.

    Grade O cortical stromal hyperplasia.

    Note the thin cortex. (H. & E.)

PHOTO 4.

    Grade I cortical stromal hyperplasia. Most of the
cortex is thickened. The medulla is not involved.
(H. & E.)
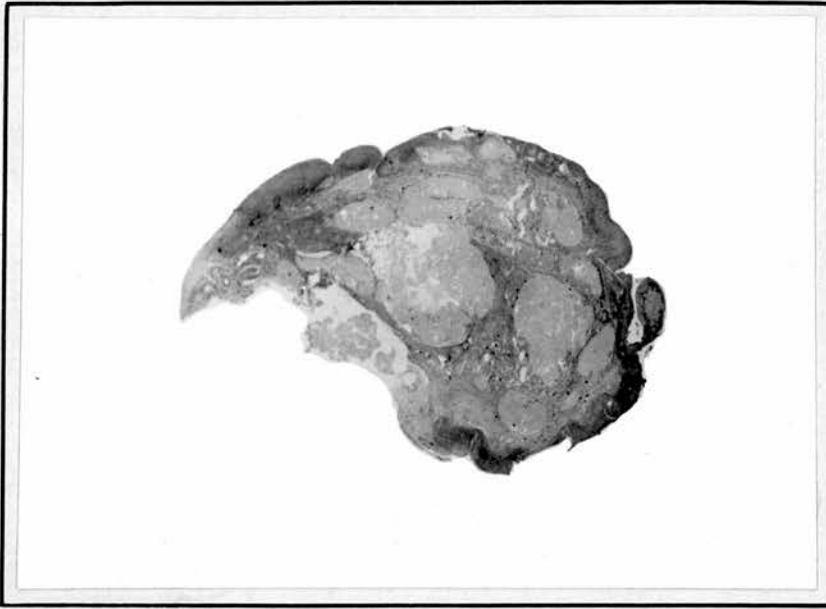
Photo 3.

Photo 4.

PHOTO 5.

Grade II ovarian stromal hyperplasia. The cortex
and part of the medulla are hyperplastic (taking the
HX stain in contrast to the inactive hyaline fibrous
tissue.)

PHOTO 6.

Grade III ovarian stromal hyperplasia. Most of
the cortex and medulla are hyperplastic. (H. & E.)
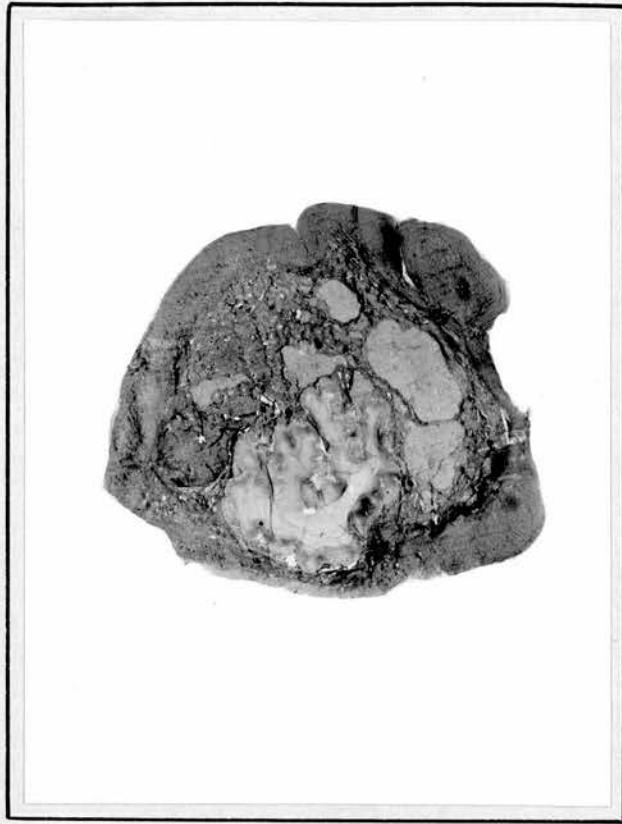
Photo 5.
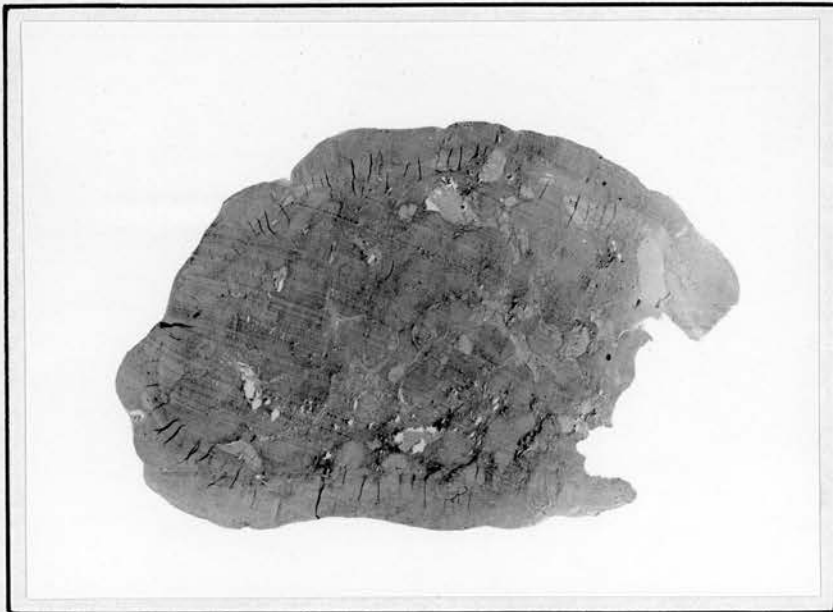
Photo 6.

PHOTO 7.　X 250.

　　An ordinary fibroma showing thin fibroblasts in
the characteristic feather-stitch arrangement.　(H. & E.)

PHOTO 8.　X 160.

　　Adenofibroma.　Ascinar structures amidst the
fibroblasts.　(H.& E.)
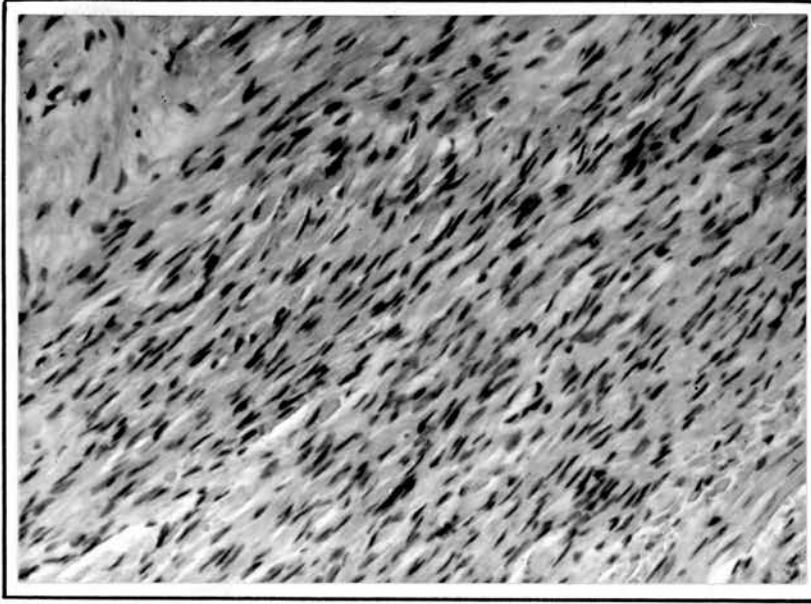
Photo 7.   X 250
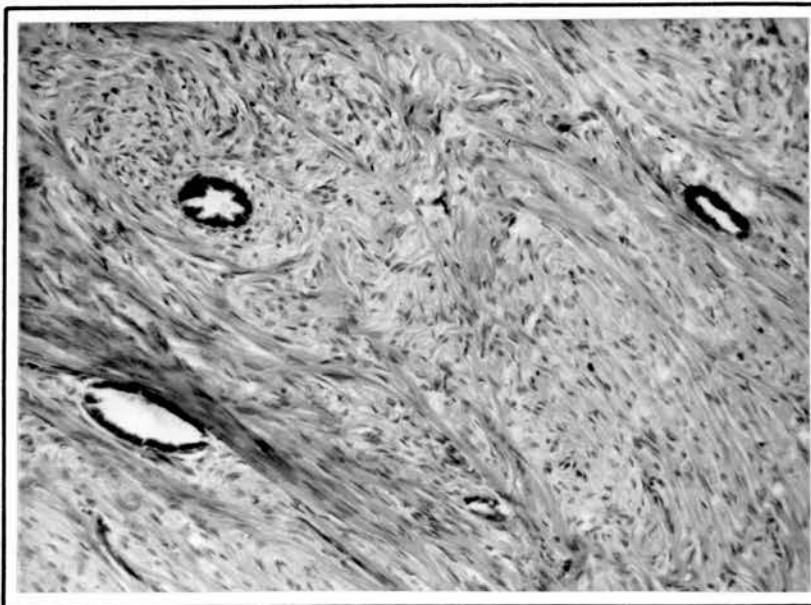
Photo 8.   X 160

PHOTO 9.   X 310.

Ovarian fibrosarcoma.

Note the irregularity in size and shape of the
nuclei, the mitotic figures and the giant cells.
(H. & E.)
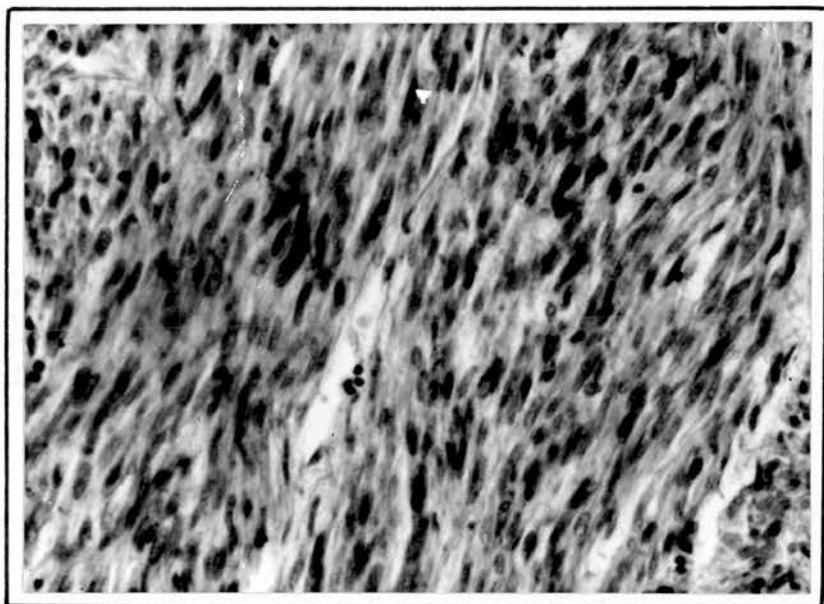
Photo 9.   X 310

PHOTO 10. X300.

    Case 1. (A.7567.)

      Fibroma with thecomatous elements. The theca
cells are plump and vacuolated. (H. & E.)

PHOTO 11. X 160.

      Endometrium of the above case, showing cystic
glandular hyperplasia. (H. & E.)

Photo 10. X 300
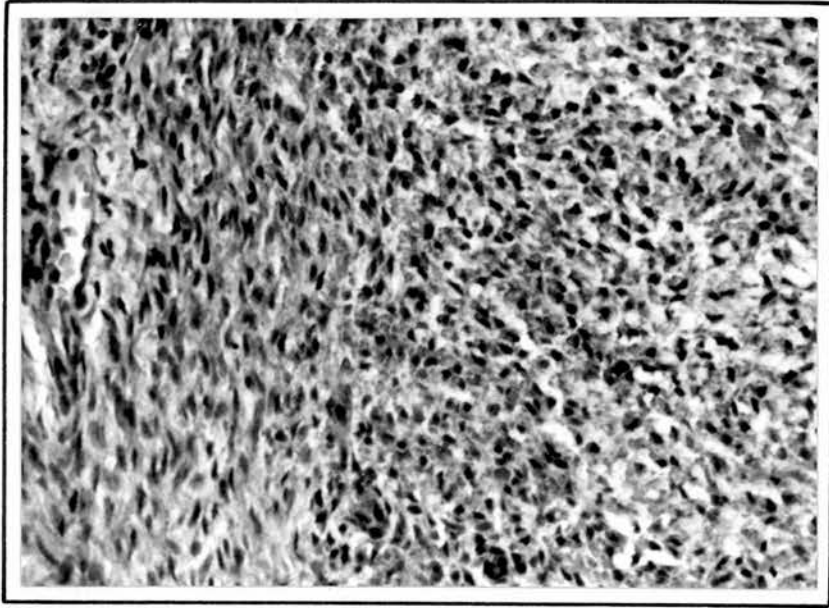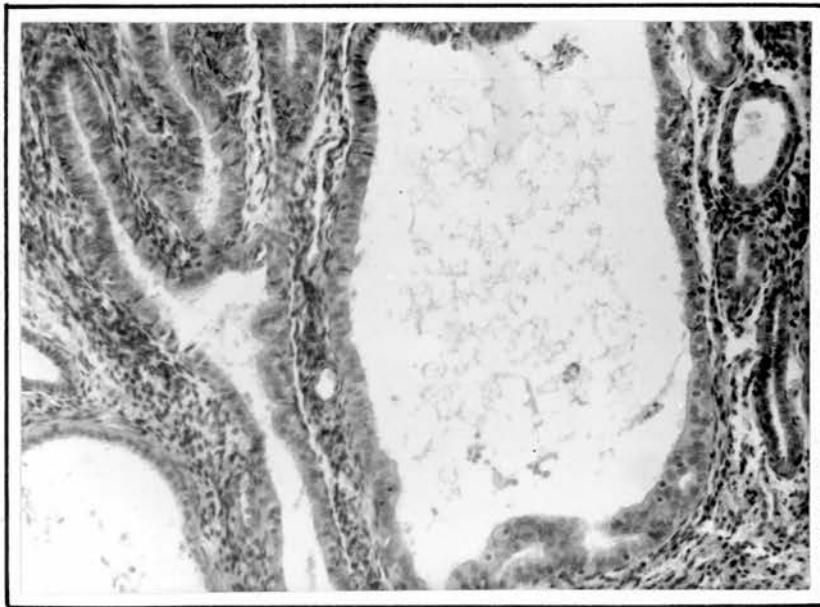
Photo 11. X 160

PHOTO 12. X 300.

Case 2. (E.310).

Cortical granuloma in the other ovary.

Note the giant cell in the centre.   (H. & E.)

PHOTO 13. X 180.

Endometrium of the above case, showing cystic
glandular hyperplasia.   (H. & E.)
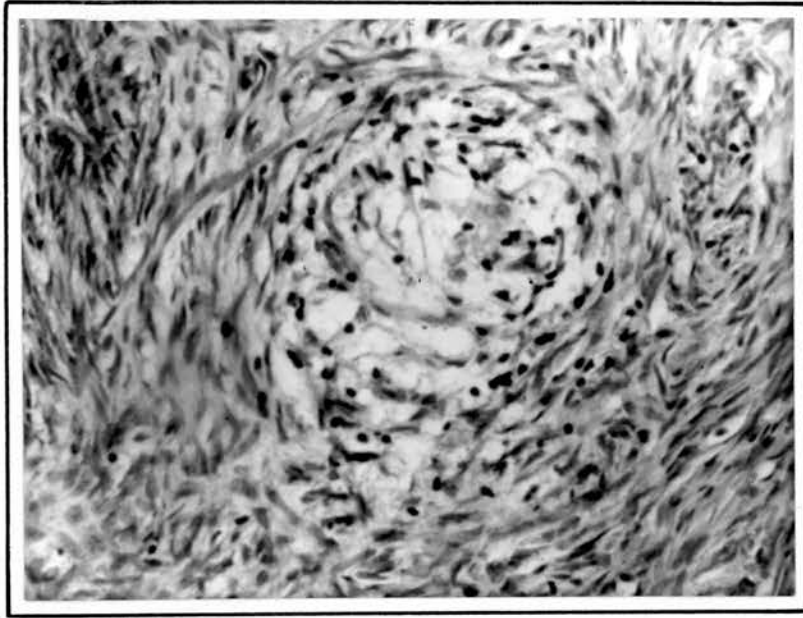
Photo 12.   X300
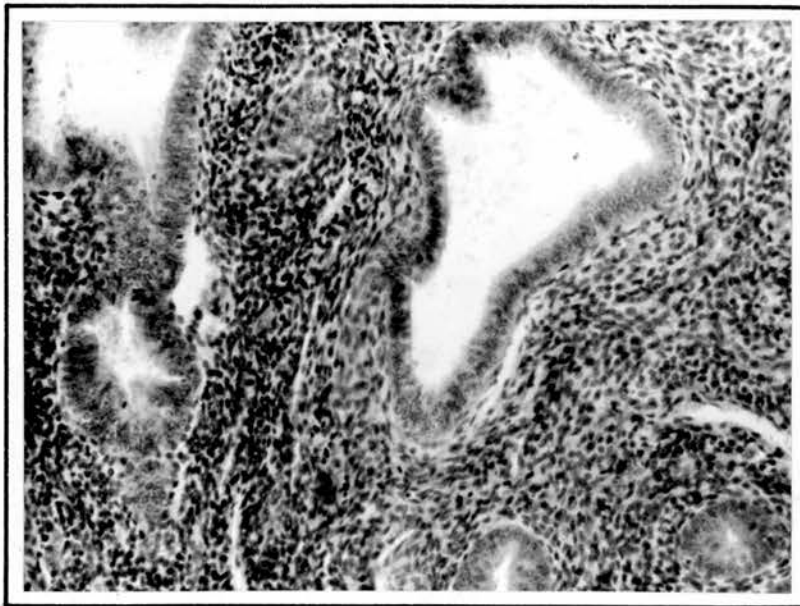
Photo 13.   X180

PHOTO 14.   X 300.

   Case 3. (E.3871).

   Thecomatosis, passing into a stage of cortical granuloma.

   Note the giant cell in the centre.   (H. & E.)

PHOTO 15. X 180.

   Endometrium of the above case, showing active proliferation.   (H. & E.)
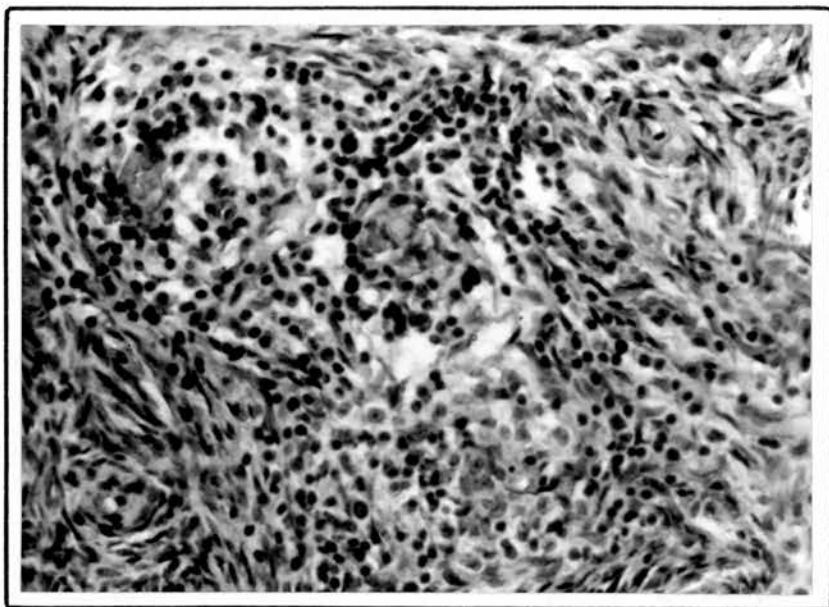
Photo 14.   X300
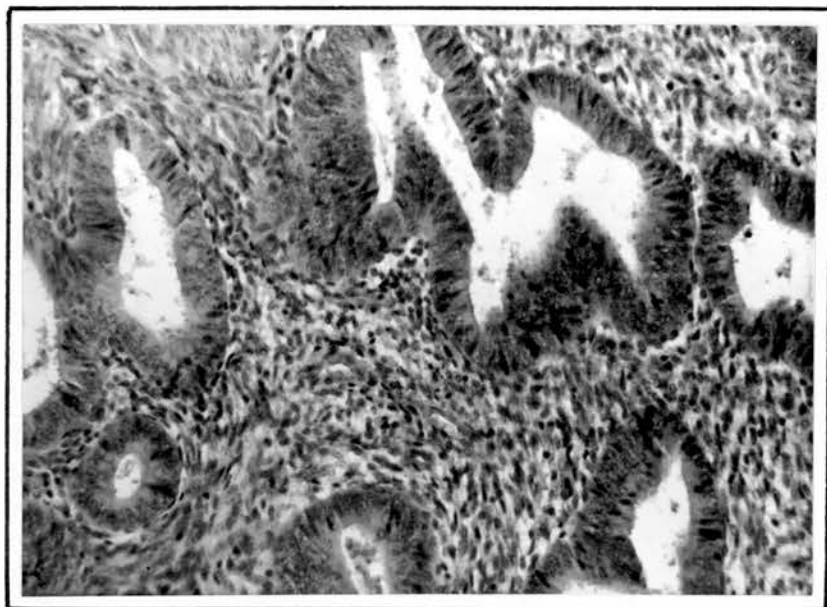
Photo 15.   X180

PHOTO 16.   X 230.

    A.5477.

      Hyaline plaques in a thecoma.   (H. & E.)

PHOTO 17.   X 220.

    Case 1.   (D.7582)

      Thecoma.   The cells are plump and mostly
vacuolated.   (H. & E.)
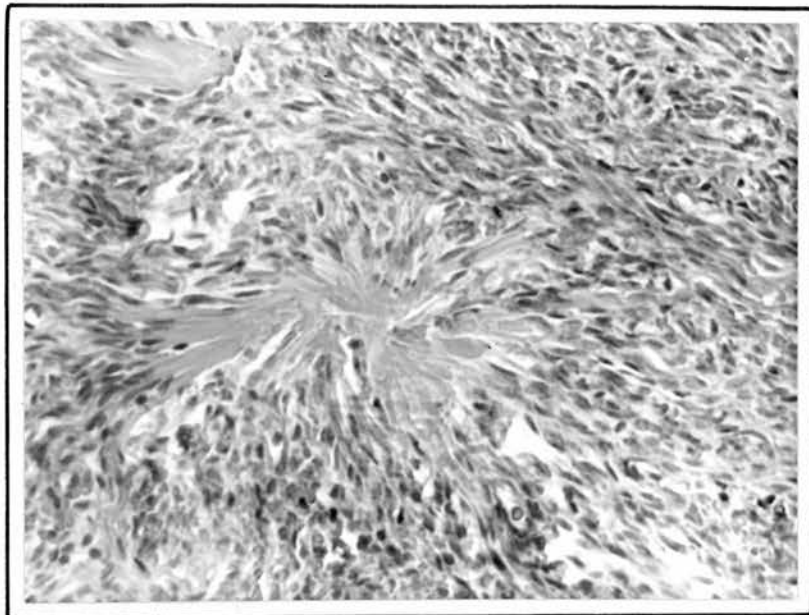
Photo 16.   X230
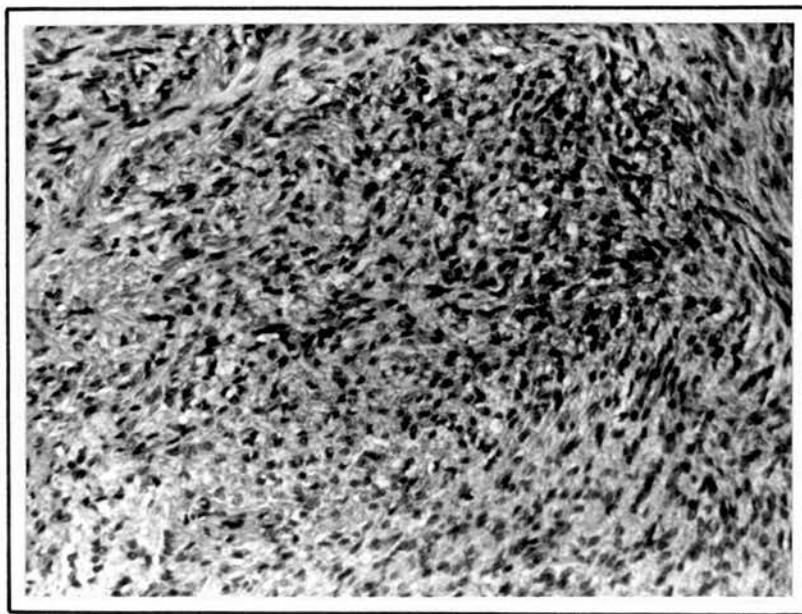
Photo 17.   X220

PHOTO 18. X 260.

   Case 1. (D.7582).

   Thecoma.   Reticular fibrils encircle each
individual cell.   The cells are clear.

   (Gordon and Sweet reticulum stain.)

PHOTO 19. X 280.

   Case 1. (D.7582)

   Thecoma.

   Thecomatosis in the same ovary harbouring the
above tumour. (H. & E.)
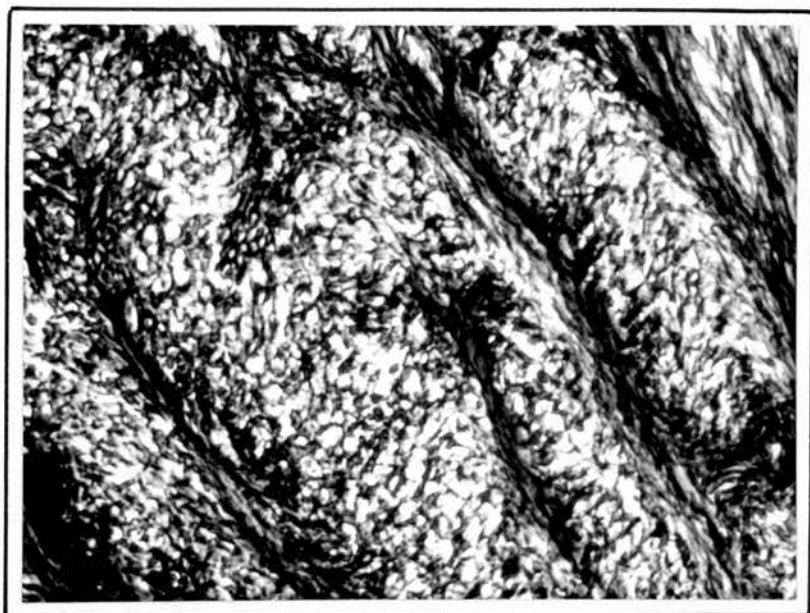
Photo 18.   X260
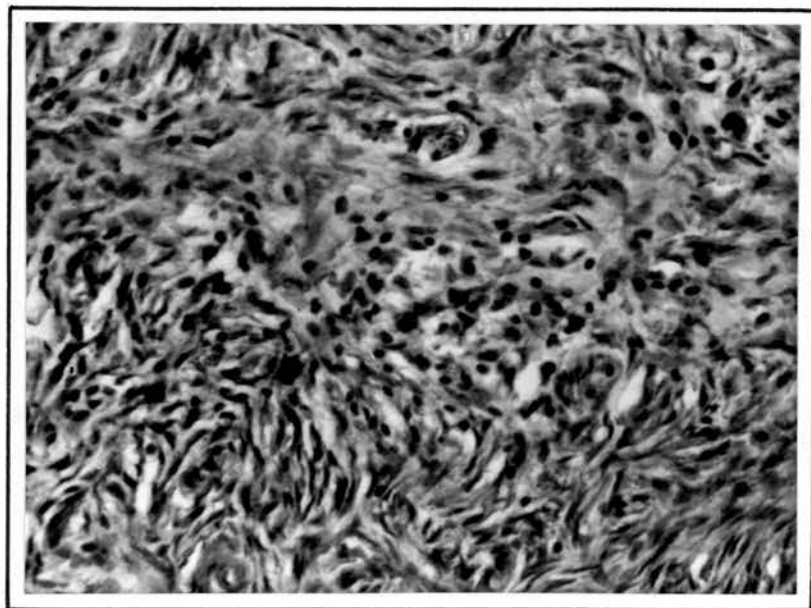
Photo 19.   X280

PHOTO 20.   X 280.

    Case 1.   (D. 7582)

,   Thecoma.   Two cortical granulomas in the other
ovary of the same case.

    Note the giant cell at the upper pole of each.
(H. & E.)

PHOTO 21.   X 220.

    Endometrium of the above case, showing a well-
differentiated adeno-carcinoma.
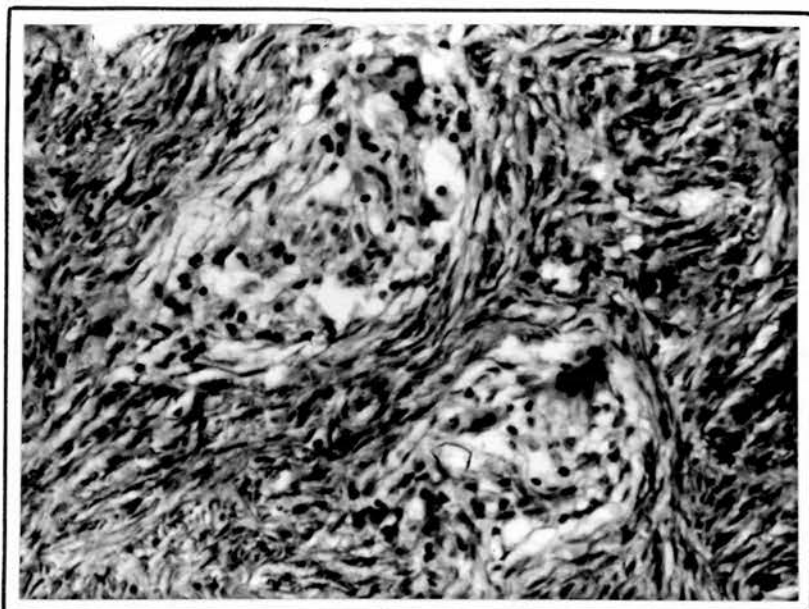
Photo 20.   X280
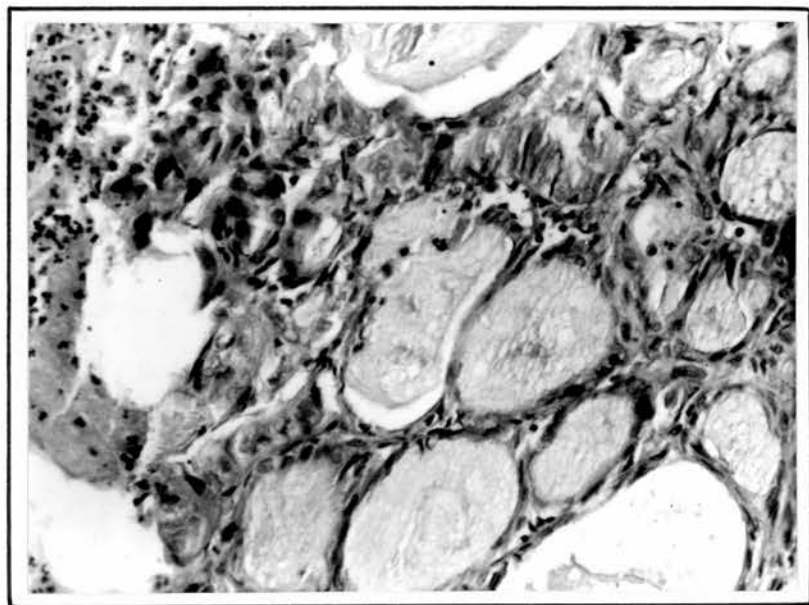
Photo 21.   X220

PHOTO 22. X 200.

Case 1. (A.5304)

Granulosa-cell tumour showing the micro-folliculoid and the gyriform patterns.

Note the stroma-theca cells at the upper right corner.

PHOTO 23. X 140.

Case 1. (A.5304)

Reticular fibrils encircle the whole island but not individual granulosa cells which are seen to contain argentophillic granules.

