

# **FEMALE GENITAL SYSTEM PATHOLOGY**

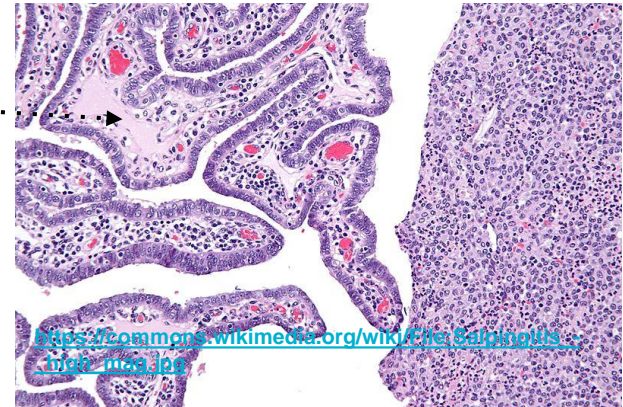
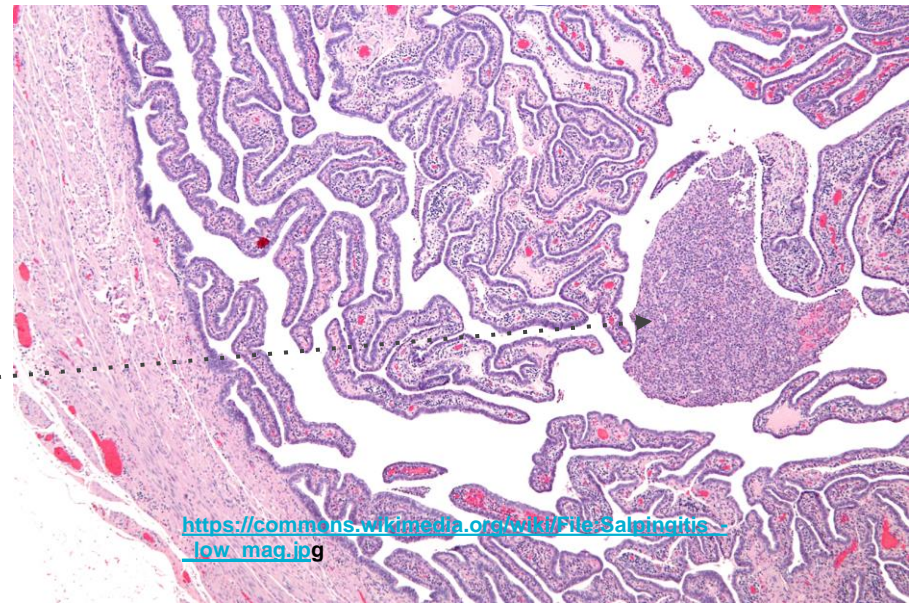
# FALLOPIAN TUBES DISORDERS

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**Acute** and **chronic** SALPINGITIS typically results from **ascending infections** of the lower genital tract. The most common causative organisms are **N. gonorrhoeae**, **E. coli**, **Chlamydia** and **Mycoplasma**.

In most cases, chronic salpingitis develops only after repeated episodes of acute salpingitis.

In acute salpingitis microscopic examination reveals a marked inflammatory infiltrate of polymorphonuclear leukocytes, in association with marked edema and congestion of the mucosal folds.



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The fallopian tubes allow ascending microorganisms from the lower genital tract to reach the peritoneal cavity, a journey that leads to peritonitis and pelvic inflammatory disease. The adjacent ovary may also be involved in the process, sometimes giving rise to a **tubo-ovarian abscess**.

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www.unibas.ch/patho

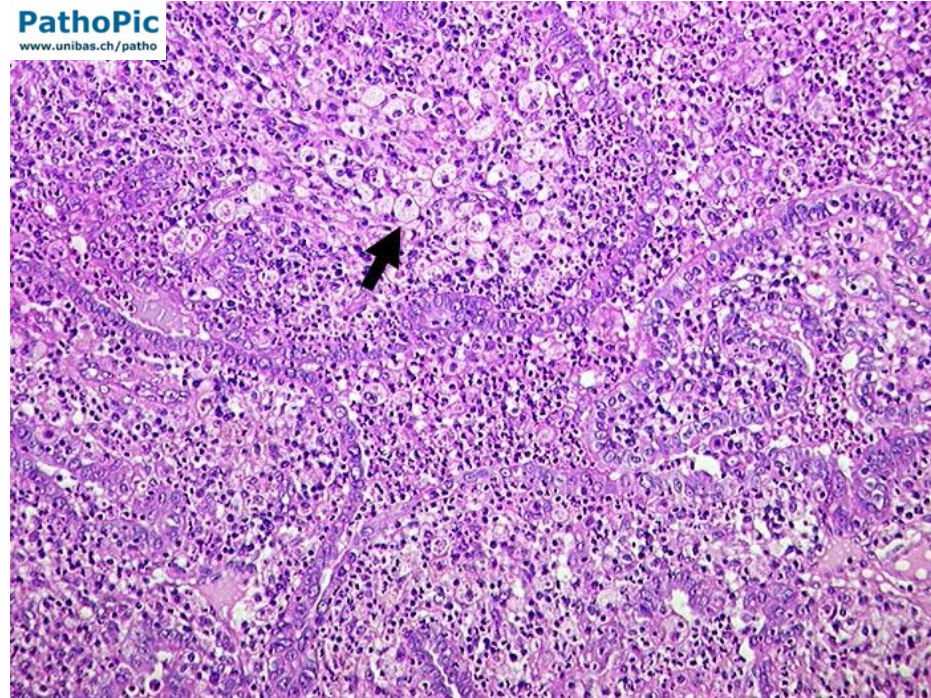




Stroma of the tube mucosa and tube lumen densely infiltrated with neutrophilic granulocytes and foam cells (macrophages) at the arrow.

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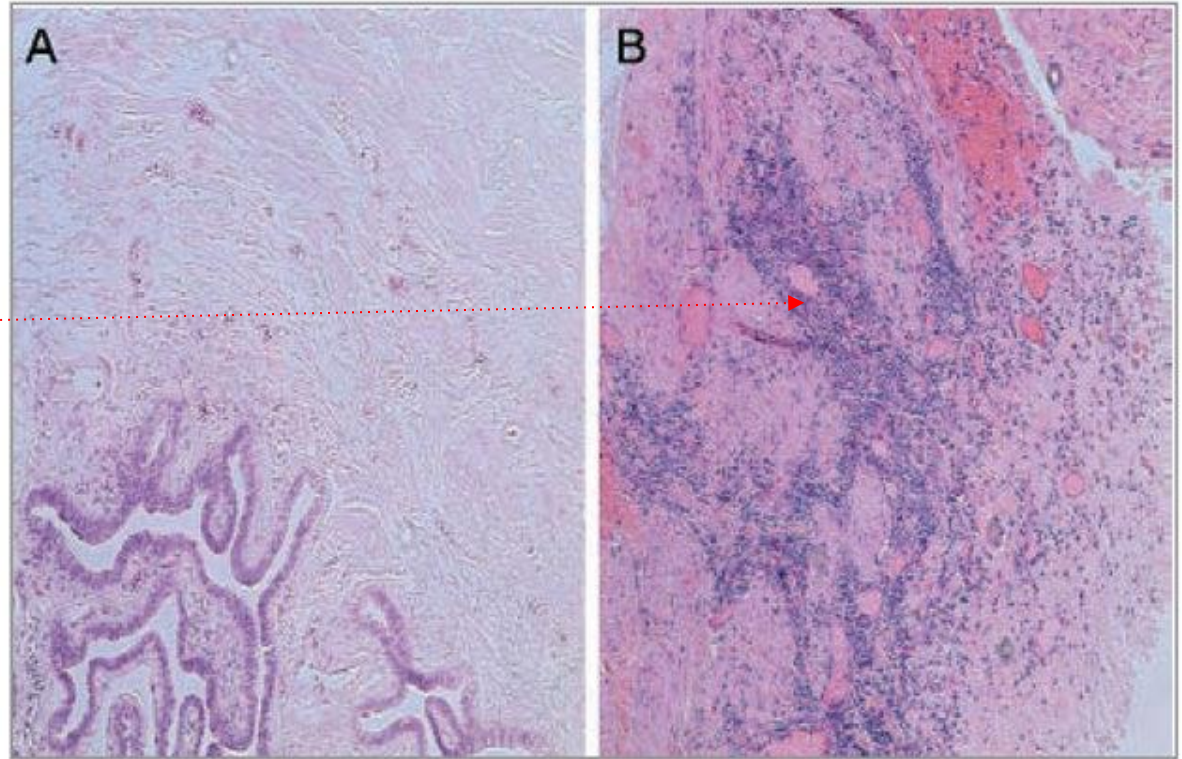
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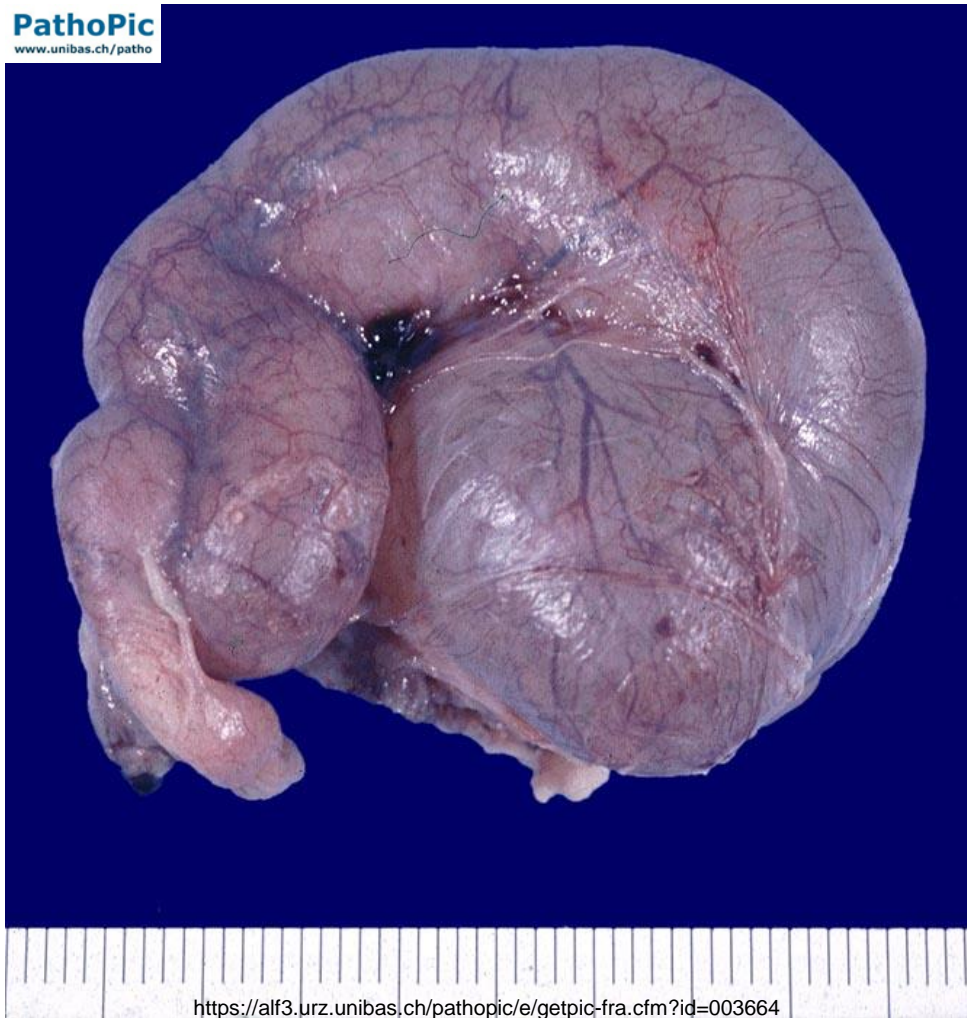
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The inflammatory infiltrate in **chronic salpingitis** is composed of lymphocytes and plasma cells; the edema and congestion tend to be minimal. In **late stages**, the fallopian tube may seal and become distended with pus (**pyosalpinx**) or an acellular transudate (**hydrosalpinx**).



King M, Poya H, Rao J, Natarajan S, Butch AW, Aziz N, Kok S, Chang MH, Lyons JM, Ault K, Kelly KA. CXCL13 expression in Chlamydia trachomatis infection of the female reproductive tract. *Drugs of today (Barcelona, Spain: 1998)*. 2009 Nov;45(Suppl B):125.



## Hydrosalpinx

The damage wrought by **chronic salpingitis** often poses a mechanical obstruction to the passage of sperm, in which case infertility results. Also, chronic salpingitis is a common cause of **ectopic pregnancy**, since adherent mucosal plicae create pockets in which ova can become entrapped.

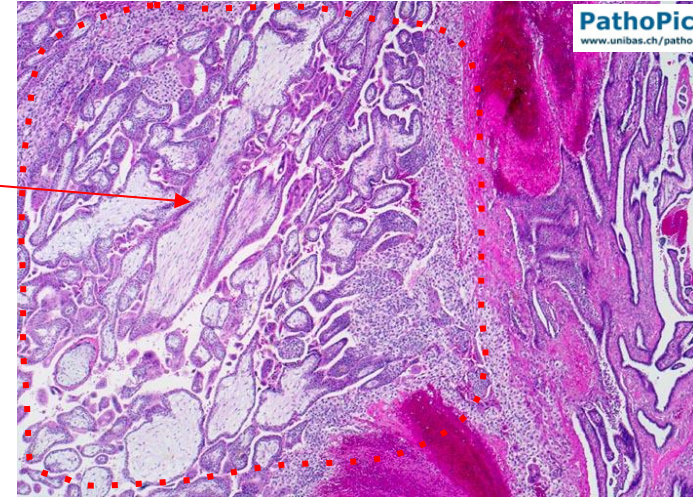


# ECTOPIC PREGNANCY

PathoPic  
www.unibas.ch/patho



**Implantation** of a fertilised egg that develops outside the endometrium. Over **95% of ectopic pregnancies occur in the fallopian tube**, mostly in the distal and middle thirds. An ectopic pregnancy results when the passage of the conceptus along the fallopian tube is impeded, for example, by mucosal adhesion or abnormal tubal motility secondary to inflammatory disease or endometriosis.



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# ECTOPIC PREGNANCY

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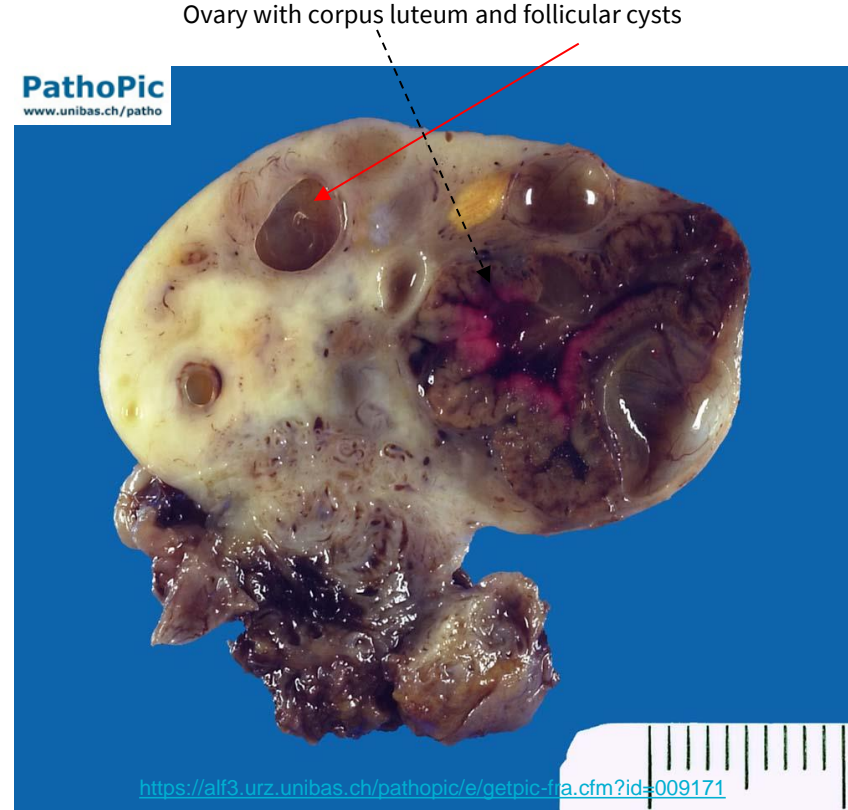
## **Evolution & complication:**

- trophoblast readily penetrates the mucosa and wall of the tube.
- the fertilized egg can't survive and the thin tubal wall usually ruptures by the 12<sup>th</sup> week of gestation.
- tubal rupture is life threatening, because it can result in rapidly exanguinating hemorrhage

# OVARIAN PATHOLOGY

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**NON-NEOPLASTIC CYSTS** are the most **common cause of enlarged ovaries**. Excluding cysts that arise from the invaginated surface epithelium of the ovary (serous cysts) almost all arise from **ovarian follicles**.



