

Female Genital System

Part 3: Ovary and Fallopian Tube

APPROVED

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Goals for Today's Lecture

By the end of the lecture you should be able to:

- Recognize and describe the pathology of the major ovarian neoplasms
- Compare the incidence and mortality rates for ovarian cancer vs. other gynecologic cancers
- Predict the behavior of benign, borderline and malignant ovarian epithelial neoplasms
- Classify the common forms of gestational trophoblastic disease

A few things about pregnancy are discussed in the last part of lecture



Fallopian tube (brief)

Ovary

Non-neoplastic

Neoplastic

Pregnancy-related

Fallopian Tubes-Developmental

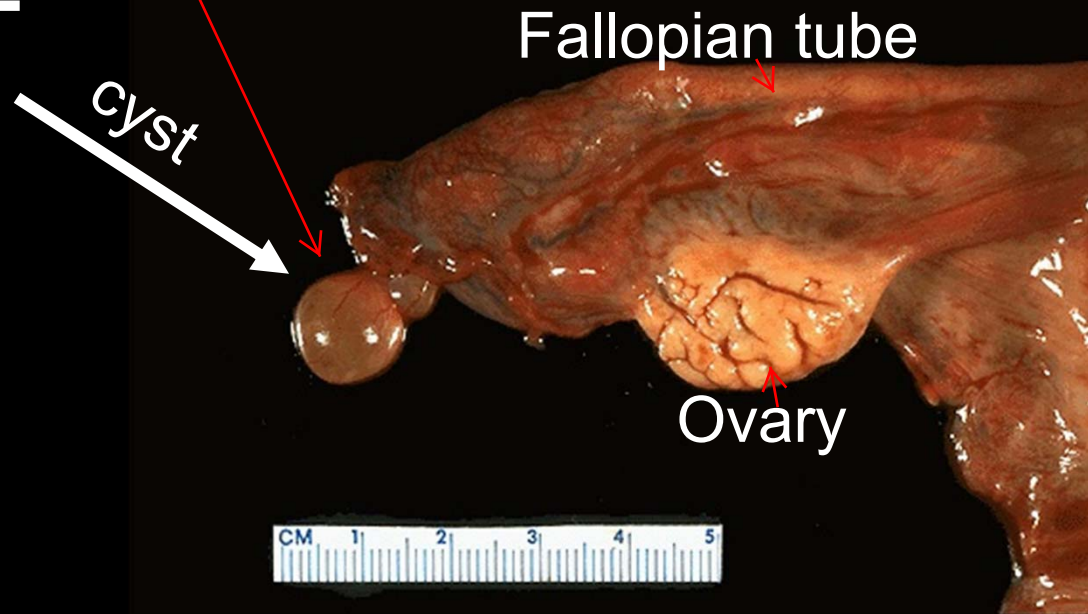
- Paratubal cysts
 - Usually small, less than 2 cm

usually no clinical significance

This is apparently no big deal

Near fimbria =
“Hydatids of Morgagni”
No clinical significance

Cyst near fimbria is called Hydatids of Morgagni. Remember this if you want to sound very clever. Honestly, sounds like something that came out of Lord of the Rings.



Disease of the Fallopian tubes is frequently inflammatory

Fallopian Tubes-Inflammatory

- Pelvic Inflammatory Disease (PID)
 - Ascending infection from STD's
 - Acute infection of upper gyn structures, typically involves tubes and ovaries, but neighboring structures involved.
 - Tuboovarian abscess (“**TOA**”) is common.

Inflammation not limited to the tubes, can see a lot of structures stuck together in one ugly mess

Pelvic Inflammatory Disease

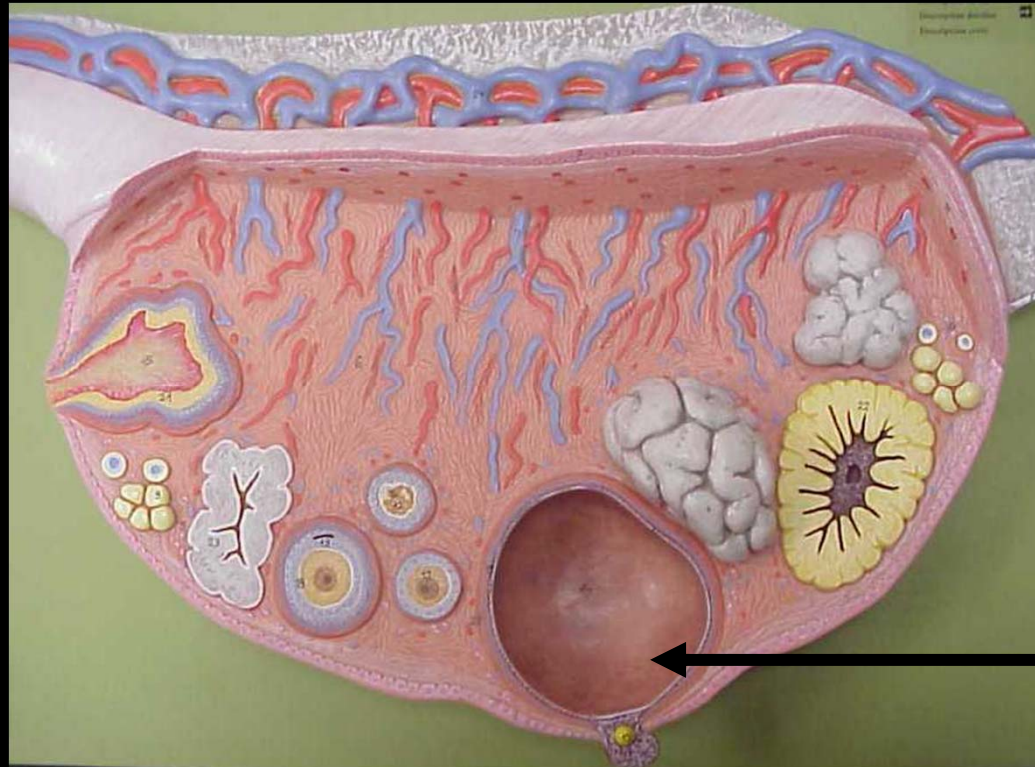
- 2.5 million outpatient visits
- 200,000 hospitalizations
- 100,000 surgical procedures remove abscesses
- Most common gyn cause of ER visit
- Estimated cost \$5 billion/year in U.S.
- Major long-term sequelae i.e. It is a big deal.
 - Infertility Due to scarring
 - Ectopic pregnancies egg can't move into uterus
 - Pelvic pain