(Gordon and Sweet reticulum stain.)
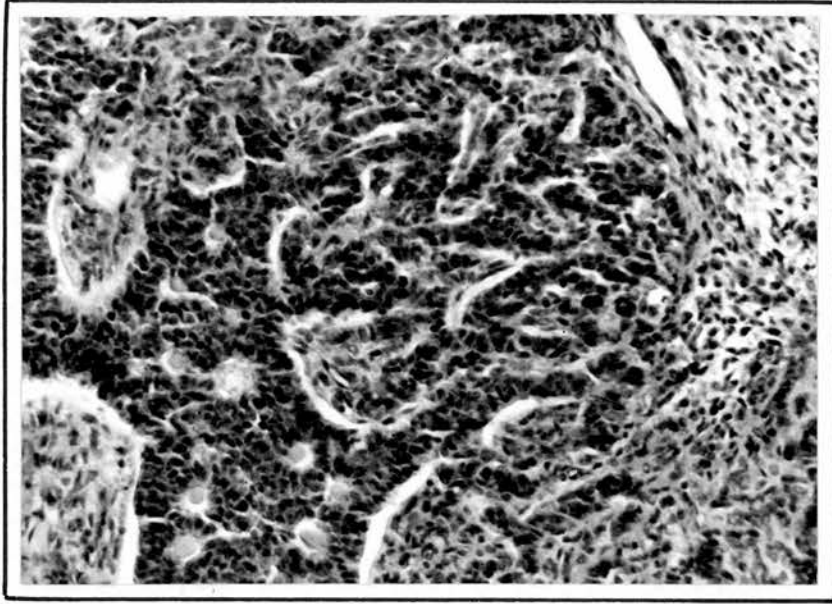
Photo 22.   X200
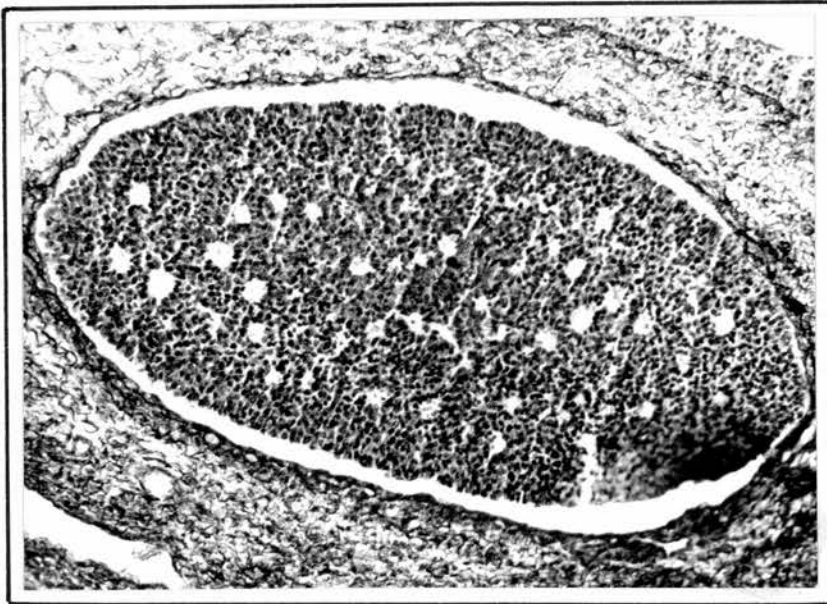
Photo 23.   X140

PHOTO 24.   X 300.

  (A.5304.)

    Thecomatosis in the other ovary of the same case.

(H. & E.)

PHOTO 25.   X 280.

    Malignant granulosa-cell tumour.

    Note the mitotic figures and malignant giant

cells.
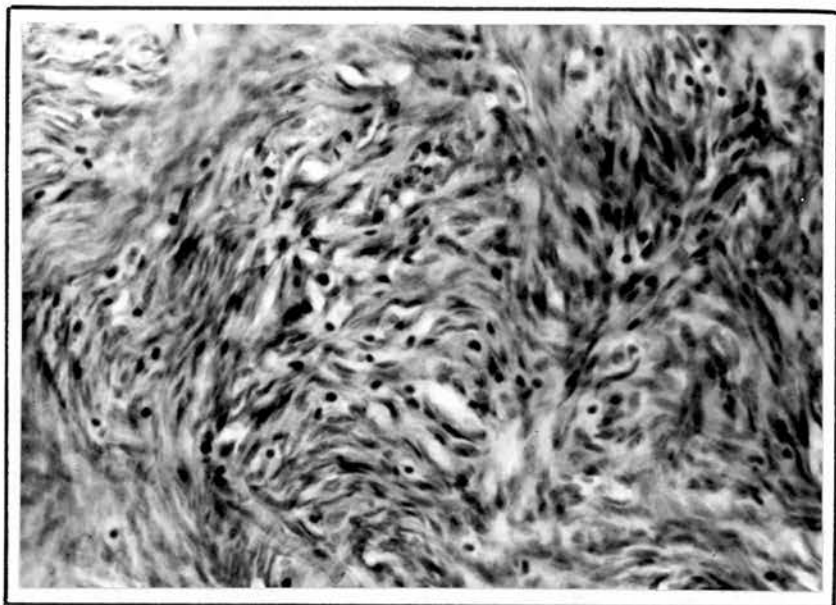
Photo 24.   X 300
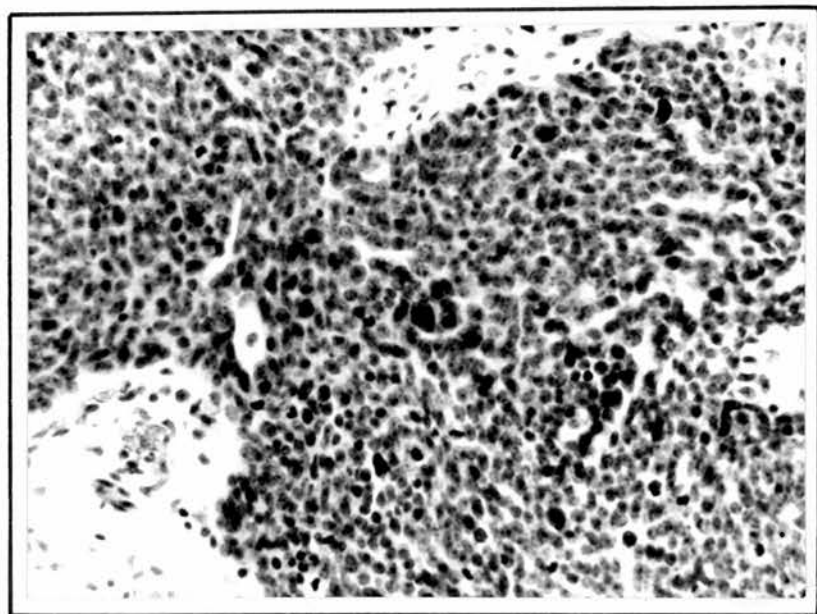
Photo 25.   X 280

PHOTO 26. X 180.

    Case 1. (C.5429.)

    Brenner-cell tumour.

    Note the gradual transition into pseudo-mucinous
epithelium. (H. & E.)
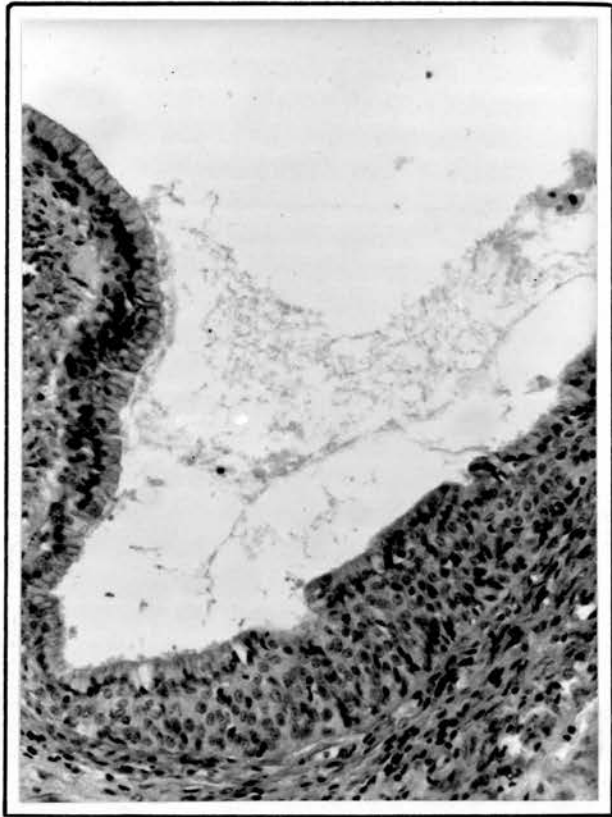
Photo 26.   X180

PHOTO 27. X 180.

   Case 1. (C.5429)

    Glycogen granules inside Brenner cells.

    (Best's Carmine Stain.)

PHOTO 28. X 180.

   Case 1. (C.5429)

    Glycogen control after diastase digestion.

Photo 27.   X180

Photo 28.   X180

PHOTO 29.   X 880.

    Case 1.   (C.5429)

    Brenner cells showing nuclear grooving or coffee-bean appearance of the nuclei.

PHOTO 30.   X 300.

    Case 1.   (C.5429)

    Plump theca-like cells are seen in the stroma.
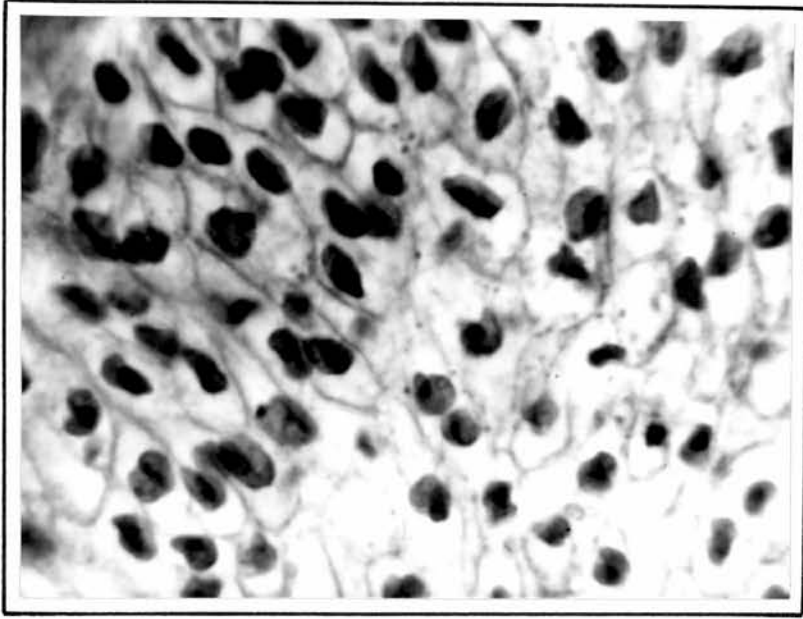
Photo 29.   X880
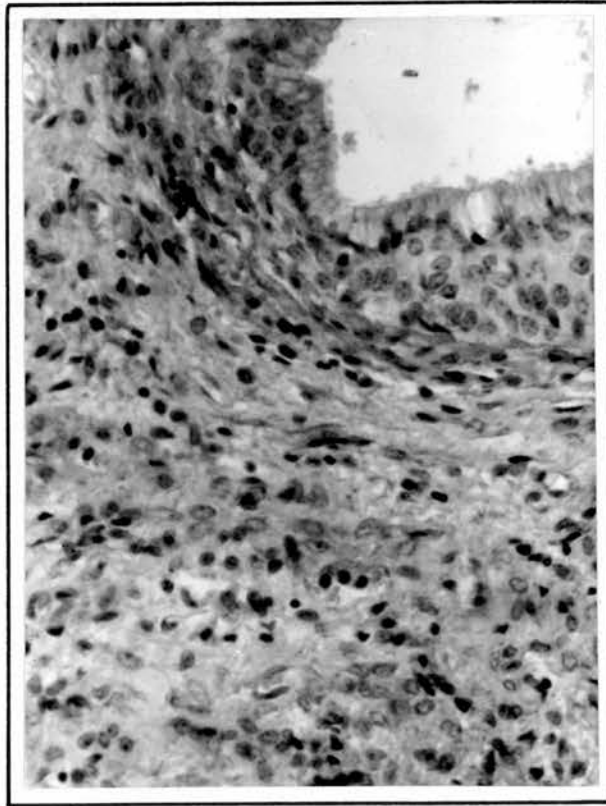
Photo 30.   X300

PHOTO 31. X 280.

Endometrium of the same case, showing proliferative
activity.

PHOTO 32. X 280.

Case 2. (B.982)

An island of Brenner cells surrounded by hyaline
fibrous tissue comparable in type to that found in
a thecoma. (H. & E.)
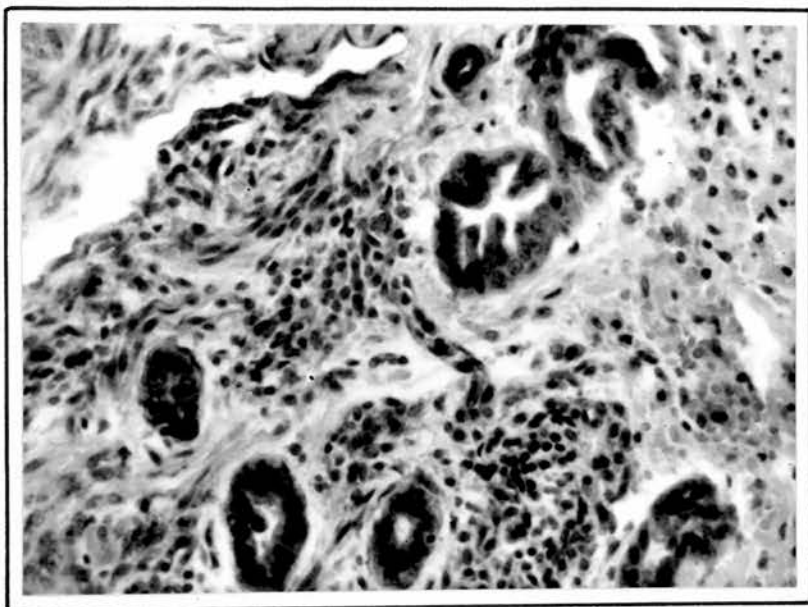
Photo 31.   X280
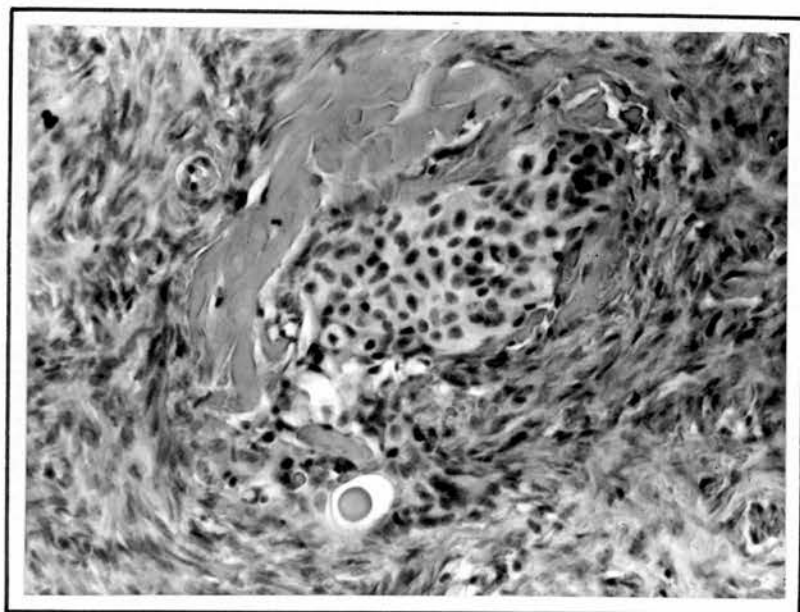
Photo 32.   X280

PHOTO 33.   X 300.

   Case 2.   (B.982)

      Thecomatosis in the other ovary.

PHOTO 34.   X 180.

      Endometrium of the same case showing cystic
hyperplasia.
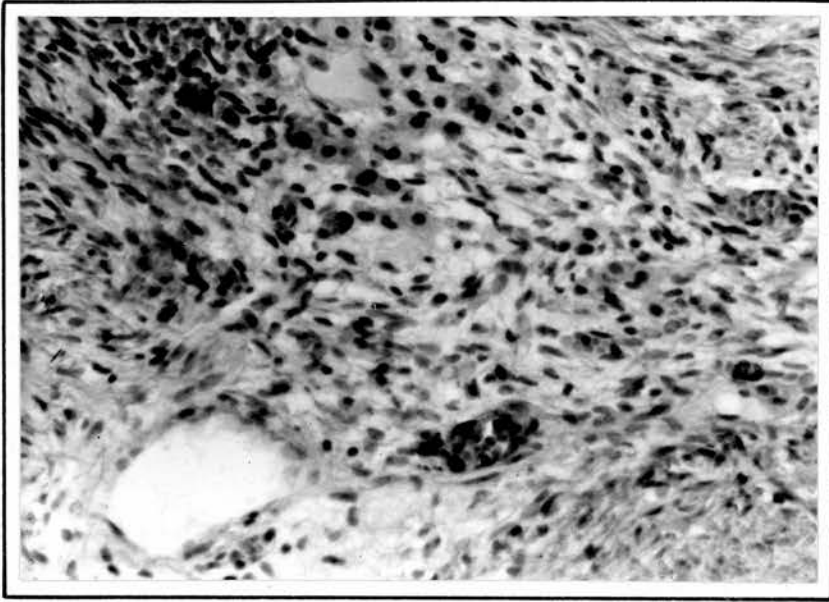
Photo 33   X 300
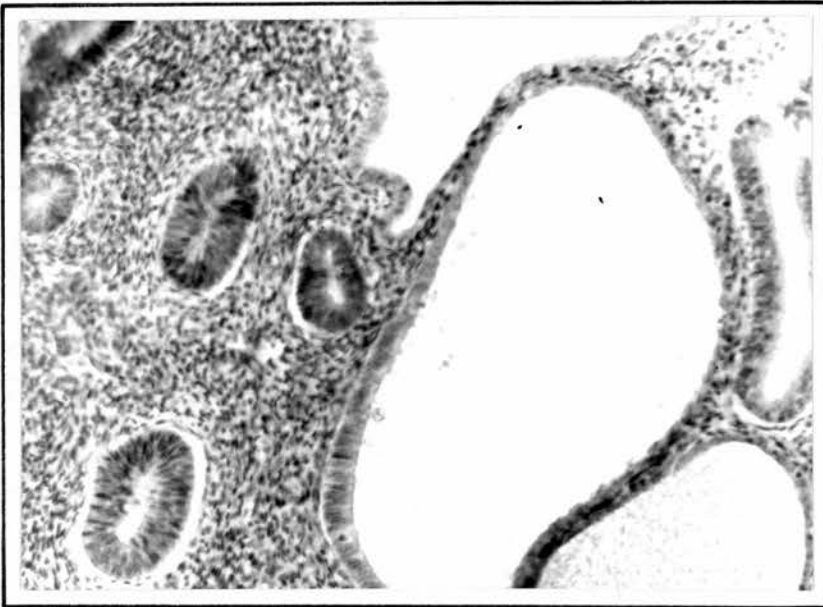
Photo 34.   X 180

PHOTO 34a.

Case 1. (F.480)

Dysgerminoma associated with a dermoid cyst.

Note the stratified squamous epithelium lining the cyst.

Photo 34 a.   X 130

PHOTO 34b.

Case 1. (F.480)

Dysgerminoma - The tumour cells are large and discrete. They are intersected by bands of connective tissue showing lymphocytic infiltration.

PHOTO 34c.

Case 1. (F.480)

An area of the above neoplasm showing a foreign body giant cell.
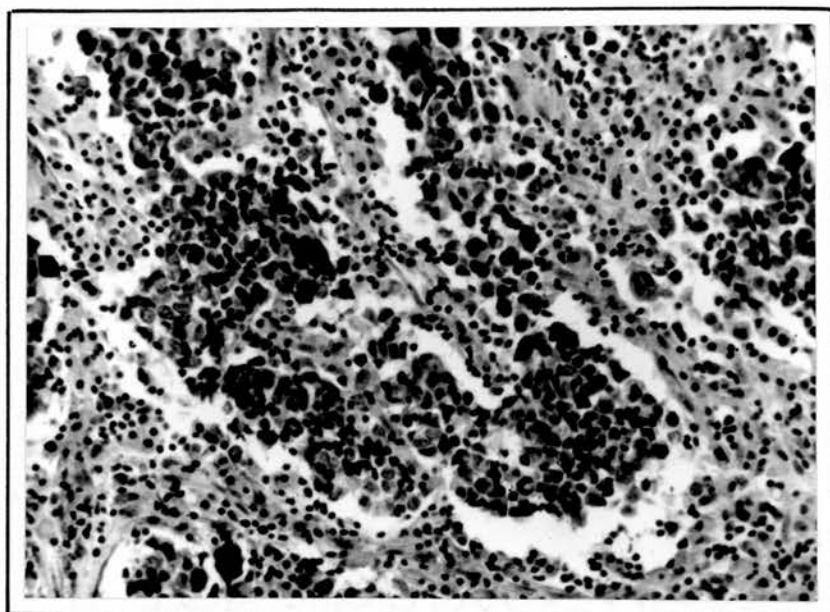
Photo 34b.   X 210
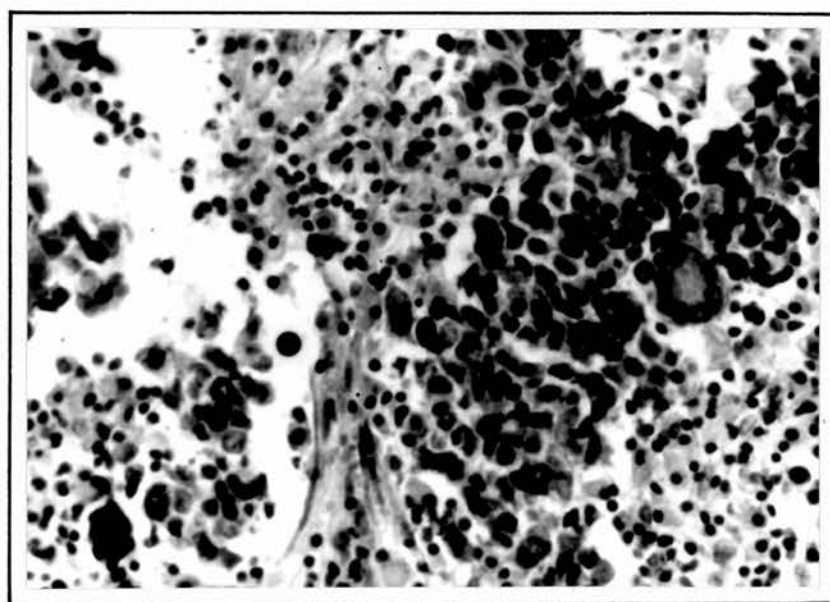
Photo 34c.   X 330

PHOTO 35. X 180.

Case 1,   Arrhenoblastoma. (Diffuse pattern.)

Groups of Leydig cells can be seen on the upper right.
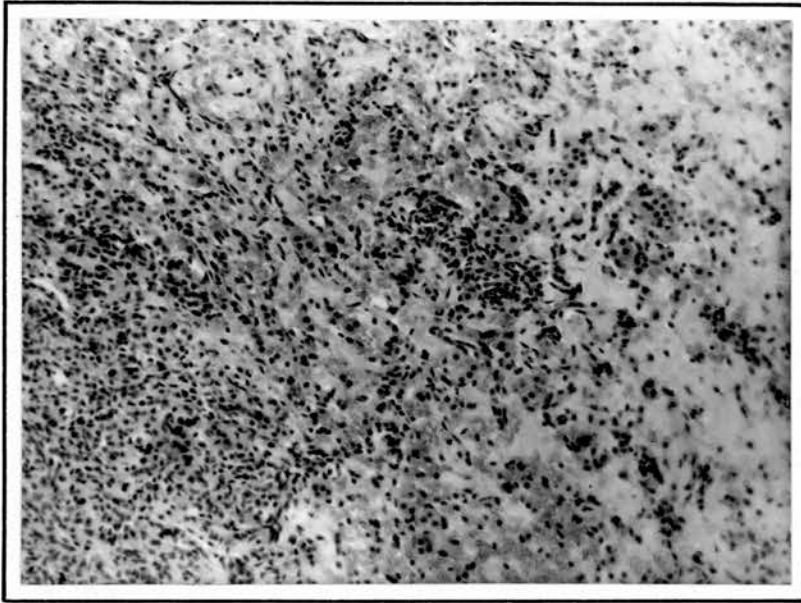
Photo 35   X180

PHOTO 36.   X 740.

   (A.6237.)

   Goblet cells in the lining of a pseudomucinous

cystadenoma.

PHOTO 37.   X 100 (reduced).

   A benign and a border line malignant area

in a pseudomucinous cyst.   (H. & E.)

PHOTO 38.   X 140 (reduced).

   A frankly malignant area in the same cyst.
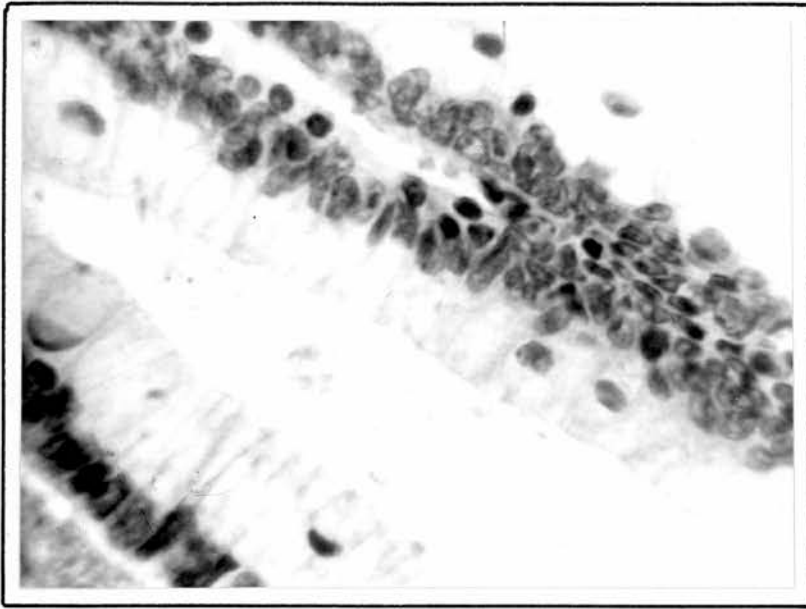
Photo 36. X740
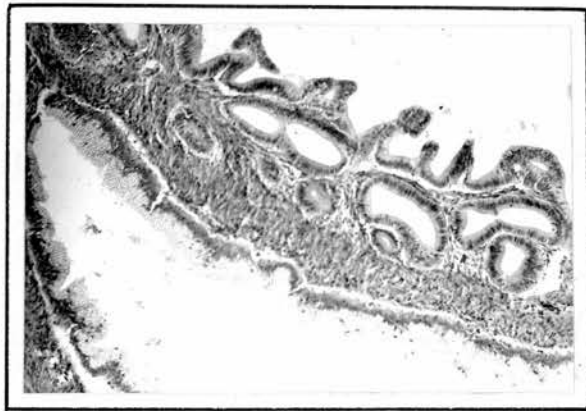
Photo 37.
X100(reduced)
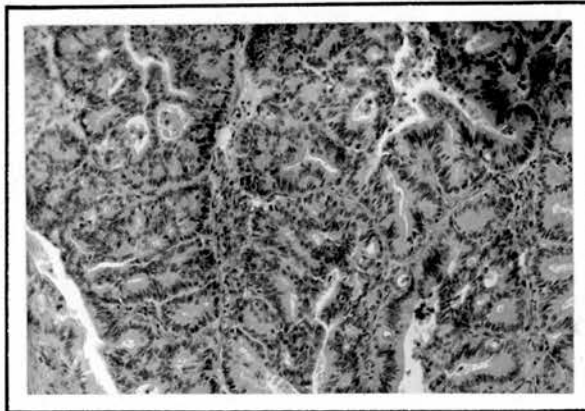
Photo 38.
X140(reduced)

PHOTO 39. X 180.

Case 1. (C.8912)

Luteinised theca-like cells in the stroma of
a pseudomucinous cystadenoma. (H. & E.)

PHOTO 40. X 300.

Case 1. (C.8912)

Thecomatosis in the other ovary. (H. & E.)
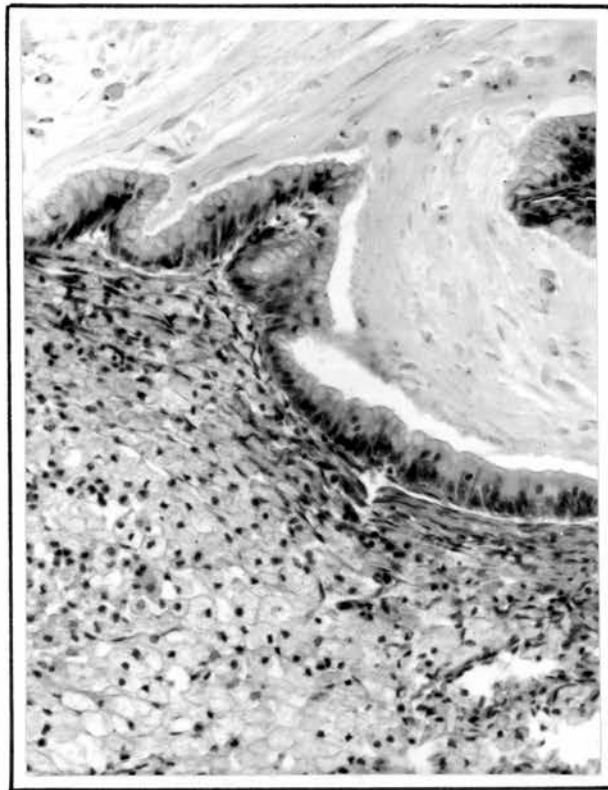
Photo 39.   X180
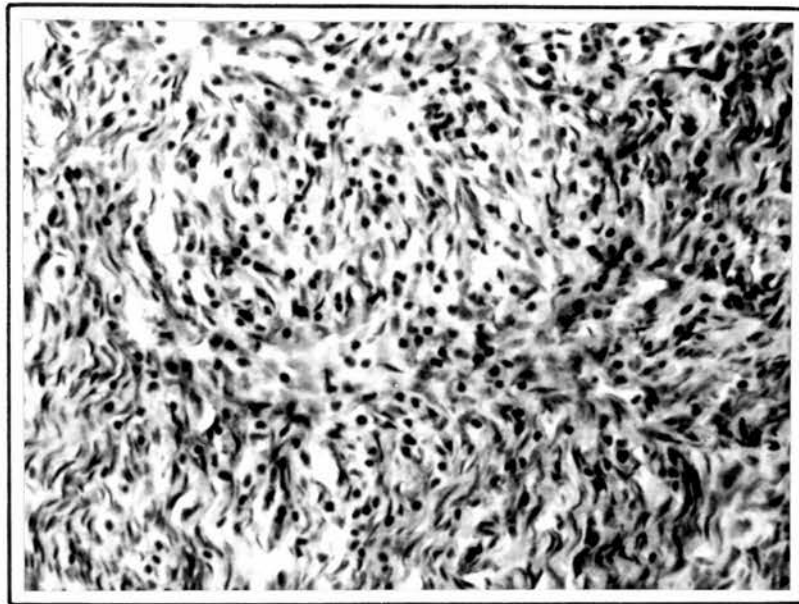
Photo 40.   X300

PHOTO 41. X 200.

Case 1. (C.8912)

Endometrium of the above case showing cystic
glandular hyperplasia.

Photo 41.   X200

PHOTO 42. X 290.

Case 2. (D.4600)

Typical theca cells in the stroma of
a pseudomucinous cystadenoma just underneath the
epithelium.

PHOTO 43. X 120.