# Follicle cyst

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**thin-walled**, fluid-filled structure that is lined internally by granulosa cells and externally by a layer of theca interna cells. **Rarely exceed 5 cm in diameter** and occur at any age up to the menopause. **Follicular cysts** are **unilocular** and may be **single** or **multiple**, **unilateral** or **bilateral**.

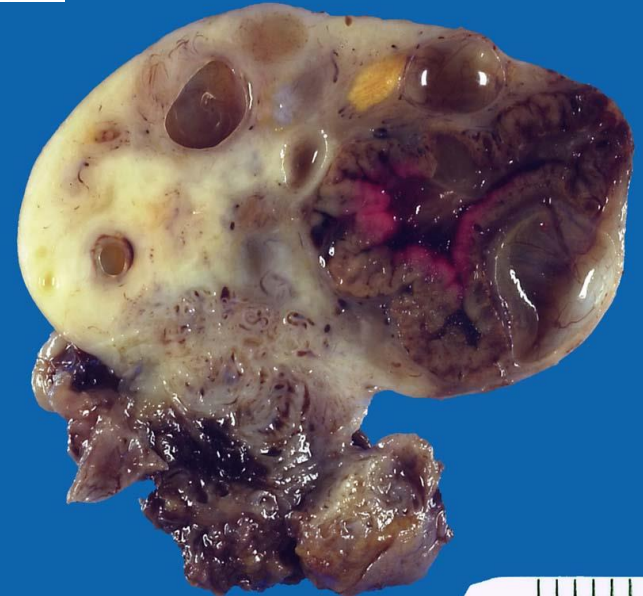


# Corpus luteum cyst

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results from the **delayed resolution of the central cavity of a corpus luteum**. Continued progesterone synthesis leads to menstrual irregularities. A corpus luteum cyst is typically **unilocular** and **3 to 5 cm in diameter**, with a yellow wall. The contents of the cyst vary from **serosanguineous fluid** to clotted blood. **Microscopic** examination shows numerous, large luteinized granulosa cells.

PathoPic  
www.unibas.ch/patho



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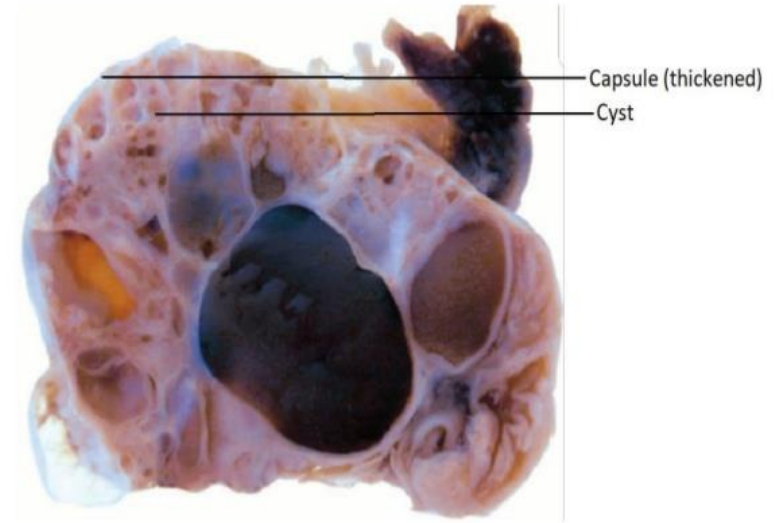


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**Corpus  
luteum  
cyst**



**Polycystic ovary syndrome** (*Stein-Leventhal syndrome*) was described initially as secondary amenorrhea, hirsutism, and obesity.

**On gross examination** both ovaries are enlarged. The surface is smooth, an appearance reflecting the absence of ovulation. **On cut section, the cortex is thickening and numerous subcortical cysts,** typically less than 1 cm in diameter, are seen.

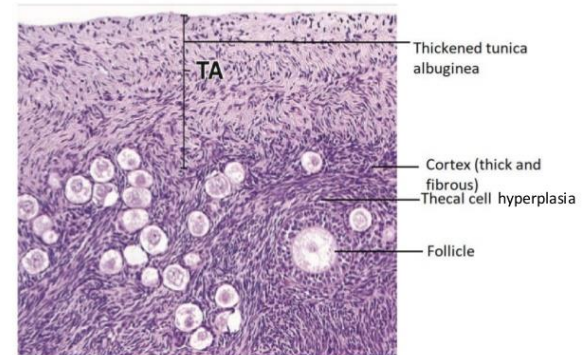
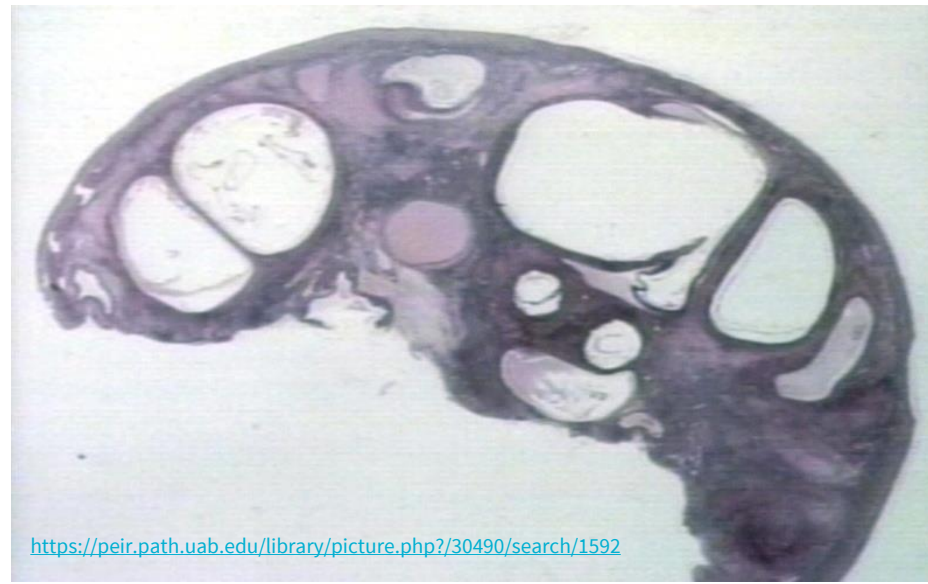


<https://www.slideshare.net/DevlopShrestha/describe-the-gross-and-microscopic-features-of-polycystic-ovaries-111385385>

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**Microscopically**, the following features are present: numerous follicles in early stages of development, follicular atresia, stroma with luteinized cells (hyperthecosis), and morphologic signs of an absence of ovulation (thick, smooth capsule and absence of corpora lutea and corpora albicantia). Many of the subcapsular cysts are lined by thick zones of theca interna, some cells of this structure may be luteinized.

<https://www.slideshare.net/DevlopShrestha/describe-the-gross-and-microscopic-features-of-polycystic-ovaries-111385385>



# TUMORS OF THE OVARY

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- more than 25 major types of ovarian neoplasms.
- most frequently encountered tumors arise from the **surface epithelium** and are termed **common epithelial tumors**.
- Other important groups include **germ cell** tumors, **sex cord/stromal** tumors, and **metastatic** tumors to the ovary.



## Common epithelial tumors

Benign common epithelial tumors are almost always **serous** or **mucinous** and generally arise in women between the age of 20 and 60 years.

Frequently large, **15 – 30 cm in diameter**. Some of these tumors, particularly the **mucinous** variety, reach a truly massive proportion, exceeding 50 cm in diameter.

Serous cystadenoma of the ovary, cut surface of the ovary with multilocular cyst.



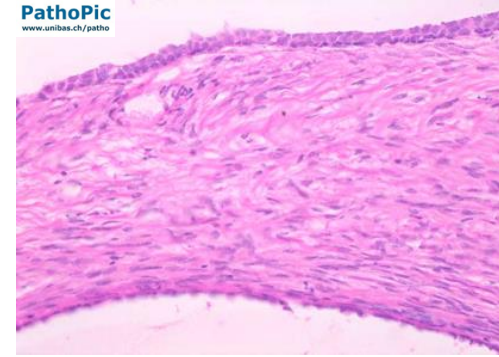
Benign epithelial tumors are typically **cystic**, hence the term **cystadenoma**.

**Serous cystadenomas** are more commonly bilateral (15%) than mucinous cystadenomas and tend to be **unilocular**.

By contrast, mucinous tumors are characteristically composed of hundreds of small cysts.

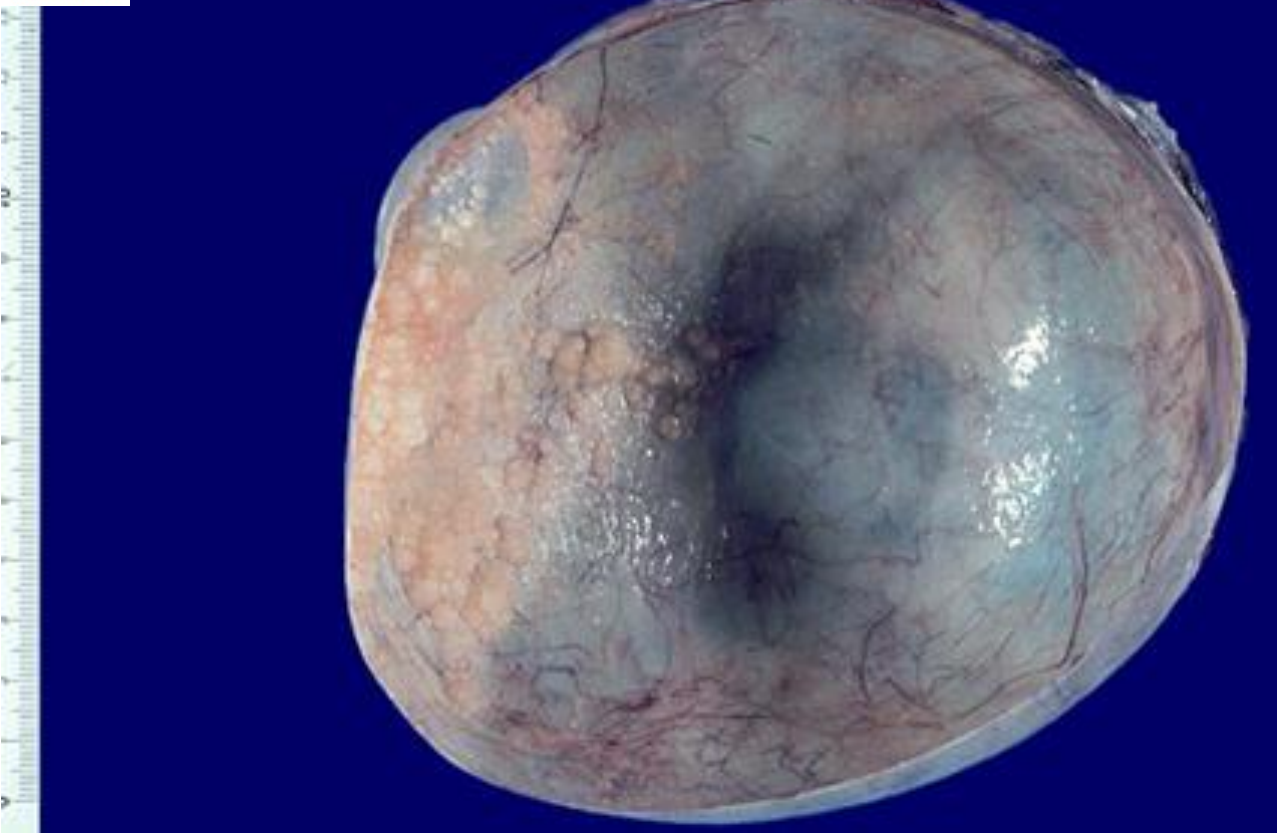
As opposed to their malignant counterparts, benign epithelial tumors of the ovary tend to have **thin walls and lack solid areas**.

**Microscopically**, a **single layer of tall columnar epithelium lines the cysts**. **Papillae**, when present, consist of fibrovascular core covered by a single layer of tall columnar epithelium identical to that of the cyst lining.

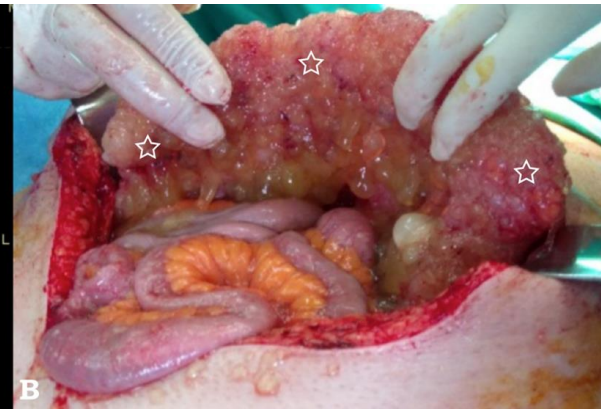




Serous cystadenoma of the ovary  
Multilocular cystic tumor with papillary formations on the inside of the cyst.







Up to **5% of mucinous tumors of the ovary** are complicated by the **implantation** of numerous **mucus-producing cells** on the peritoneal surfaces. This results in the massive accumulation of gelatinous material in the abdominal cavity, similar to that seen in **pseudomyxoma peritonei** associated with **mucocoele of the appendix**. Some believe that these lesions represent metastases from appendiceal mucinous tumors of low malignant potential. Histologically, the peritoneal implants are composed of regular, mucus-containing columnar cells, without atypia and mitoses.

**Figure 1: Pseudomyxoma peritonei, (patient #1)**

(A) Axial computed tomography (CT) slice demonstrates a large hypodense lobulated omental mass (white stars) and (B) demonstrates a corresponding perioperative view of the greater omentum with extensive tumor seeding (white stars)

Pantiara EV, Massaras D, Koutalas J, Melemini A, Fragulidis GP.  
Pseudomyxoma Peritonei: Presentation of Two Cases and  
Challenging Issues in the Literature. Cureus. 2018 Dec;10(12).

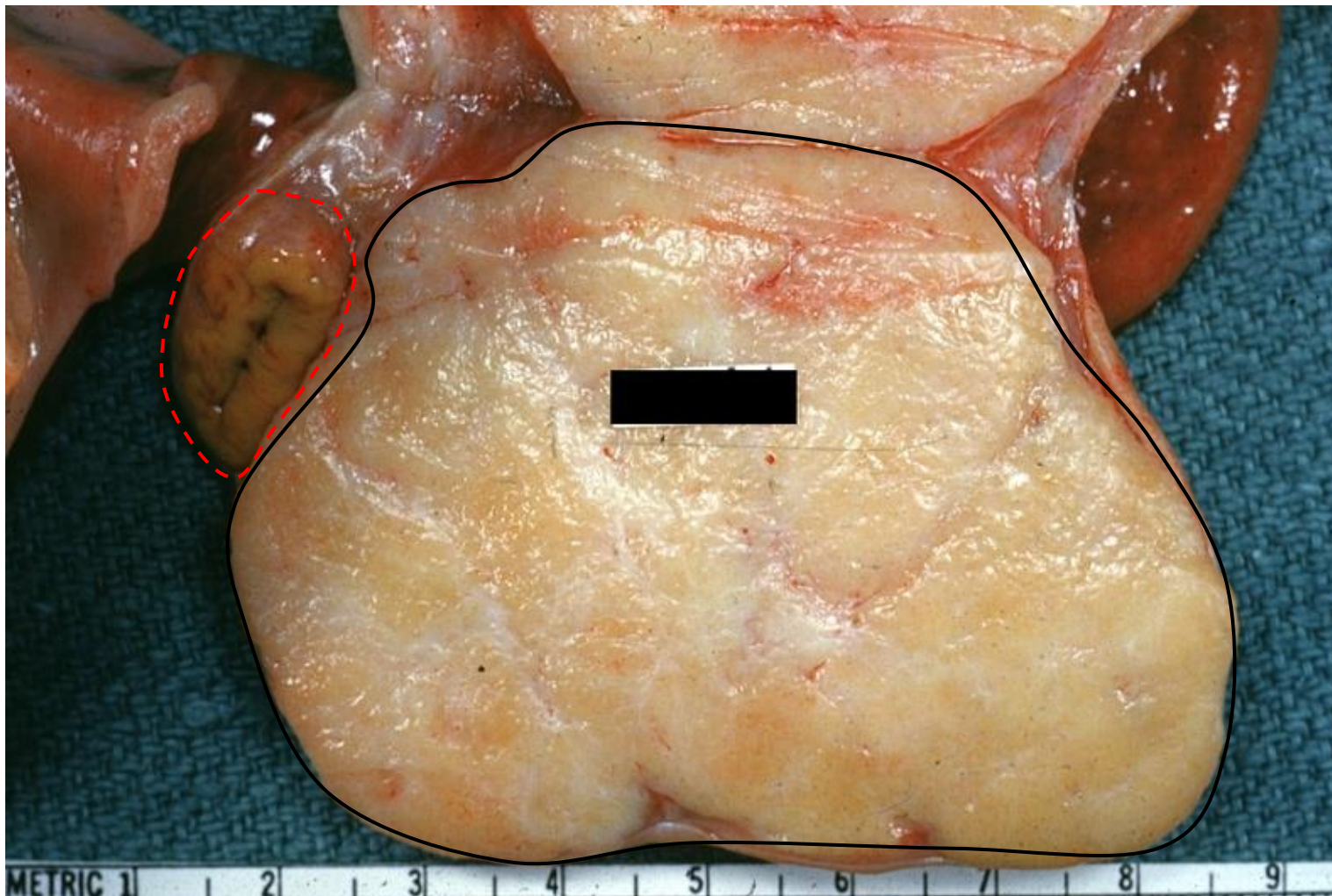
# Brenner tumor

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**Brenner tumor** is benign and occurs at all ages, with half of the cases presenting in women over 50 years of age.