Ovary

- Follicular cysts (normal)
- Polycystic Ovaries
- **Ovarian neoplasms**

NORMAL OVARY

Follicles/Follicular Cysts



Oocytes mature and form big cystic structures lined with single layer of granulosa cells. (Graafian follicle). Sometimes these follicles don't rupture and can grow quite large, but it is still a normal ovary. Though these cysts are often incidental findings on imaging studies, sometimes patient gets unnecessary surgery on a normal ovary to rule out cancer. Sometimes docs wait to see if the cyst change over time. If it is a follicular cyst, it will eventually regress, but cancer won't.

Follicular Cyst

Normal follicles can be **large** ("follicular cysts), and are **sometimes suspicious on imaging studies**

Review: How does Progesterone opposes Estrogen?
1. E stimulates synthesis of both E and P receptors in target tissues
2. P inhibits synthesis of both E and P receptors
3. P increases cellular estradiol dehydrogenase, which converts estrogen to less potent estrone, decreasing estrogenic activity

Polycystic Ovary Disease

infrequent menses, >35 day menstrual cycle according to first-aid

excess body hair, masculinization

particularly central obesity, e.g. belly fat

- Syndrome of oligomenorrhea, anovulation, hirsutism, infertility and obesity (“Stein-Leventhal Syndrome”).

- Unopposed estrogen, high risk of endometrial carcinoma

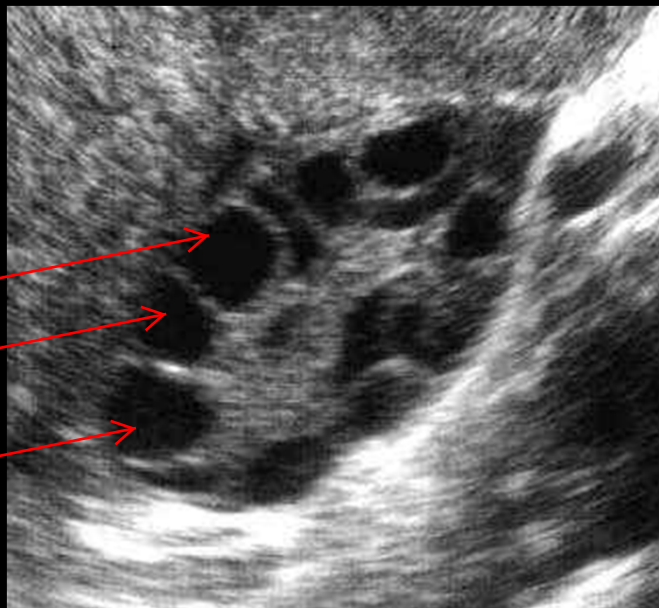
These patients can develop endometrial cancer as early as their 20s whereas in general, women don't start to get endometrial cancer until their 40s.

- Pathogenesis poorly understood; related to insulin resistance?

Because of lack of ovulation, have unopposed estrogen. Remember, corpus luteum (left-over follicle after rupture/ovulation) secretes progesterone which opposes estrogen.

Patients may present in their teens for irregular menses. This (POD) is asymptomatic before puberty.