Endometrium of the above case showing cystic
glandular hyperplasia.
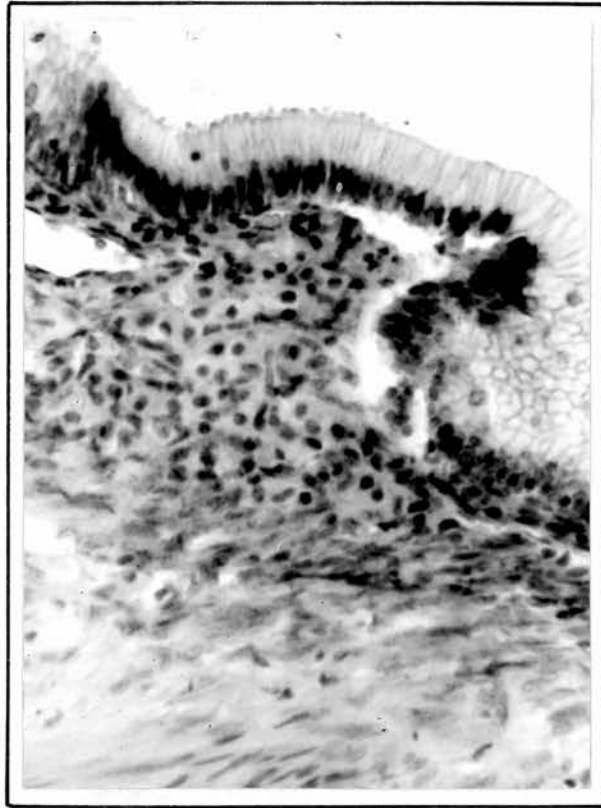
Photo 42.   X 290
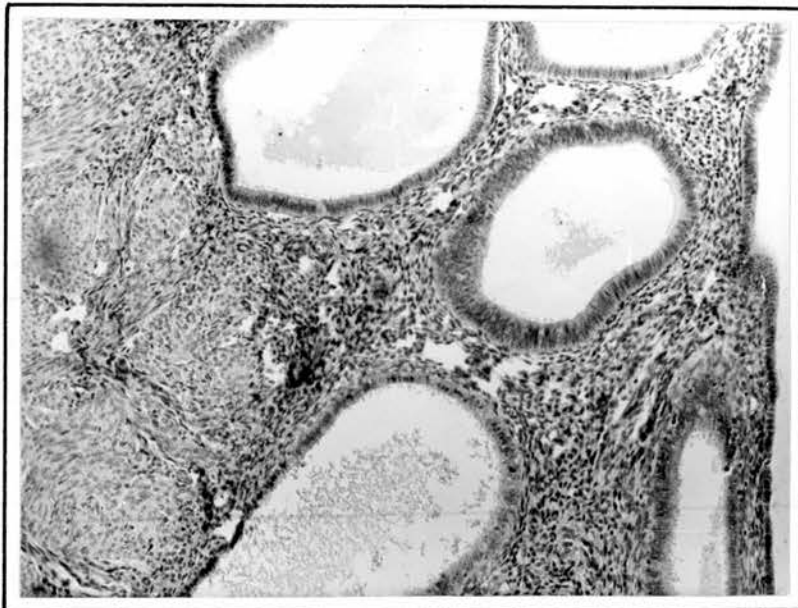
Photo 43.   X 120

PHOTO 44.   X 300.

   (A.1018)

      Tubal type of epithelium, lining a simple

serous cyst.   (H. & E.)

PHOTO 45.   X 180.

   (E.244.)

      Psammoma bodies (calcified papillae) in a serous

cyst.   (H. & E.)
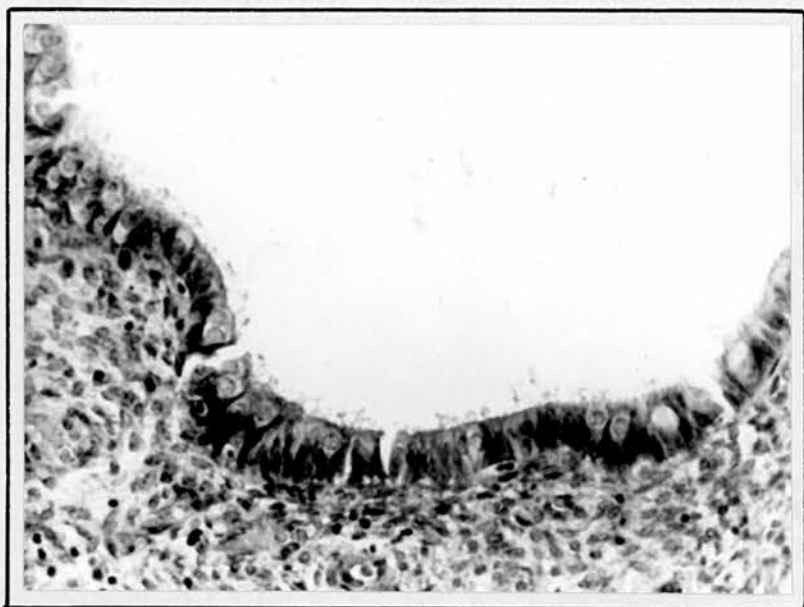
Photo 44.   X 300
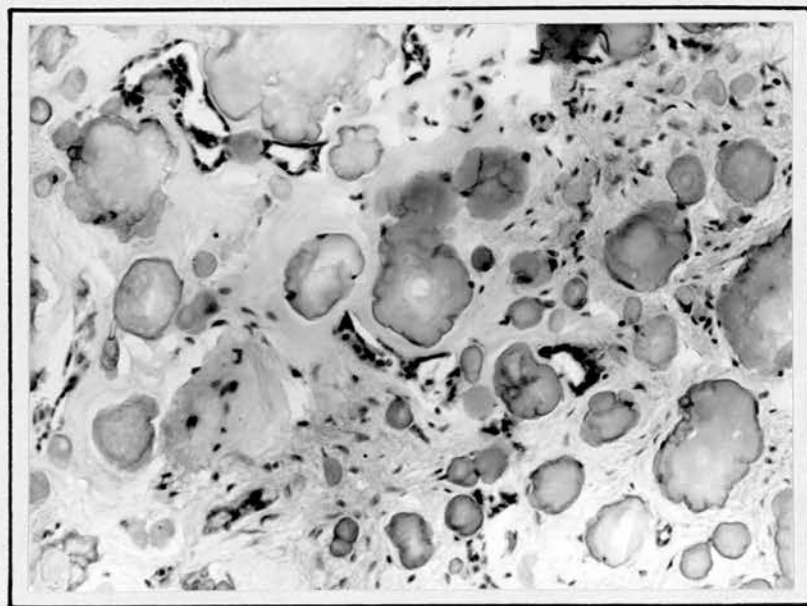
Photo 45.   X180

PHOTO 46.   X 60.

   (E.4765)

     Papillae, resembling chorionic villi, in a serous

cystadenoma.   (H. & E.)

PHOTO 47.   X 50.

   (F.786)

     Borderline and malignant areas, in one field,

in a serous cyst. (H. & E.)

Photo 46.   X 60
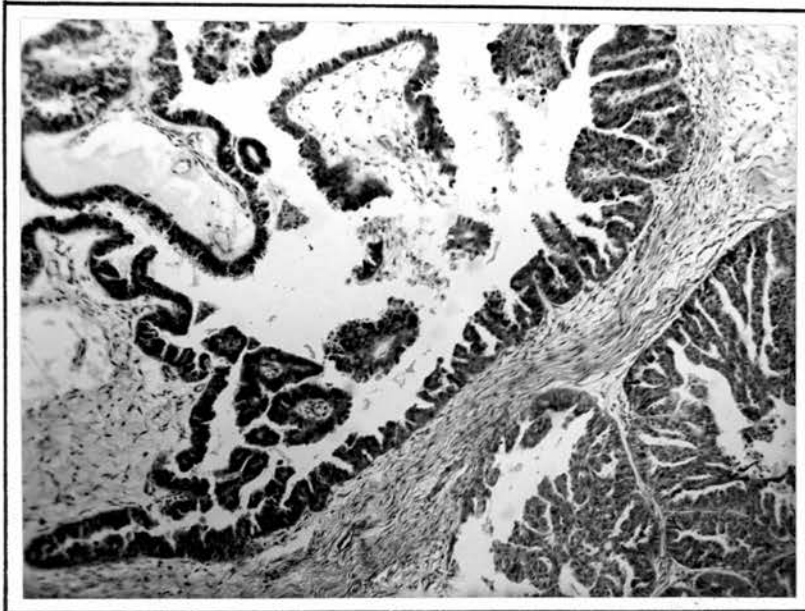
Photo 47.   X 50

PHOTO 48. X 200.

   (E.5691)

     Benign area in a serous cyst.   The papillae
are lined by one layer of cubical epithelium. (H. & E.)

PHOTO 49. X 250.

     Borderline malignant area in the same cyst.
(No stromal invasion.)

PHOTO 50. X 250.

     Frankly malignant area in the same cyst.
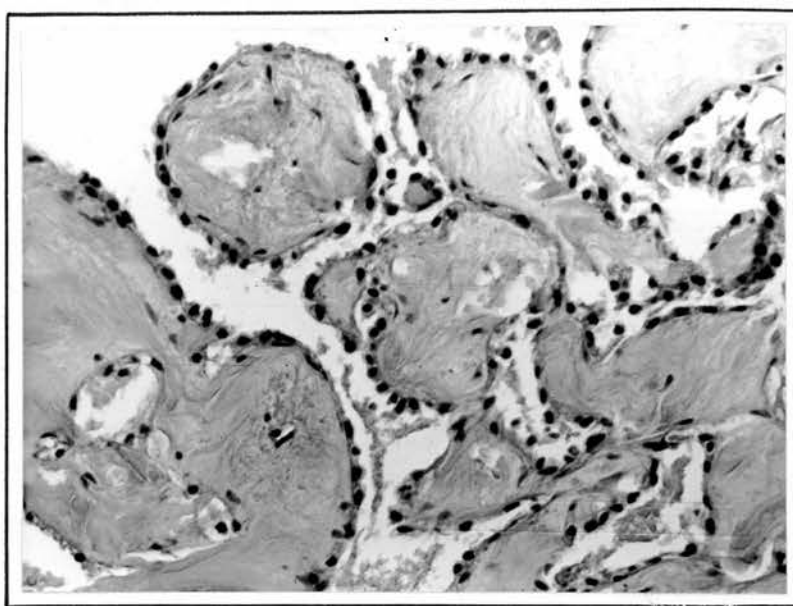
Photo 48.   X 200
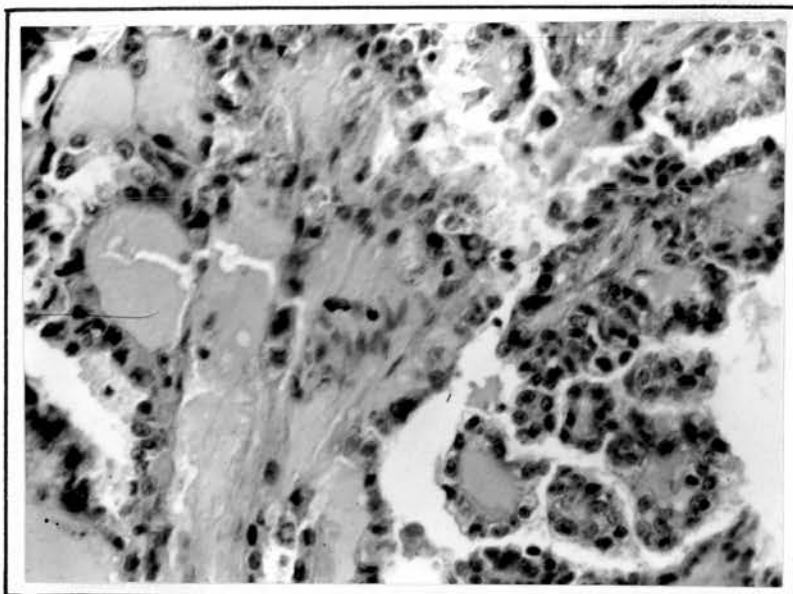
Photo 49.   X 250
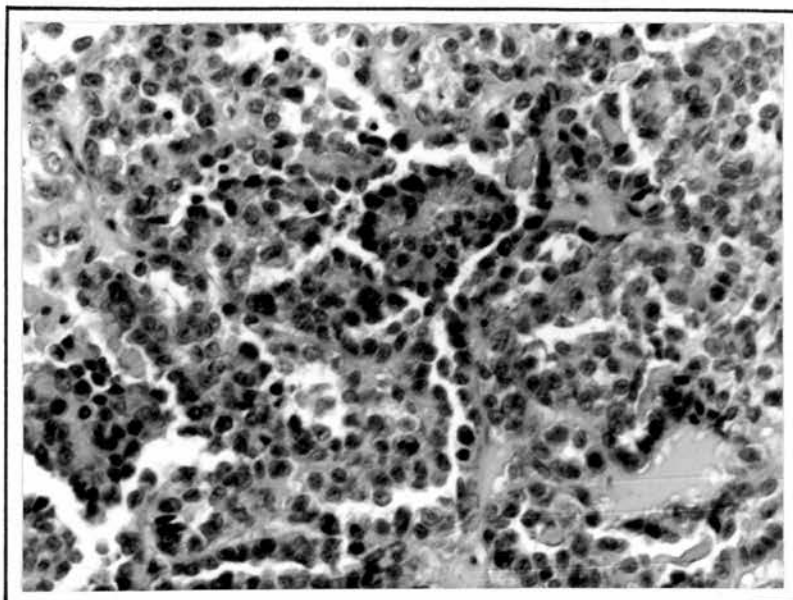
Photo 50.   X 250

PHOTO 51.   X 200.

Case I. (B.1197)

Theca-like cells in the stroma of a well differentiated
primary adeno-carcinoma of the ovary.   (Note the upper
left corner.)

PHOTO 52.   X 260.

Case I. (B.1197)

Same tumour.   This section shows the stromal theca
cells to a better advantage.
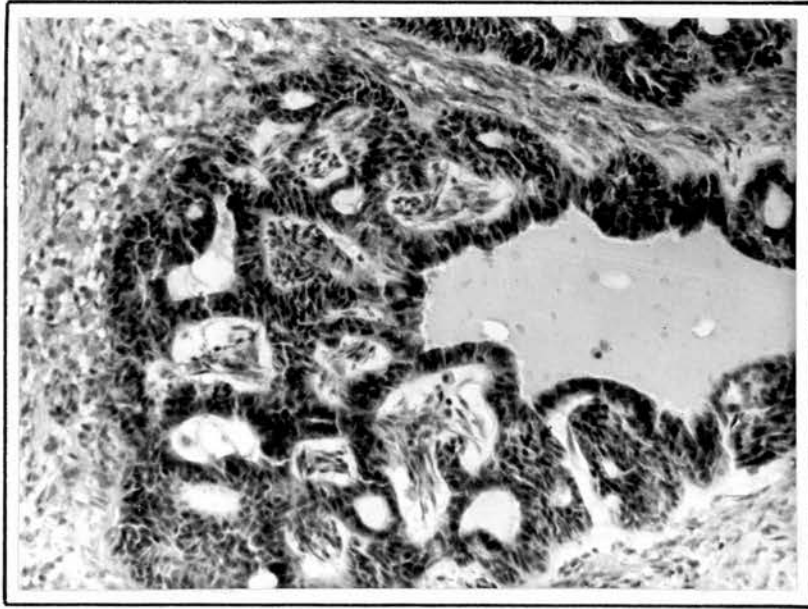
Photo 51.   X200
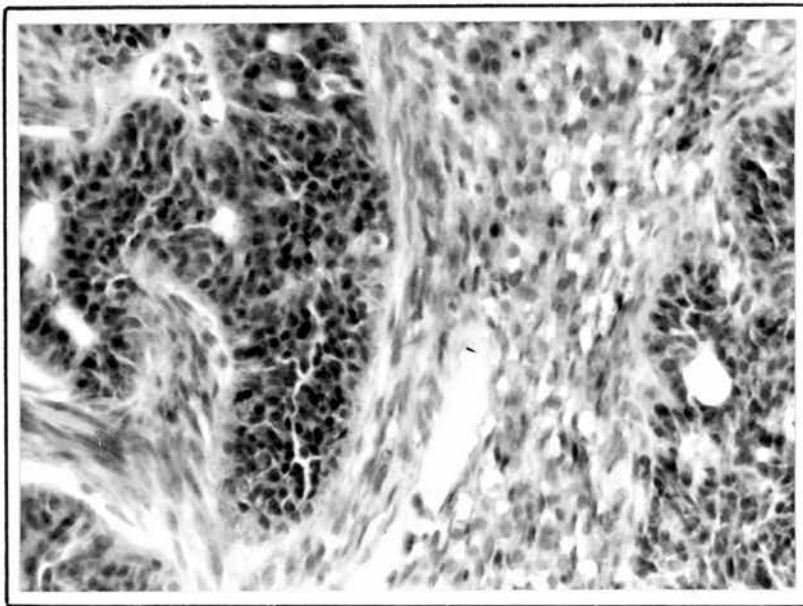
Photo 52.   X260

PHOTO 53. X 150.

(B.1197)

Hyperplastic cortical nodule in the other ovary of
the same case. Note the plump whirly fibroblasts (H. & E.).

PHOTO 54. X 180.

(B.1197)

Endometrium of the same case showing cystic glandular
hyperplasia.
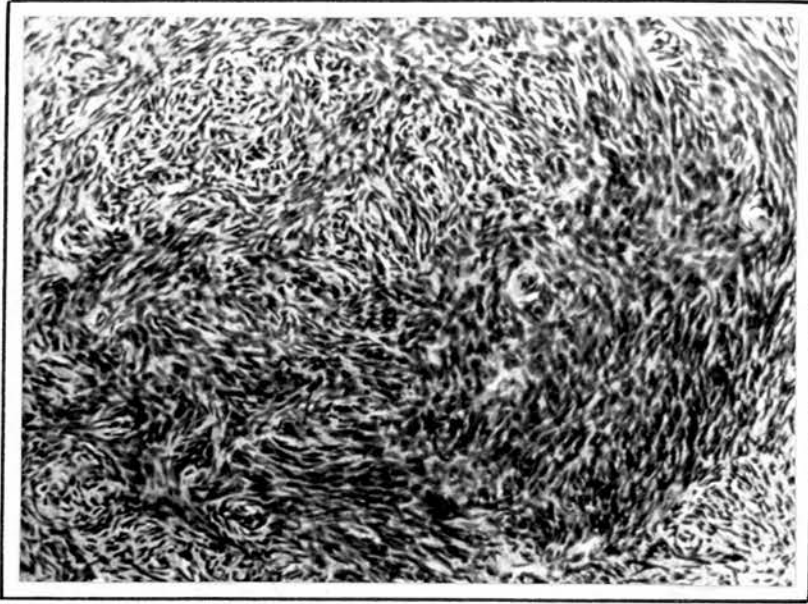
Photo 53.   X150

Photo 54.   X180

PHOTO 55. X 180.

(E.3543)

Typical thyroid ascini filled with colloid in the
wall of a dermoid cyst.

PHOTO 56. X 50.

(E.4281)

Pseudomucinous cystadenocarcinoma taking origin in a
dermoid cyst. Note the transition of the stratified
squamous epithelium into pseudomucinous epithelium.
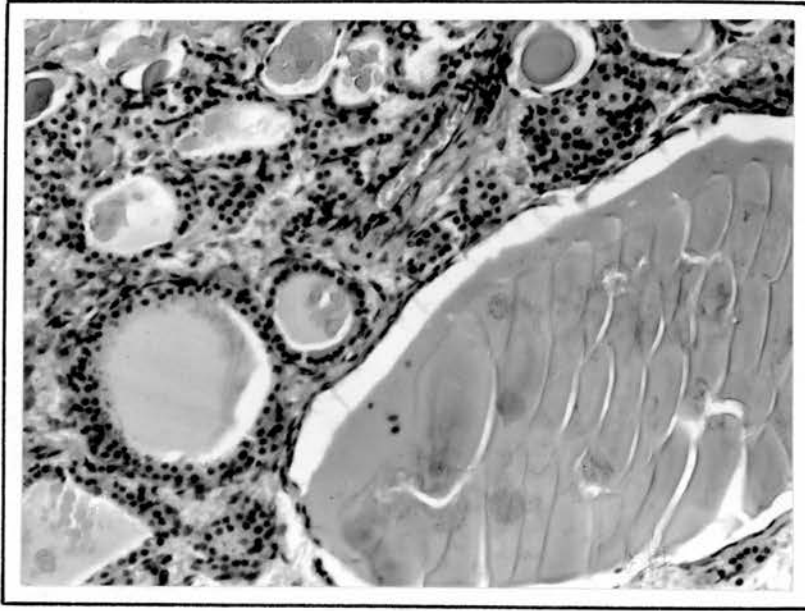
Photo 55.   X180
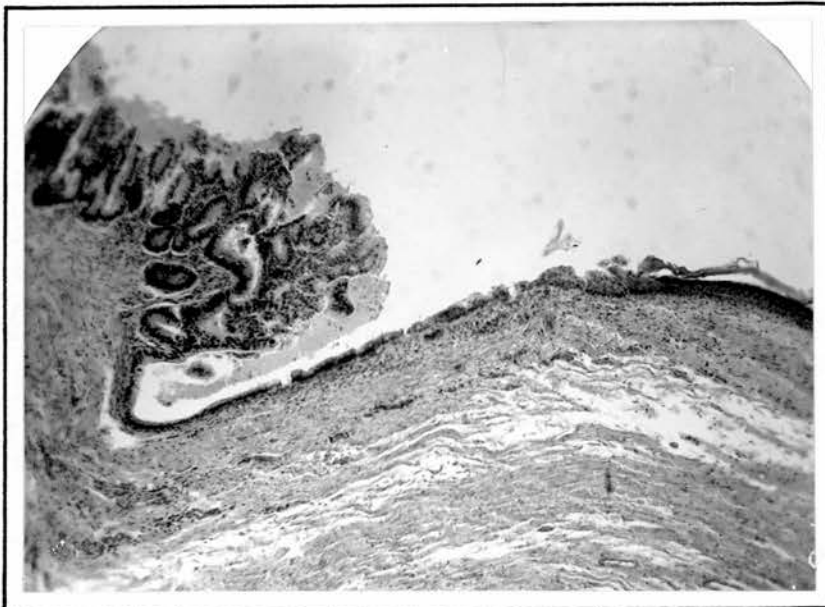
Photo 56.   X50

PHOTO 57. X 260.

(E.4281)

Pseudomucinous cystadenocarcinoma shown to a better
advantage.

PHOTO 58. X 160.

(E.4281)

The dermoid portion of the same cyst showing skin
and a sebaceous gland.
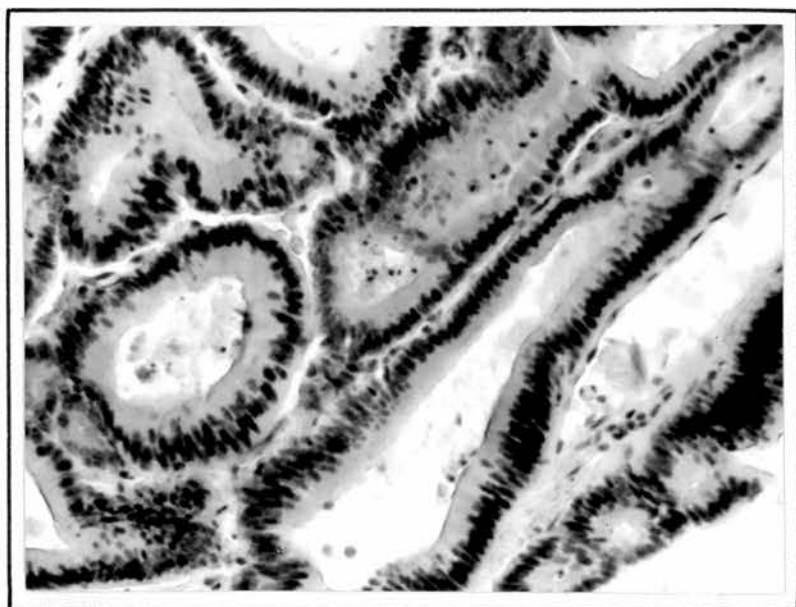
Photo 57.   X260
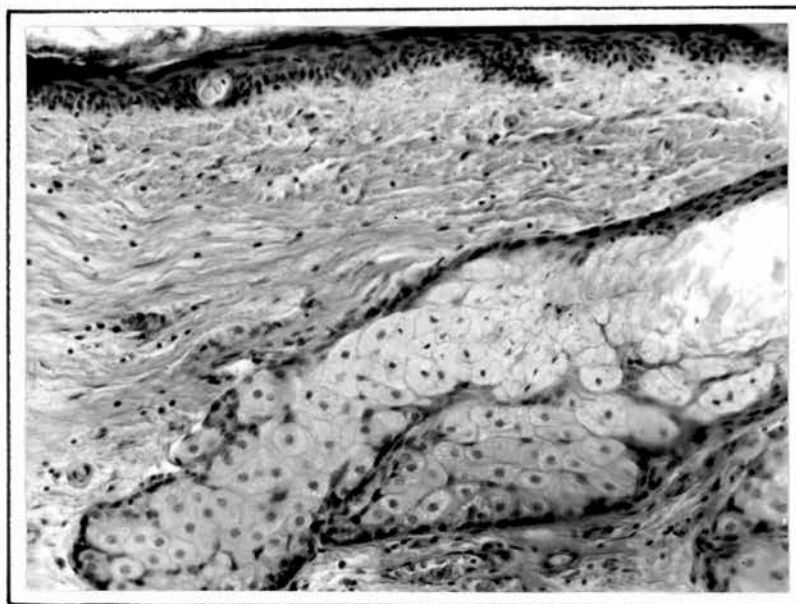
Photo 58.   X160

PHOTO 59.   X 15.

(C.7237)

An adenocarcinoma taking origin in a dermoid cyst.
(Apparently from the sweat glands.)   (H. & E.)

PHOTO 60.   X 100.

Case 3 (A.6964)

Malignant teratoma in the form of a squamous cell
carcinoma.
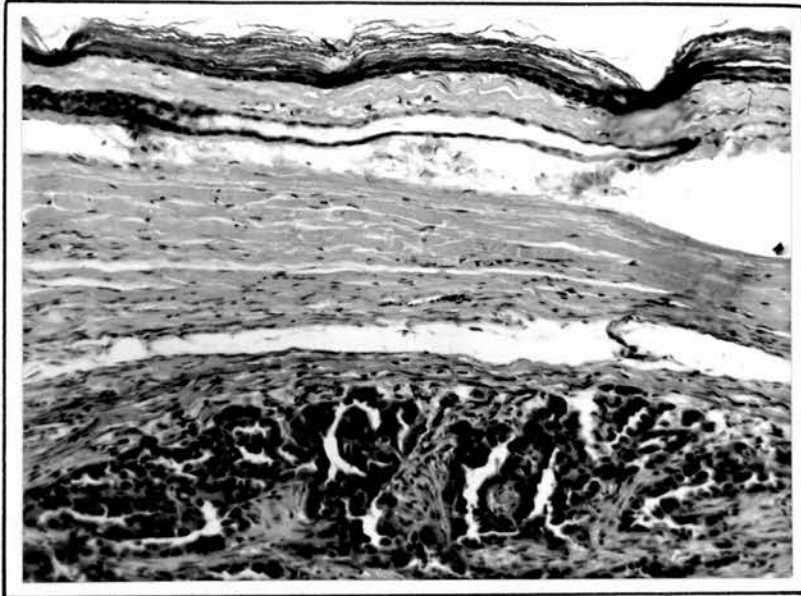
Photo 59.   X15
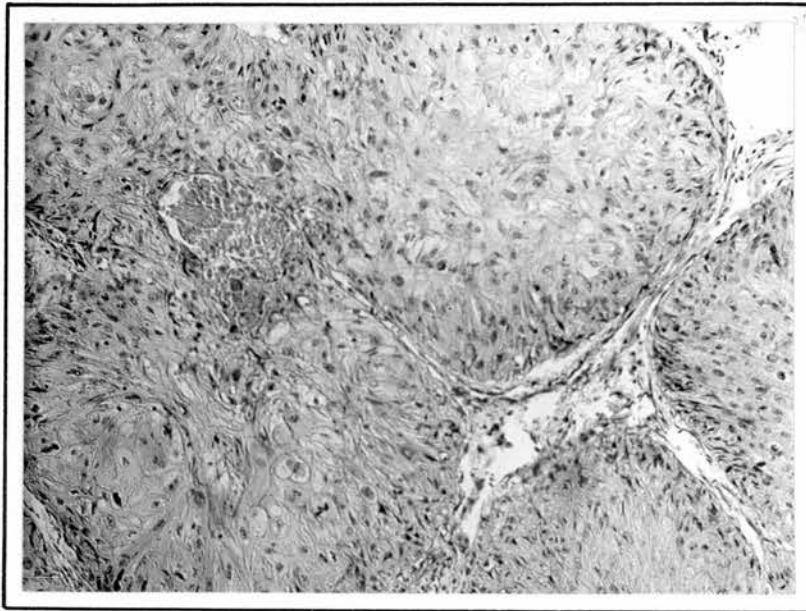
Photo 60.   X100

PHOTO 61.

    Case 4 (F.191)

    Gross specimen of ovarian teratoma. The presence
of hairs in one of the cystic cavities was a clue to the
possibility of its being a teratoma.

PHOTO 62.   X 150.

    Case 4 (F.191)

    Glandular tissue (quite benign). (H. & E.)

Photo 61.

Photo 62.   X150

PHOTO 63.   X 180.

(Case 4. F.191)

Nervous tissue in a teratoma. (H. & E.)

PHOTO 64. X 90.

Case 4. (F.191.)

A structure very similar to choroid plexus, adjacent
to nervous tissue in a teratoma. (H. & E.)
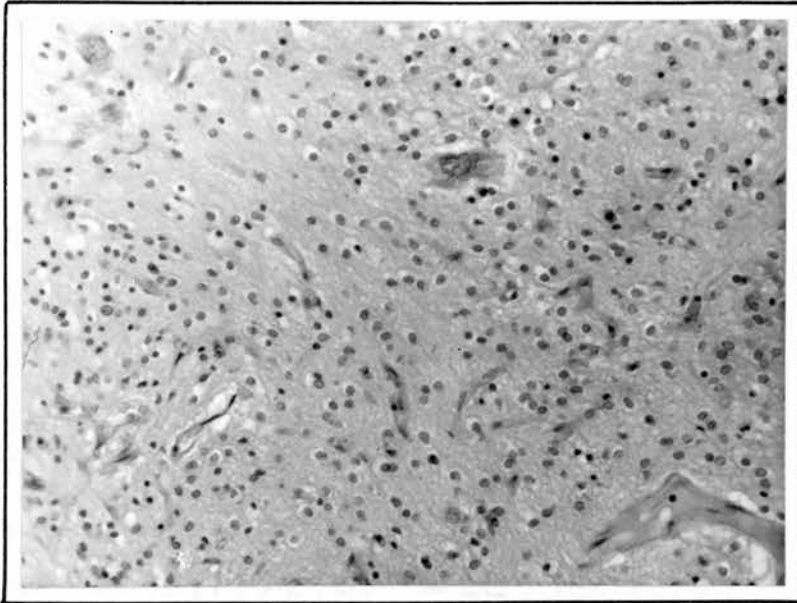
Photo 63.   X180

Photo 64.   X90

PHOTO 65.   X 180.

   Case 4.   (F.191.)

     Osseus tissue in a teratoma.   (H. & E.)

PHOTO 66.   X 250.

   Case 4.   (F.3059.)

    Undifferentiated malignant embryonic cells found in
a metastatic peritoneal nodule 7 months after removal of
the above teratoma.   These cells might be of nervous
origin.   (H. & E.)
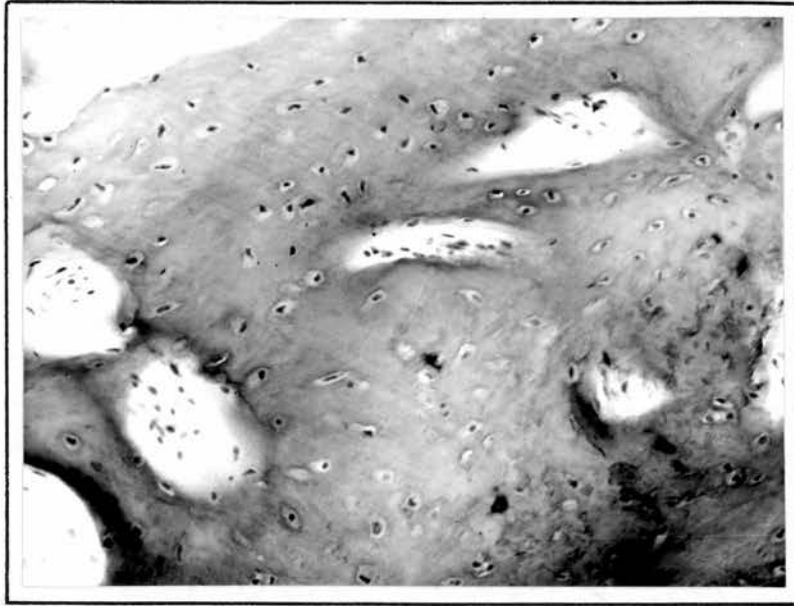
Photo 65.   X180
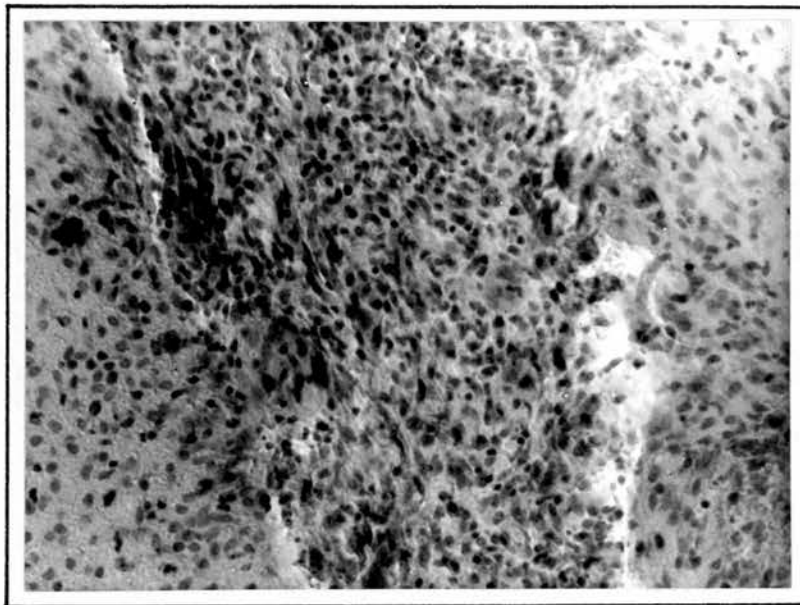
Photo 66.   X250

PHOTO 67. X 300.