**Size varies** from a microscopic focus to masses as large as 8 cm or more in diameter.

**Histologically**, Brenner tumor is composed of solid nests of **transitional-like (urothelium-like)** cells enclosed in a dense, fibrous stroma. The most superficial epithelial cells may exhibit mucinous differentiation.



Red dashed line indicates the normal ovarian gross appearance

The black line indicates the gross appearance of Brenner Tumor



## Brenner tumor

Histologically,  
Brenner tumor is  
composed of solid  
nests of  
**transitional-like**  
**(urothelium-like)**





# Borderline tumors (tumors of low malignant potential)

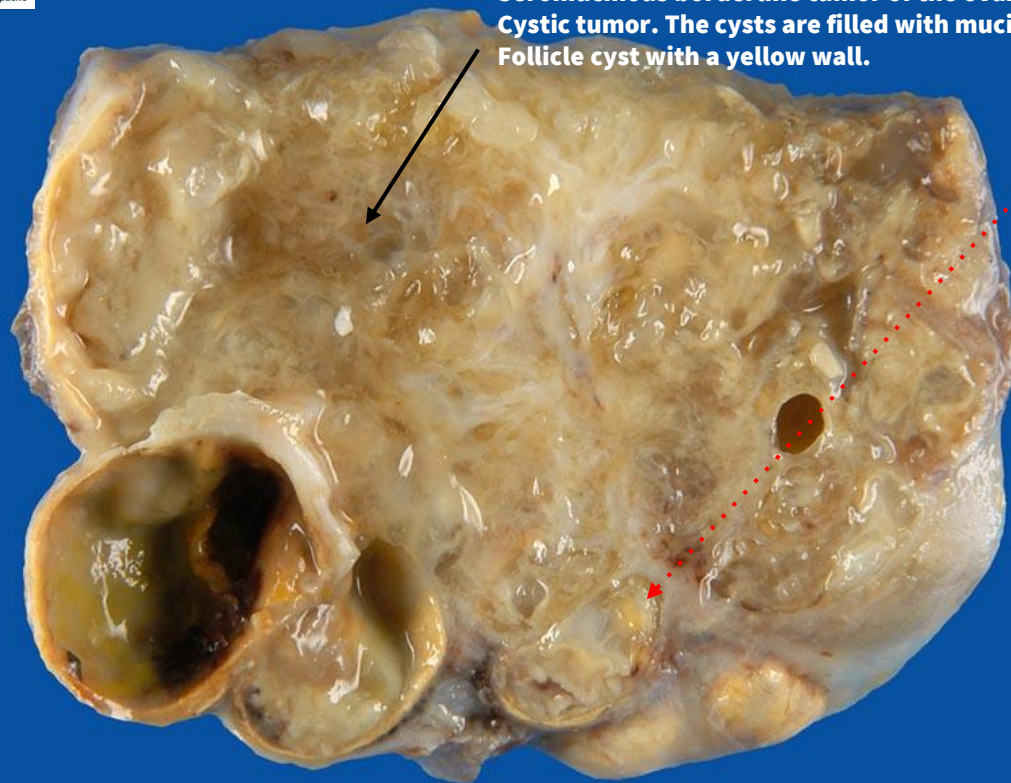
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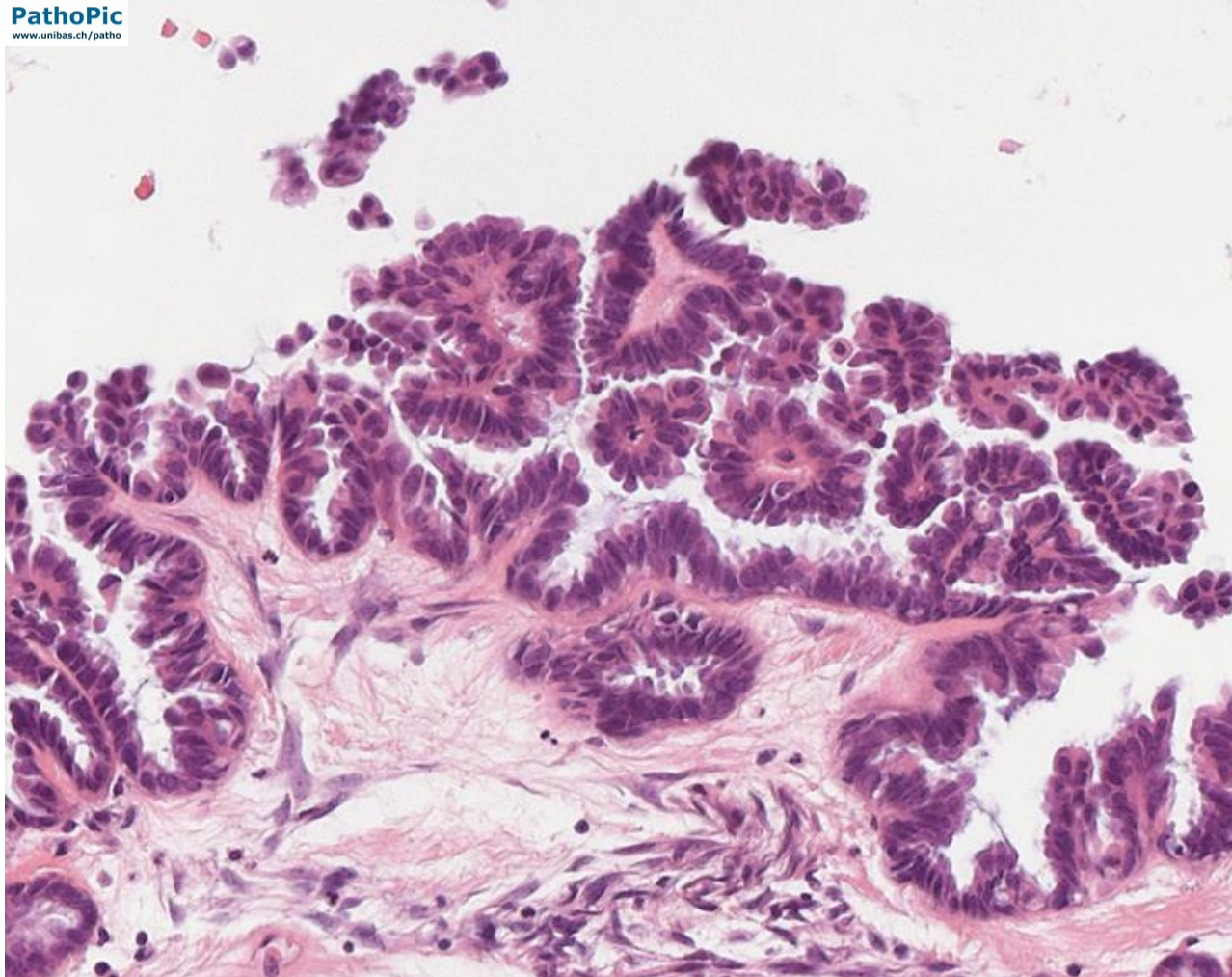
The designation “borderline malignancy” is an important concept of recent vintage.

Group of ovarian tumors that share an excellent prognosis, despite certain histologic features that suggest cancer.

These are characterized by epithelial cell proliferation and nuclear atypia, but not a destructive stromal invasion.

**Seromucinous borderline tumor of the ovary**  
**Cystic tumor. The cysts are filled with mucin.**  
**Follicle cyst with a yellow wall.**





**Microscopically**, these structures resemble the papillary fronds in benign cystadenoma but are distinguished from them by epithelial stratification, nuclear atypia, and mitotic activity. The same criteria apply to borderline mucinous tumors, although papillary projections are less conspicuous. **By definition**, the **presence of stromal invasion in the primary tumor removes it from the category of borderline malignancy and identifies it as frankly malignant.**

# Malignant epithelial tumors of the ovary

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Most common between the ages of 40 and 60 years and are rare under the age of 35.

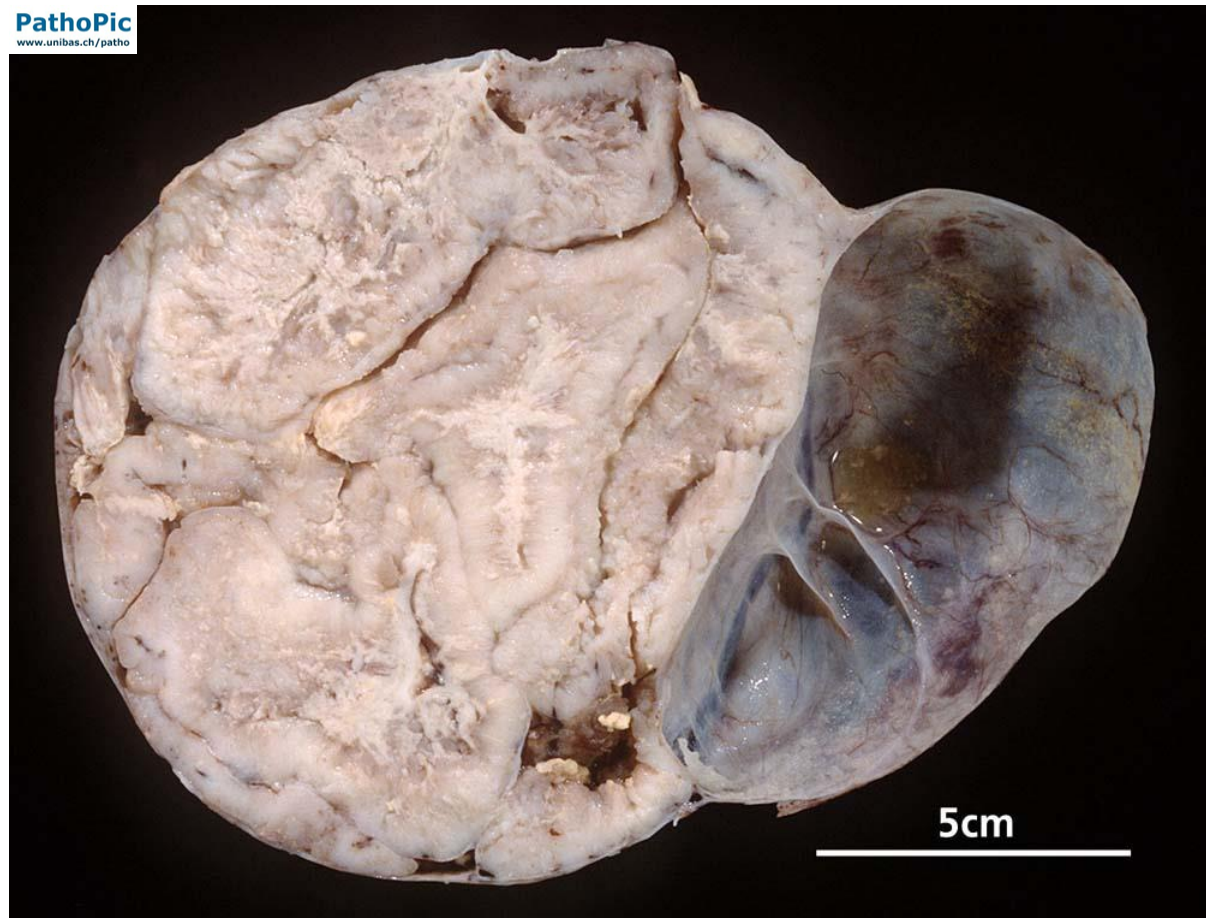
By the time a carcinoma reaches a size of 10 to 15 cm, it often has already spread beyond the ovary and seeded the peritoneum.



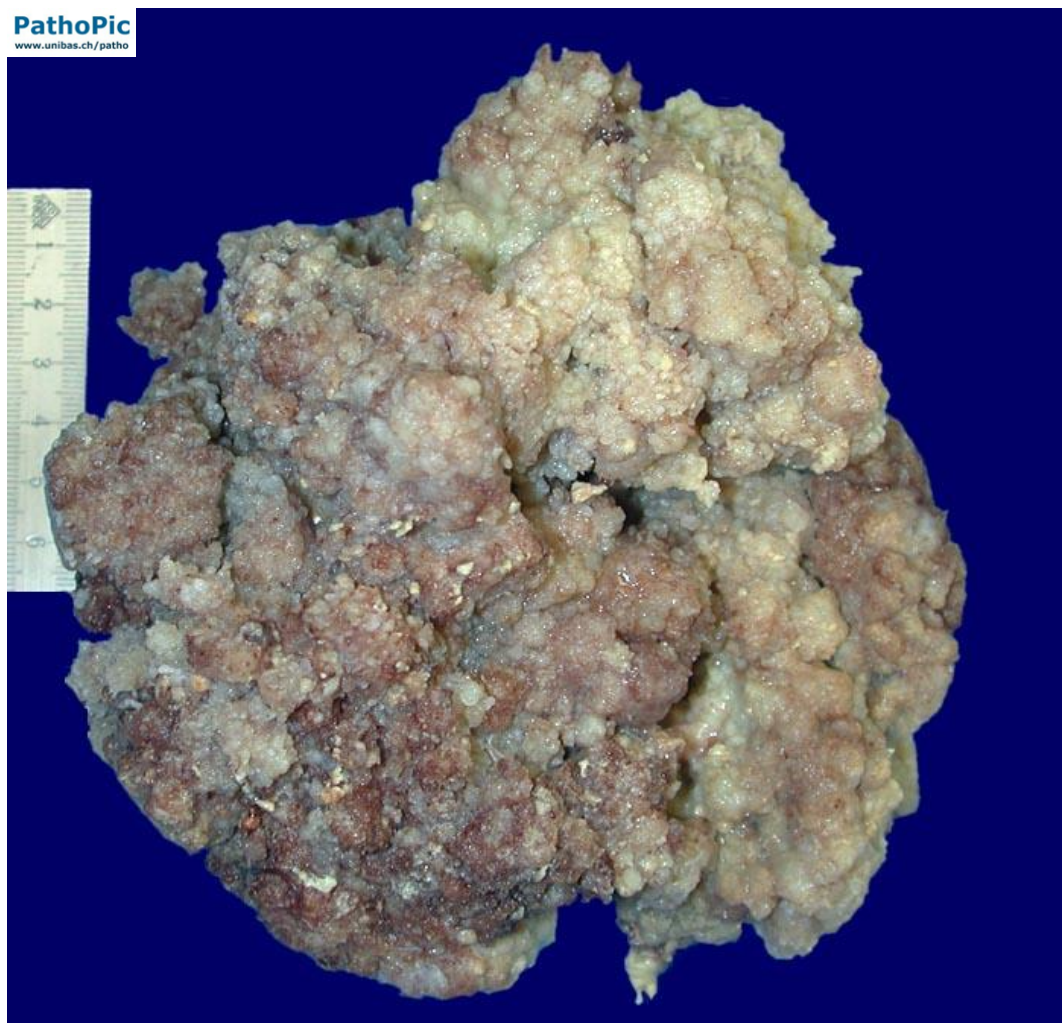
**Serous cystadenocarcinoma** is the most common malignant ovarian tumor, accounting for a third of all cancers of the ovary.