Polycystic Ovaries



can see cysts on ultrasound

Ultrasound

Numerous cysts

Ovarian Neoplasms

Gyn Cancers - 2006

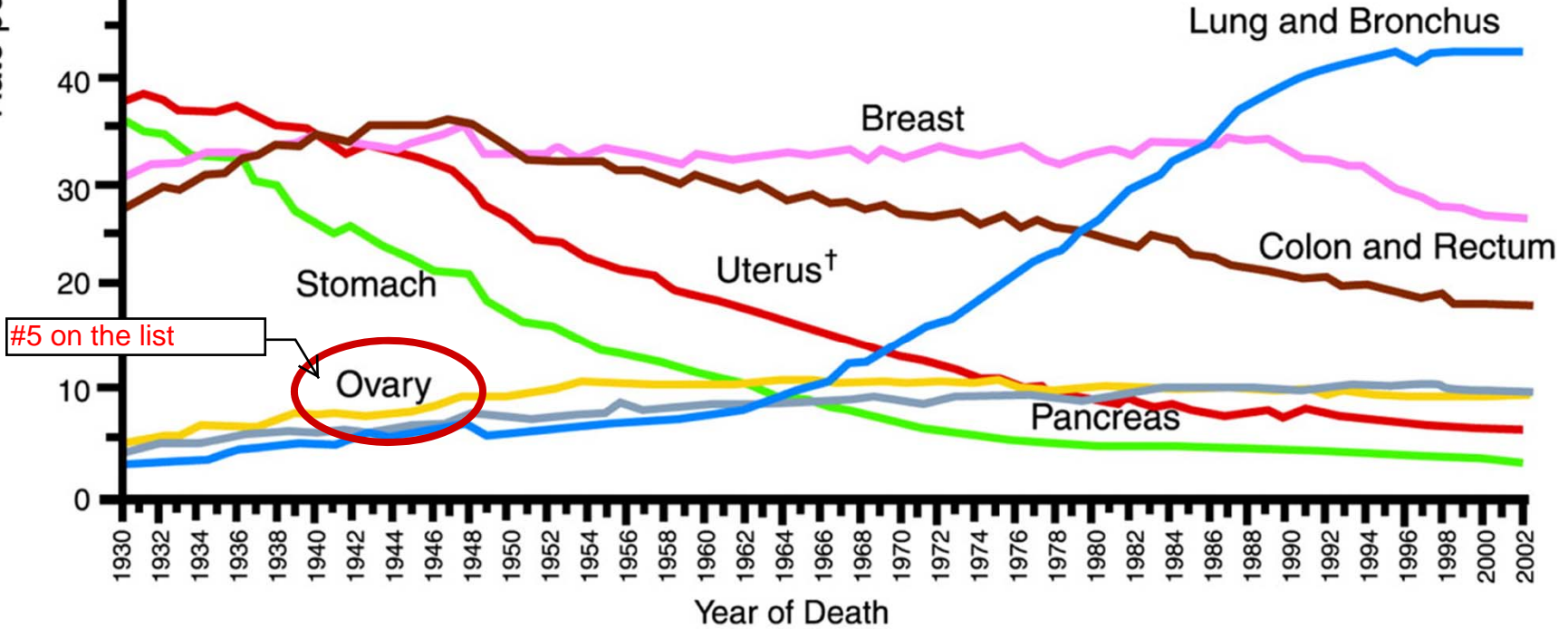
	<u>New cases</u>	<u>Deaths</u>
Corpus	41,200	7,350
Ovary	21,180	15,310
Cervix	9,710	3,700
Vulva	3,740	800
Vagina/ other	2,420	820

Although not the most common cancer in the GYN

....It is the most deadly, bad actor

Death rates in women for common cancers in the U.S.

Rate per 100,000 Population



#5 on the list

Ovary

Ovarian Cancer

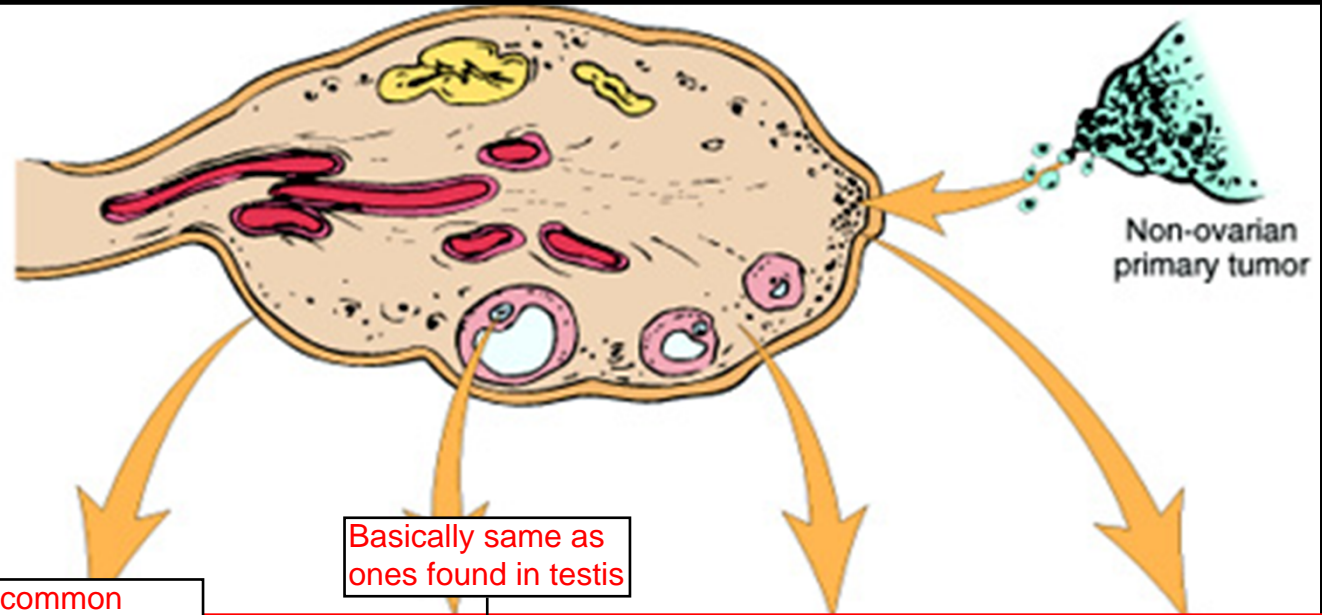
A lot of women undergo surgery to rule out cancer, but cancer is only 1 in 5 tumors.

- 3% of cancers in women
- 6% of cancer deaths in women (5th)
- **Only 20% of ovarian tumors are malignant**
 - Oophorectomy or cystectomy to r/o cancer is very common.
 - 7% of women will have ovarian mass that requires evaluation.

← Quite common

Key Point: A large variety of tumors can be found in ovaries because of the different tissues there. Mets like ovaries too, watch for them as well.