(B.641.)

Krukenberg tumour. Note the acinar structures and
signet ring cells. (H. & E.)

PHOTO 68. X 100.

(E.1260.)

Metastatic ovarian adeno-acanthoma. Note the islands
of squamous epithelium amidst the malignant acini.
(H. & E.)
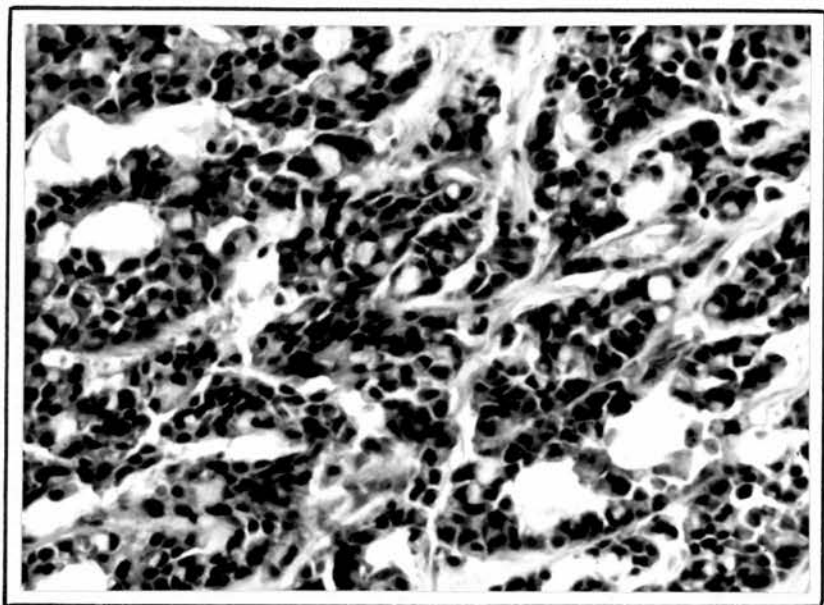
Photo 67.   X 300
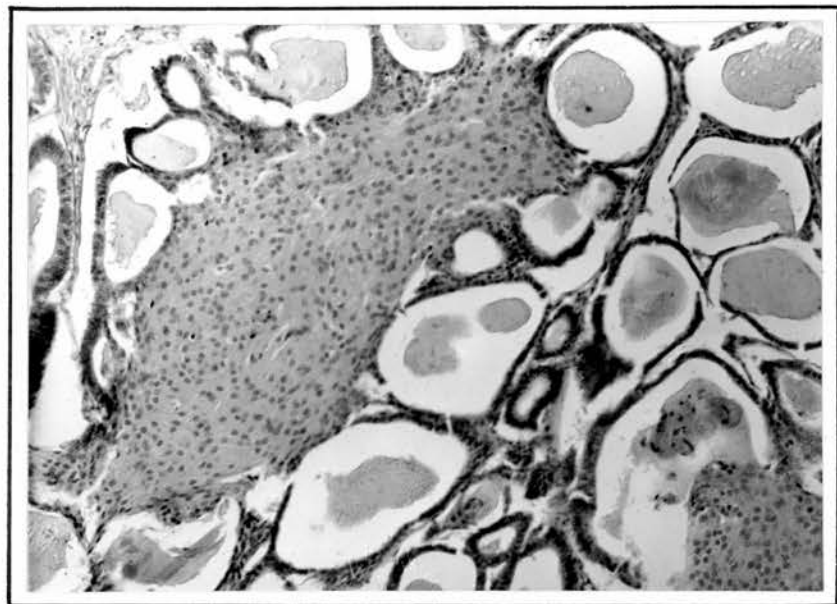
Photo 68.   X 100

PHOTO 69.   X 300.

   (B.9174.)

   Metastatic ovarian oat-cell carcinoma secondary to
a lung cancer.   (H. & E.)

PHOTO 70.   X 260.

   (C.5923.)

   Metastatic ovarian schirrhous carcinoma secondary to
a known breast cancer.   (H. & E.)
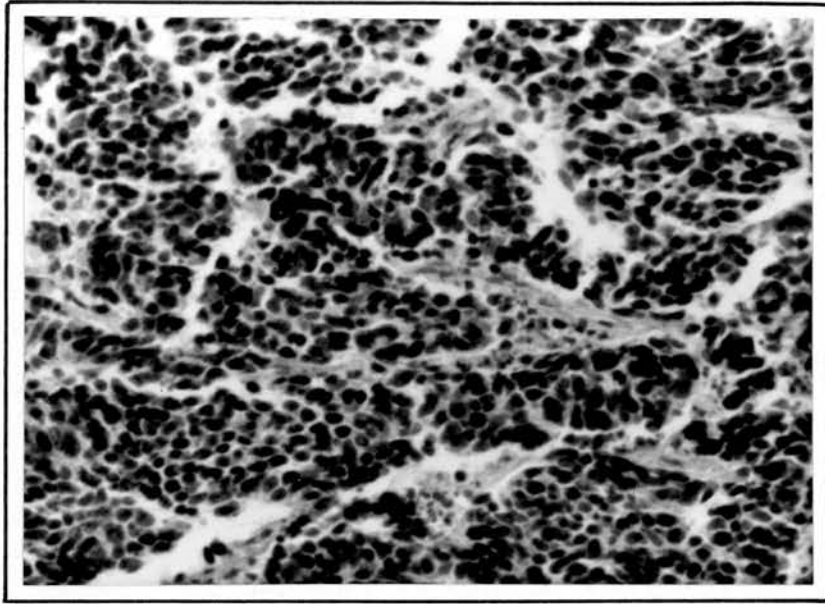
Photo 69.   X300
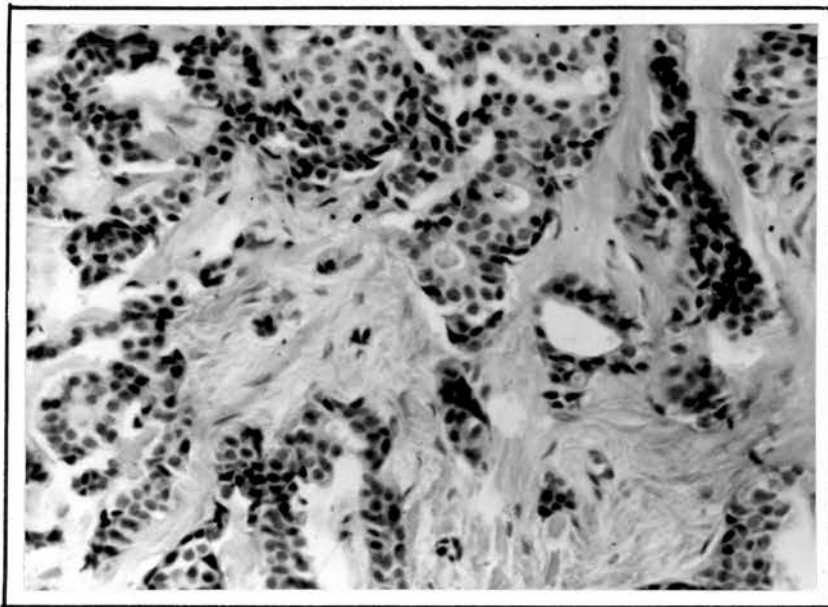
Photo 70.   X260

PHOTO 71. X 200.

Case I. (1343/61.)

Granulosa-cell tumour.

Sudanophillic red droplets of fat are only present
in theca-like stromal cells. None in granulosa cells.
Sudan IV Stain.

PHOTO 72. X 180.

Case I. (1343/61.)

Granulosa-cell tumour.

Birefringent crystals are seen in the same sites, i.e.,
theca-like stromal cells.
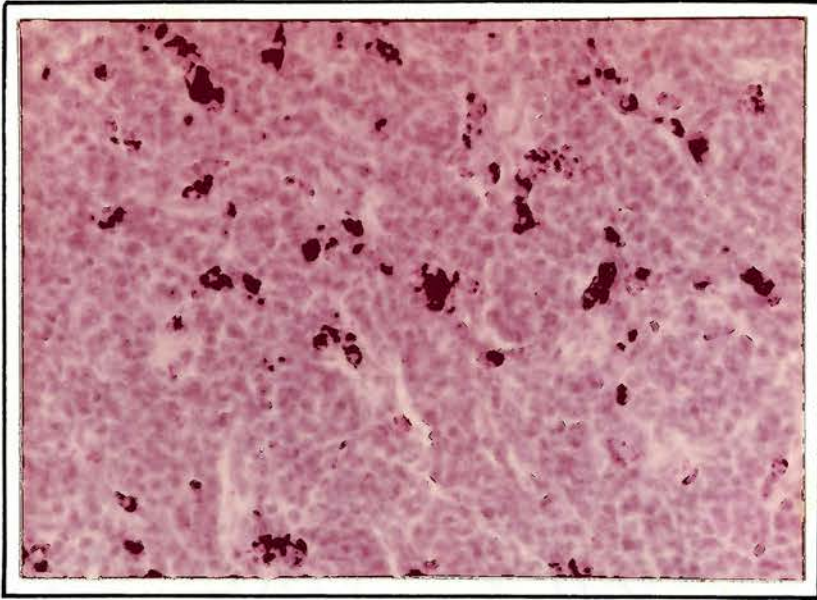
Photo 71.   X200
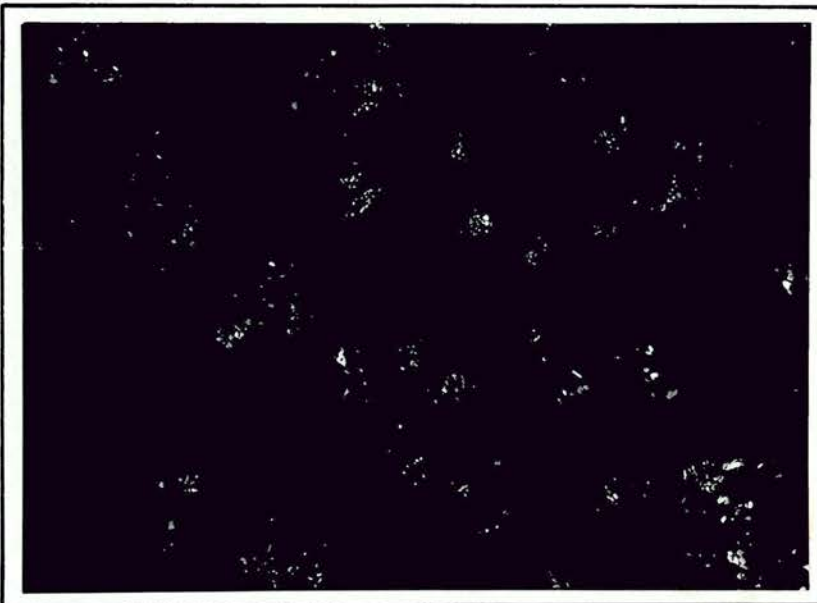
Photo 72.   X180

PHOTO 73.   X 240.

   Case I.   (1343/61.)

      Granulosa-cell tumour.

      Schultz test. Green droplets are present only in
theca-like stromal cells (none in granulosa cells).

         (Black and white.)

PHOTO 74.   X 200.

   Case I.   (1343/61.)

      Ashbel-Seligman test.   Purple-blue granules are seen
inside stromal theca cells only.

         (Black and white.)
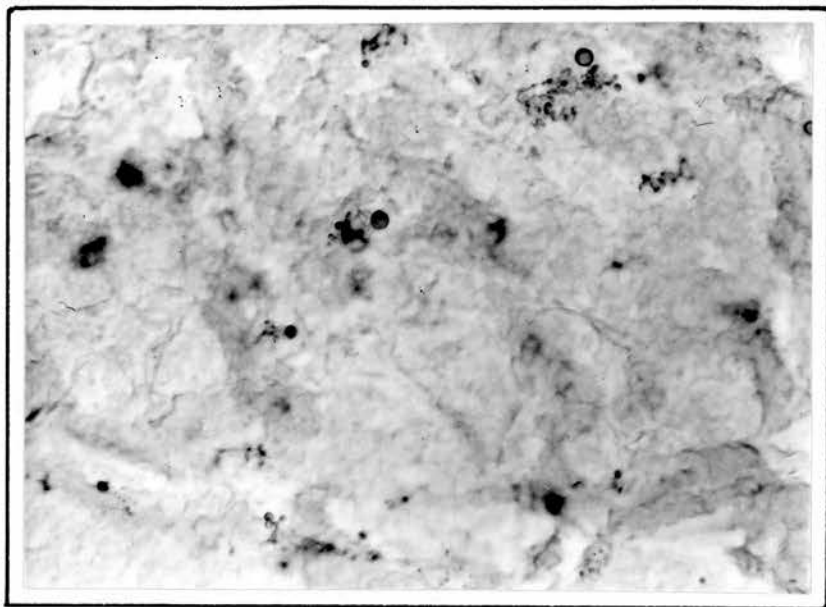
Photo 73.   X240
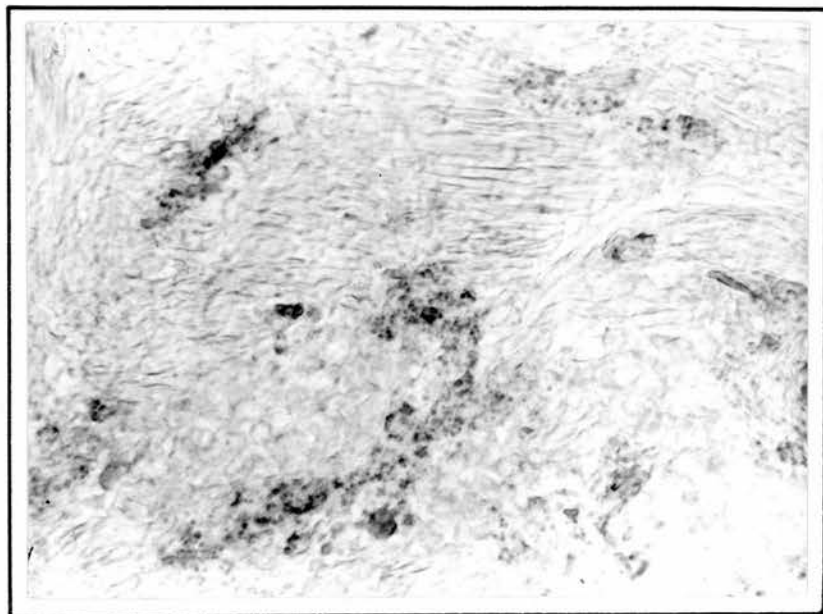
Photo 74.   X200

PHOTO 75.   X 280.

   Case I. (1343/61.)

   An area of thecomatosis passing into a cortical granuloma
around a blood vessel in the cortex of contra-lateral ovary.
(H. & E.)

PHOTO 76.   X 150.

   Case I. (1343/61.)

   Endometrium showing cystic glandular hyperplasia.

(H. & E.)
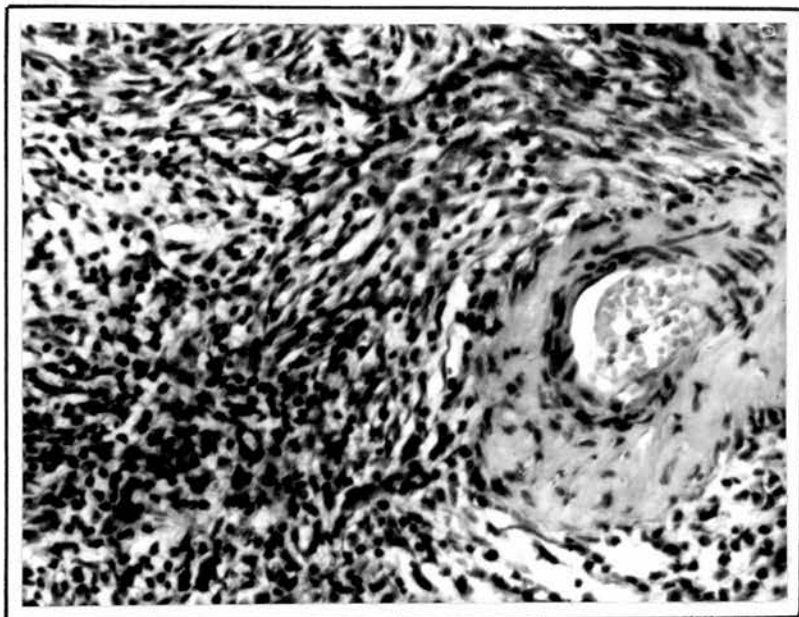
Photo 75.   X280

Photo 76.   X150

PHOTO 77. X 280.

Case 2. (5818/61.)

Luteinized granulosa-cell tumour.

The cytoplasm of granulosa cells is filled with
large vacuoles which were filled with fat. (H. & E.:
Frozen Section.)

PHOTO 78. X 150.

Case 2. (5818/61.)

A section from the same block revealing the high
concentration of red fat droplets in the luteinized
granulosa cells and in the stromal theca cells.
(Sudan IV.)
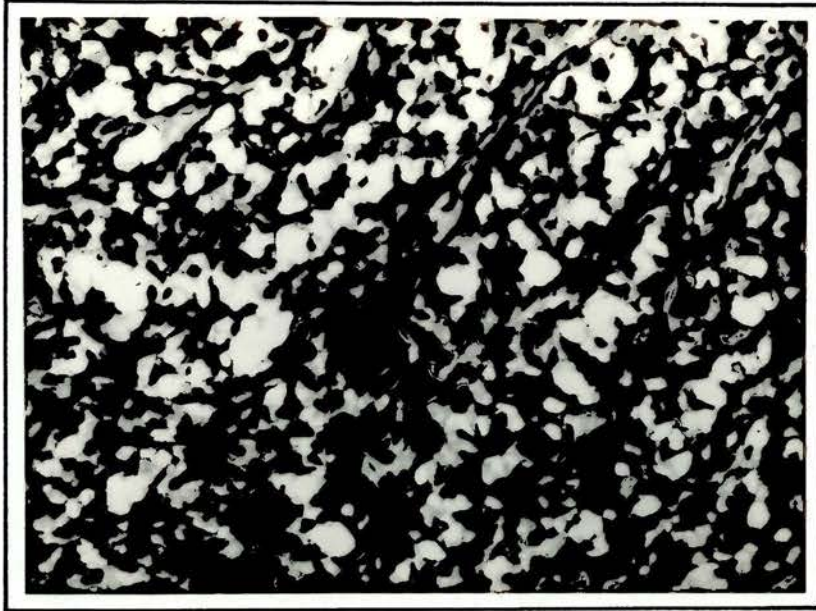
Photo 77.   X280
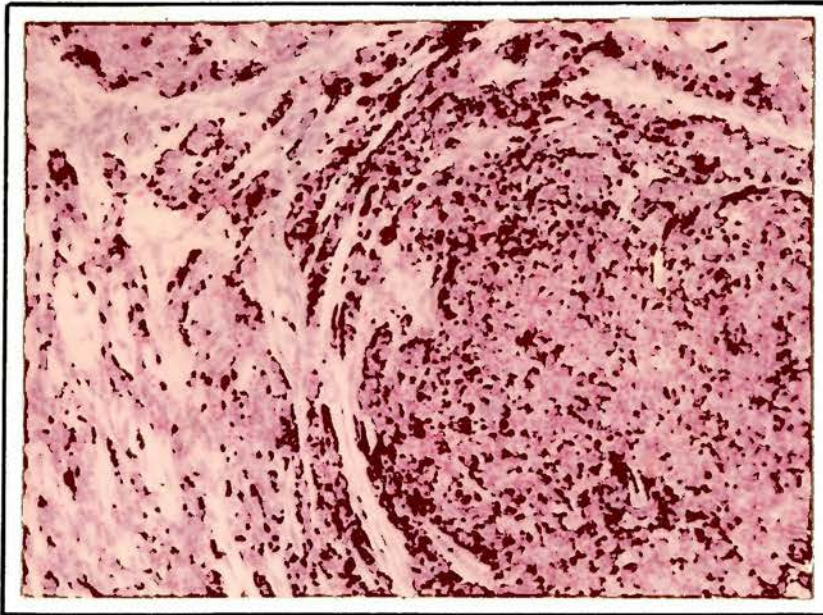
Photo 78   X150

PHOTO 79. X 160.

Case 2. (5818/61.)

Birefringent crystals seen in both the luteinized granulosa and the stromal theca cells.

PHOTO 80. X 140.

Case 2. (5818/61.)

Endometrium showing cystic glandular hyperplasia.
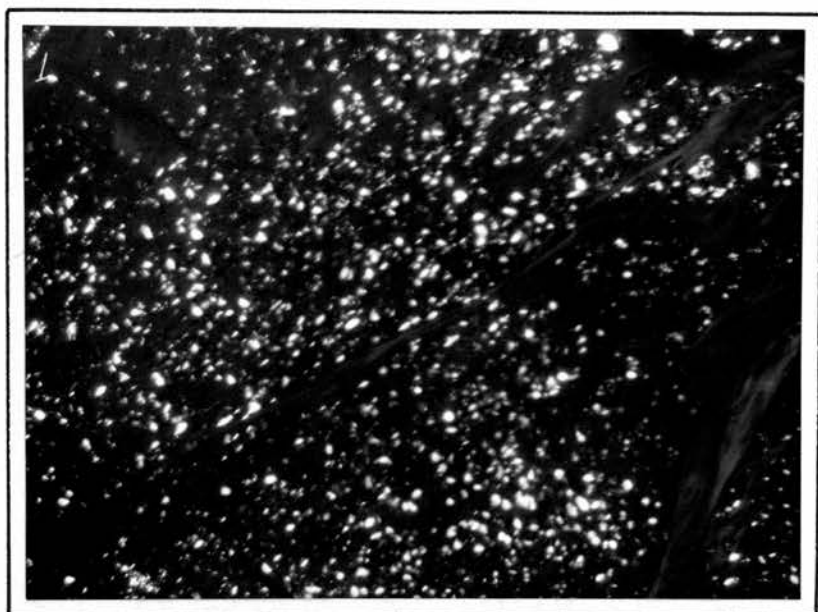
Photo 79   X160
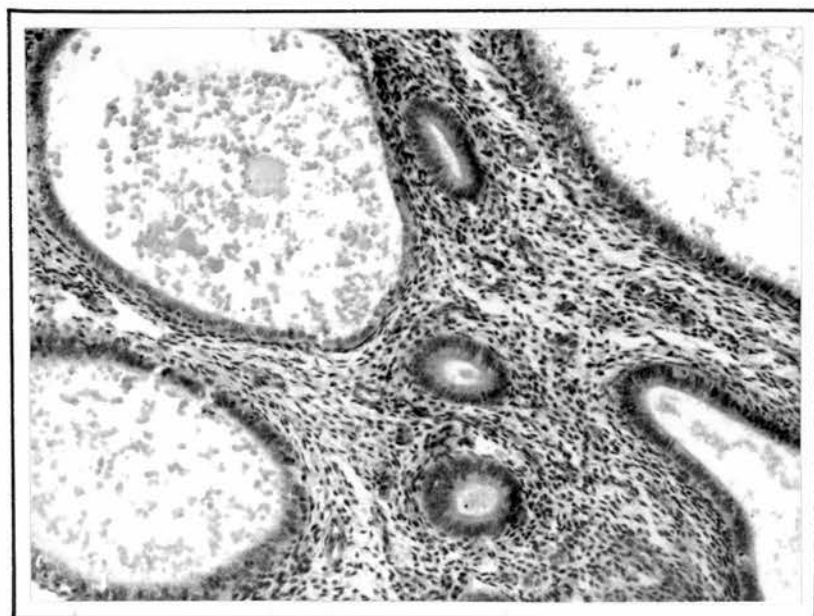
Photo 80.   X140

PHOTO 81.

Case 9. (83/61.)

Naked-eye photograph of the pathological specimen.

Note the profuse polypoidal endometrium.

The cervix shows Nabothian follicle formation.

PHOTO 82.

Case 9. (83/61.)

Cut section of left ovary showing a whitish-fibroma
and a smaller yellow central thecoma surrounded by
haemorrhage.
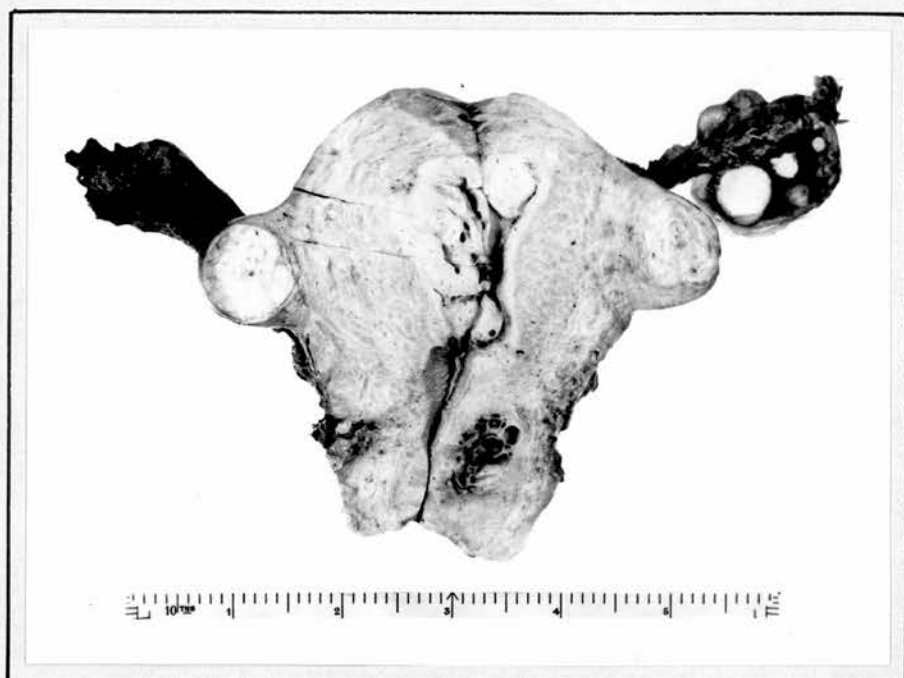
Photo 81.
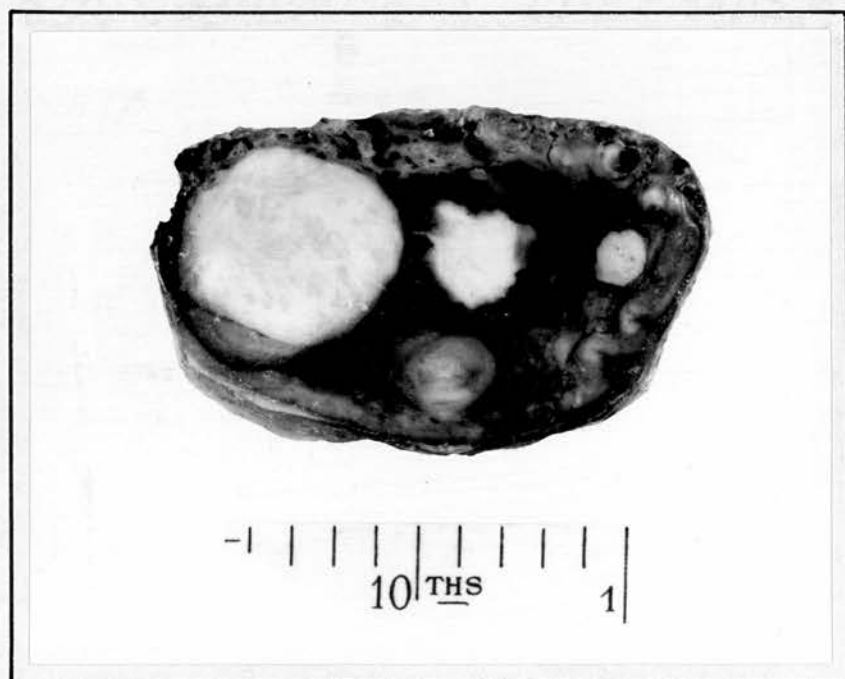
Photo 82.

PHOTO 83.   X 250.

Case 9. (83/61.)

Section of the yellow central nodule of left
ovary showing a typical thecoma. (H. & E.)

PHOTO 84. X 250.

Case 9. (83/61.)

Reticular fibres surrounding clear individual
theca cells of the above tumour.

(Gordon and Sweet Reticulum Stain.)
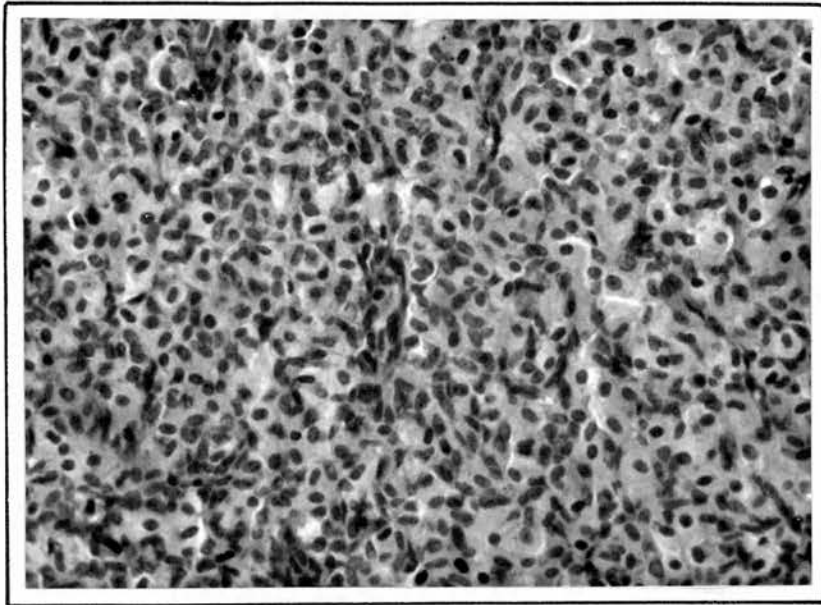
Photo 83.   X 250
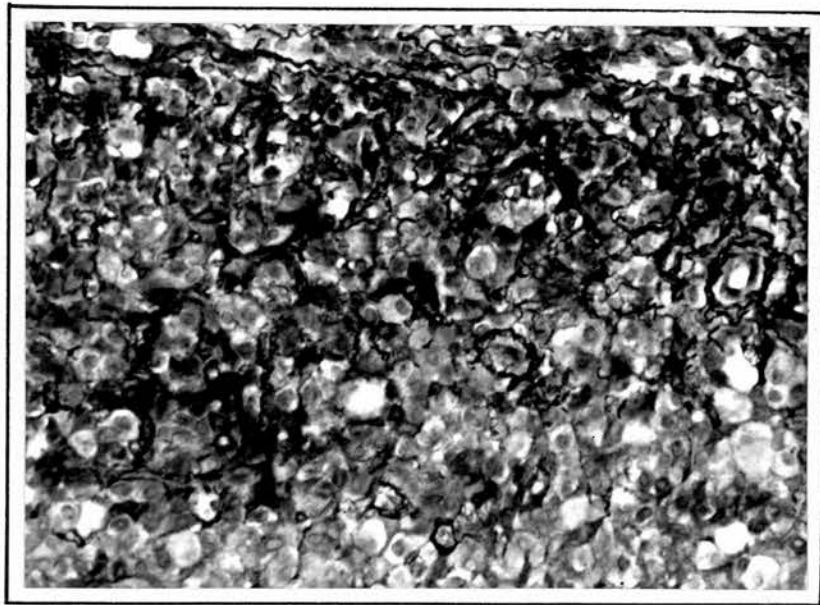
Photo 84.   X 250

PHOTO 85. X 180.