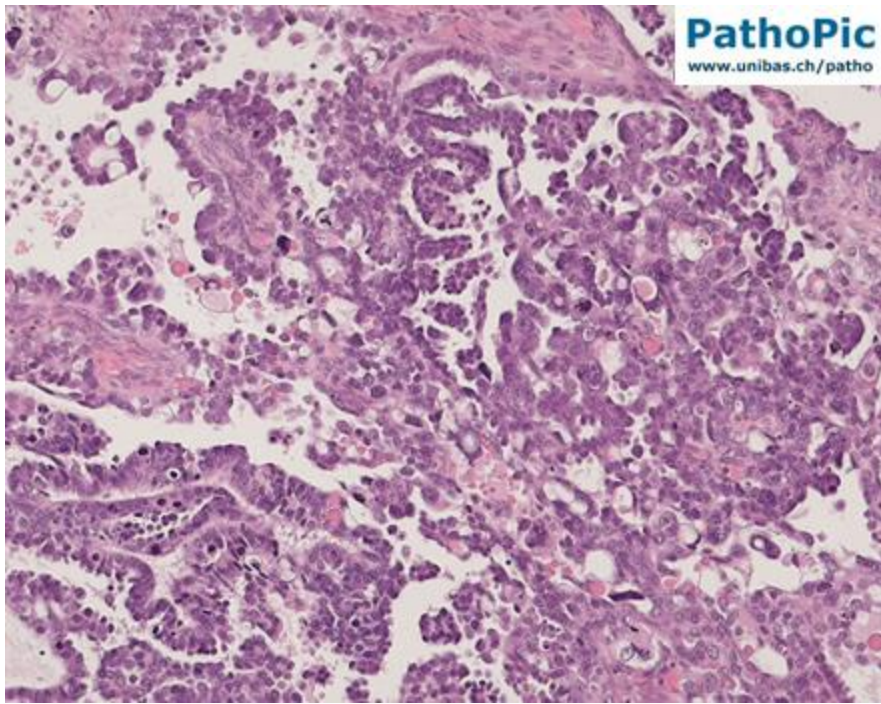
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**On gross examination**, serous cystadenocarcinoma usually is a multiloculated tumor, with soft, delicate papillae lining the entire surface. Solid areas, often with zones of necrosis and hemorrhage, are commonly present.



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Serous papillary  
adenocarcinoma of the ovary  
- Exophytic papillary tumor

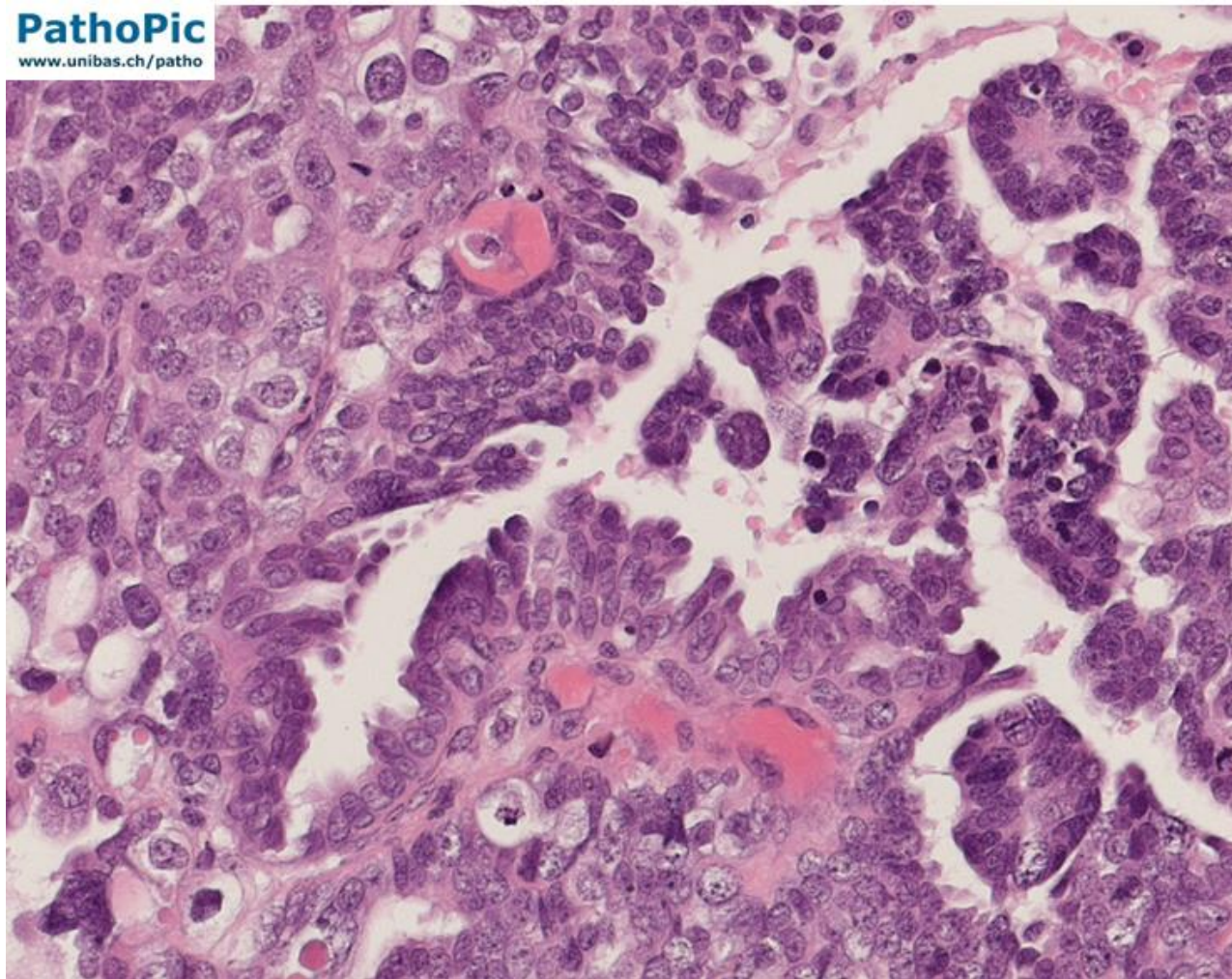




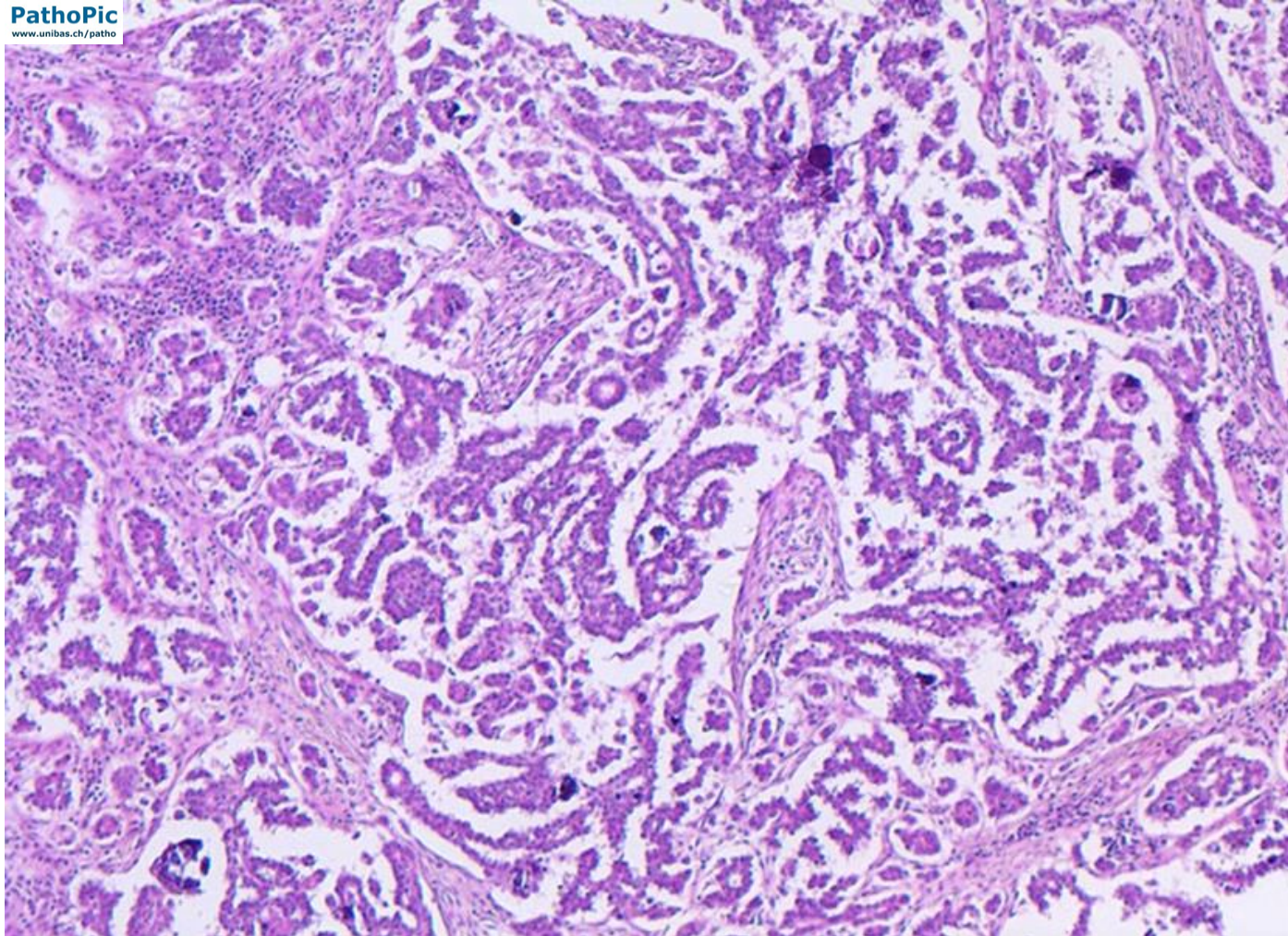
**Microscopically**, serous cystadenocarcinomas vary from well-differentiated to poorly differentiated tumors. In the latter, the papillary pattern may be inconspicuous, with most areas being composed of solid sheets of malignant cells. Stromal and capsular invasion by the tumor cells is evident. Laminated calcified concretions, referred to as psammoma bodies, are present in one-third of the cases.

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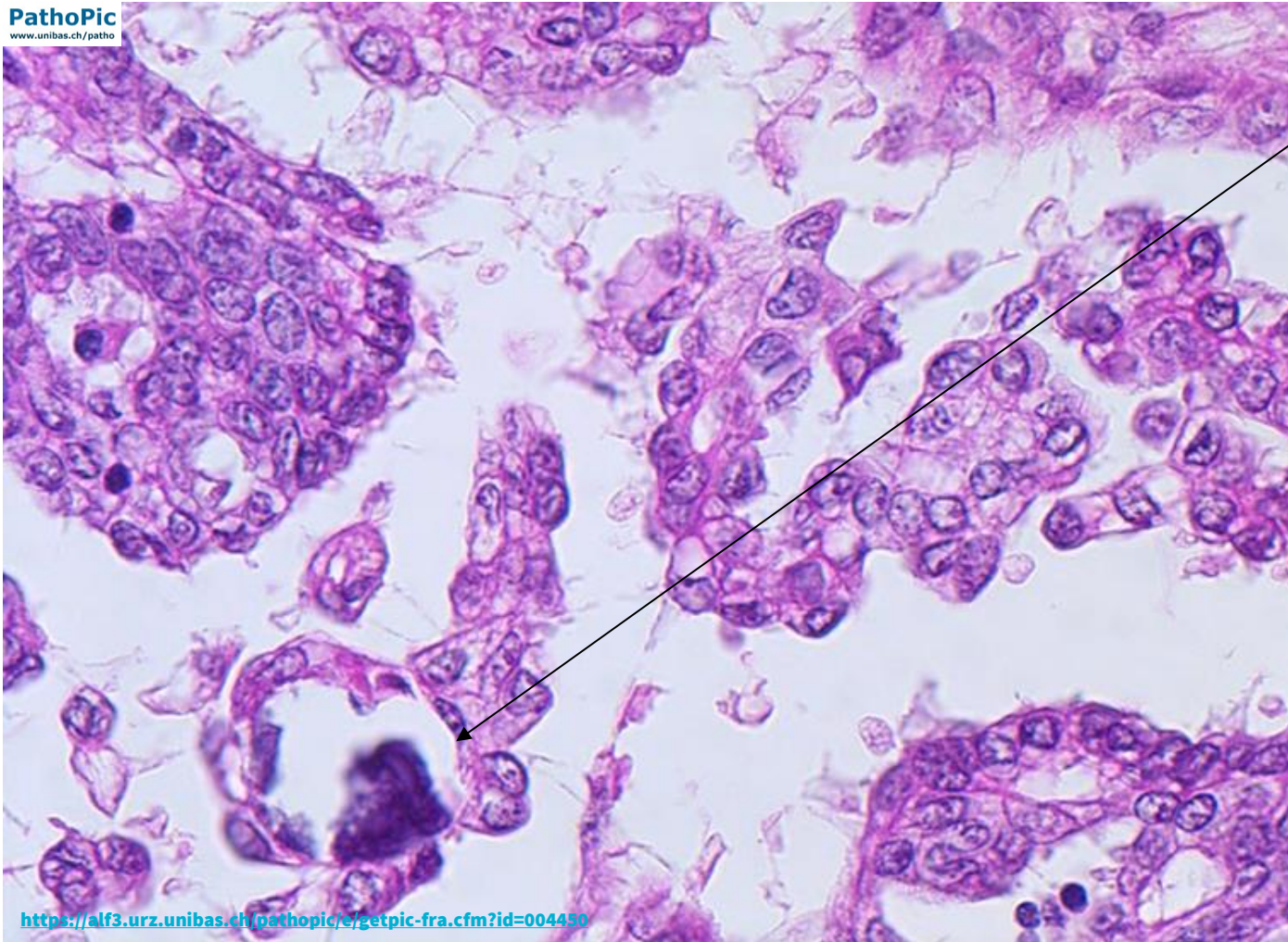












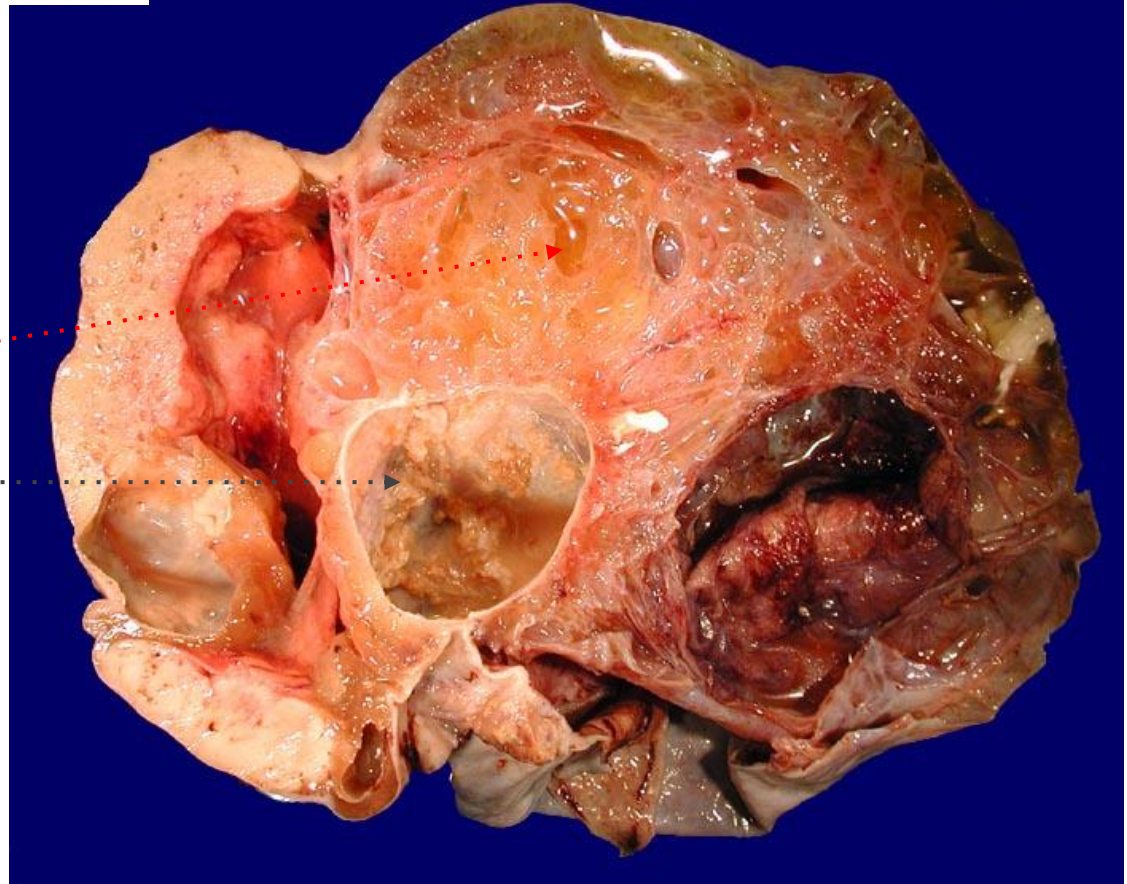
Laminated calcified concretions, referred to as psammoma bodies, are present in one-third of the cases.