Categories of Ovarian Tumors



Most common

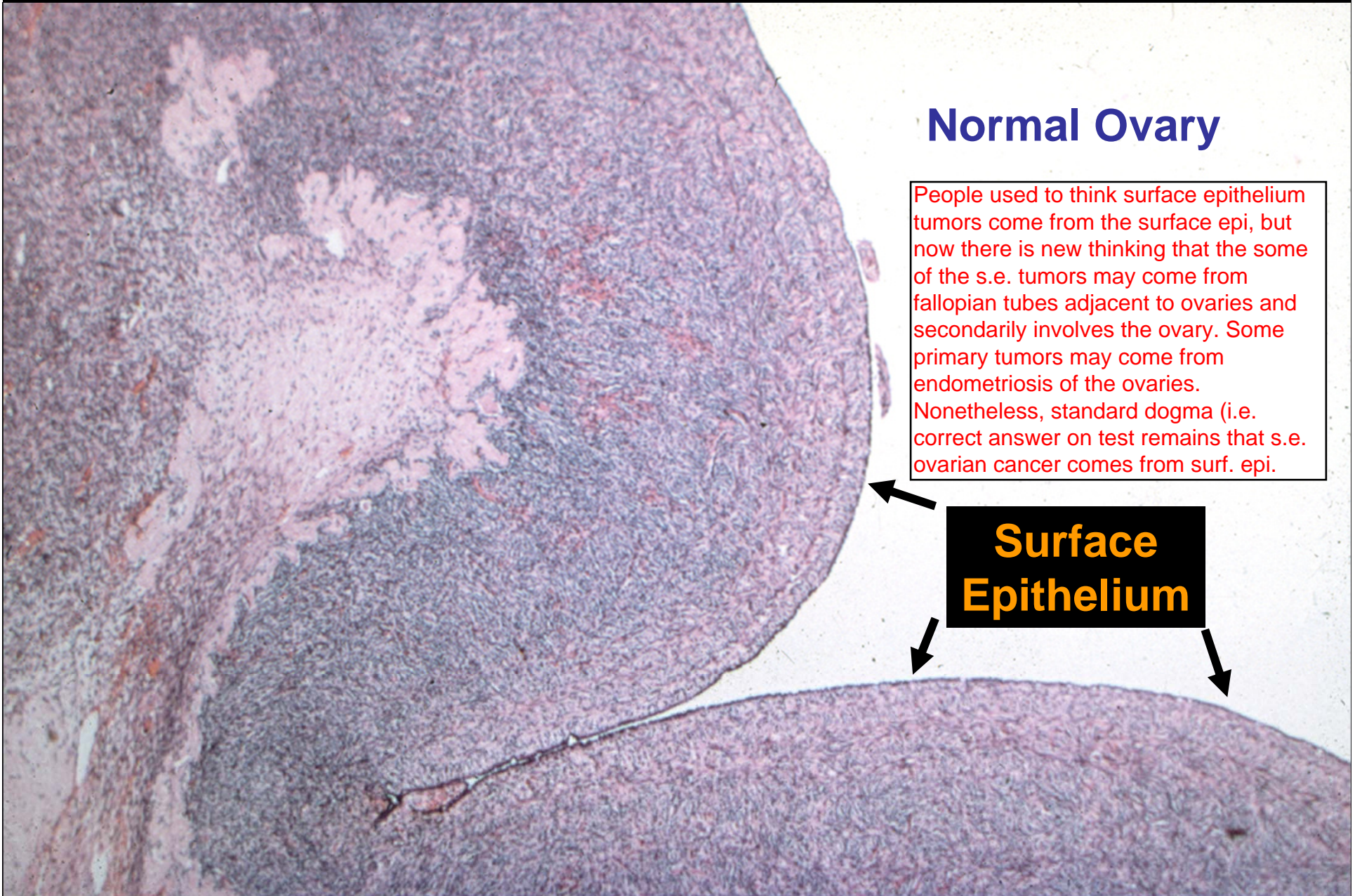
Basically same as ones found in testis

ORIGIN	SURFACE EPITHELIAL CELLS (Surface epithelial-stromal cell tumors)	GERM CELL oocyte tumors	SEX CORD-STROMA Support cell tumors	METASTASIS TO OVARIES
Overall frequency	65%-70%	15%-20%	5%-10%	5%
Proportion of malignant ovarian tumors	90%	3%-5%	2%-3%	5%
Age group affected	20+ years	0-25+ years	All ages	Variable
Types	<ul style="list-style-type: none"> • Serous tumor • Mucinous tumor • Endometrioid tumor • Clear cell tumor • Brenner tumor • Cystadenofibroma 	<ul style="list-style-type: none"> • Teratoma • Dysgerminoma • Endodermal sinus tumor • Choriocarcinoma 	<ul style="list-style-type: none"> • Fibroma • Granulosa-theca cell tumor • Sertoli-Leydig cell tumor 	