Case 9. (83/61.)

Theca cell tumour showing high content of red fat droplets in all the cells.

(Sudan IV Stain)

(Black and white.)

PHOTO 86. X 180.

Case 9. (831/61.

Birefringent crystals are present practically in every cell of the theca cell tumour.
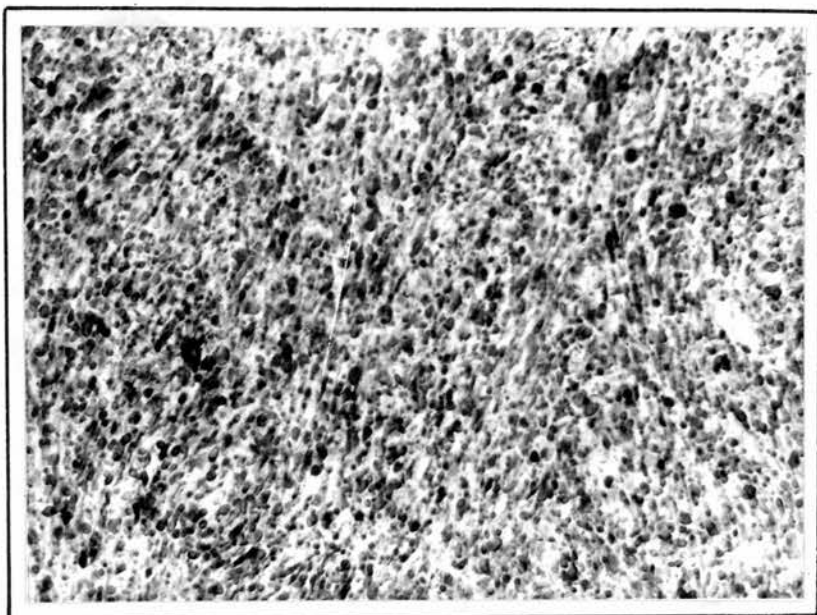
Photo 85.   X180
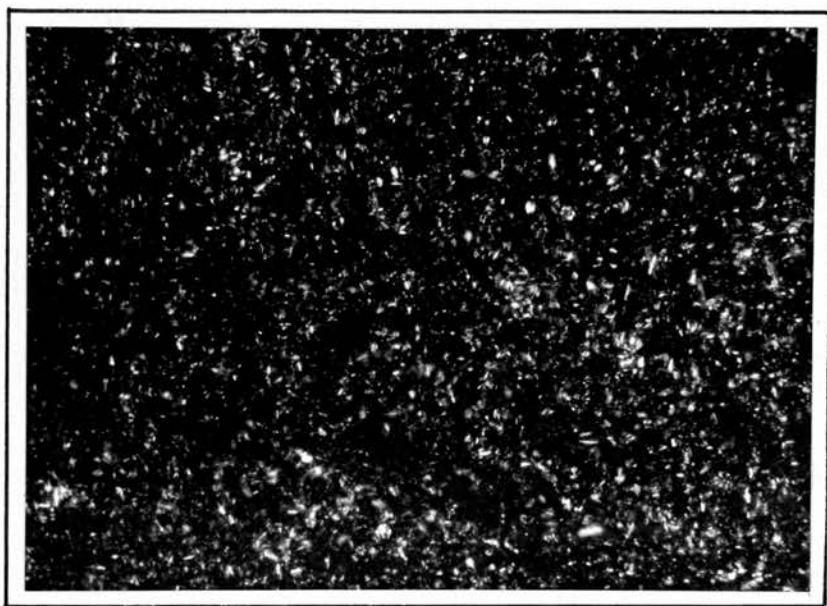
Photo 86.   X180

PHOTO 87. X 180.

Case 9. (83 /61.)

Thecoma.   Schultz Test - green droplets are seen
diffusely all over the section.

(Black and white.)

PHOTO 88. X 250.

Case 9. (83/61.)

Thecoma. Ashbel-Seligman ketosteroid test.

The cells show high content of dark blue granules.

(Black and white.)
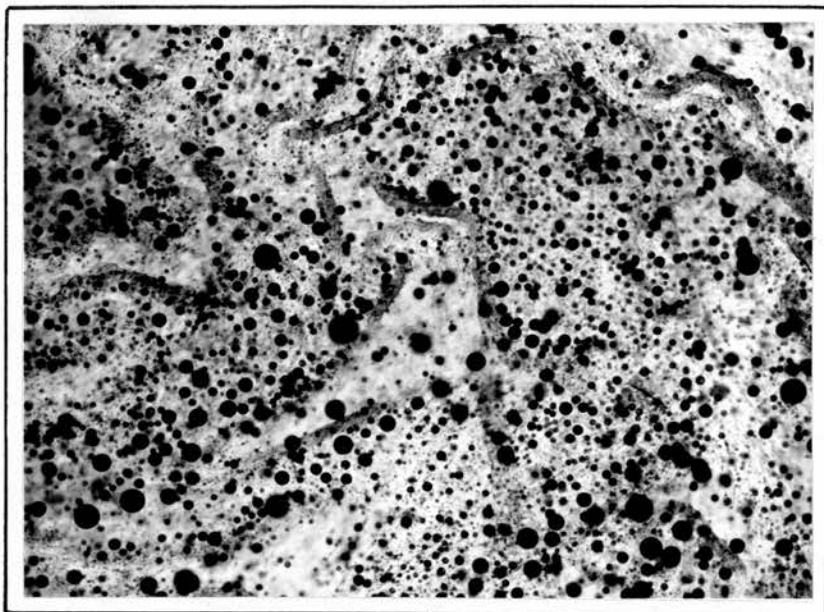
Photo 87.   X180
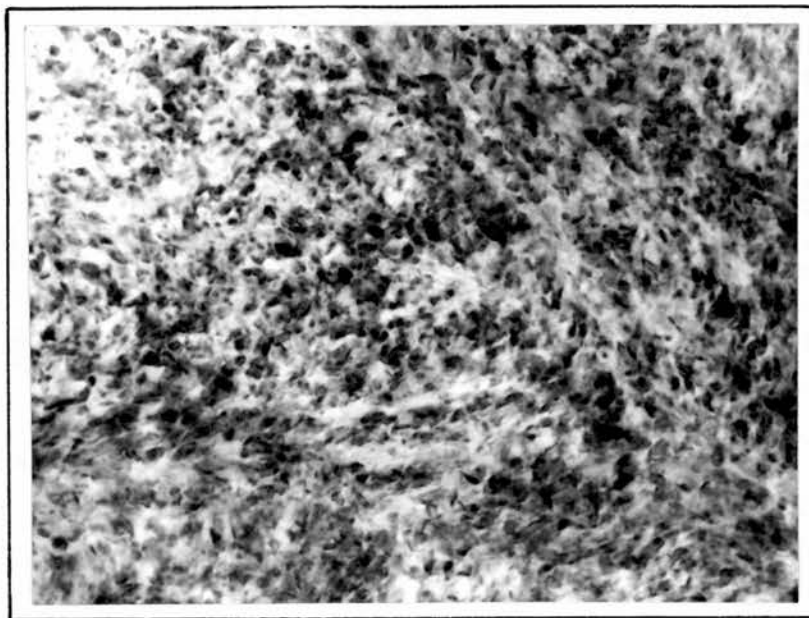
Photo 88.   X250

PHOTO 88a. X 180.

Case 9. (83/61.)

The endometrium showing cystic glandular hyperplasia.
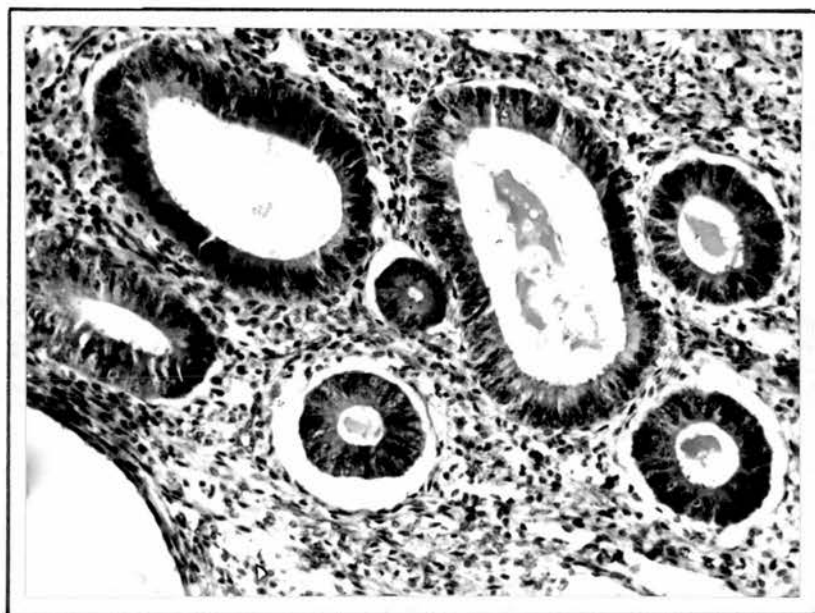
Photo 88a.   X180

PHOTO 89. X 180.

Case 11. (5500/61.)

Malignant thecoma.   Note the variation in size
and shape of the nuclei and the mitotic figures.
(H. & E.)

PHOTO 90. X 220.

Case 11. (5500/61.)

Malignant thecoma.

Reticular fibres surrounding clear individual cells.
(Gordon and Sweet reticulum stain.)
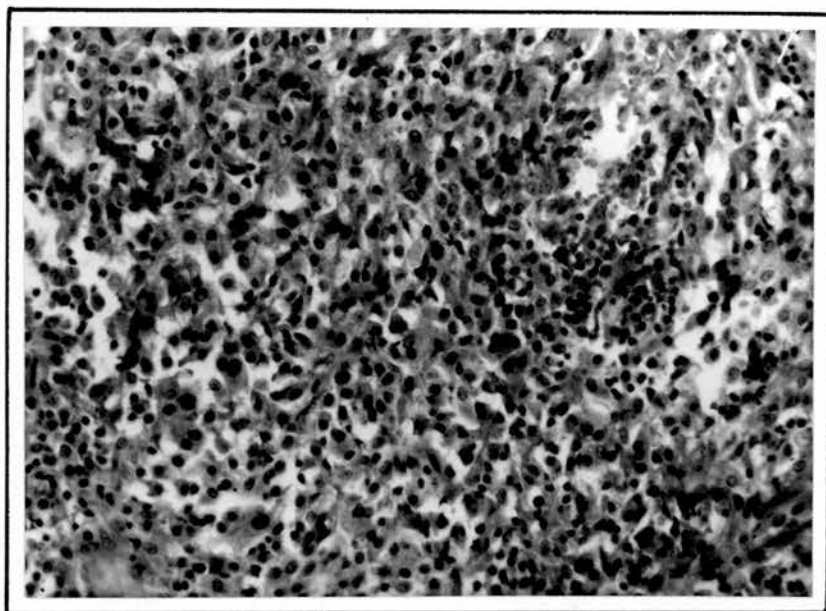
Photo 89.   X180
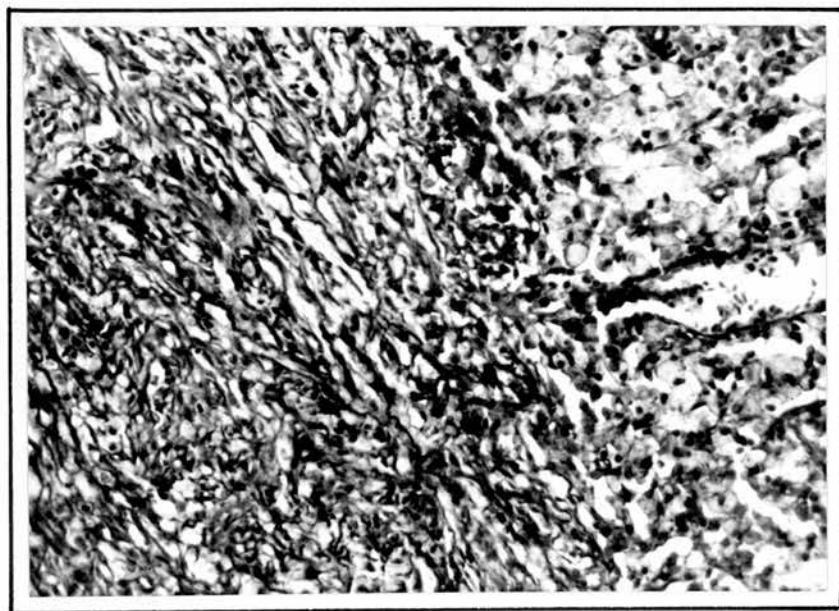
Photo 90.   X220

PHOTO 91.   X 140.

    Case 11.   (5500/61.)

      Malignant thecoma.

      A section showing high content of red fat droplets.

      (Sudan IV.)

      (Black and white.)

PHOTO 92.   X 180.

    Case 11.   (5500/61.)

    Malignant thecoma cells showing high concentration of birefringent crystals.
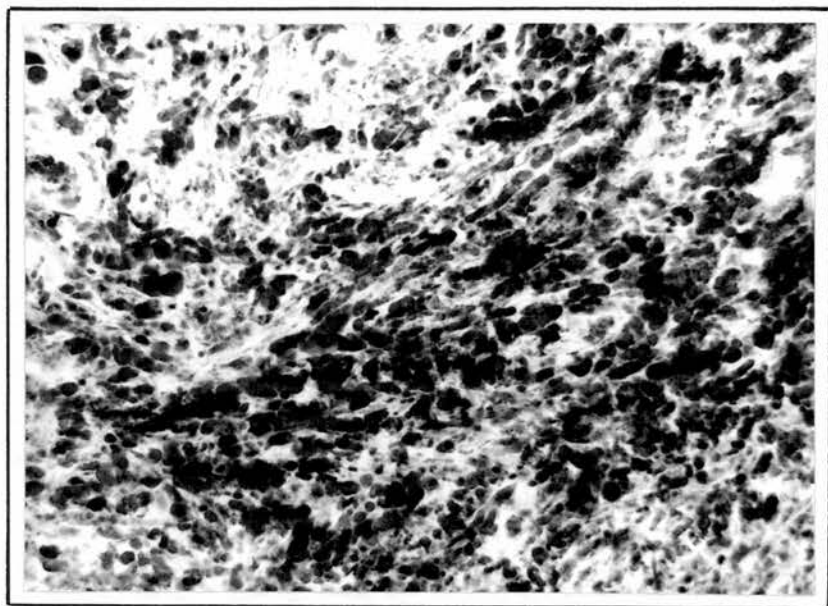
Photo 91.   X140
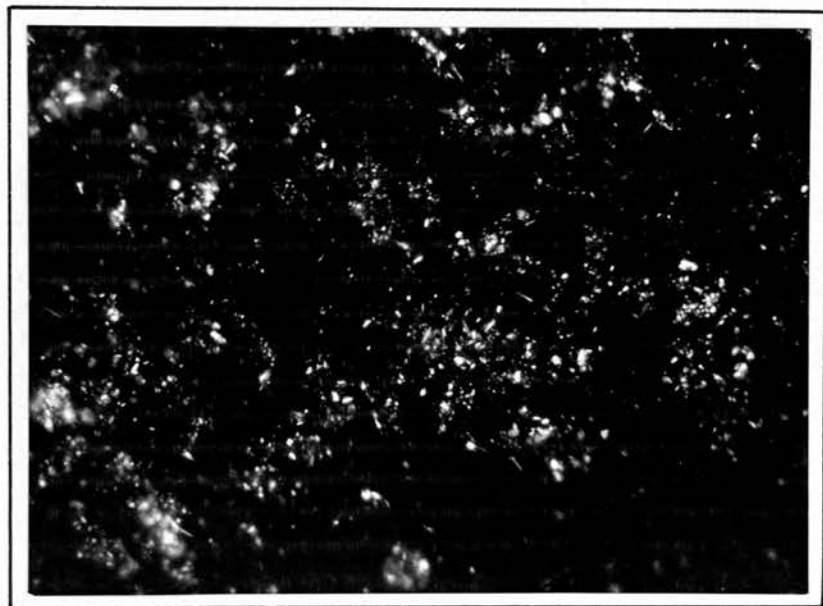
Photo 92.   X180

PHOTO 93. X 300.

Case 11. (5500/61.)

Malignant thecoma.

Schultz test.   Green droplets are scattered
diffusely all over the section.

PHOTO 94. X 230.

Case 11. (5500/61.)

Malignant thecoma.

Ashbel-Seligman Ketosteroid reaction.

Dark blue granules are present in most of the cells.

(Black and white.)
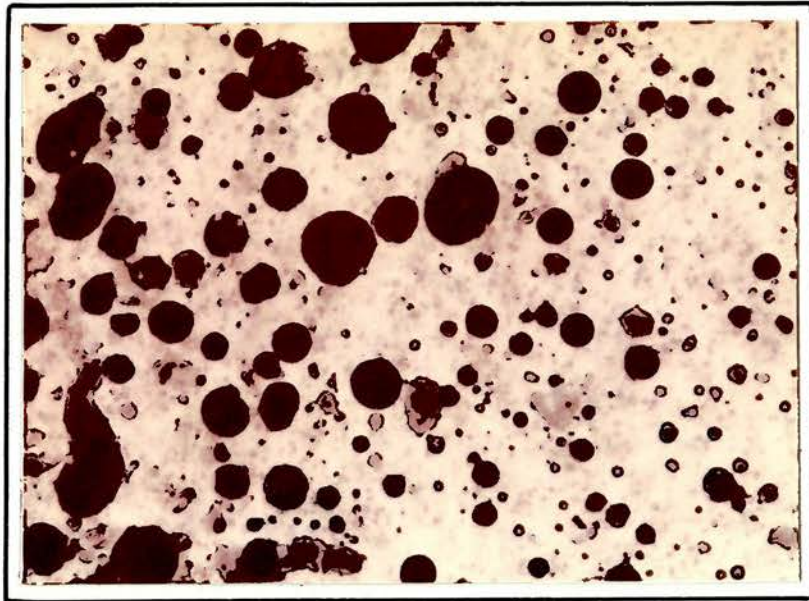
Photo 93.   X300
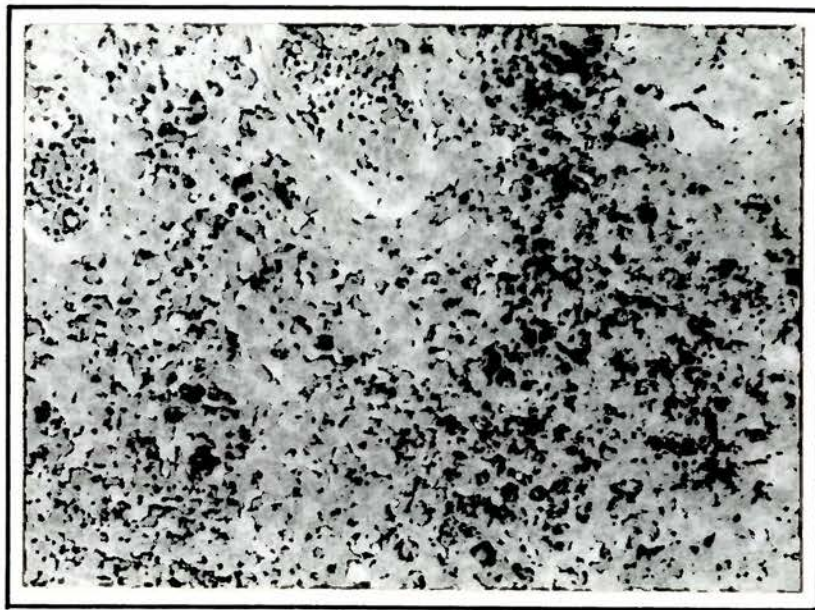
Photo 94.   X230

PHOTO 95.

Case 13. (200/61.)

Naked eye photograph of the pathological material.
The right ovary harbours a tiny whitish nodule. The left
ovary is the seat of a follicular cyst.

Note the thickened uterine wall and the profuse
endometrium.

PHOTO 96. X 180.

Case 13. (200/61.)

Fibroma with thecomatous elements.

Birefringent crystals are present in a far less
degree than in the case of thecoma.
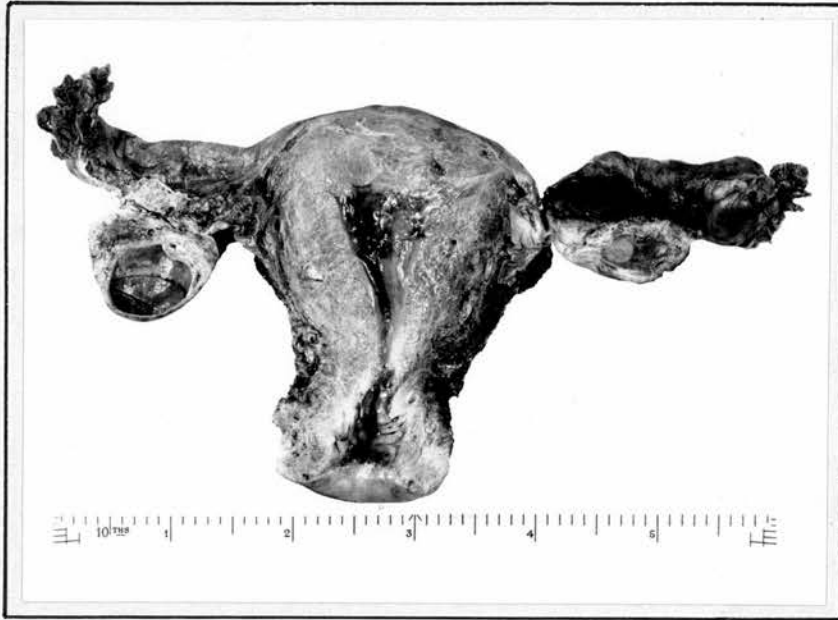
Photo 95.
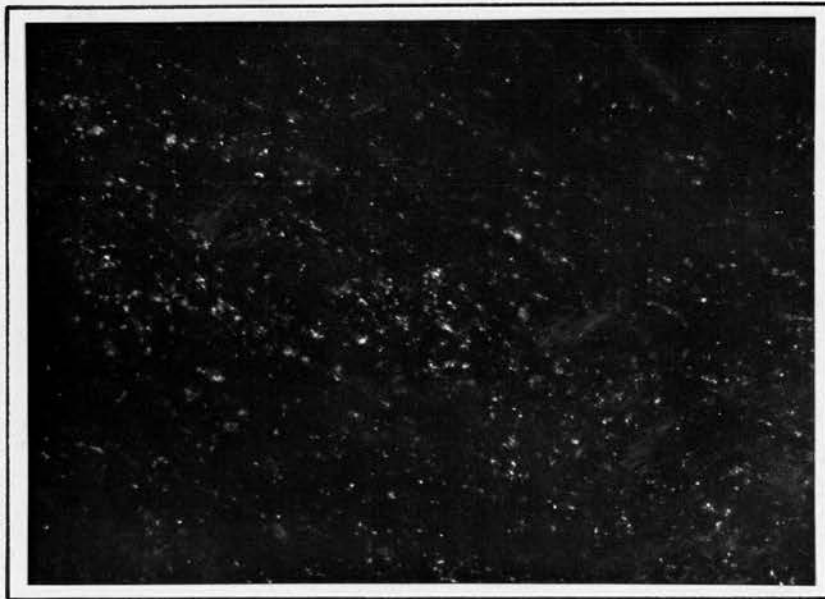
Photo 96. X180

PHOTO 97. X 260.

Case 13. (200/61.)

An area of thecomatosis in the cortex of the tumour-bearing ovary. (H. & E.)

PHOTO 98.

Case 18. (4619/61.)

Naked eye photograph of the pathological material. The uterine cavity is filled with a haemorrhagic, friable polypoid mass which proved to be a sarcomatous fibroid.

PHOTO 99.

Case 18. (4619/61.)

The right ovary showed few surface papillomata and contained a fibroma with a yellow centre, much resembling a corpus luteum.
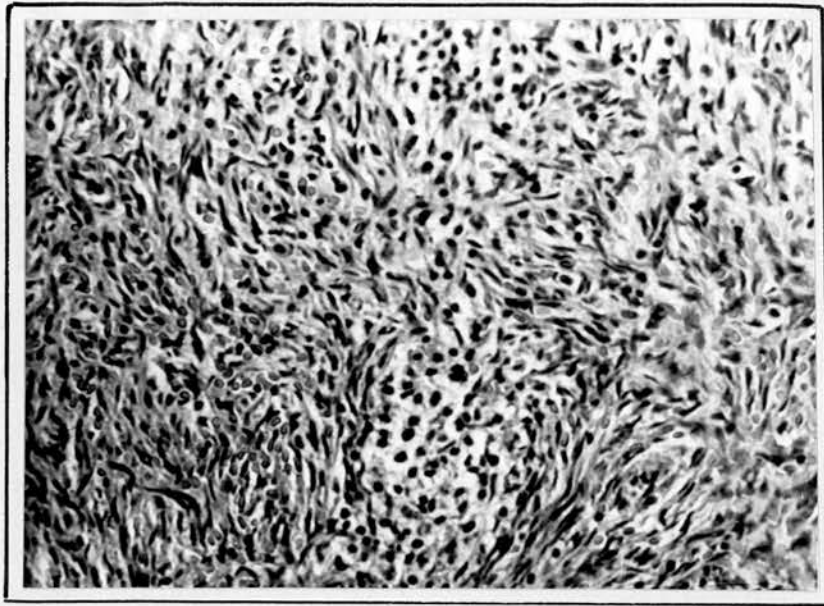
Photo 97.   X260
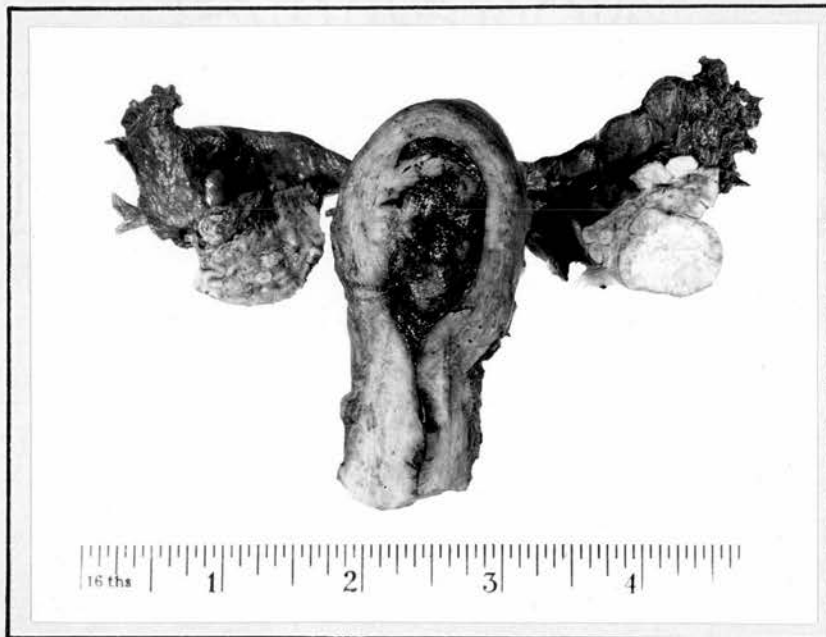
Photo 98.

Photo 99.

PHOTO 100.   X 140.

Case 18. (4619/61.)

Fibroma with thecomatous elements.   Clusters of
theca-like cells containing red fat droplets are present
amidst the fibroblasts.

(Sudan IV.)

(Black and white photograph.)

PHOTO 101.   X 220.

Case 18. (4619/61.)

The endometrium showing dilated glands and sarcomatous
fibroid with many giant cells. (H. & E.)

Photo 100.   X140
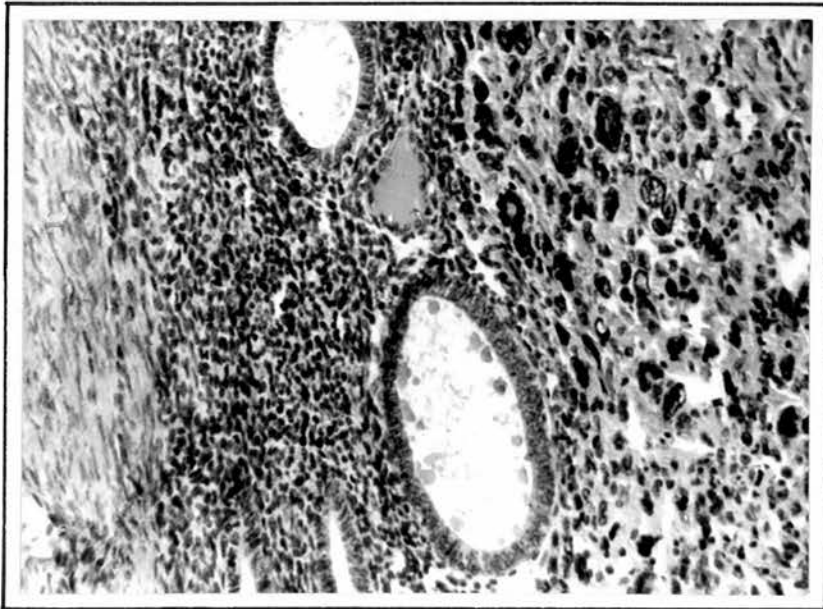
Photo 101.   X220

PHOTO 102. X 200.

Case 19. (494/62.)

Fibroma with thecomatous elements.

Schultz Test. Green droplets are present in scattered theca cells amidst the fibroblasts. The reaction is less intense than in a thecoma.
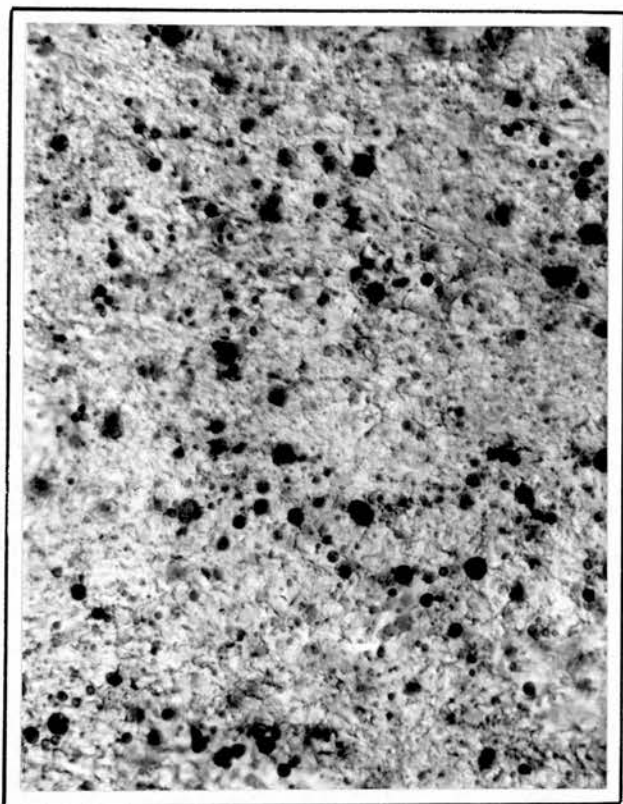
Photo 102.   X 200

PHOTO 103.   X 220.

Case 34.   (650/60.)

Brenner cell tumour.

Red fat droplets are seen inside theca-like stromal cells around the epithelial island.

(Sudan IV.)

PHOTO 104.   X 180.

Case 34.   (650/60.)

Birefringent crystals inside the stromal cells.

Note the continuous fibrillar and non-granular birefringence of the connective tissue fibres.
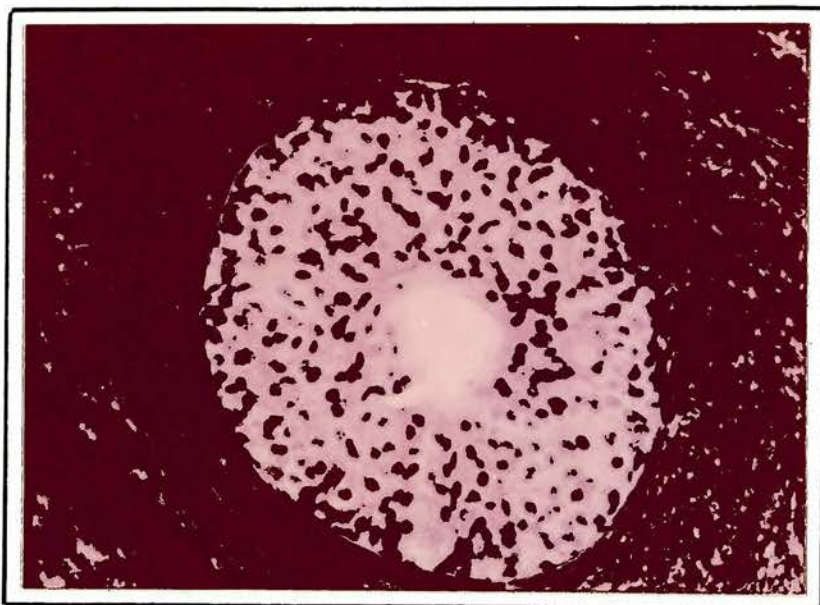
Photo 103.   X 220

Photo 104.   X 180

PHOTO 105.   X 150.