## Mucinous cystadenocarcinoma

- **10%** of all ovarian cancers.
- among the **largest tumors recorded**

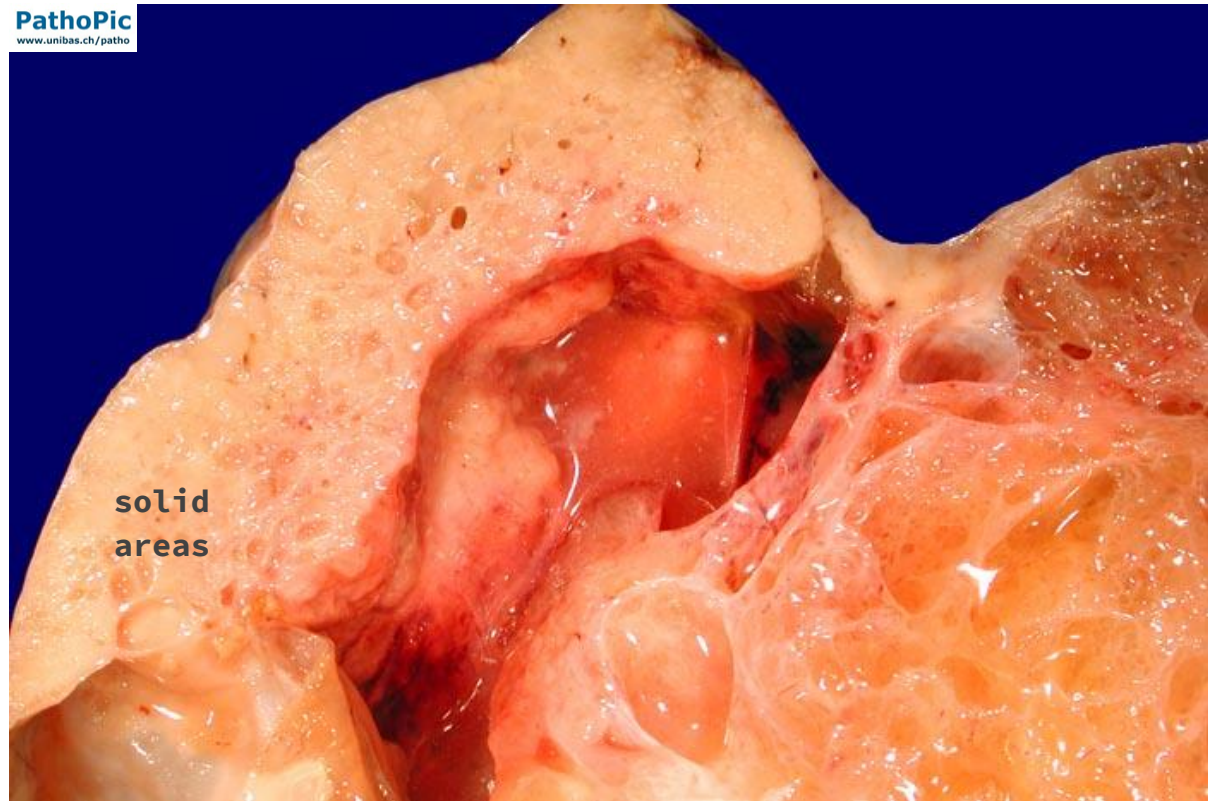
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Mucinous cancers are typically **cystic** and **multilocular**, with many **solid areas** and **papillary projections**.





**Microscopically**, similar to serous cancers, the appearance ranges from **well-differentiated** to **poorly differentiated**. The well-differentiated tumors are characterized by neoplastic glands lined by tall columnar, mucin-producing malignant cells. Poorly differentiated mucinous adenocarcinomas show irregular nests and cords of tumor cells and numerous mitoses. **Stromal invasion is the rule, and infiltration of the capsule is common.**

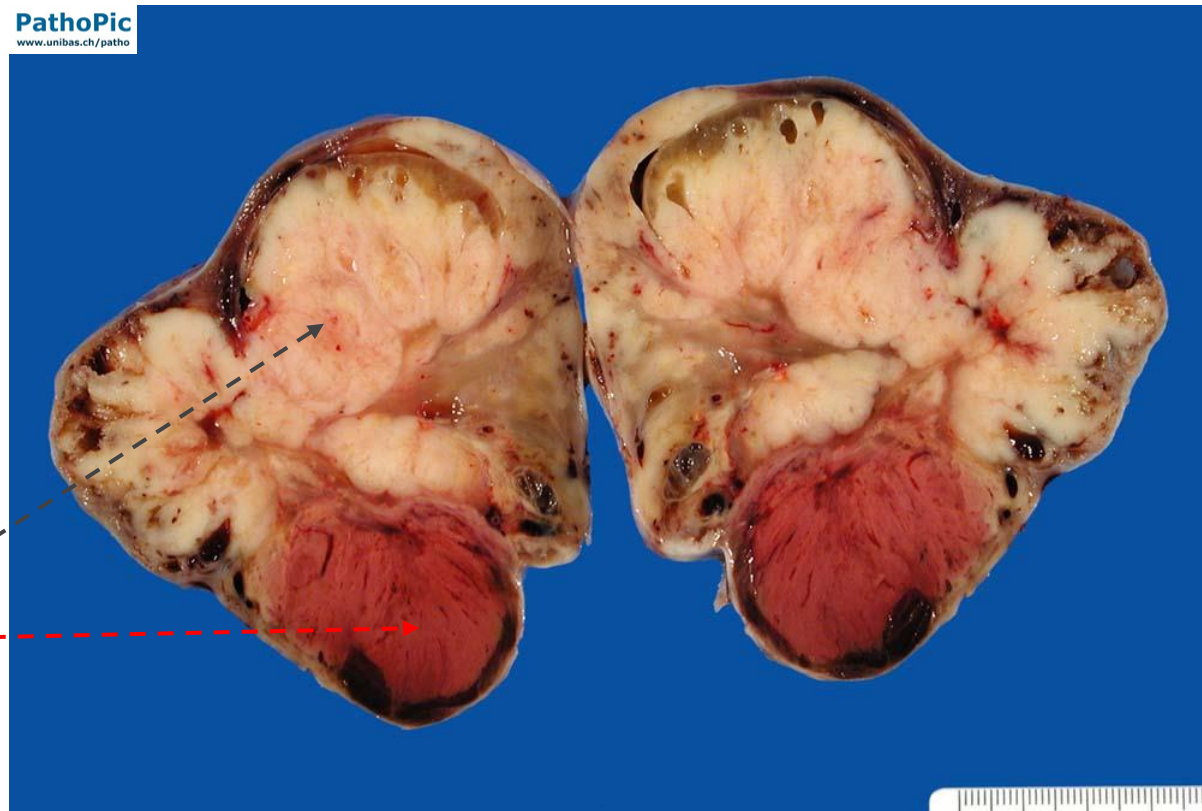


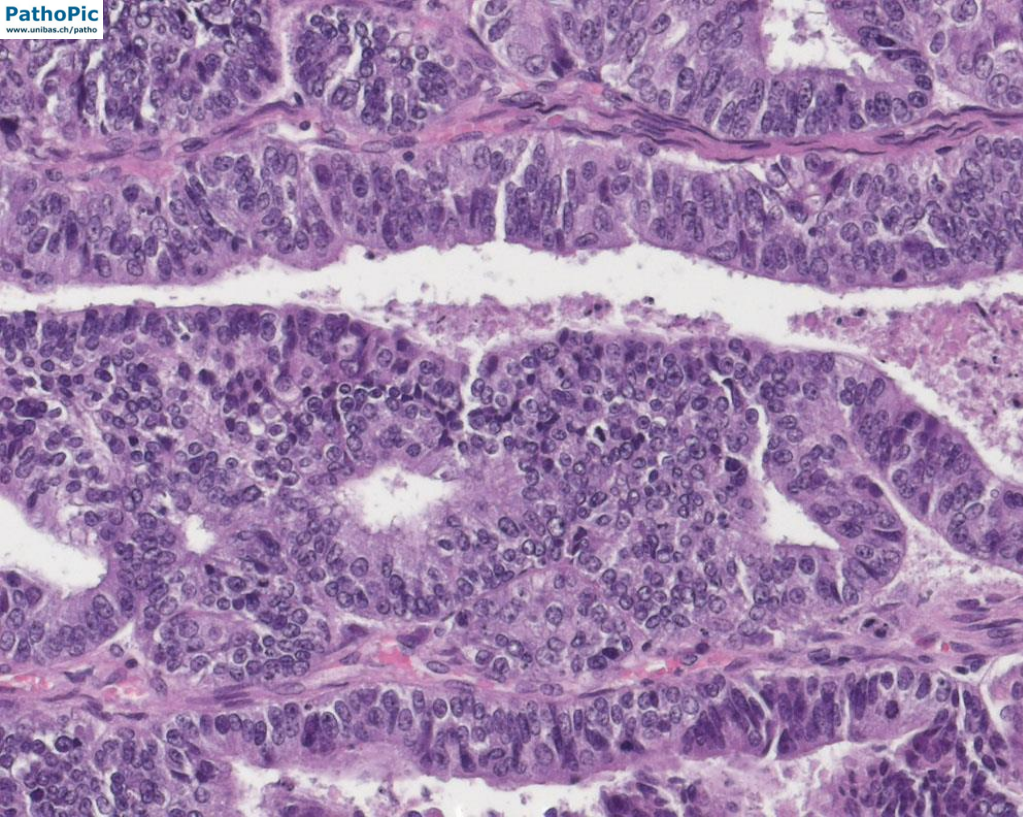


## Endometrioid adenocarcinoma

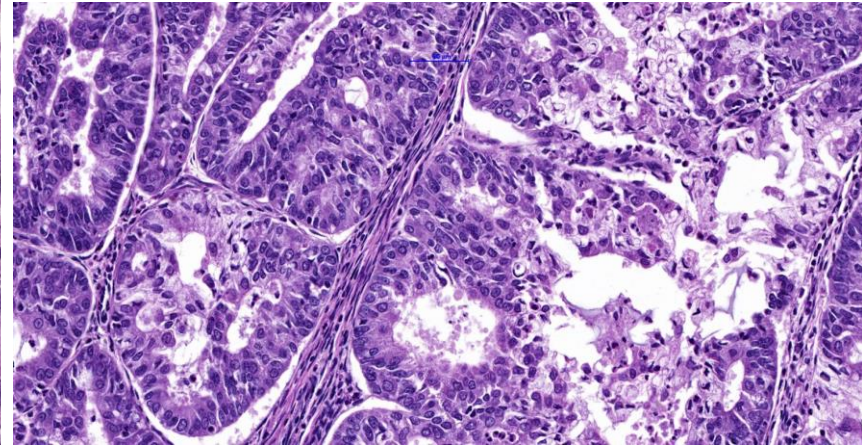
- histologically is identical to carcinoma of the endometrium.
- 20% of all ovarian cancers.

On **gross examination**, **endometrioid carcinomas** vary in size from 2 cm to more than 30 cm in diameter. They tend to be **cystic**, although some are **completely solid** and **exhibit necrotic areas**.





**Microscopically**, the tumors are graded according to the same scheme used for endometrial adenocarcinoma.



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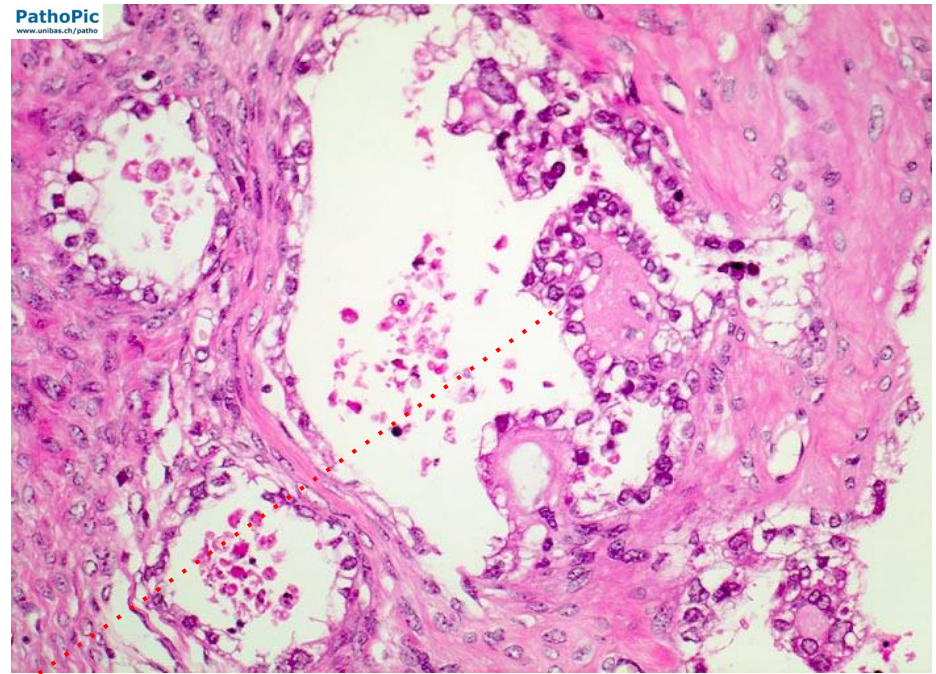
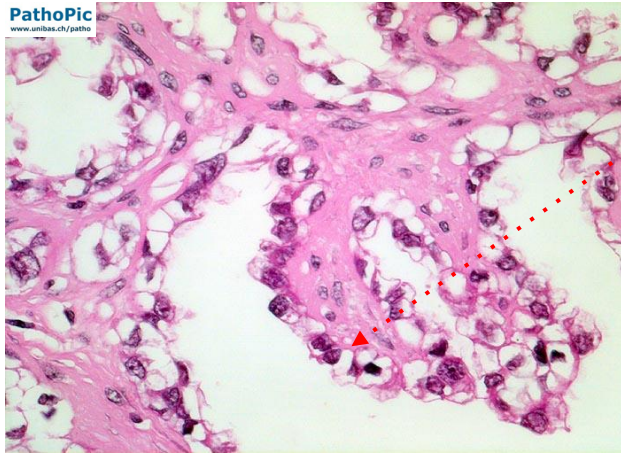
Uterine endometrioid  
adenocarcinoma for comparison;  
H&E slide from own archive



## Clear cell adenocarcinoma

- thought to be **closely related** to **endometrioid adenocarcinoma**
- often found in **association** with **endometriosis**.

It constitutes **5% to 10% of all ovarian cancers**, usually occurring **after the menopause**. The size of the tumors ranges from 2 to 30 cm in diameter, and **40% are bilateral**. The majority are **partially cystic** and **exhibit necrosis** and **haemorrhage in the solid areas**.



<https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=002991>

Survival for patients with malignant ovarian tumors is poor in general. Overall, the 5-years survival is only 35%, because in more than half cases the tumors have spread to the abdominal cavity, or elsewhere, by the time they are discovered.

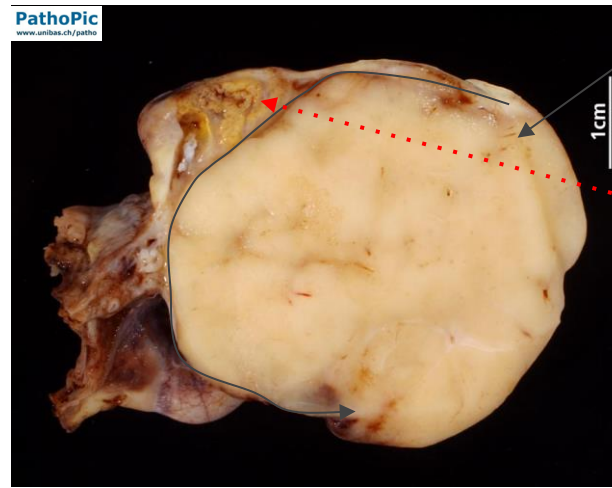
<https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=002992>

# Germ cell tumors.

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Tumors derived from the **germ cells of the ovary** represent a fourth of all ovarian tumors. In **adult women**, **germ cell tumors** are **virtually all benign** (mature cystic teratoma, dermoid cyst).

In **children and young adults** they are **largely malignant**. In children, germ cell tumors are the most common form of ovarian cancer (60%).



Dysgerminoma  
Sharply demarcated beige solid tumor of the ovary.  
Corpus luteum.