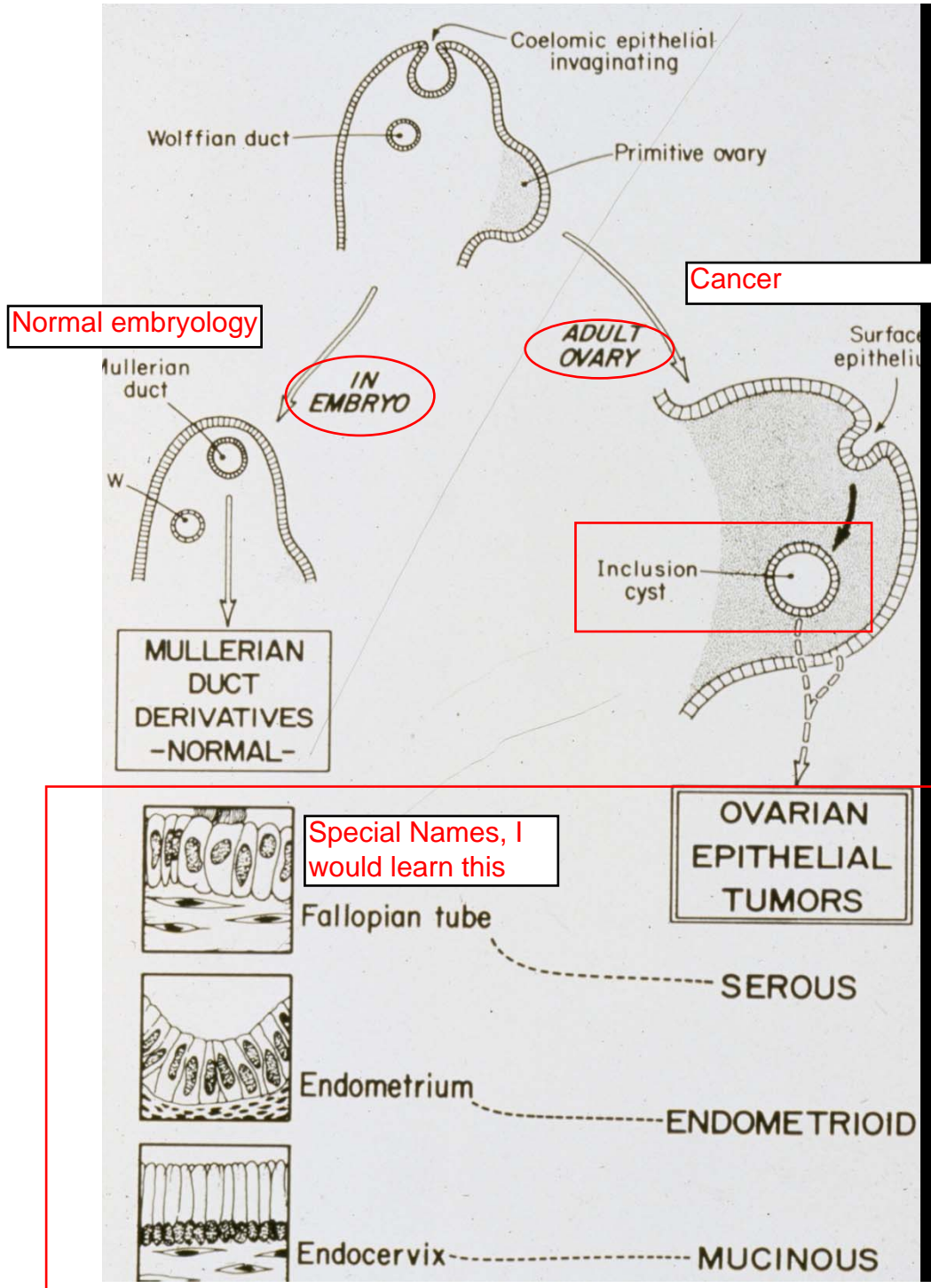
Normal Ovary

People used to think surface epithelium tumors come from the surface epi, but now there is new thinking that the some of the s.e. tumors may come from fallopian tubes adjacent to ovaries and secondarily involves the ovary. Some primary tumors may come from endometriosis of the ovaries. Nonetheless, standard dogma (i.e. correct answer on test remains that s.e. ovarian cancer comes from surf. epi.

Surface Epithelium



Ovarian Surface Epithelial Carcinoma: Pathogenesis



How does the outer surface cause cancer?
 Surface epithelium is a special form of peritoneum, but it has capability to differentiate into all different epi in GYN tract.
 Embryologically, the Mullerian tract arises from this epithelium, so it makes sense that this epi may still retain some ability to differentiate into other epi.
 The idea is that an inclusion forms from the surface epi, and the inclusion cyst can turn into all kinds of crazy epithelial tumors.

Ovarian Carcinoma

- Risk factors
 - Nulliparity (2.8x risk) Never had children
 - Family history
 - BRCA 1 (30% lifetime risk) and BRCA 2 mutations.
 - Endometriosis (?) ovarian endometriosis may lead to certain cancers.
- Protective factors
 - Use of oral contraceptives (0.64x risk)
 - Tubal ligation (0.59x risk)

More kids you have, the more protected. Risk is related to estrogen exposure, so suppression of ovulation via pregnancy, oral contraceptives helps.

Don't know why, but does work

Ovarian Epithelial Neoplasms

How to name your tumor.

Classified by

1. **Cell type**—what kind of epithelium is neoplastic?
2. **Degree of malignancy**

Epithelial Cell Types

All Mullerian Types Seen

Should probably know this.

- Fallopian Tube → **Serous**
- Endometrium → **Endometrioid**
- Gestational EM → **Clear cell**
- Endocervix → **Mucinous**
- [Bladder] → **Brenner or Transitional**

Ovarian cells can look like bladder.

Ovary-Degree of Malignancy

- Every epithelial type can be categorized into 3 general tumor types:
 - **Benign** (cystadenoma, cystadenofibroma)
 - **Low Malignant Potential** (aka Borderline, or atypical proliferating tumor)
 - **Adenocarcinoma**
- This is what determines treatment

These benign ones tend to be very cystic

Right now, cell type doesn't influence treatment, degree of malignancy does. This is critical to know about the neoplasm

Common combination

Most Common Epithelial Tumors

GERMINAL EPITHELIUM

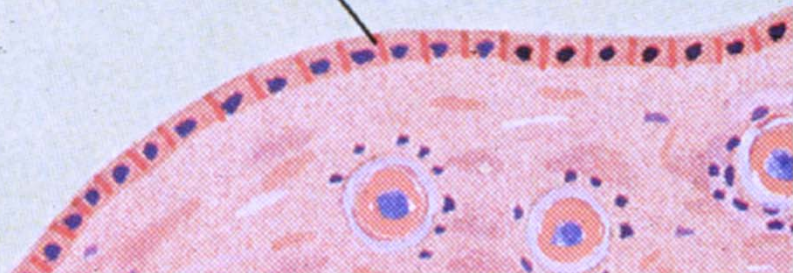
Benign— Serous cystadenoma
Mucinous cystadenoma
Brenner tumor