   Case 34.   (650/60)

   Endometrium showing cystic glandular hyperplasia.

(H. & E.)

PHOTO 106.   X 200.

   Case 35.   (1524/61.)

   Brenner cell Tumour.

   Theca-like stromal cells containing red fat droplets.

(Sudan IV.)

Photo 105.   X150
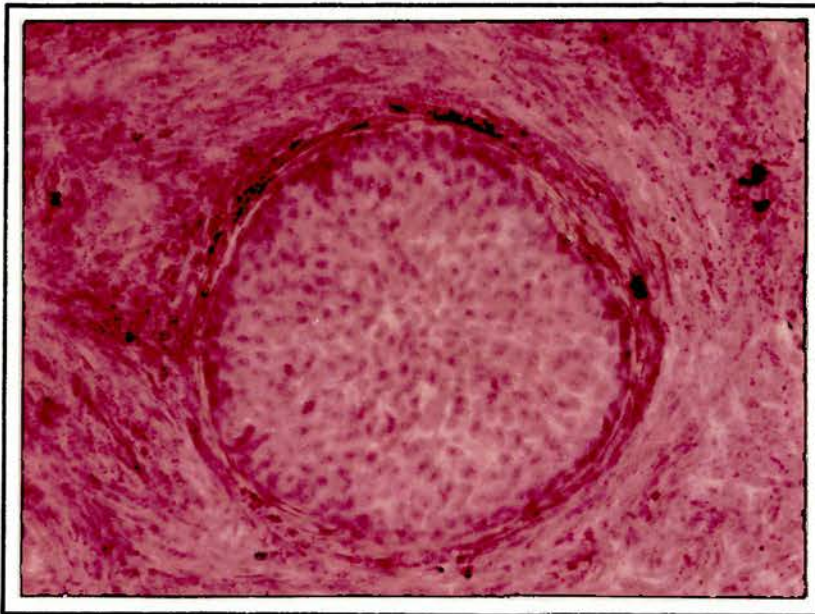
Photo 106.   X200

PHOTO 107.   X 180.

   Case 35. (1524/61.)

     Brenner cell tumour.

     Birefringent crystals inside theca-like stromal cells.

PHOTO 108.   X 250.

   Case 35. (1524/61.)

   Cystic hyperplastic glands seen in the endometrial
polypi.
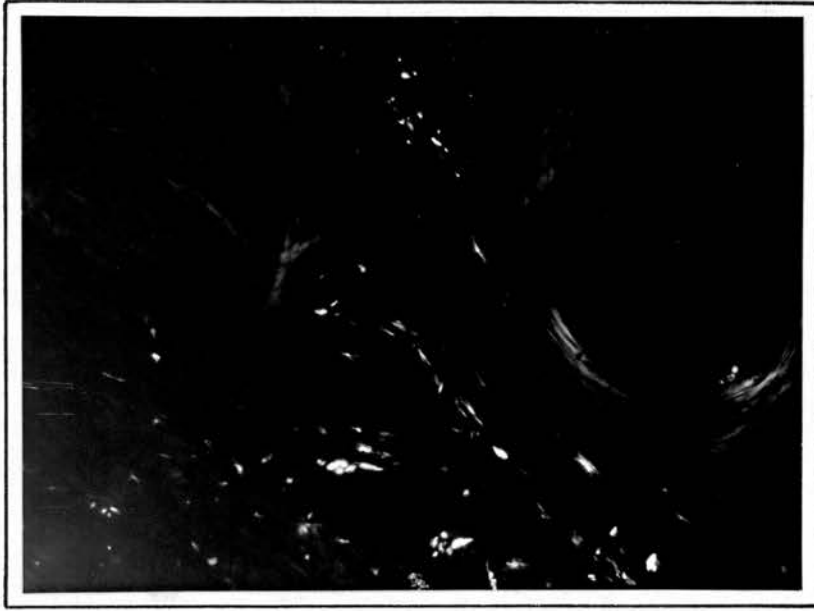
Photo 107.   X180
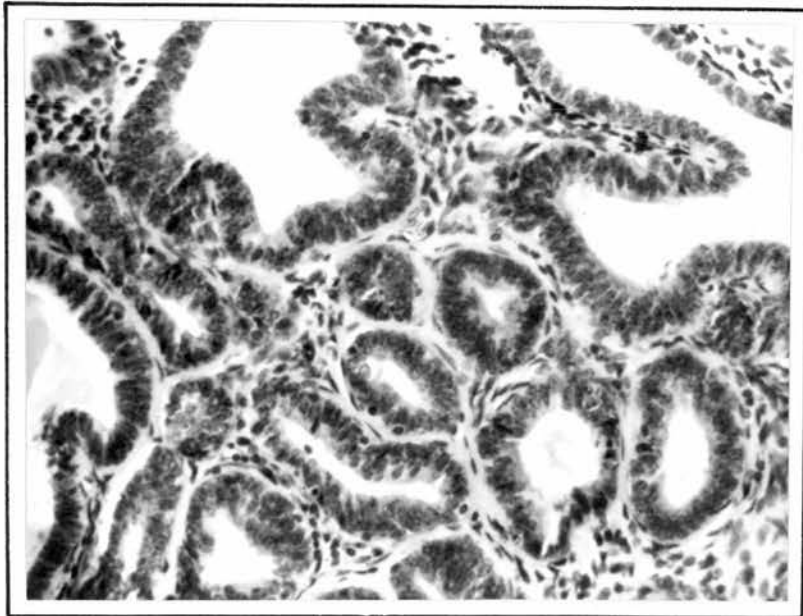
Photo 108.   X250

PHOTO 109. X 280.

    Case 39. (5876/61.)

        Pseudomucinous cystadenoma.

        Ashbel-Seligman Ketosteroid reaction.

        Dark blue material inside theca-like stromal cells.

PHOTO 110. X 260.

    Case 39. (5876/61.)

        Pseudomucinous cystadenoma.

        Black deposit underneath the epithelium indicating
marked alkaline phosphatase activity in the stroma.

        (Coupling Azo-dye technique for alkaline phosphatase.
Frozen section.)
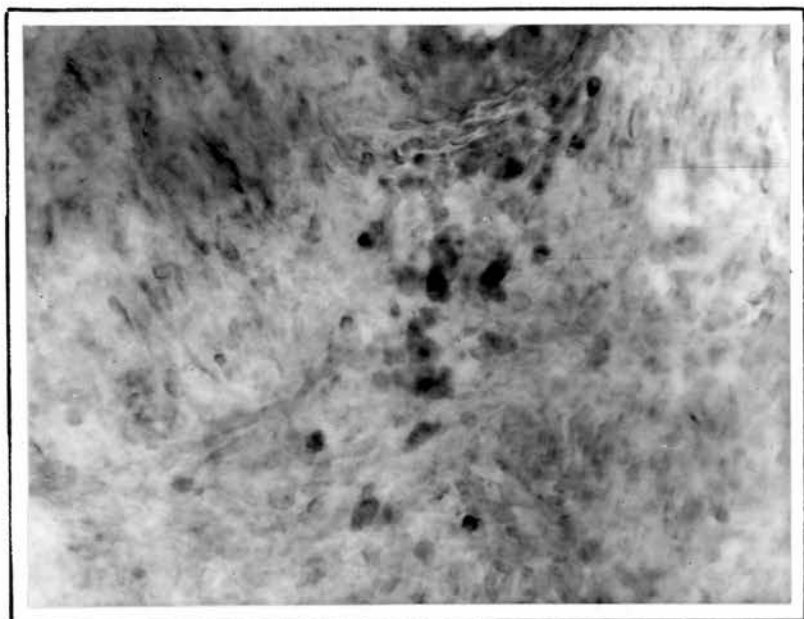
Photo 109.   X280

Photo 110.   X260

PHOTO 111.   X 180.

Case 39. (5876/61.)

Pseudomucinous cystadenoma. Black deposit indicating
marked alkaline phosphatase activity in the stroma. The
epithelium is free.

(Gomori's method - Paraffin section.)

PHOTO 112. X 175.

Case 39.   (5876/61.)

Pseudomucinous cystadenoma.

(Acid phosphatase, Burton Method - Frozen Section.)

Black deposit mainly inside the epithelial cells.

Photo III.   X180
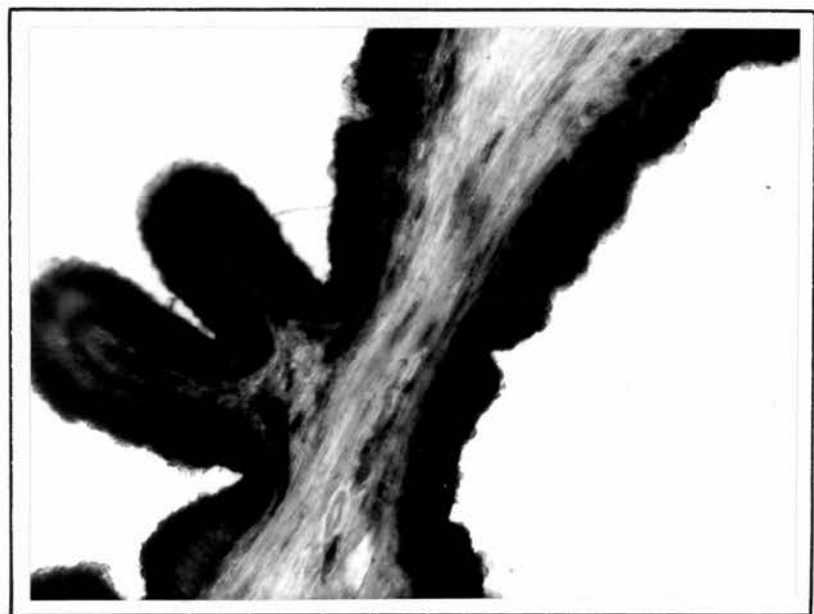
Photo 112.   X175

PHOTO 113. X 175.

Case 39. (5876/61.)

Pseudomucinous cystadenoma.

(Acid phosphatase Gomori's Method, Frozen section.)

Black deposit is again seen mainly at the tips of
epithelial cells.

PHOTO 114. X 180.

Case 39. (5876/61.)

Pseudomucinous cystadenoma.

(Acid phosphatase Gomori's Method, Paraffin section.)

Section shows black deposit inside the epithelial
cells.

Nuclear staining markedly apparent in the stromal cells,
is supposed to be due to an artifact.
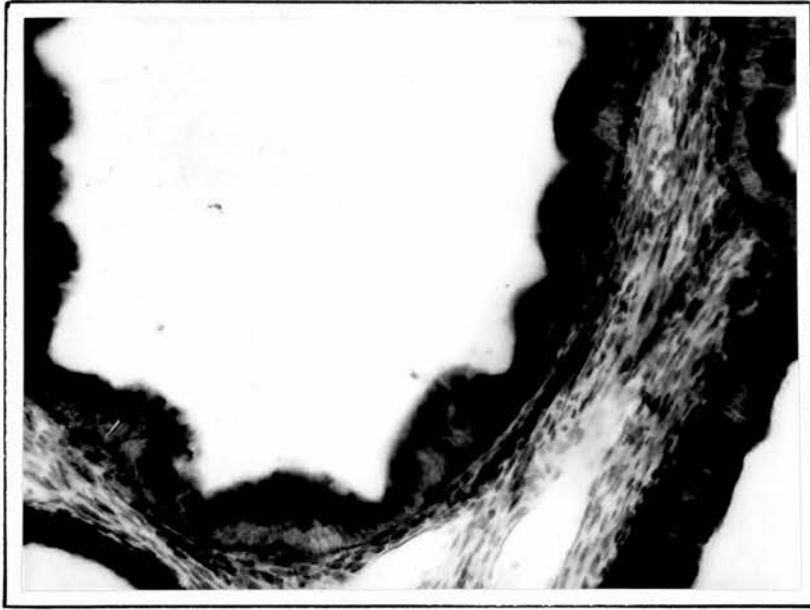
Photo 113.   X175
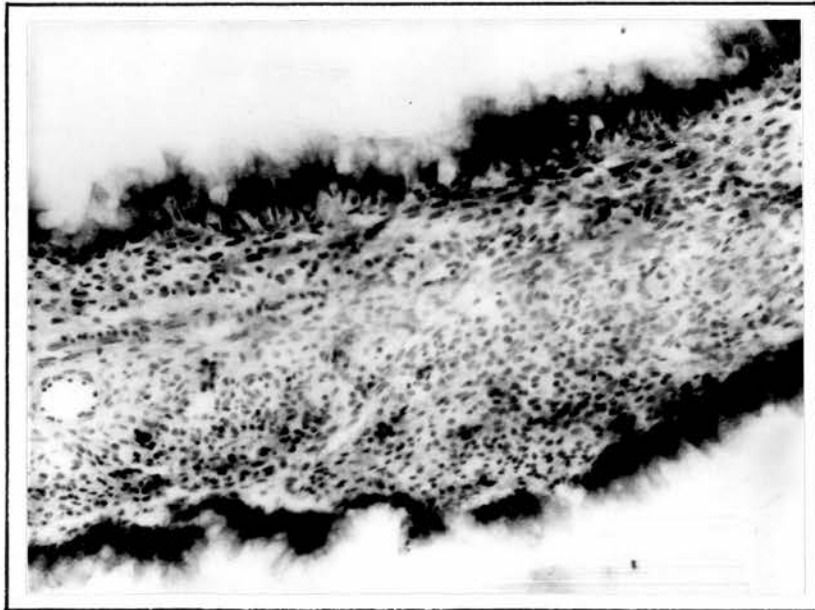
Photo 114.   X180

PHOTO 115. X 220.

Case 39. (5876/61.)

Pseudomucinous cystadenoma.

(Non-specific esterase - Frozen section.)

Black deposits are mainly inside the epithelial cells.

PHOTO 116. X 260.

Case 39. (5876/61.)

The contra-lateral ovary showing marked blue granules
indicating succinic dehydrogenase activity in the cortex.

(Nitro B.T. - Fresh frozen section.)
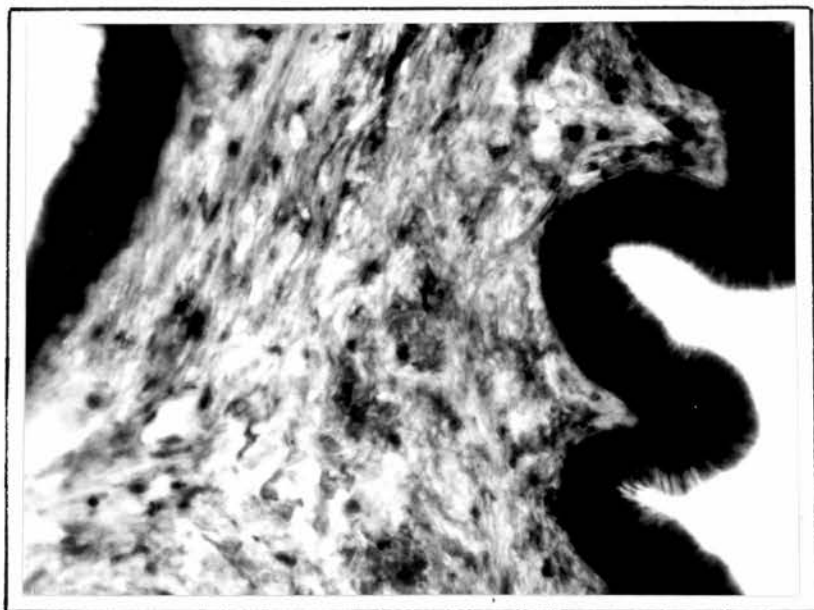
Photo 115.   X220
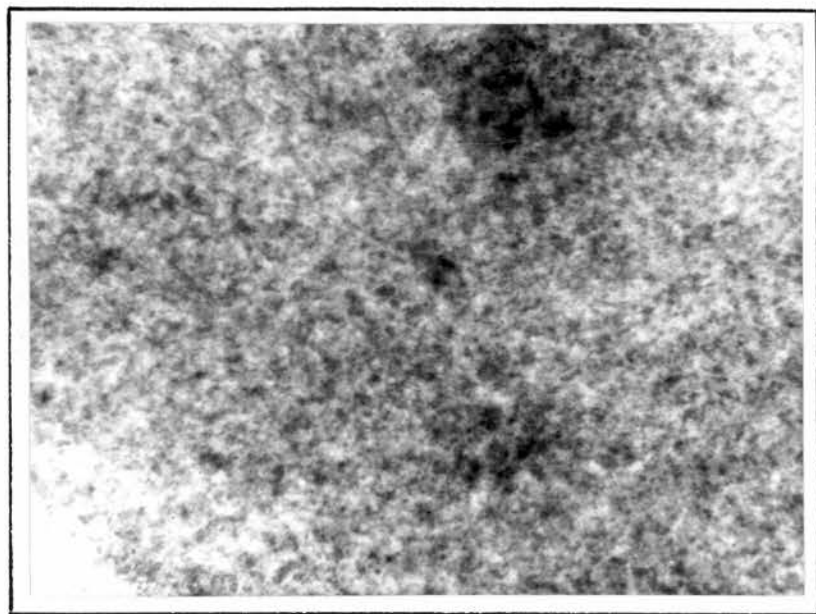
Photo 116.   X260

PHOTO 117. X 300.

   Case 40. (436/61.)

     Pseudomucinous cystadenoma.

     Stromal theca-like cells containing red fat droplets.

     (Sudan IV.)

PHOTO 118. X 280.

   Case 40. (436/61.)

     Ashbel-Seligman ketosteroid reaction.

     Theca-like stromal cells containing dark-blue granules
are seen rupturing through the epithelium.
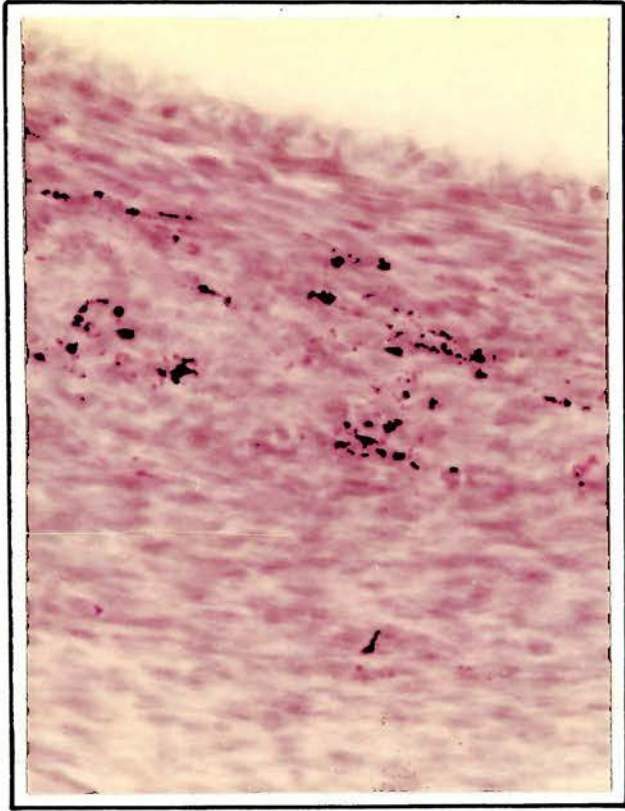
Photo 117.   X300
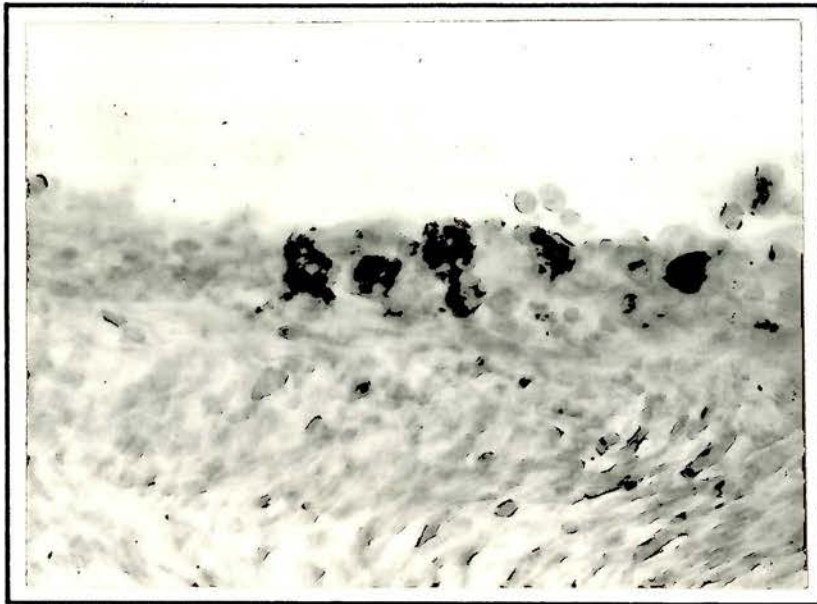
Photo 118.   X280

PHOTO 119. X 300.

   Case 40. (436/61.)

   The contra-lateral ovary showing theca-like cells
amidst the cortical fibroblasts (thecomatosis).

PHOTO 120. X 190.

   Case 40. (436/61.)

   Endometrium showing proliferative activity and
dilated glands.
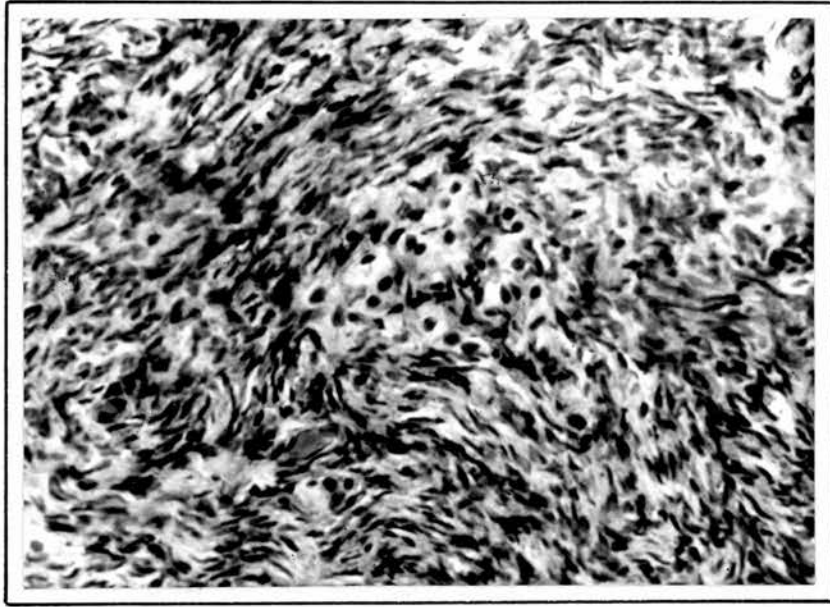
Photo 119.   X300
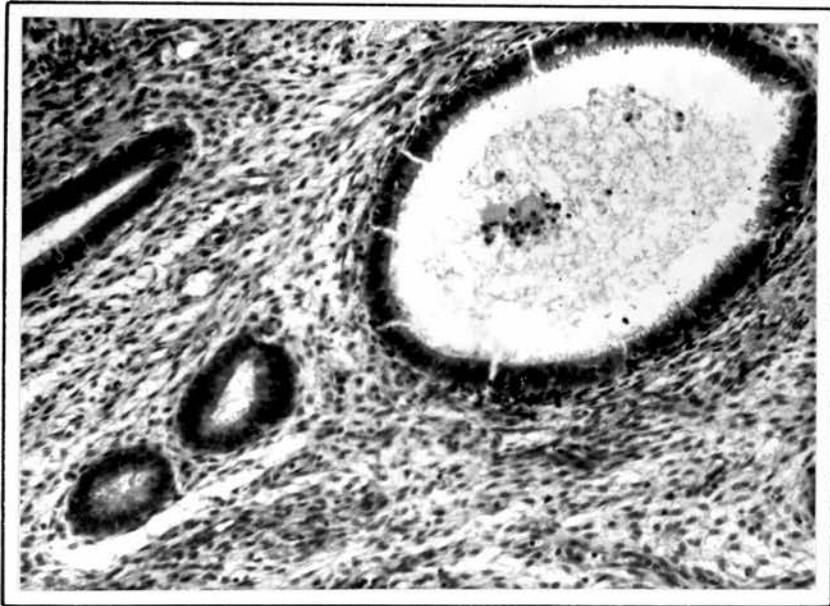
Photo 120.   X190

PHOTO 121.   X 100.

   Case 41. (3448/61.)

      Pseudomucinous cystadenoma.

      Section showing a large area of theca-like stromal
cells.   (H. & E.: Frozen section.)
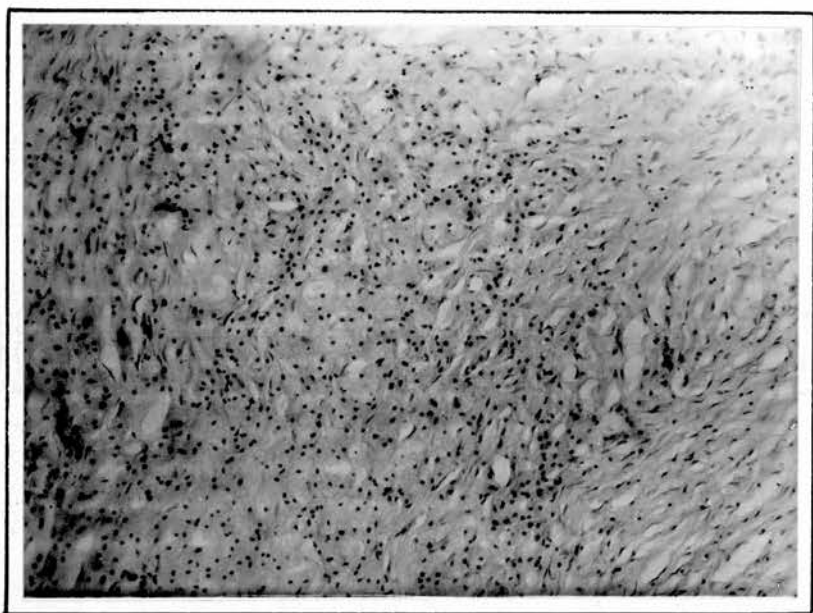
Photo 121.   X100

PHOTO 122.   X 70.

    Case 41.   (3448/61.)

      Cells of the same area as above, showing high content
of red fat droplets.

    (Sudan IV.)

PHOTO 123.   X 100.

    Case 41.   (3448/61.)

      The same area of cells showing high concentration of
birefringent crystals.
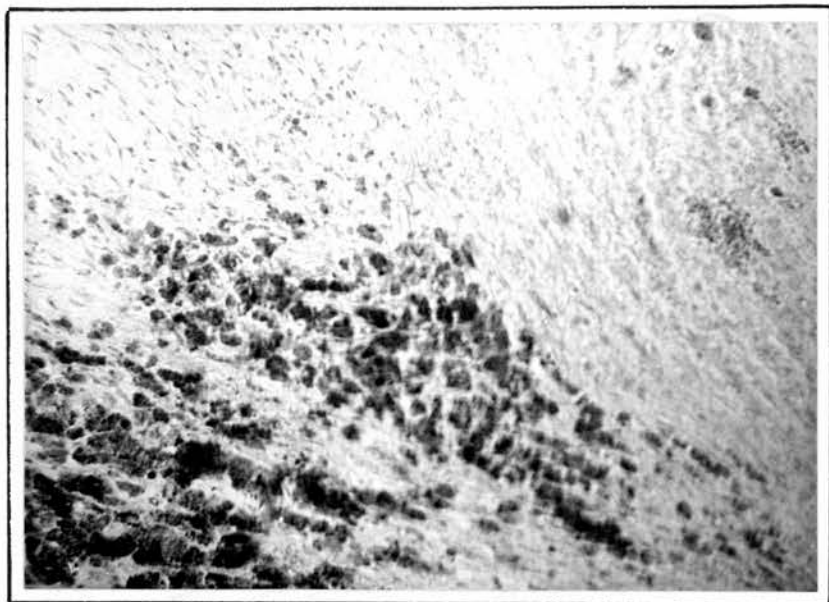
Photo 122.   X70
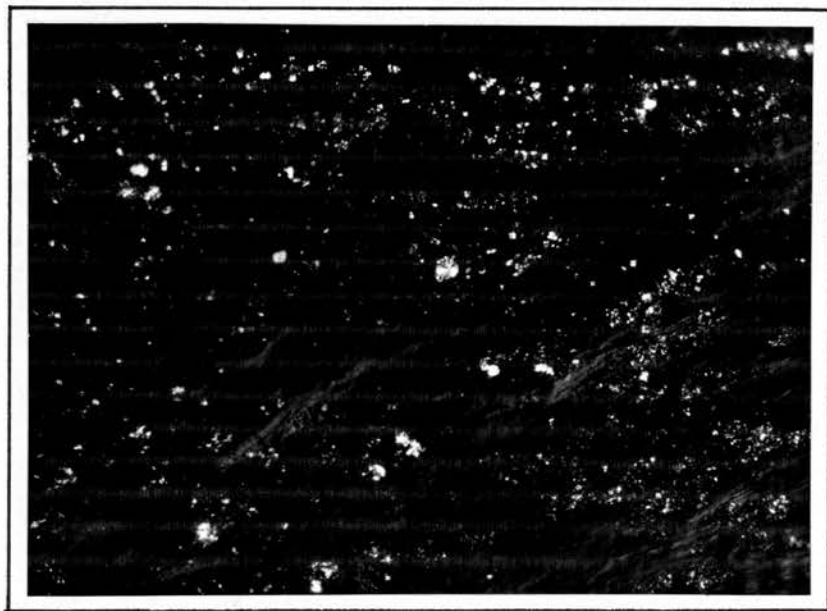
Photo 123.   X100

PHOTO 124.   X 70.

   Case 41.   (3448/61.)

    Ashbel-Seligman Ketosteroid reaction.

    Dark blue granules inside theca-like cells of the
same area.

PHOTO 125.   X 260.

   Case 41.   (3448/61.)

    The contra-lateral ovary showing blue granules in the
cortex, indicating marked succinic dehydrogenase activity.
(Nitro - B.T. fresh frozen section.)
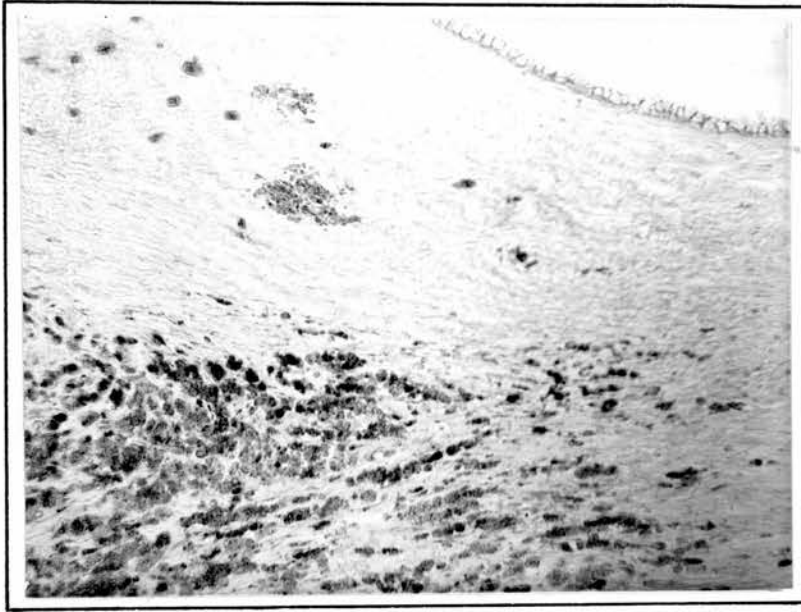
Photo 124.   X70
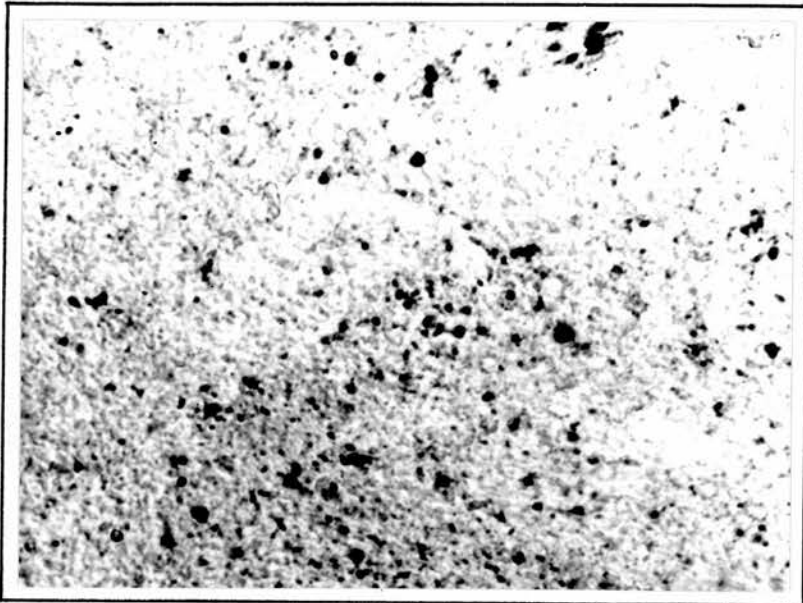
Photo 125.   X260

PHOTO 126. X 140.