<https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=009565>



Benign mature teratoma of the ovary  
Opened cyst **containing**:  
a tooth,  
**fat tissue** and  
**hair**

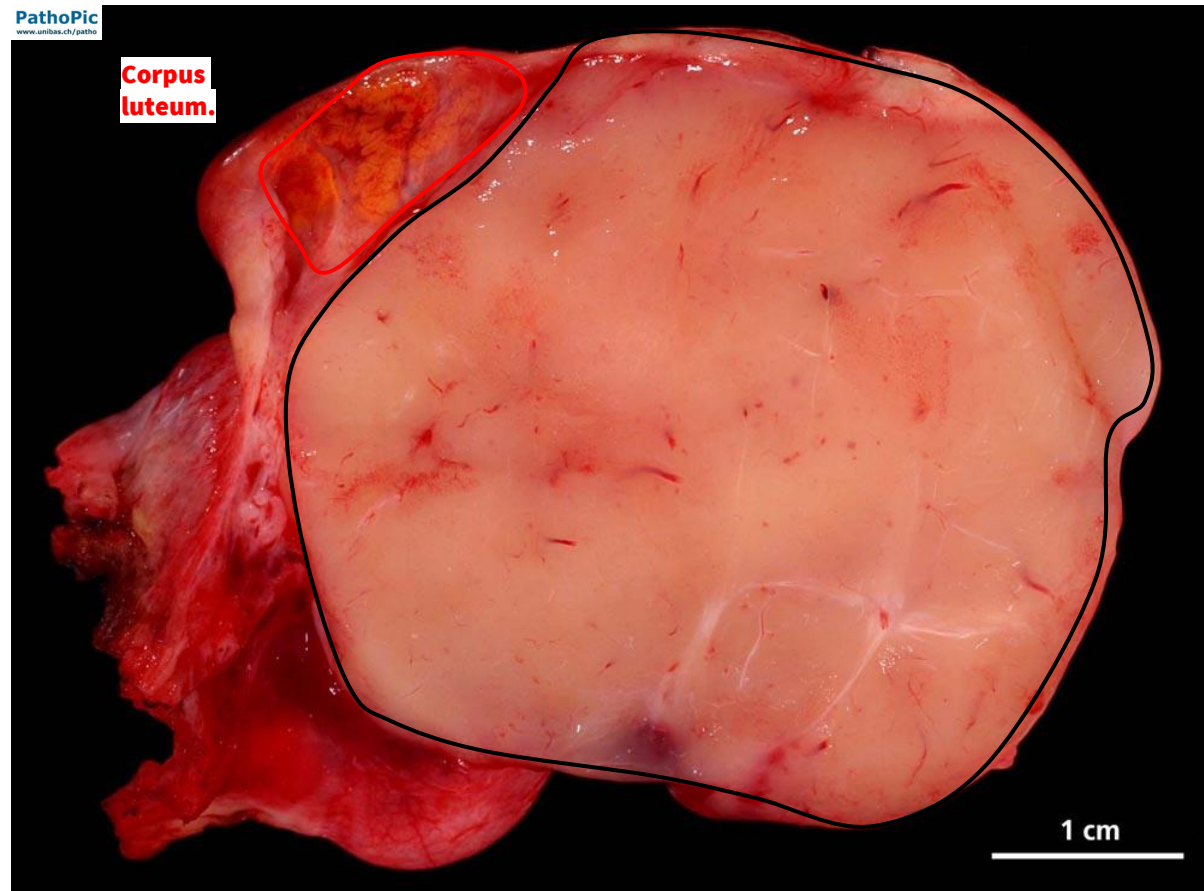
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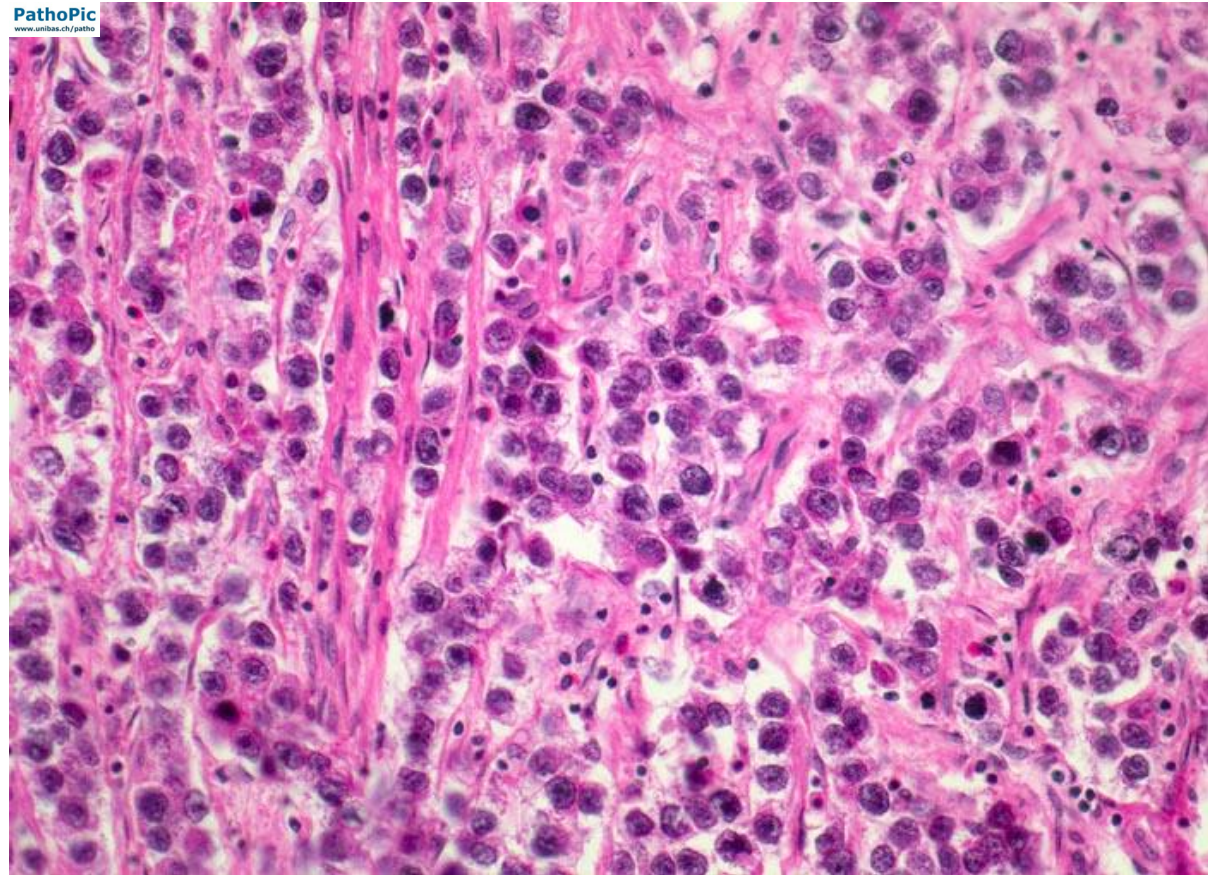
**Dysgerminoma** is the ovarian counterpart of **testicular seminoma** and is composed of **primordial germ cells**.  
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Although it accounts for less than 2% of all ovarian cancers, dysgerminoma is responsible for 10% of these cancers in women younger than 20 years of age. The tumors are bilateral in about 15% of cases.

**On gross examination, dysgerminomas** are often large and firm and have a bosselated external surface. The cut surface is often soft and fleshy.



**Dysgerminoma**  
Sharply demarcated beige solid tumor of the ovary.



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**Microscopic** examination reveals large nests of monotonous tumor cells, which have a clear glycogen-filled cytoplasm and irregularly flattened central nuclei. Fibrous septa containing lymphocytes traverse the tumor.

The 5-years survival rate for patients with stage I tumors approaches 100%. Because the tumor is highly radiosensitive, 5-years survival rates for higher stage tumors exceed 80%.

**Teratoma** is a tumor of **germ cell origin** that shows **differentiation** toward **somatic structures**.

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**Mature teratoma (dermoid cyst)** is a **benign neoplasm**, which accounts for one fourth of all ovarian tumors. The peak incidence occurs in the third decade.

**The tumor is cystic**, and more than **90% contain skin, sebaceous glands, and hair follicles**.

**Half**

**of the tumors exhibit smooth muscle, sweat gland, cartilage, bone, teeth, and respiratory tract epithelium**. Tissues such as gut, thyroid, and brain are encountered less frequently.

**Struma ovarii refers to a cystic lesion composed predominantly of thyroid tissue** (5% to 20% of mature cystic teratomas).



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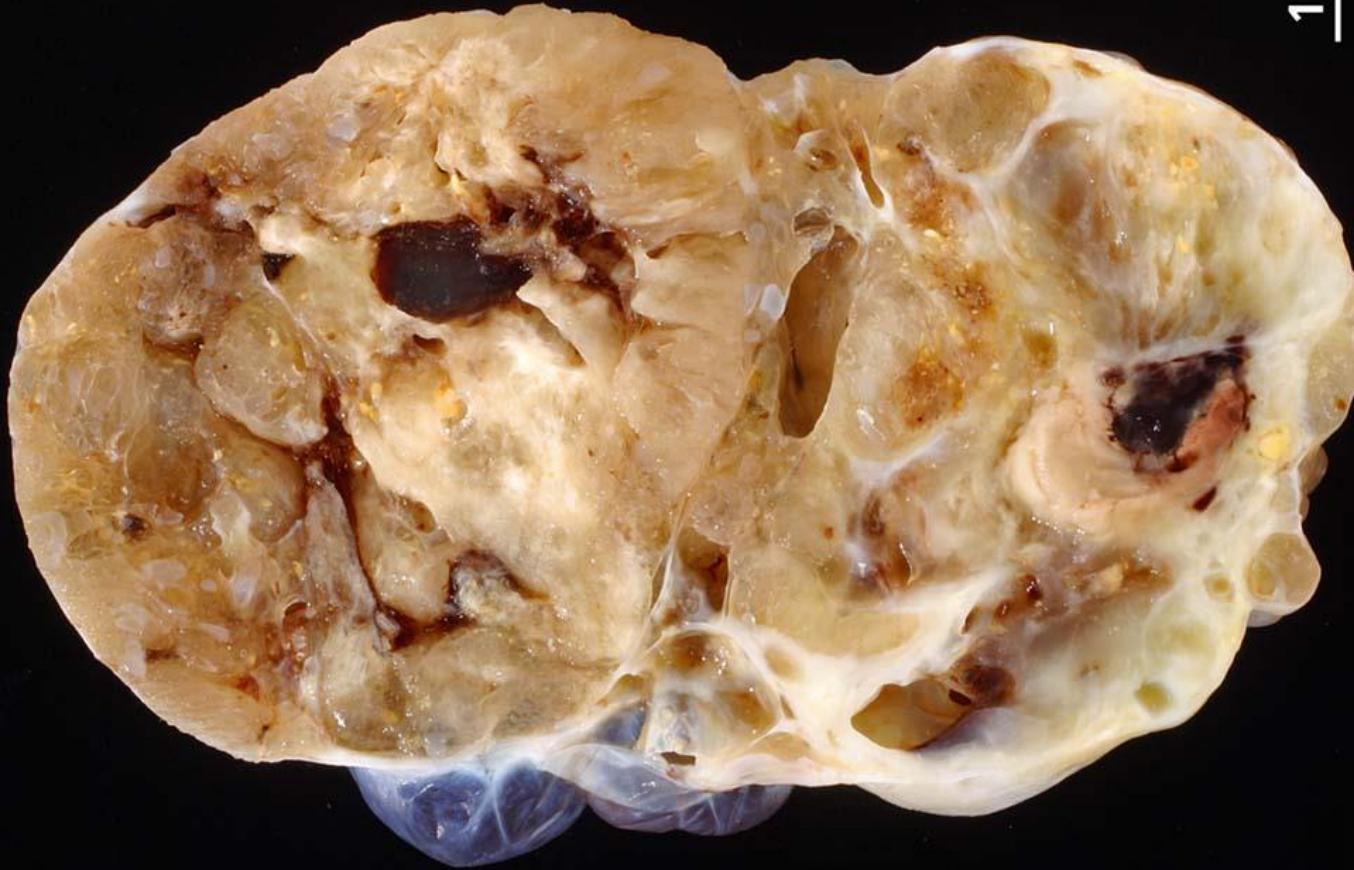




◀ 10mm ▶



1 cm

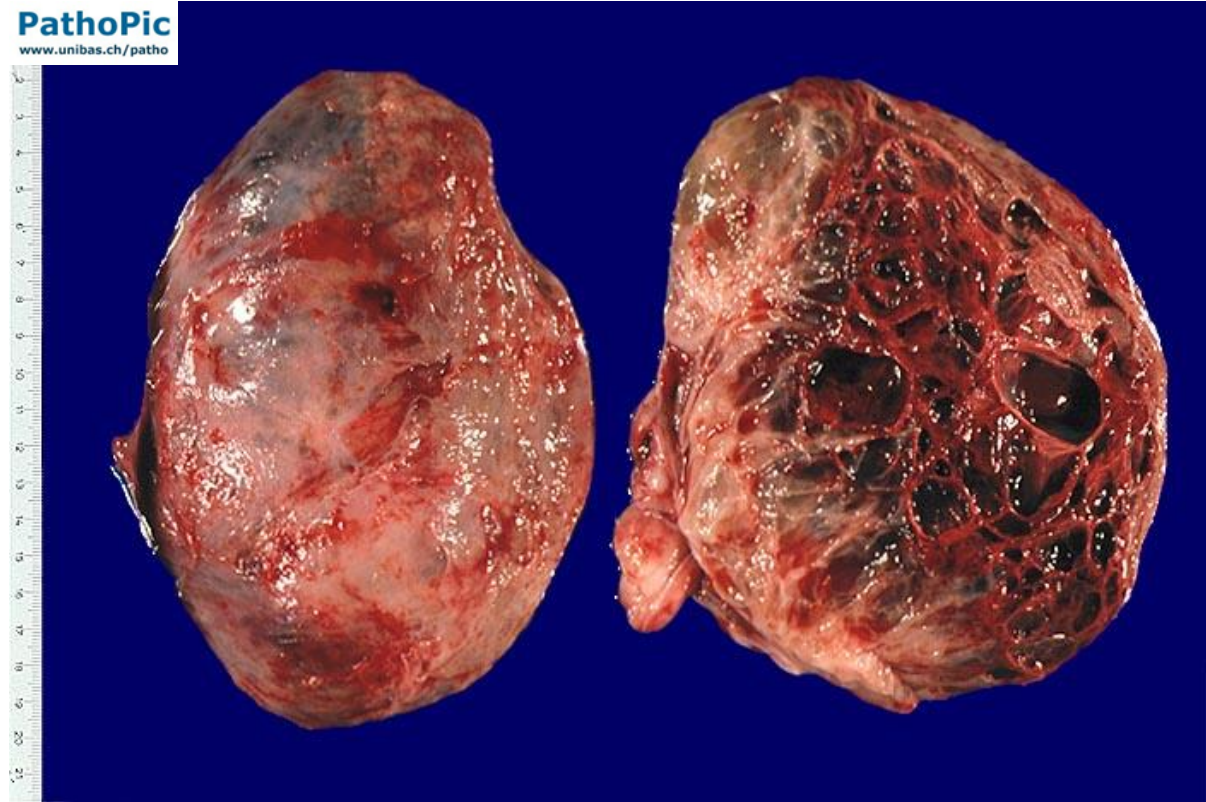


## Immature teratoma

composed of elements derived from the three germ layers. **It contains immature or embryonal tissues.**

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**Immature teratoma** is predominantly **solid and lobulated** and **contains numerous small cysts**. **Microscopically**, multiple tumor components are usually found, including those differentiating toward nervous tissue (neuroepithelial rosettes and immature glia), glands, and other structures found in mature cystic teratomas.



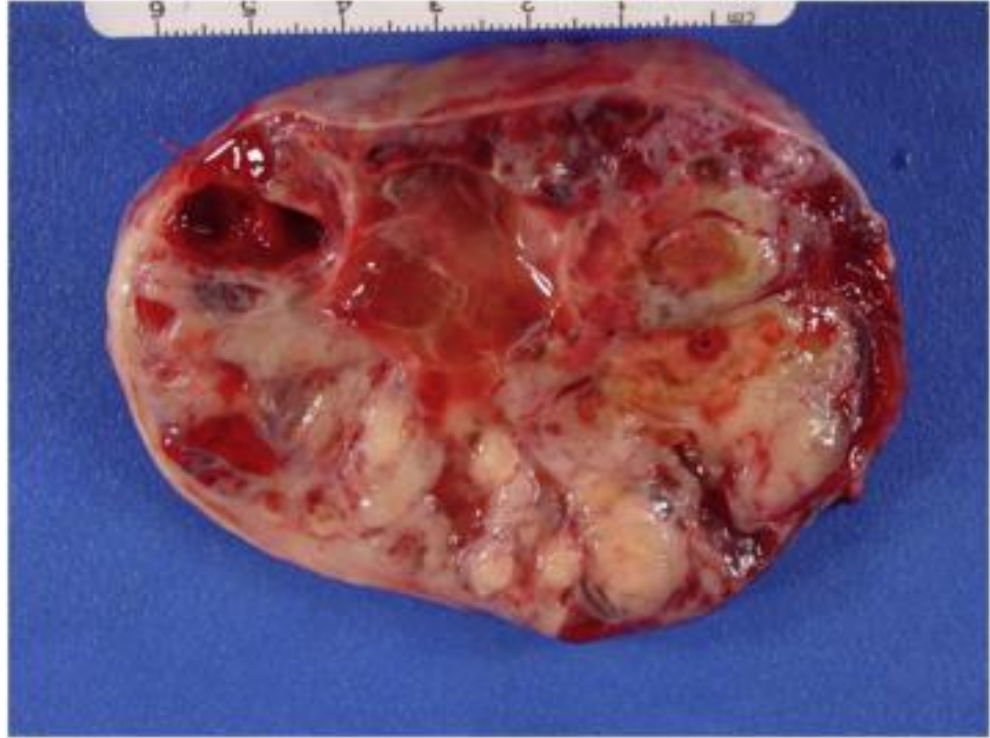
## Endodermal sinus tumor (Yolk sac carcinoma)

- **highly malignant tumor** of women younger than 30 years of age

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**Histologically** resembles the mesenchyme of the **primitive yolk sac**.