Borderline— Serous and mucinous cystadenomas

Malignant— Serous cystadenocarcinoma
Mucinous cystadenocarcinoma
Endometrioid carcinoma
Clear cell carcinoma

Others comb not
common for
borderline

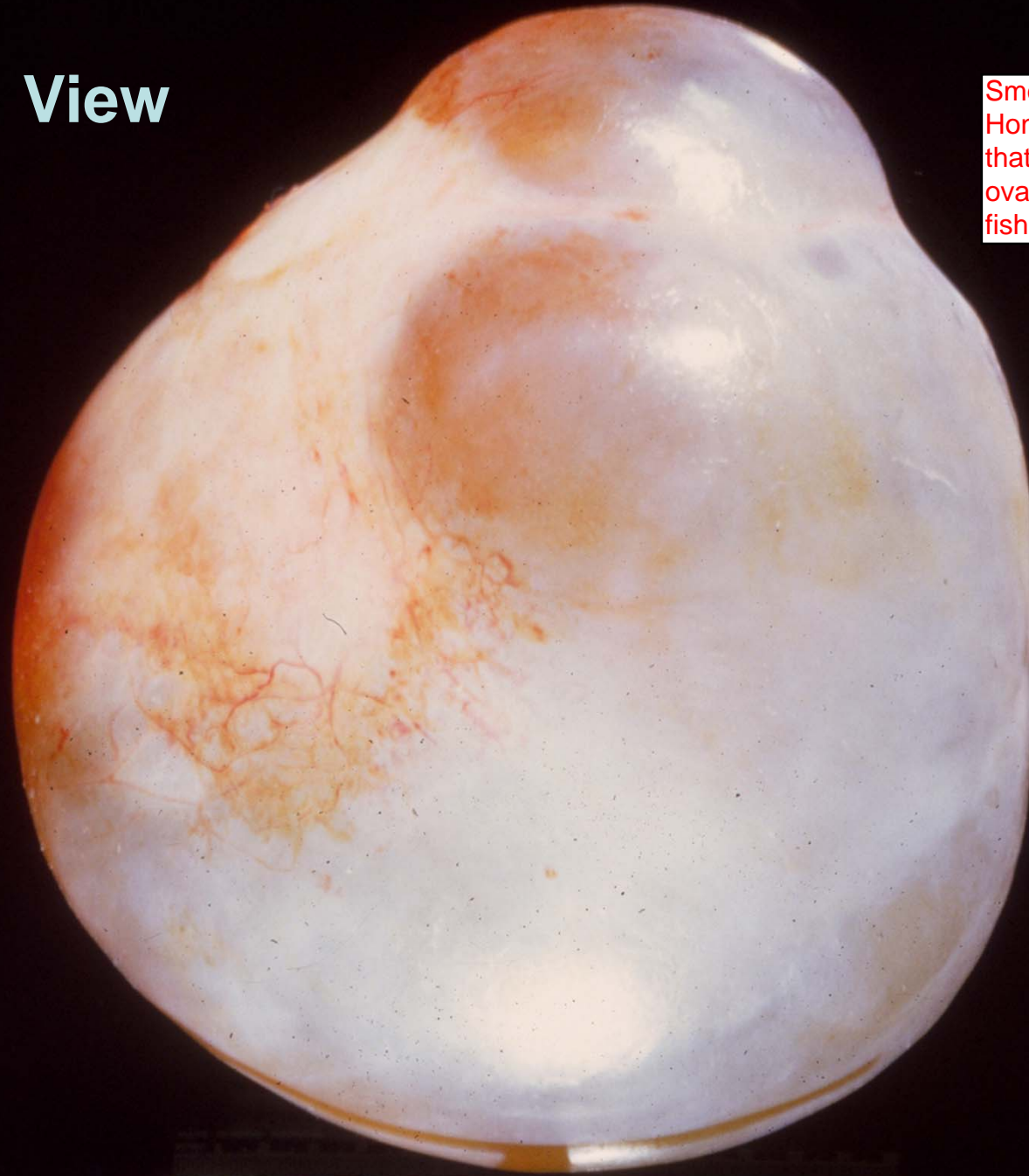
More spread-out



Case 1

Name this tumor

External View



Smooth, cysts.
Honestly can't tell
that this is an
ovary. Looks like
fish bladder to me.