   Case 41. (3448/61.)

    Endometrium showing proliferative activity.

(H. & E.)

PHOTO 127. X 180.

   Case 42. (5999/60.)

    Pseudomucinous cystadenoma.

    Birefringent crystals seen inside stromal cells underneath the epithelium.
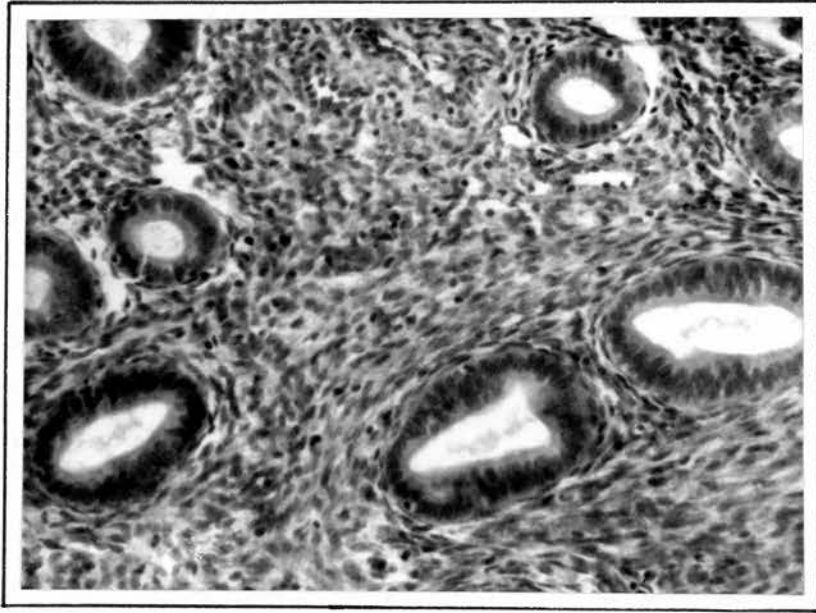
Photo 126.   X140
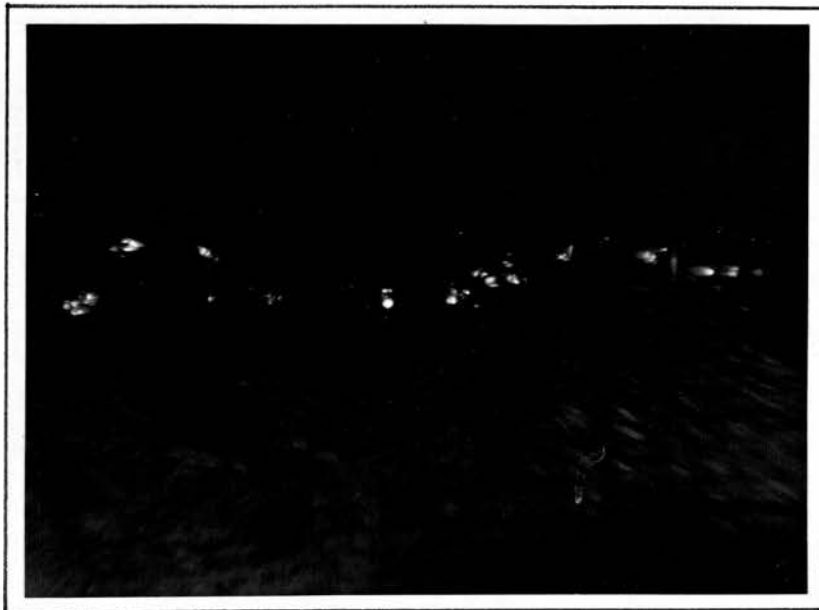
Photo 127.   X180

PHOTO 128. X 280.

Case 42. (5999/60.)

Dark blue granules inside theca-like stromal cells.

(Ashbel-Seligman Ketosteroid reaction.)

PHOTO 129. X 220.

Case 42. (5999/60.)

Pseudomucinous cystadenoma.

Theca-like stromal cells containing dark blue granules
rupturing through the epithelium.

(Ashbel-Seligman ketosteroid reaction.)
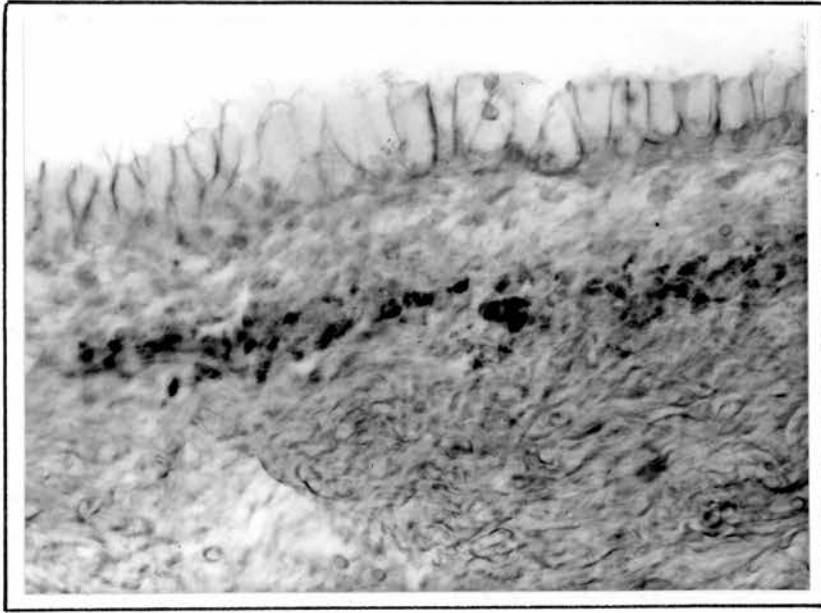
Photo 128.   X 280
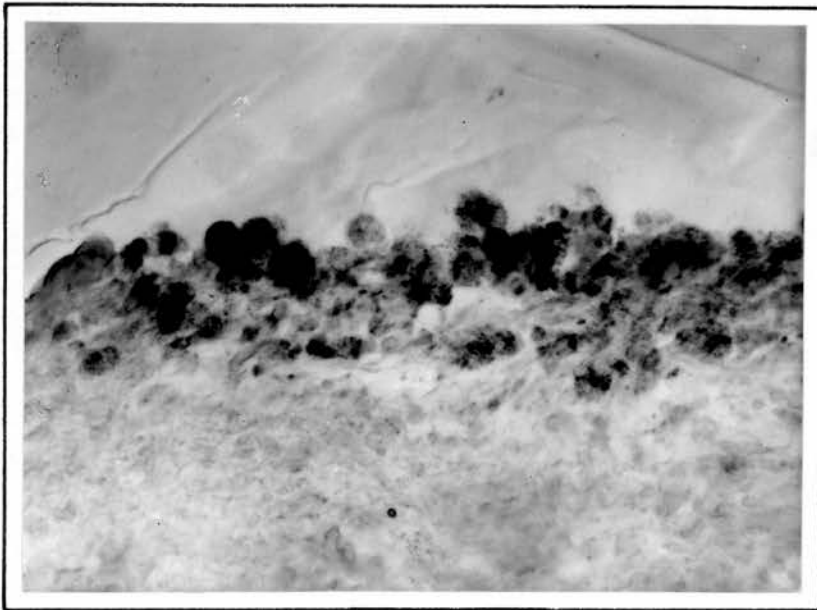
Photo 129.   X 220

PHOTO 130. X 250.

Case 42. (5999/60.)

Endometrium showing proliferative activity.

PHOTO 131. X 190 (reduced)

Case 37. (3143/61.)

A portion of the cyst lined by benign typical
pseudomucinous epithelium.

PHOTO 132. X 100 (reduced)

Case 37. (3143/61.)

Another portion of the same cyst showing benign
serous papillae.

Photo130.   X250
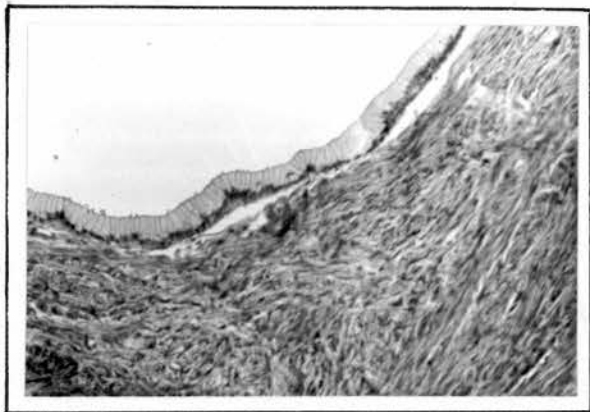
Photo 131.
X190 (reduced)
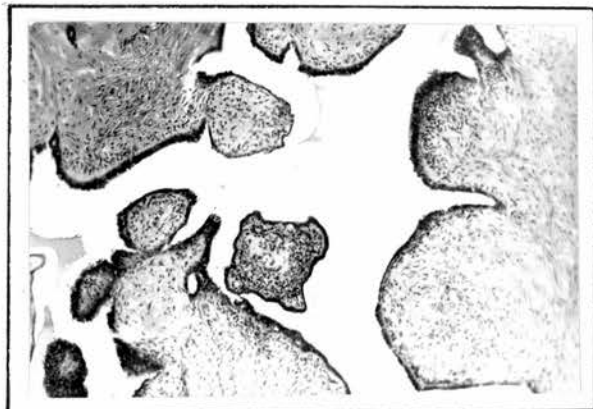
Photo 132.
X100 (reduced)

PHOTO 133. X 220.

Case 75. (4646/60.

Simple Serous cyst.

Birefringent droplets, showing the characteristic
Maltese cross, inside theca-like cells rupturing through
the epithelium.

PHOTO 134.

Case 76. (4125/61.)

Serous papilloma making a bed for itself on the
surface of the ovary.

Photo 133.   X220
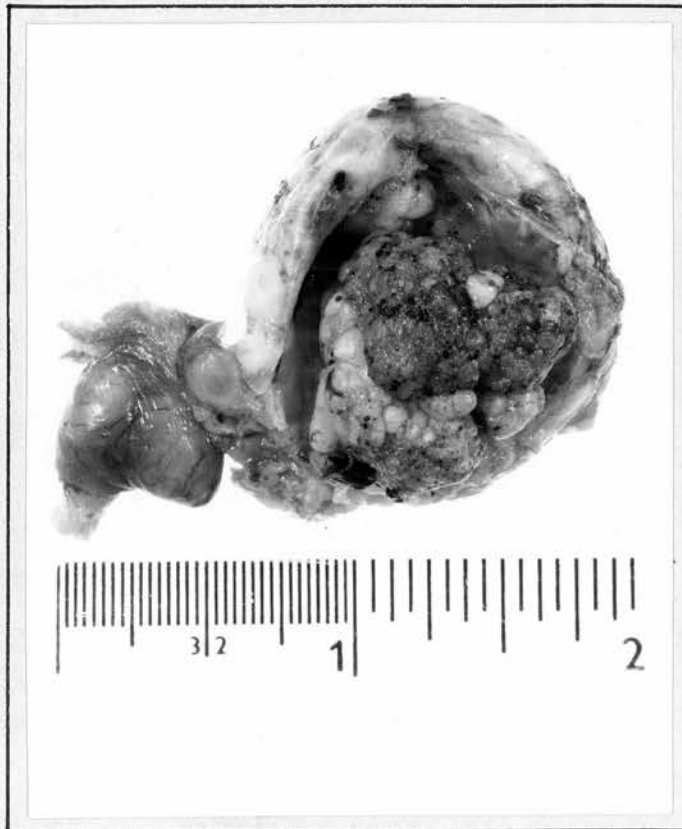
Photo 134.

PHOTO 135. X 130.

Case 77. (2326/61.)

Papillary Serous Cyst of borderline malignancy.

Theca-like cells containing red fat droplets are apparent in the stroma.

(Sudan IV.)

Black and white photograph.

PHOTO 136. X 100.

Case 77. (2326/61.)

Birefringent crystals inside stromal theca-like cells.
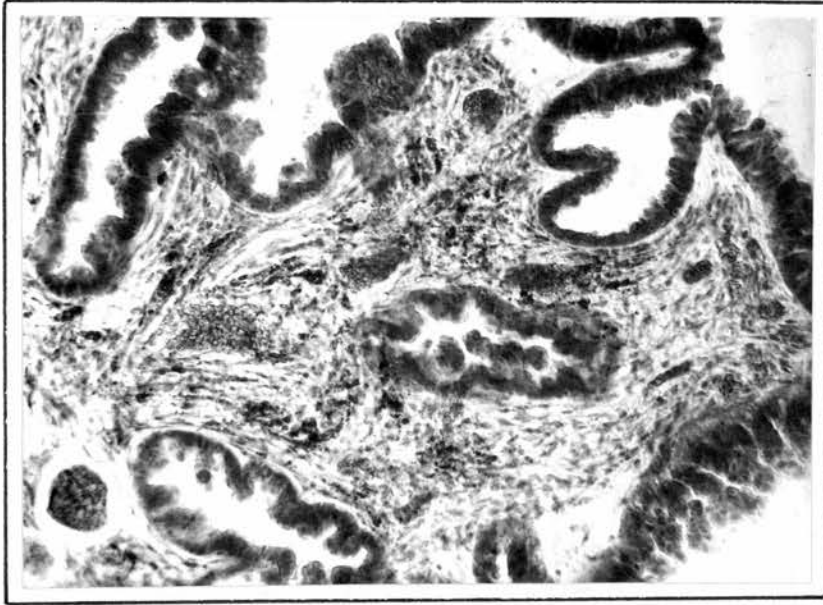
Photo 135.   X130
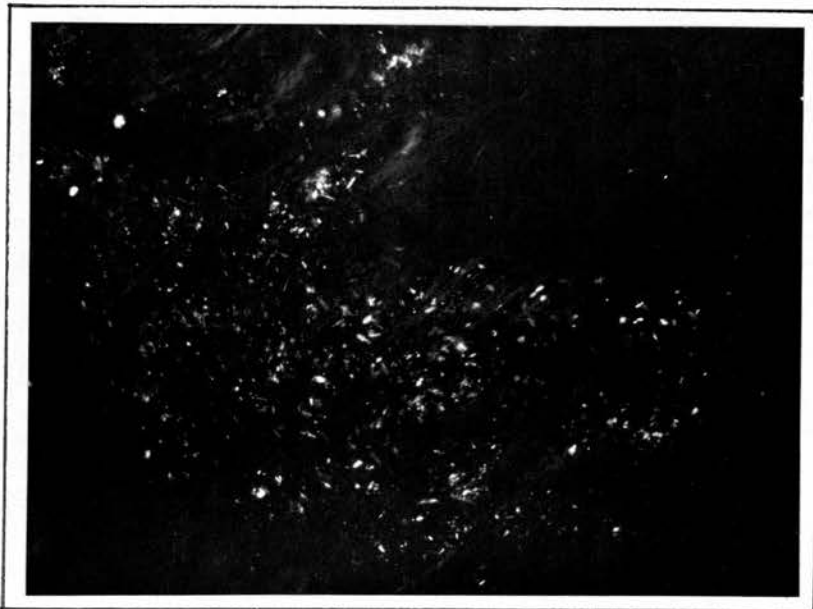
Photo 136.   X100

PHOTO 137.   X 180.

  Case 77.   (2326/61.)

    Dark blue granules inside stromal theca-like cells.

    (Ashbel-Seligman ketosteroid reaction.)

PHOTO 138.   X 60.

  Case 92.   (2209/61.)

    Contra-lateral ovary showing a hyperplastic cortical
stroma with foci of thecomatosis and cortical granuloma
which were apparent as yellow specks on the cut surface.

Photo 137.   X180
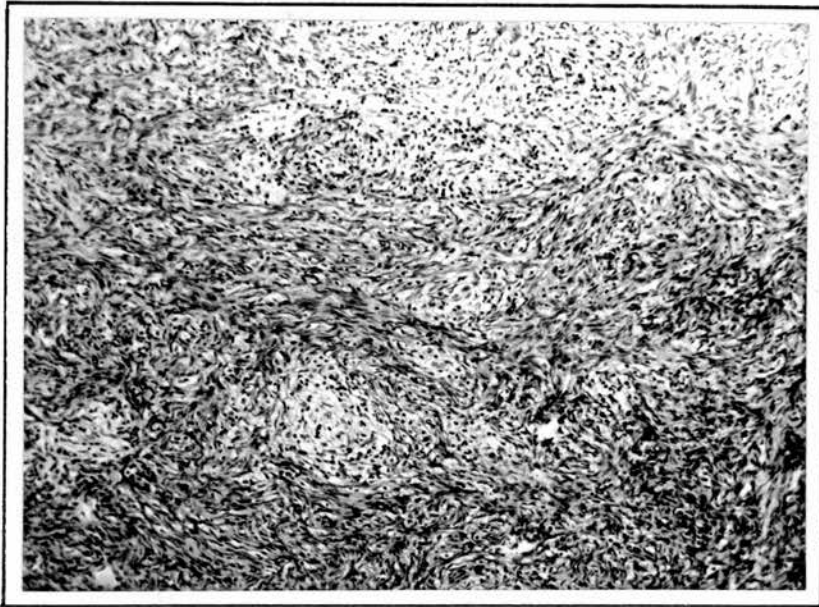
Photo 138.   X60

PHOTO 139. X 200.

Case 92. (2209/61.)

A higher magnification of one of the cortical granulomas seen in the preceding photograph.

PHOTO 140.

Case 97. (52/61.)

Primary ovarian adenocarcinoma. Red fat droplets inside theca-like stromal cells.

(Sudan IV.)
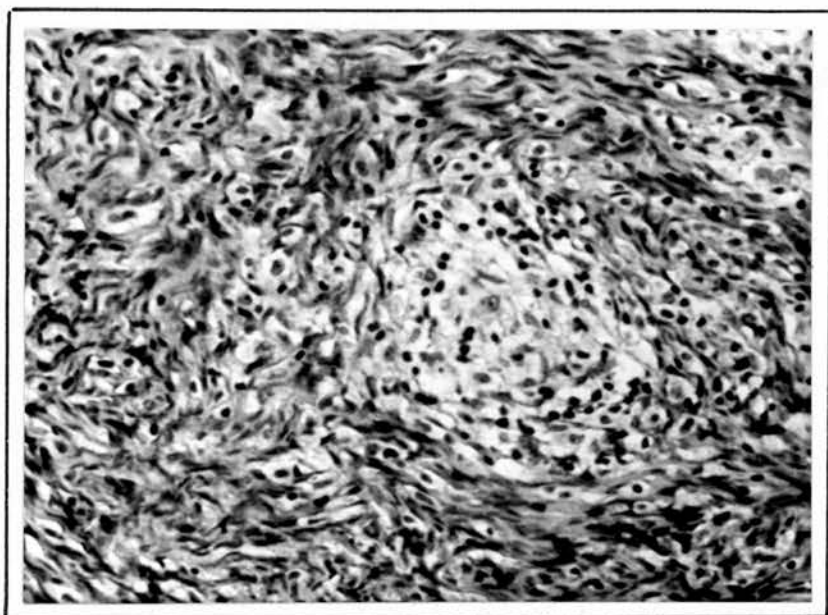
Photo 139.   X 200
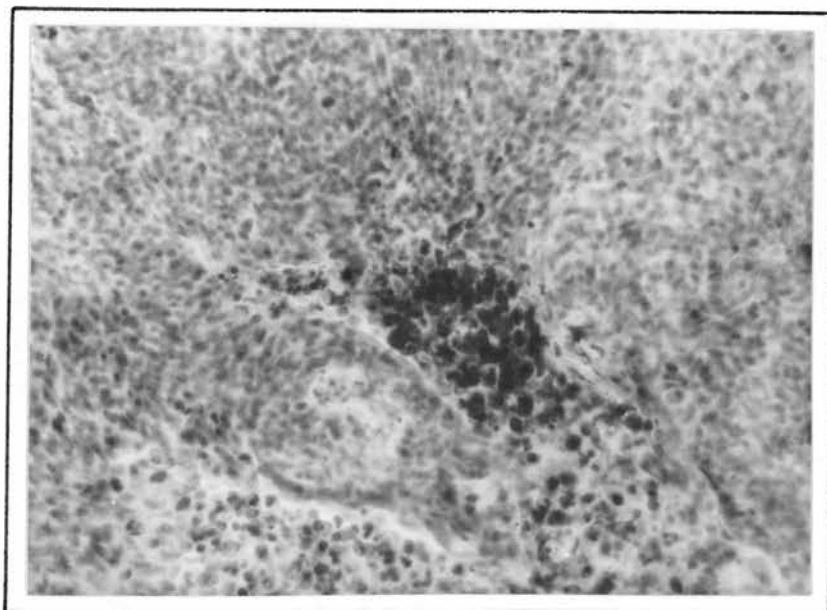
Photo 140.

PHOTO 141. X 100.

Case 97. (52/61.)

Primary adenocarcinoma. Green droplets inside theca-like stromal cells.

(Schultz test.)

PHOTO 142. X 240.

Case 97. (52/61.)

Primary ovarian adenocarcinoma. Dark blue granules inside theca-like stromal cells.

(Ashbel-Seligman ketosteroid reaction.)
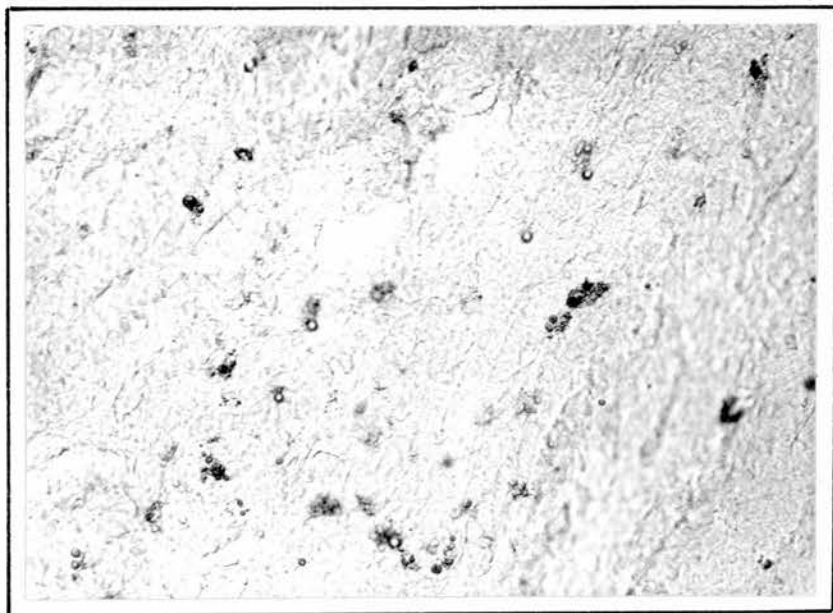
Photo 141.   X100
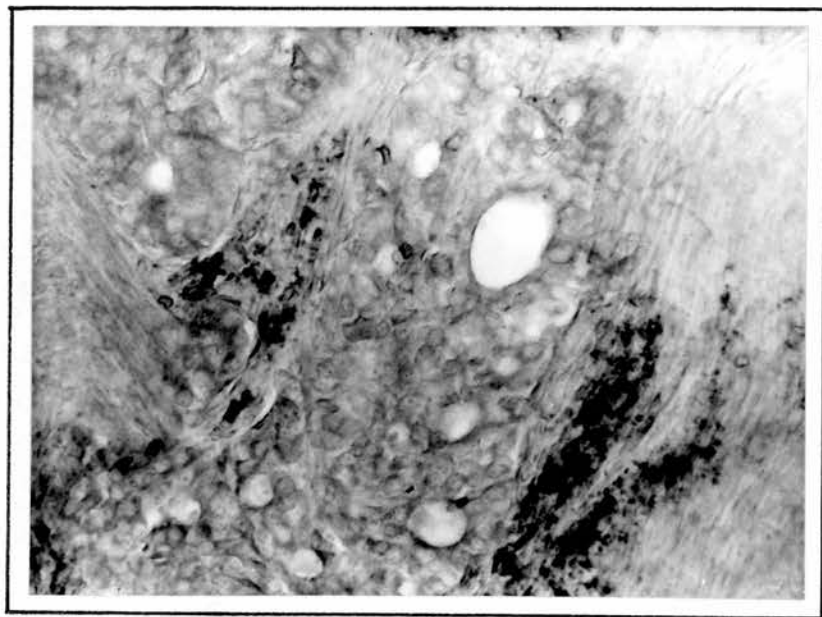
Photo 142.   X240

PHOTO 143.

   Case 97. (52/61.)

     Contra-lateral ovary showing an area of thecomatosis
passing into a cortical granuloma formation.

PHOTO 144. X 230.

   Case 99. (1951/60.)

    Primary ovarian adenocarcinoma.   Green droplets inside
the cytoplasm of stromal theca-like cells.

     (Schultz test.)
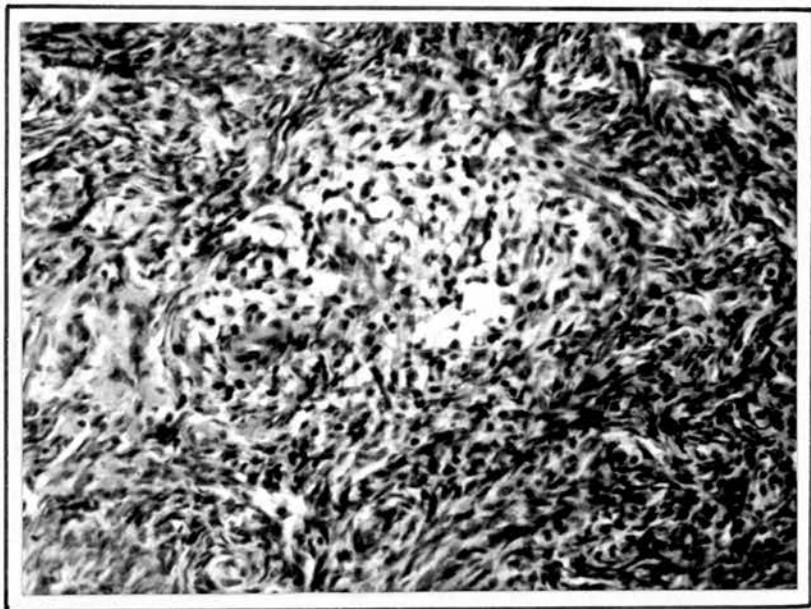
Photo 143.   X230
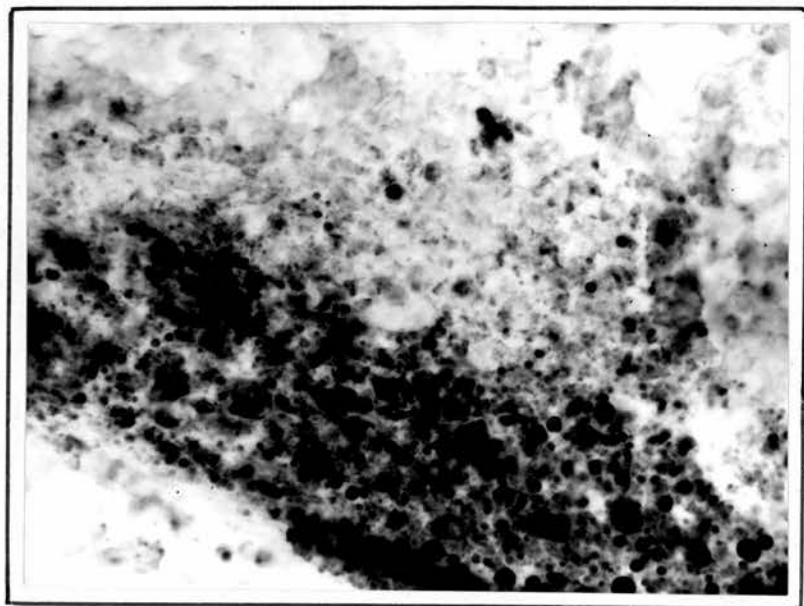
Photo 144.   X230

PHOTO 145.   X 100.

Case 99.   (1951/60.)

Primary ovarian poorly differentiated adenocarcinoma.
Section shows dark blue granules inside the cytoplasm of
theca-like stromal cells.

(Ashbel-Seligman ketosteroid reaction.)

PHOTO 146.

Case 101.   (3417/60.)

Primary ovarian adenocarcinoma.   Section shows
theca-like stromal cells containing green droplets.

(Schultz test.)
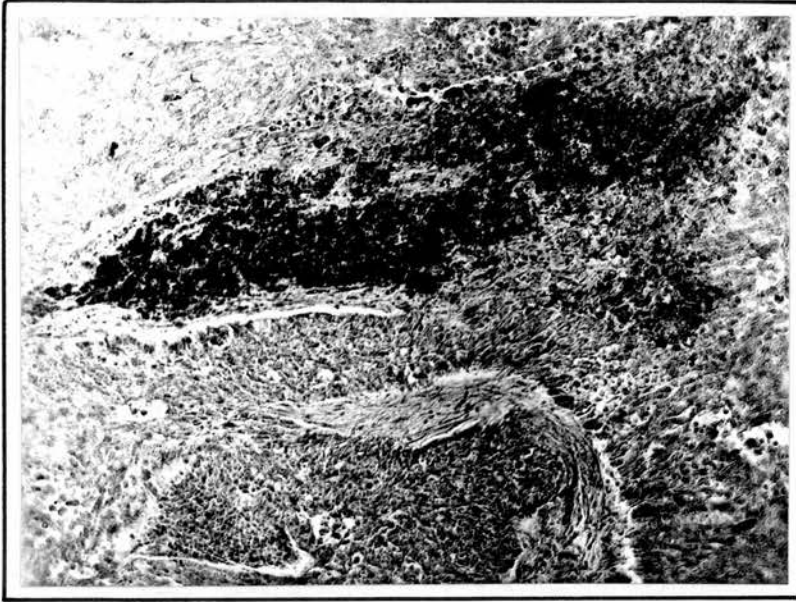
Photo 145.   X100
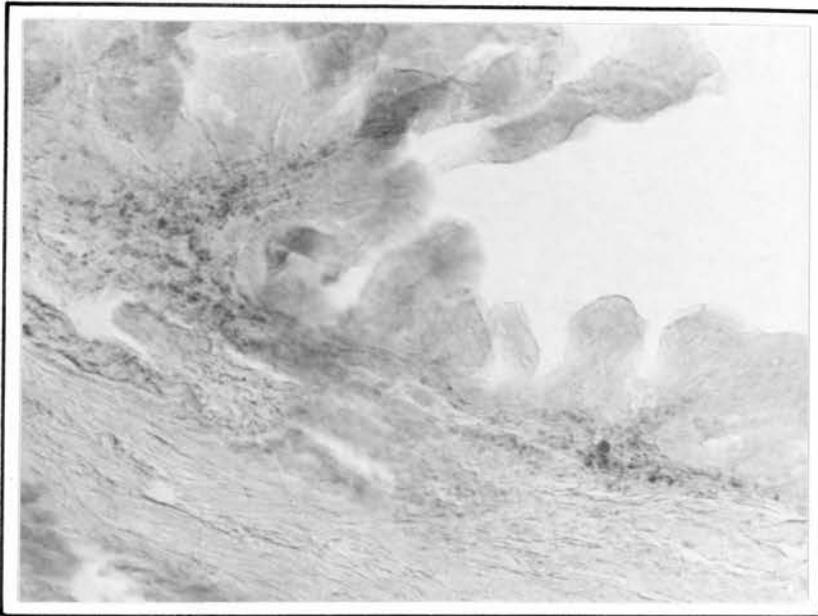
Photo 146.

PHOTO 147. X 250.