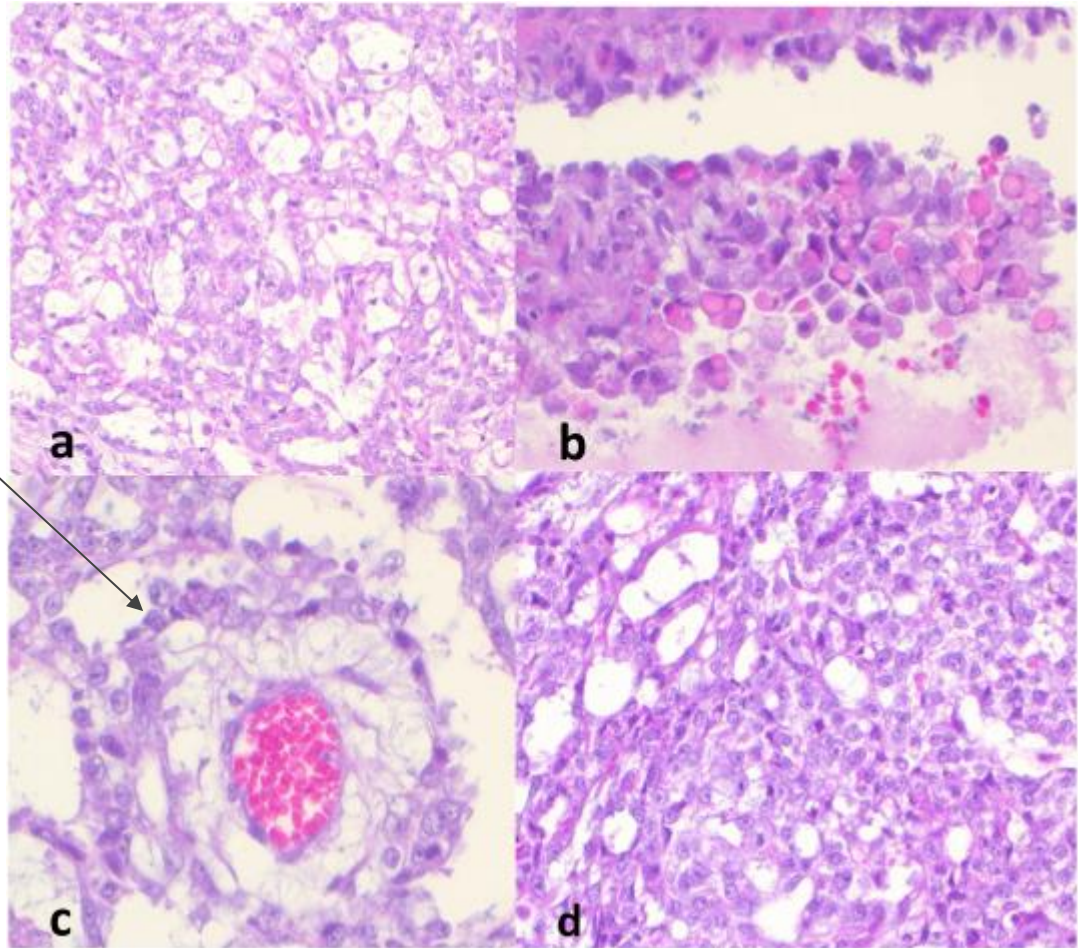
**Typically**, the endodermal sinus tumor **is large and displays extensive necrosis and hemorrhage**.





Dunn TN, Khazaeian K, Coffey DM, Rohozinski J, Kovanci E, Edwards CL, Tung CS. Successful yolk-sac tumor treatment with fertility-sparing partial oophorectomy. Gynecologic oncology reports. 2019 Feb 1;27:22-4.

The most common appearance is a reticular, honeycombed pattern of communicating spaces lined by primitive cells. Schiller-Duval bodies are characteristic of the tumor. These structures consist of papillae that protrude into a space lined by tumor cell. The papillae are covered by a mantle of embryonal cells and contain a fibrovascular core and a central blood vessel.



# Sex cord/stromal tumors.

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**Tumors of the sex cord** and **stroma** are derived from **either** the **primitive sex cords** or the **mesenchymal stroma** of the developing gonad.

**They account for 10% of all ovarian tumors.** The tumors range from benign to **low grade malignant** and are frequently differentiated towards **female (granulosa and theca cells)** or **male (Sertoli and Leydig cells) structures.**

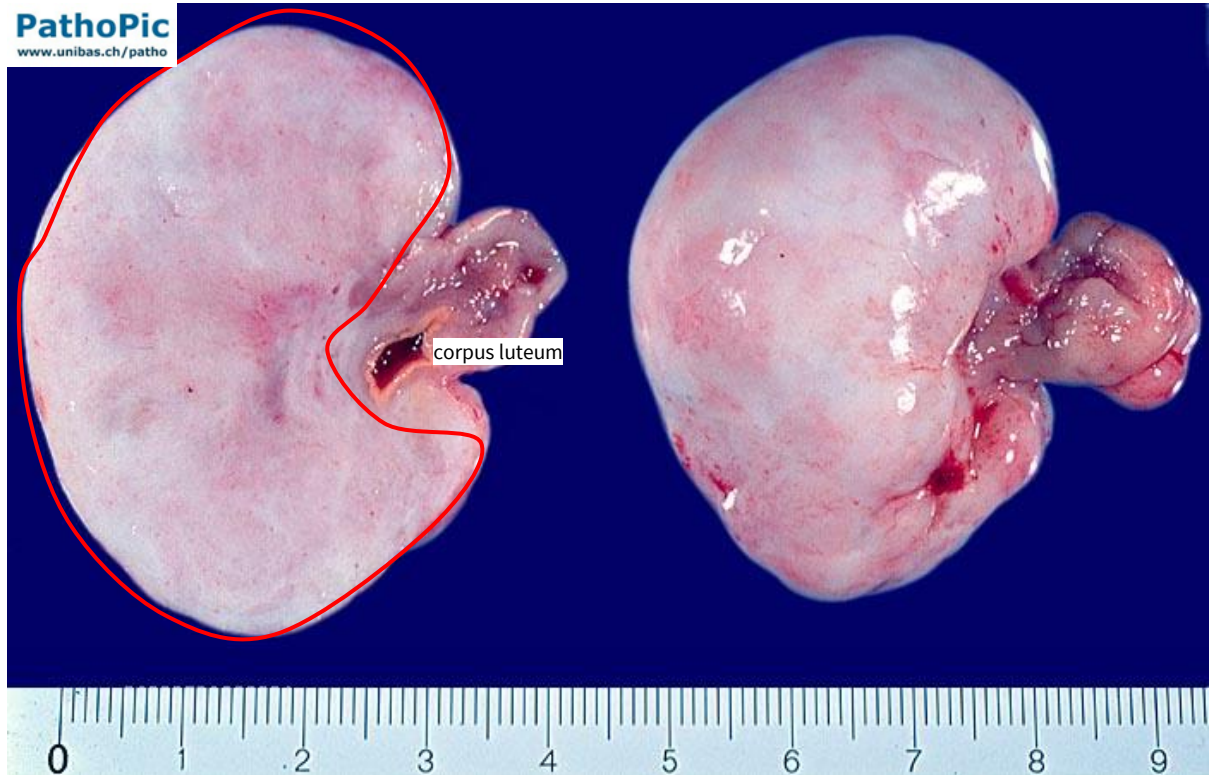
**Sex cord/stromal tumors** account for **most** of the **clinically functional ovarian tumors.**

## Ovarian fibroma

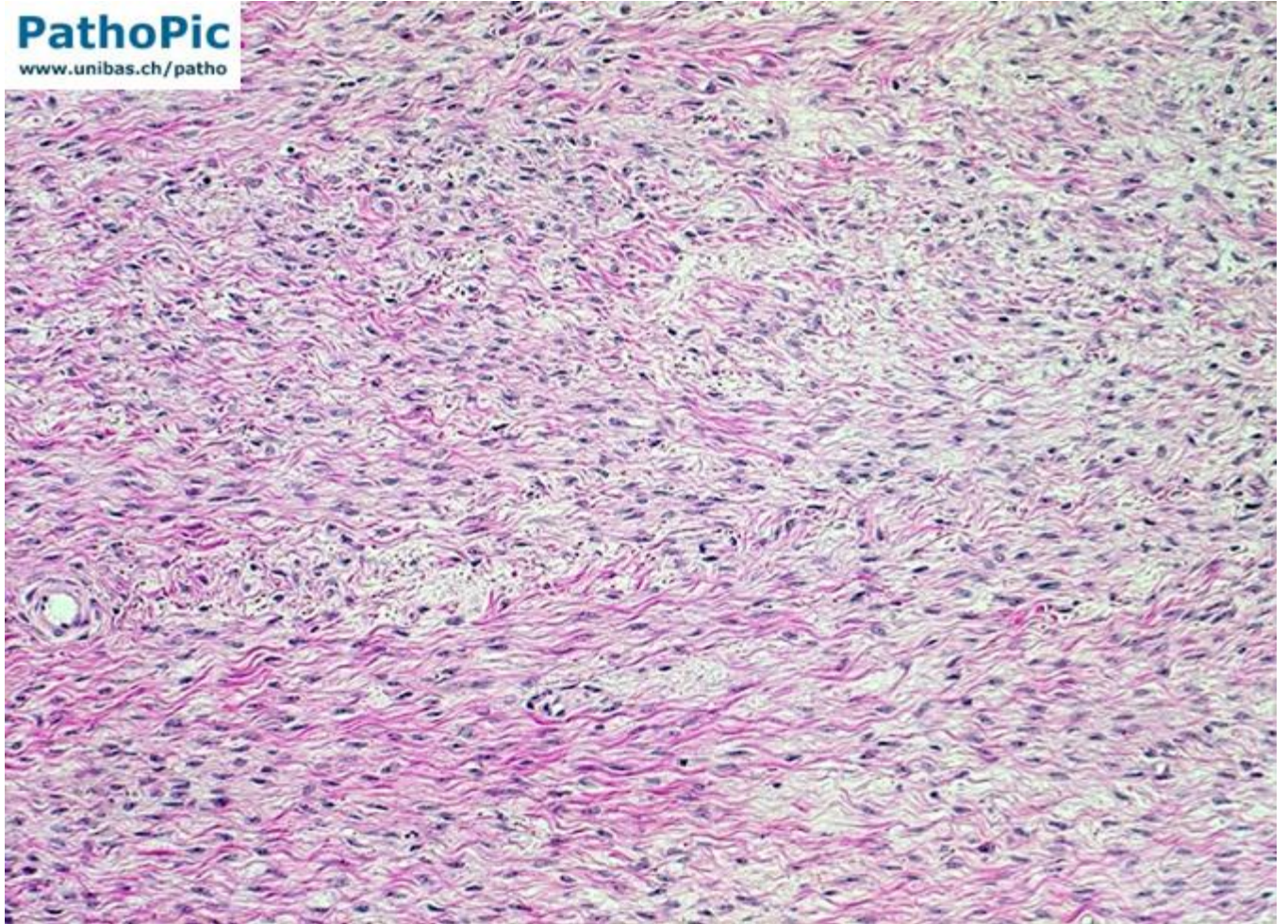
- most common ovarian stromal tumor.
- virtually always benign.

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The tumor is solid, firm, and white.







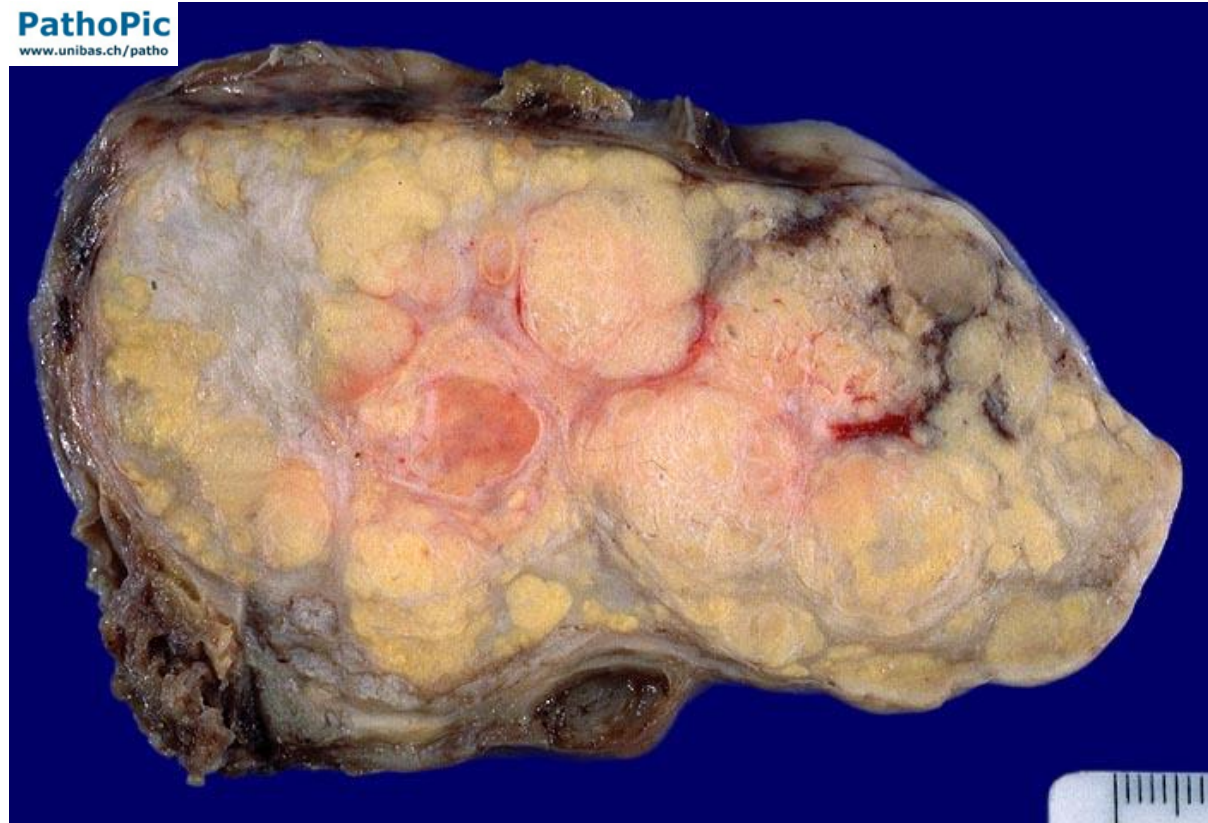
**Microscopically**, the cells resemble the stroma of the normal ovarian cortex, being composed of well-differentiated fibroblasts and variable amounts of collagen. Half of the larger tumors are associated with ascites and, rarely, with ascites and pleural effusions (Meigs syndrome).