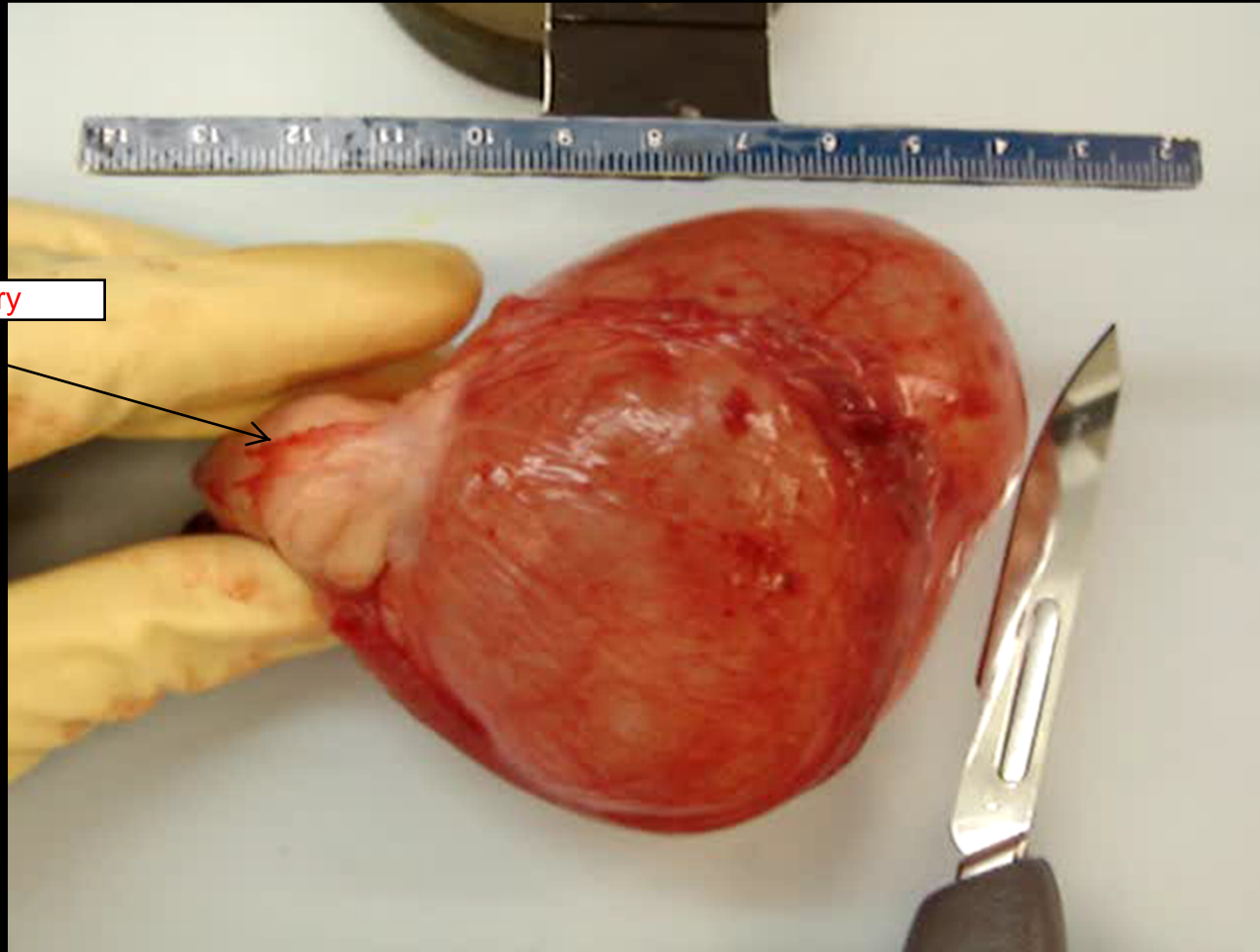


A brief video...

Video #1

Basically, when you cut it open, clear liquid oozes out, like a water ballon ruptured. Open it up, wall is like plastic wrap. No solid areas, no masses. When you cut open the normal part of ovary, just normal looking