    Case 101. (3417/60.)

      Primary ovarian adenocarcinoma.

      Section shows theca-like cells containing dark blue
granules.

      (Ashbel-Seligman ketosteroid reaction.)

PHOTO 148.   X 50.

    Case 101. (3417/60.)

      Endometrium showing a small area of adenocarcinoma
on top of a generalised cystic glandular hyperplasia.
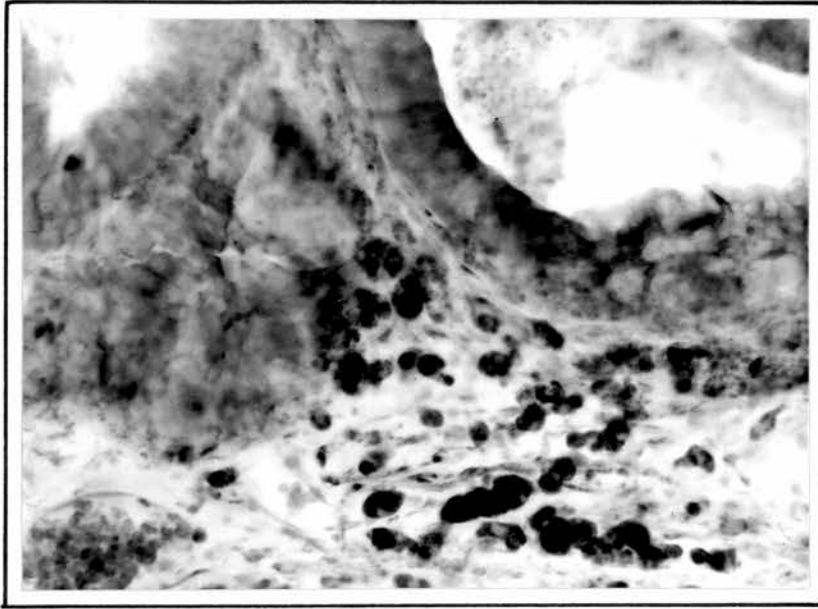
Photo 147.   X250
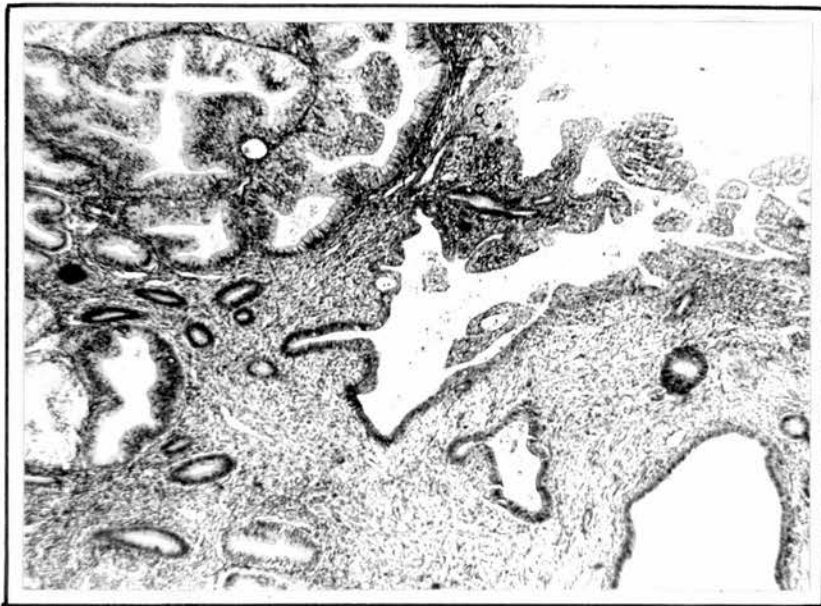
Photo 148.   X50

PHOTO 149. X 260.

   Case 103. (6149/61.)

     Primary ovarian adenocarcinoma.

     Dark blue granules inside theca-like stromal cells.

     (Ashbel-Seligman ketosteroid reaction.)


PHOTO 150.   X 220.

   Case 103. (6149/61.)

   Primary ovarian adenocarcinoma.

   Black deposits indicating sites of alkaline phosphatase
activity are almost absent.

     (Coupling Azo-dye method. Frozen section.)
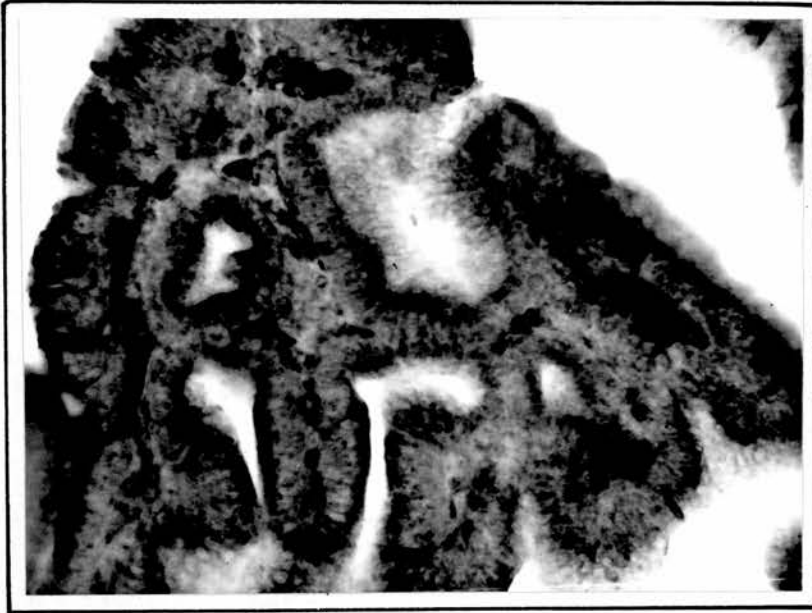
Photo 149.   X260
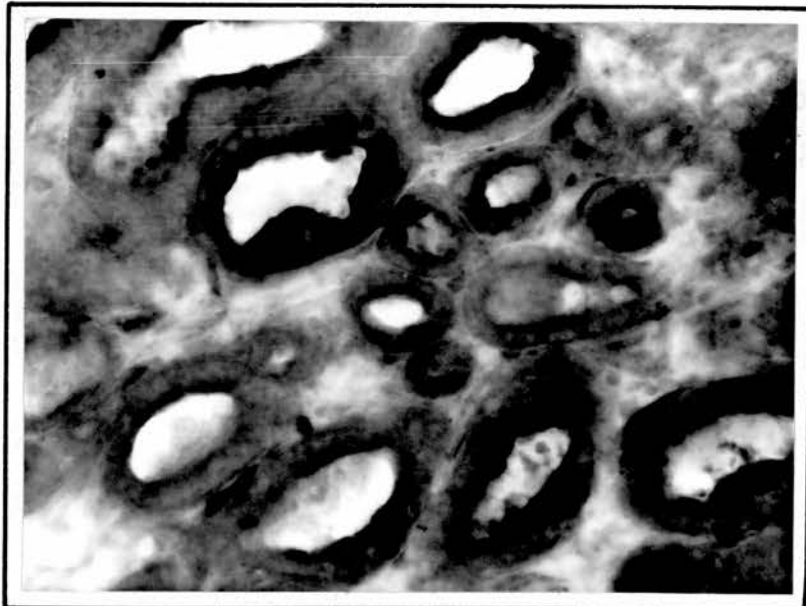
Photo 150.   X220

PHOTO 151.   X 200.

Case 103. (6149/61.)

Primary ovarian adenocarcinoma. High concentration
of acid phosphatase indicated by black deposits especially
in the epithelium.

(Burton Method - Frozen section.)

PHOTO 152.   X 280.

Case 103. (6149/61.)

Primary ovarian adenocarcinoma. Black deposits in
the epithelium indicating marked activity of non-specific
esterase.

(Frozen section.)
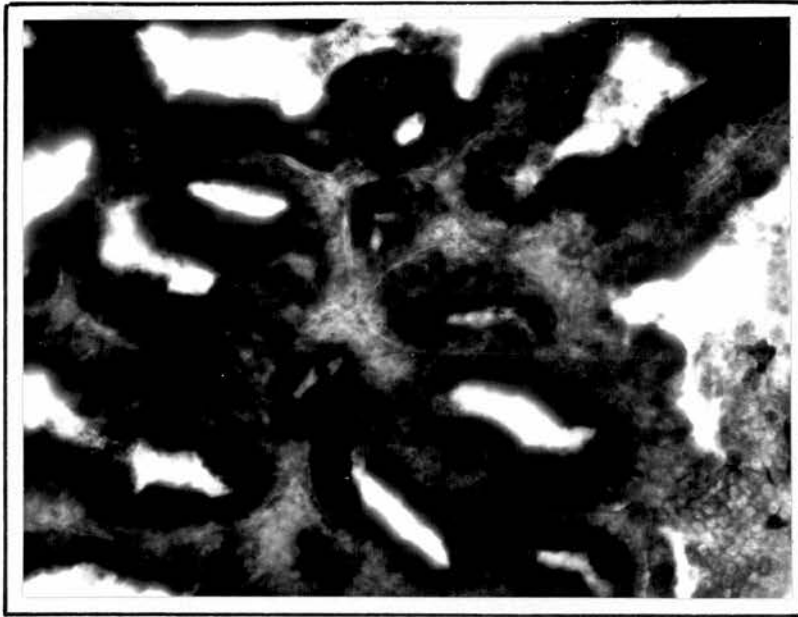
Photo 151.   X200
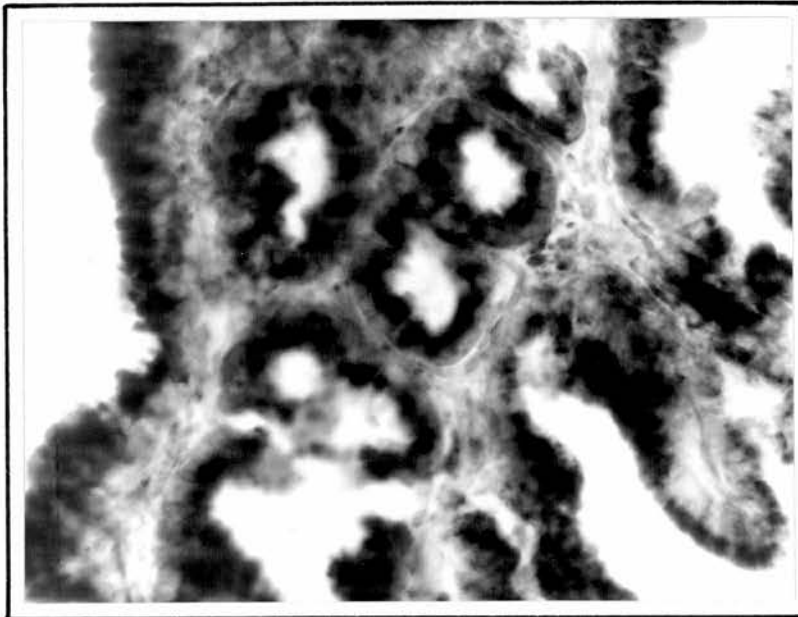
Photo 152.   X280

PHOTO 153.   X 190.

Case 105.   (4544/60.)

Primary ovarian medullary carcinoma.   Note the extreme cellularity of the tumour.   (H. & E.)

PHOTO 154.   X 100.

Case 105.   (4544/60)

Primary ovarian carcinoma.

Birefringent crystals scattered in the stroma of the tumour.
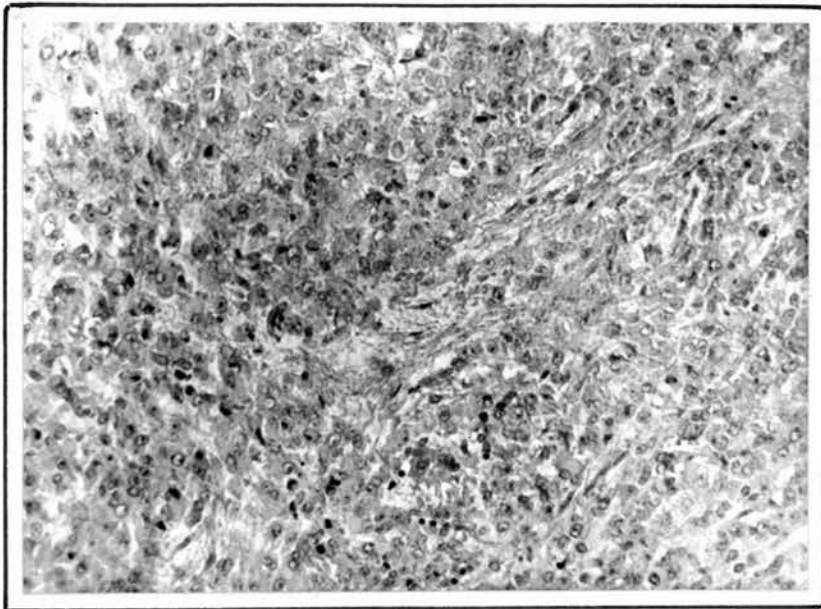
Photo 153.   X190
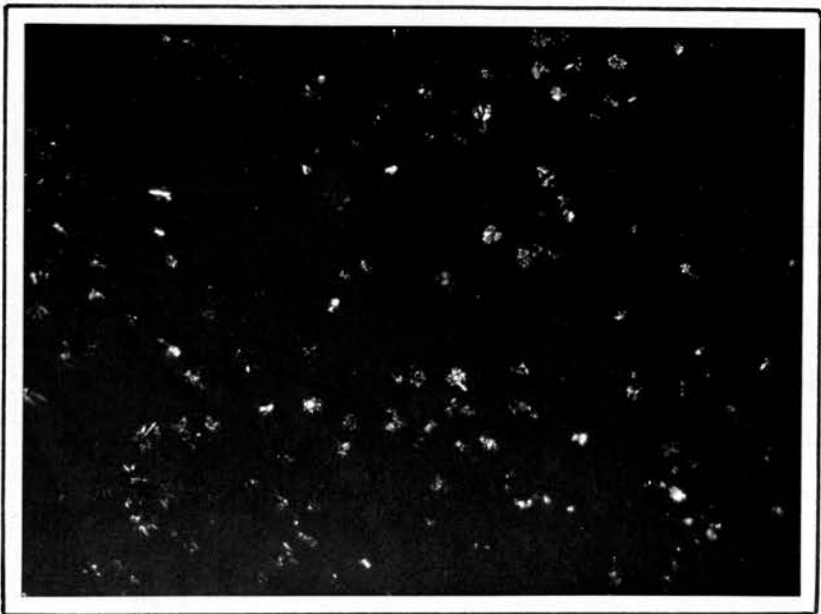
Photo 154.   X100

PHOTO 155. X 180.

Case 105. (4544/60.)

Primary ovarian carcinoma.   Green droplets
inside theca-like stromal cells.

(Schultz test.)

PHOTO 156. X 240.

Case 105. (4544/60.)

Primary ovarian carcinoma.

Dark blue granules filling the cytoplasm of theca-
like stromal cells.

(Ashbel-Seligman ketosteroid reaction.)
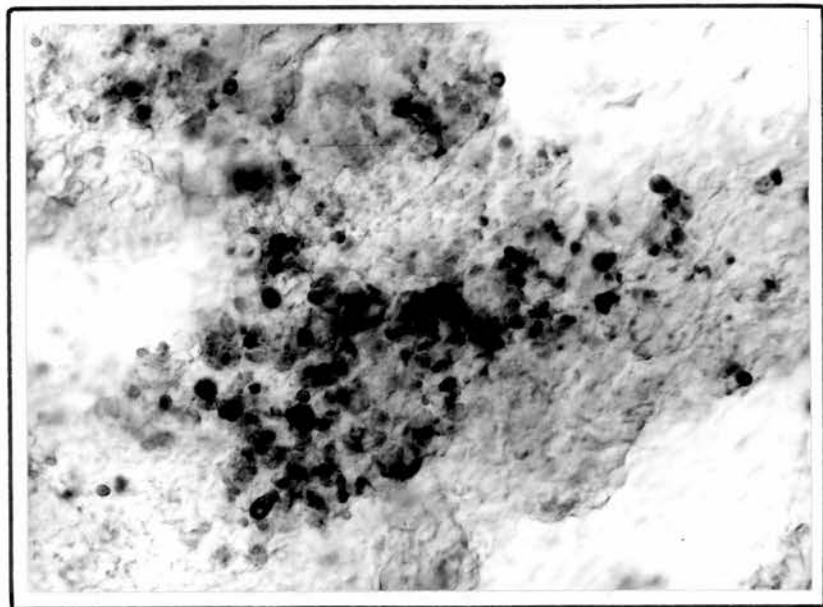
Photo 155.   X180
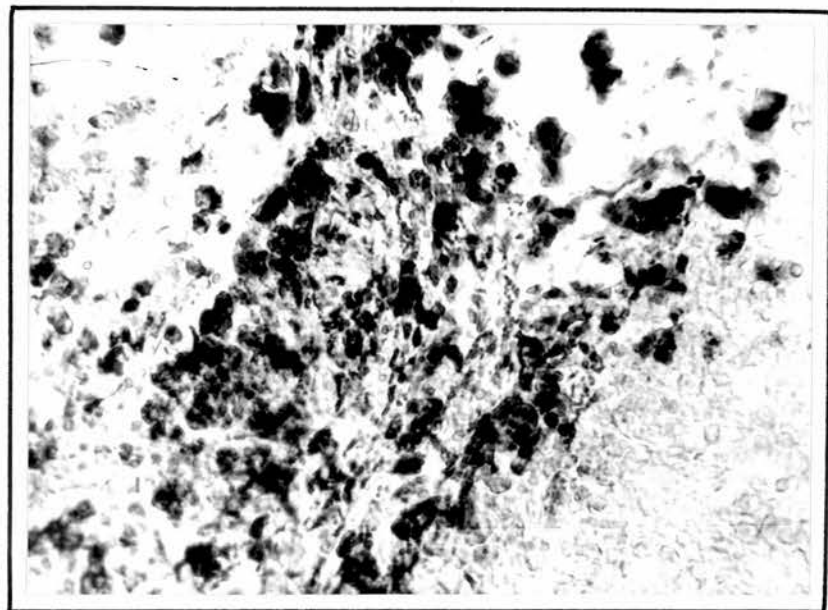
Photo 156.   X240

PHOTO 157.   X 150.

Case 105.   (4544/60.)

Endometrium showing an adeno-acanthoma with a well-marked squamous element.   (Quite different from the preceding ovarian tumour, see Photo 153.)

PHOTO 158.   X 150.

Case 105.   (4544/60.)

Contra-lateral ovary showing a metastatic adeno-acanthoma from the uterus.
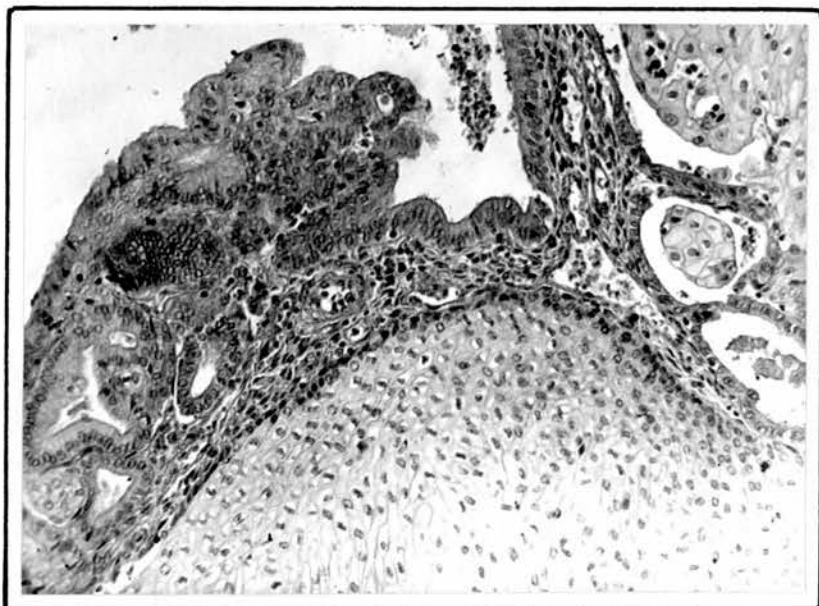
Photo 157.   X150
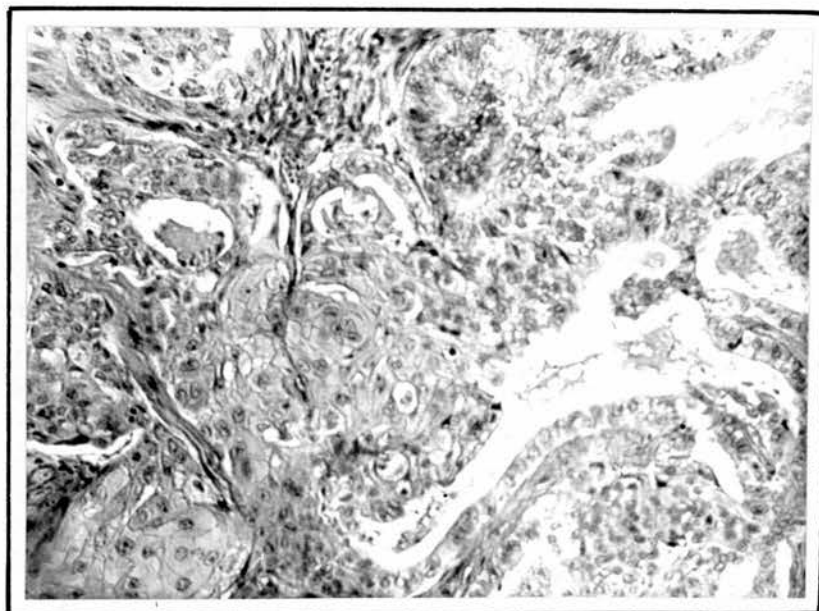
Photo 158.   X150

PHOTO 159.

Case 114. (4429/60.)

Metastatic ovarian adenocarcinoma secondary to endometrial adenocarcinoma.

Red fat droplets are seen inside theca-like stromal cells.

(Sudan IV.)

PHOTO 160.   X 180.

Case 114. (5429/60)

Metastatic ovarian adenocarcinoma.

Birefringent crystals inside theca-like stromal cells.
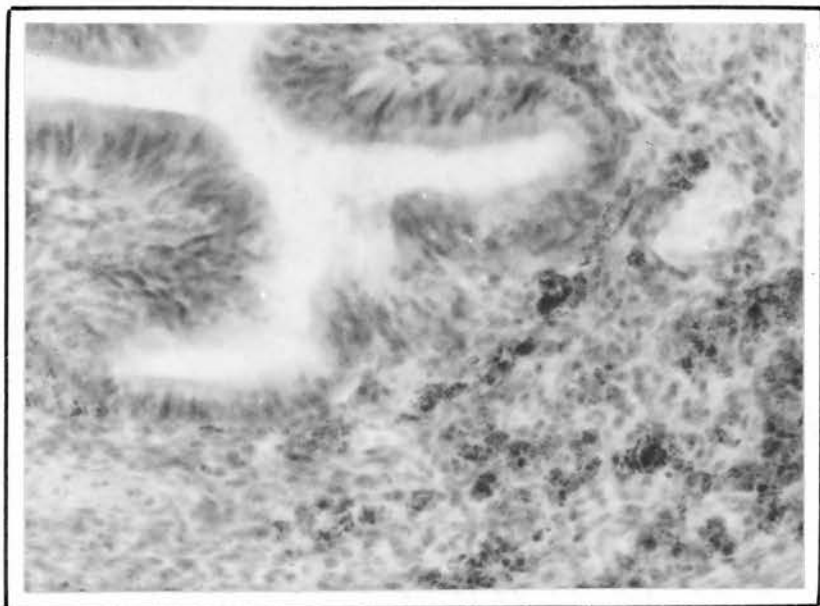
Photo 159.

Photo 160.   X180

PHOTO 161.

   Case 114. (5429/60.)

     Metastatic ovarian adenocarcinoma.

     Green droplets inside theca-like stromal cells.

     (Schultz test.)

PHOTO 162.

   Case 114. (5429/60.)

     Metastatic ovarian adenocarcinoma.

     Purple blue granules inside theca-like stromal cells.

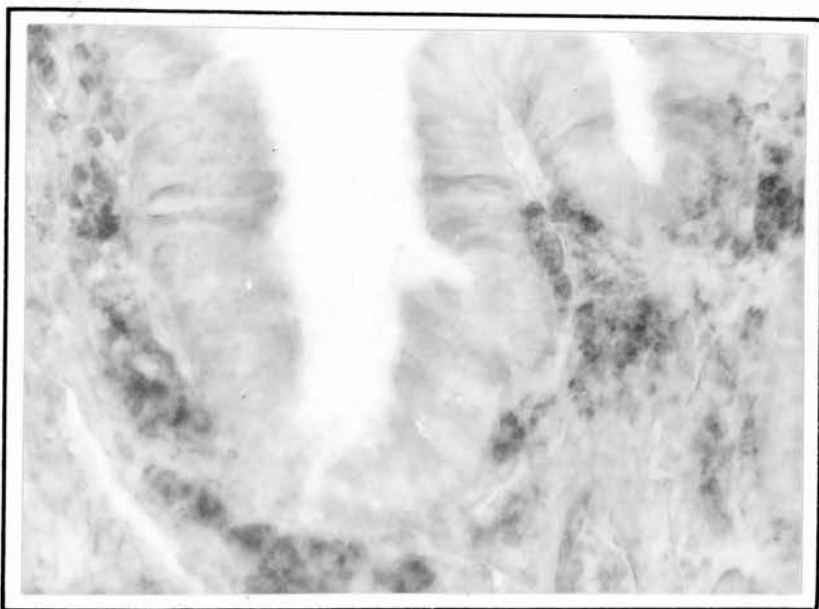   (Ashbel-Seligman ketosteroid reaction.)
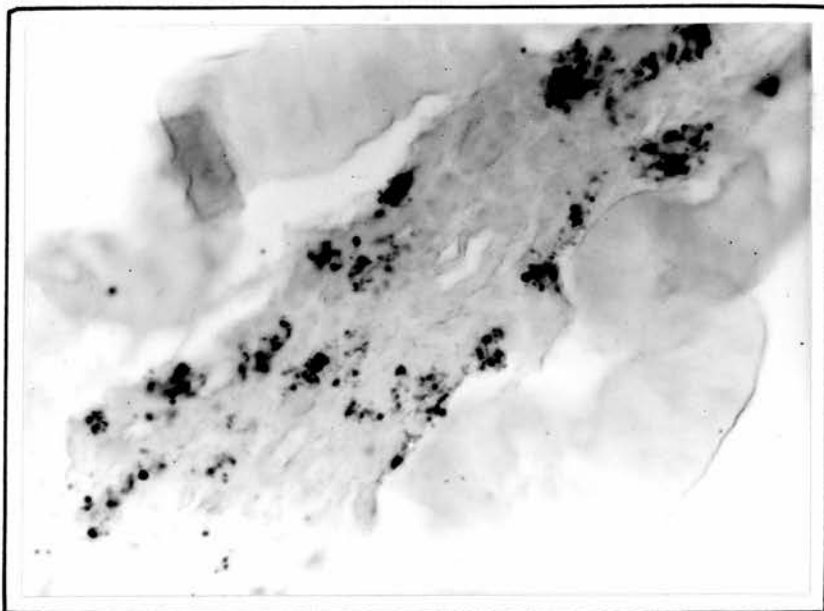
Photo 161.   X 300

Photo 162.   X 200

PHOTO 163. X 140.

Case 114. (5429/60.)

Same photograph as the above but in black and white.

PHOTO 164.

Case 114. (5429/60.)

Contra-lateral ovary showing a hyperplastic cortex
and thecomatosis.
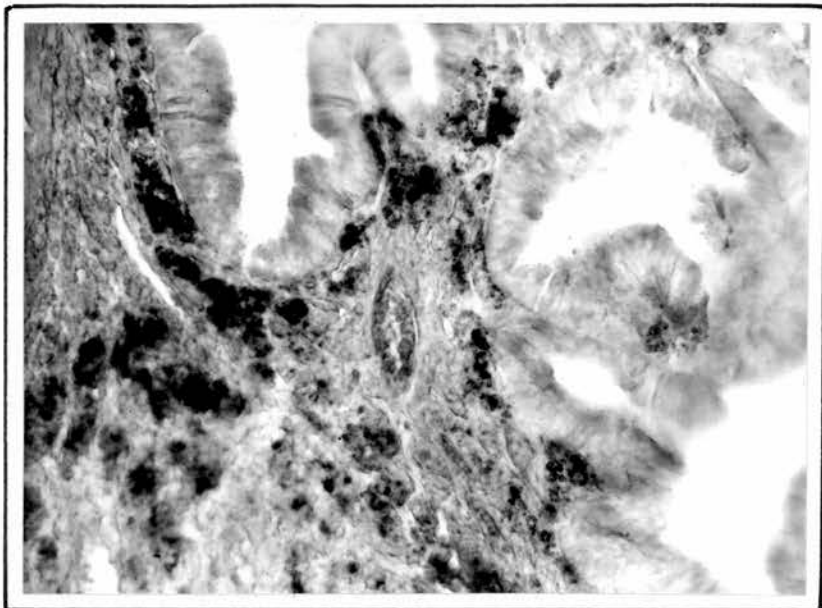
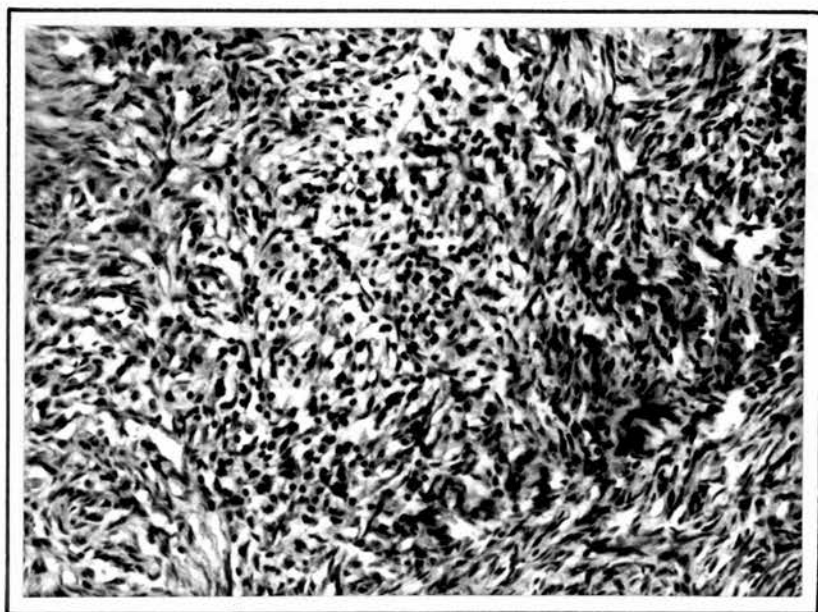Photo 163.   X140

Photo 164.   X180

PHOTO 165.   X 140.

Case 114. (5429/60.)

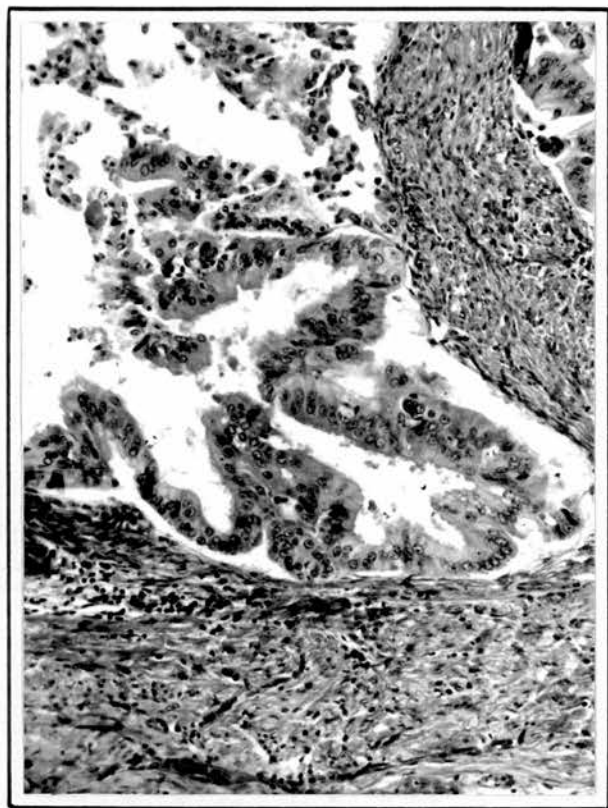Endometrium showing an adenocarcinoma invading the myometrium.

Photo 165.   X140