## Thecoma

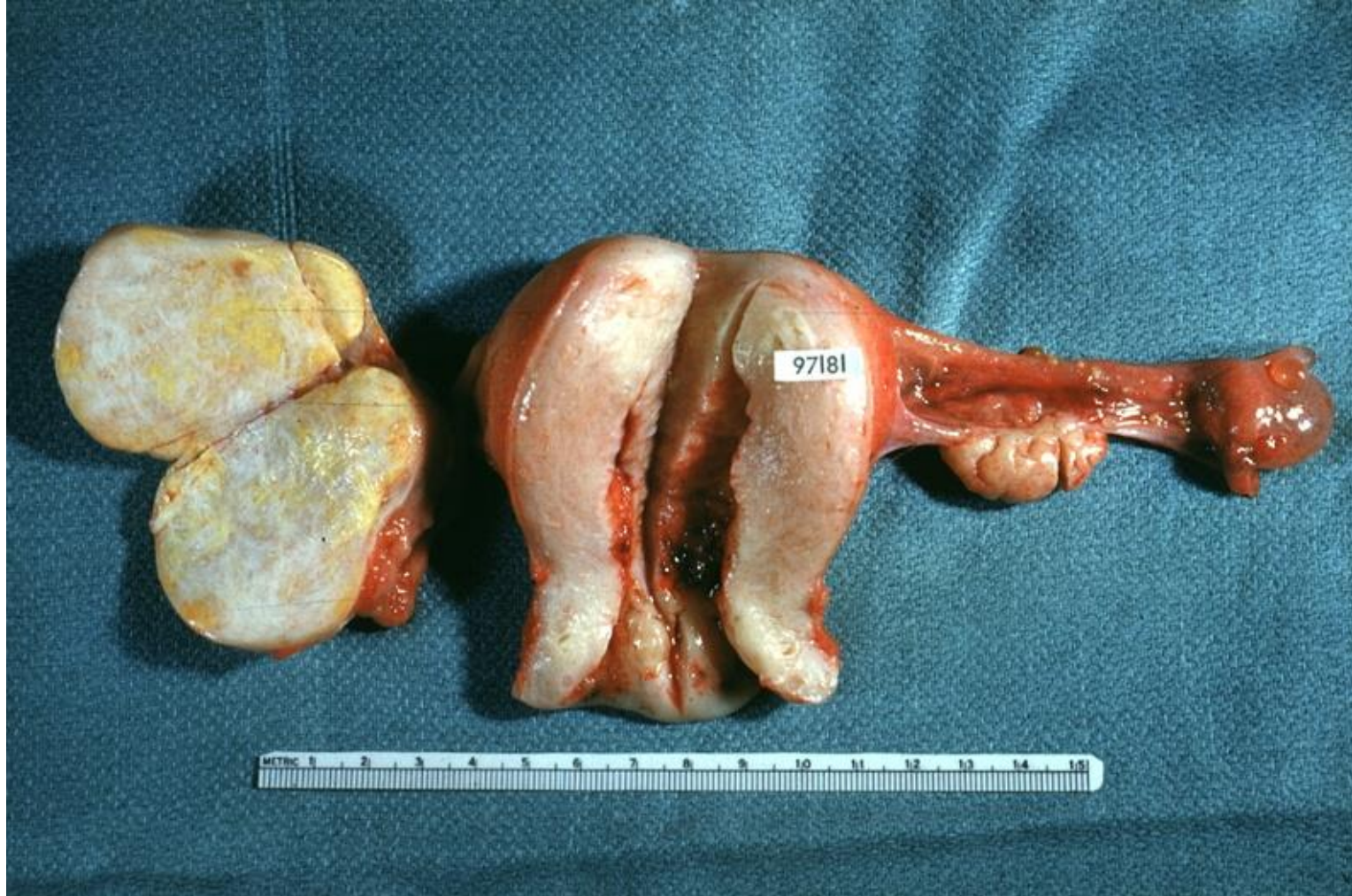
- functional ovarian tumor that arises in postmenopausal women.

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In the majority of cases, it produces signs of estrogen production. Thecomas are solid tumors, mostly 5 to 10 cm in diameter. The cut section is yellow, owing to the presence of many lipid-laden theca cells.

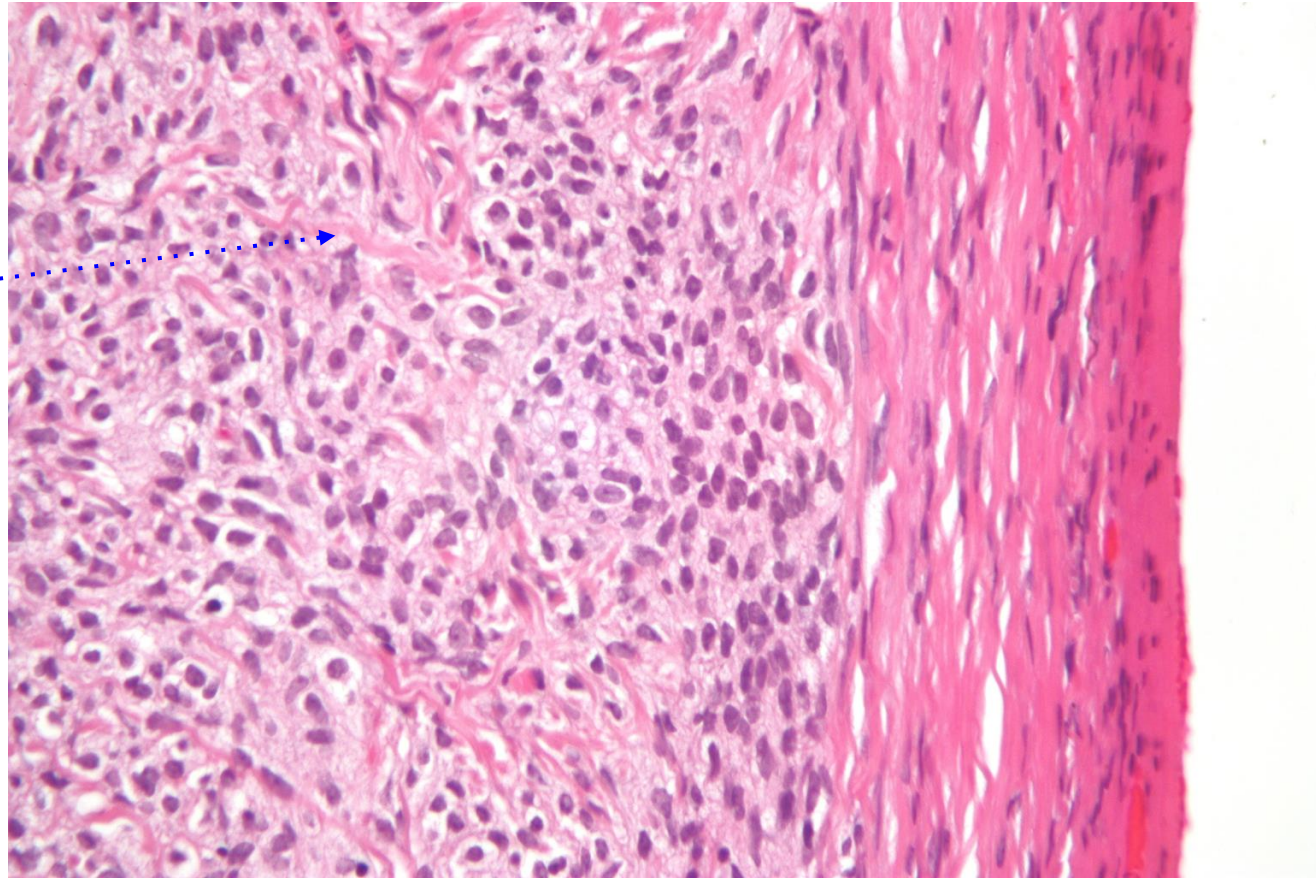








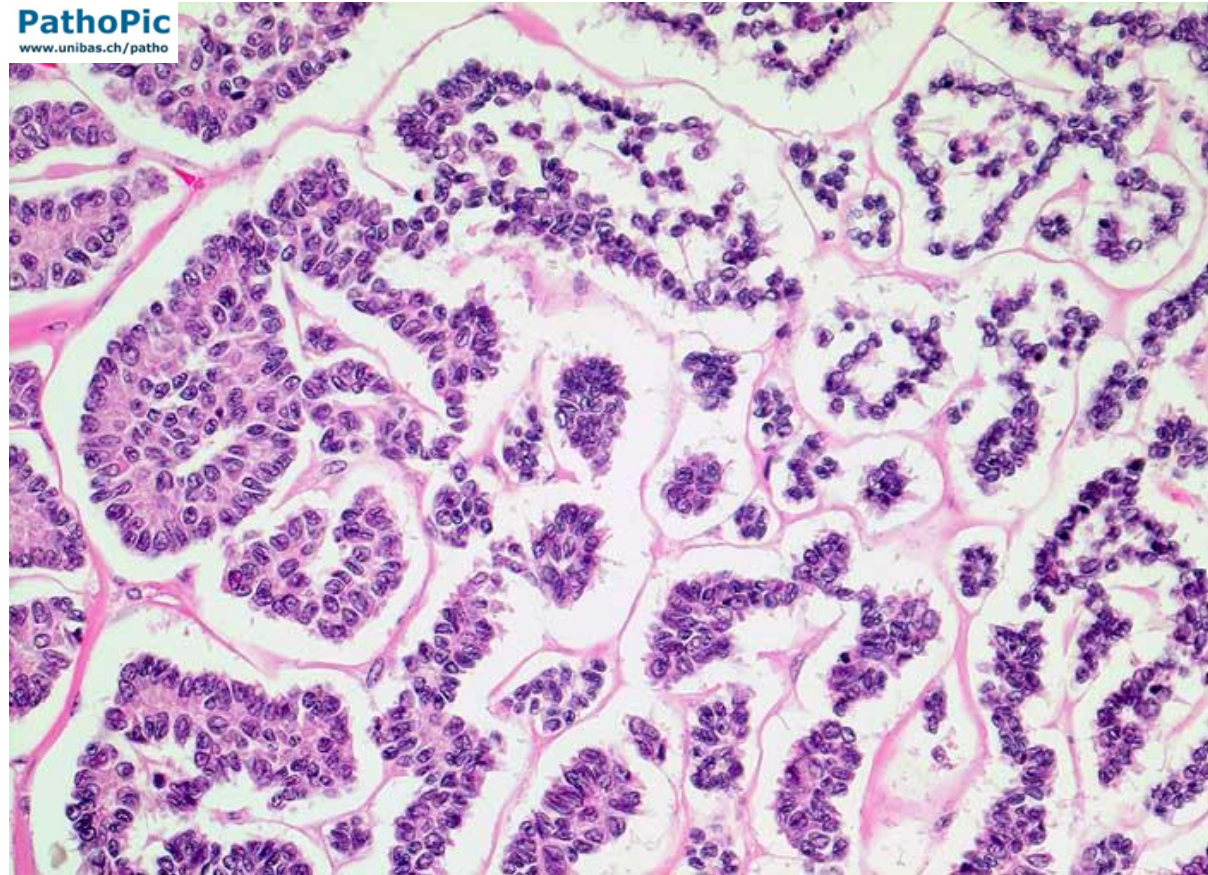
**Microscopically**, the cells are large and oval to round, with a vacuolated cytoplasm that contains lipid. Bands of **hyalinized collagen** separate nests of theca cells. **Thecomas are virtually always benign**. Because of estrogen output by the tumor, thecomas commonly cause irregularity in menstrual cycles and breast enlargement. Endometrial hyperplasia or cancer may be the complications of the tumor.



Granulosa cell tumor is the prototypical functional neoplasm associated with estrogen secretion.

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This tumor should be considered malignant, because of its potential for local spread and the rare occurrence of distant metastases. Most granulosa cell tumors occur after the menopause, and they are unusual before puberty.

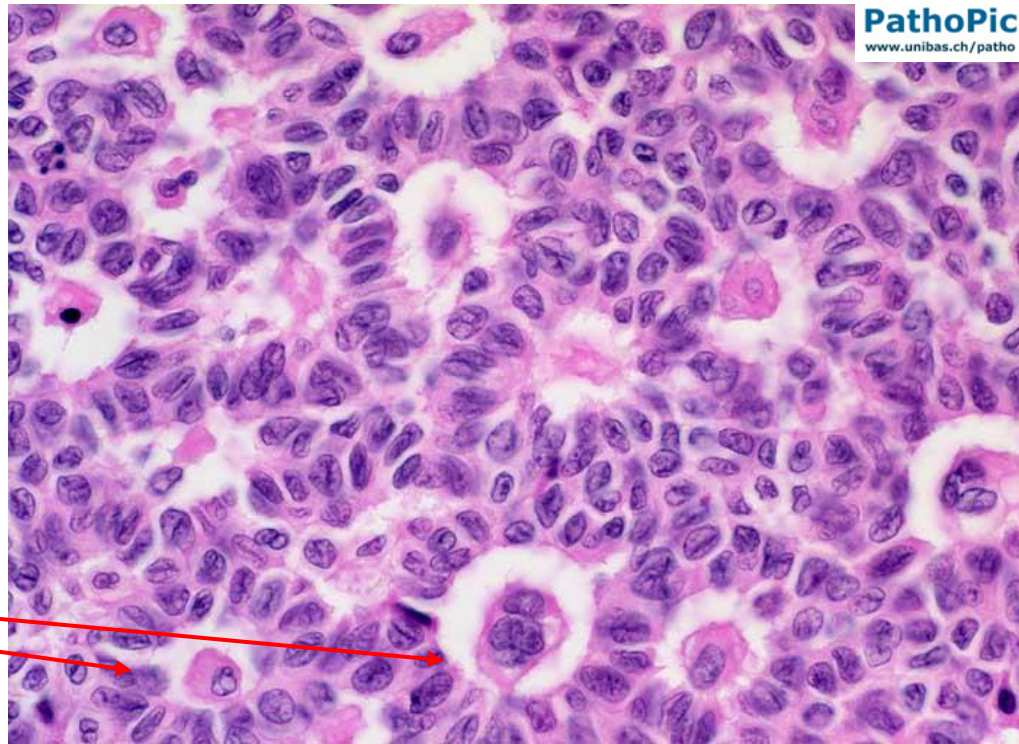




**Granulosa cell tumors** are large and focally cystic to solid.

**Characteristically, the tumor has yellow areas, representing lipid-laden luteinized granulosa cells, white zones of stroma, and focal hemorrhages. Microscopically, granulosa cell tumors display an array of growth patterns: (1) diffuse (sarcomatoid), (2) insular (islands of cells), or (3) trabecular (anastomotic bands of granulosa cells).**

**The orientation of the cells about a central space (Call-Exner bodies)** results in a characteristic follicular pattern. The tumor cells are typically spindle shaped and have a cleaved, elongated nucleus (coffee bean appearance).



Three-fourths of granulosa cell tumors are functional, means that they secrete estrogens. Consequently, endometrial hyperplasia is a common presenting sign. Hyperplasia may progress to endometrial adenocarcinoma if the functioning granulosa cell tumor remains undetected.



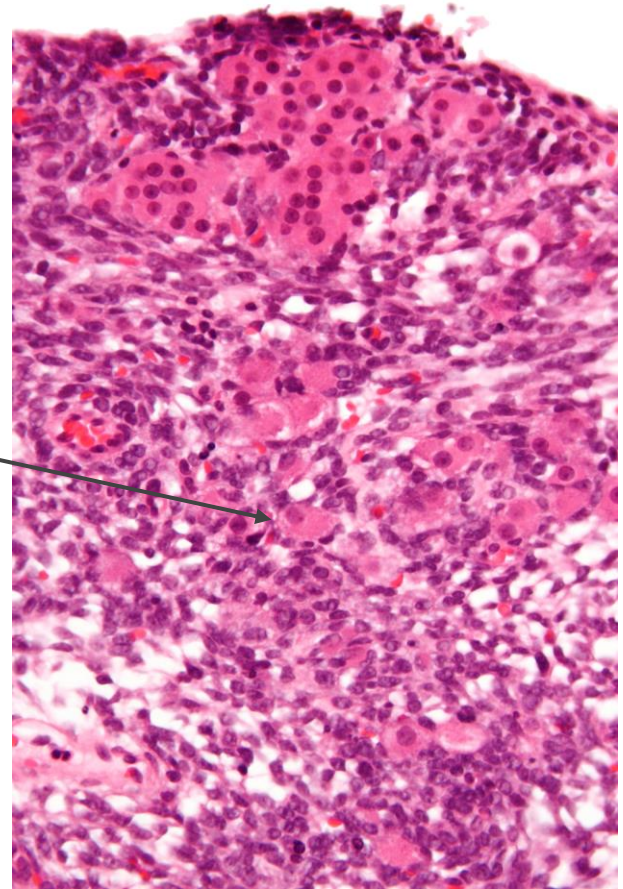
**Sertoli-Leydig cell tumor** (arrhenoblastoma or androblastoma) is a rare mesenchymal neoplasm of the ovary of **low malignant potential**.  
           

It is the **prototypical functional tumour-associated with androgen secretion**. It occurs at all ages but is most common in young women of child-bearing age. **Sertoli-Leydig cell tumors are unilateral and vary in size from microscopic foci to very large lesions**, most measuring between 5 and 15 cm in diameter. They tend to form **lobulated, solid, yellow or tan masses**.



**Microscopically**, the tumors vary from well-differentiated to poorly differentiated, and some exhibit heterologous elements (papillae, glands, cartilage). **The most characteristic features are large Leydig cells, which have abundant eosinophilic cytoplasm**, and fine trabeculae of sex cords, which are immature solid tubules of embryonic Sertoli cells. **Patients with functioning tumors (about half of them) present with signs of virilization, evidenced by hirsutism, deep voice.** The initial signs of the tumor are often defeminization, manifested as breast atrophy, amenorrhea, and loss of hip fat. Both virilization and defeminization result from the secretion of testosterone and other androgenic hormones by the Sertoli-Leydig cell tumor.

**Leydig cells**



# Tumors metastatic to the ovary.

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About 3% of ovarian cancers arise outside the ovary, the most common primary sites being in descending order: breast, large intestine, stomach, and other genital organs. The tumors vary in size from microscopic lesions to large masses, bilateral ovarian involvement being an important clue to the diagnosis.

Krukenberg tumors are ovarian metastases in which the tumor appears as nests of mucin-filled “signet-ring” cells within a cellular stroma derived from the ovary. The stomach is the primary site in 75% of the cases, and most of other Krukenberg tumors are from the colon.