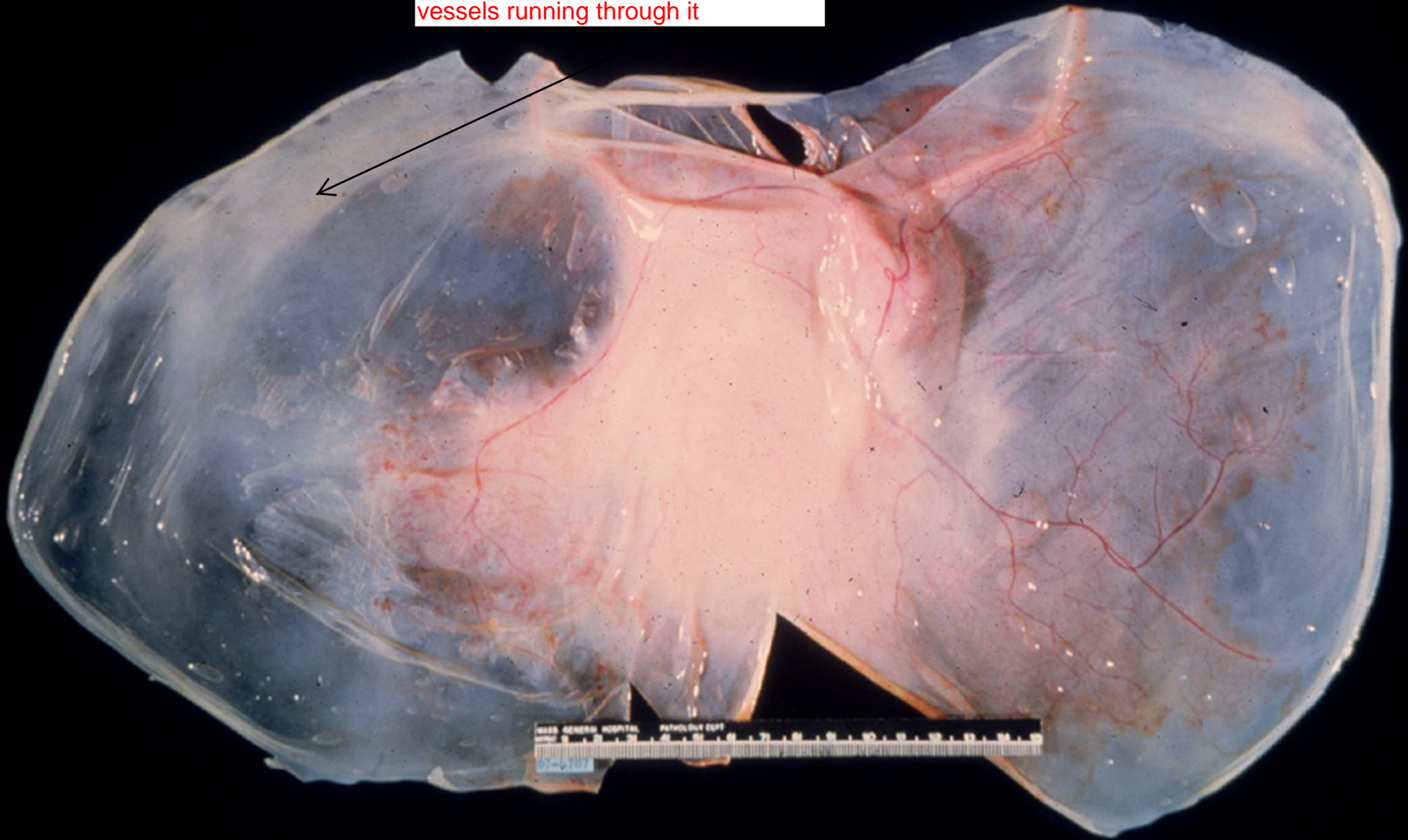
Normal Ovary



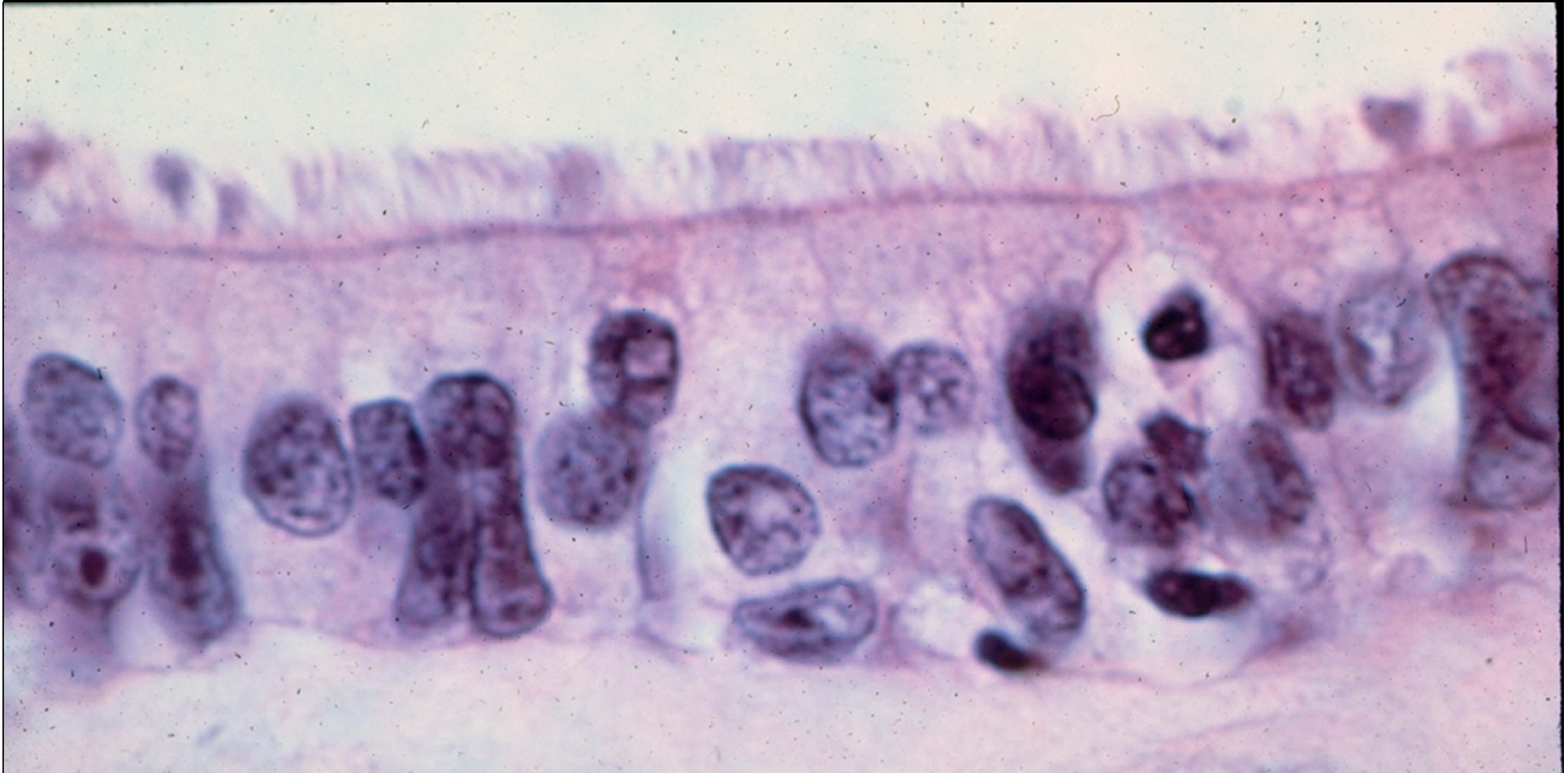
<http://www.youtube.com/user/ProfBentley#p/u/3/s4nMSNnCxOs>

Internal View

Thin translucent wall, can see vessels running through it



Simple, thin-walled cyst



Lining cells: ciliated, resembling fallopian tube

Case1

Add everything
up...

- Cell type: fallopian tube = serous
- Behavior: Large simple **cyst** lined by benign cells = cystadenoma
- **Final DX: “SEROUS CYSTADENOMA”**

Q: Is this from autopsy?

A: no patient waiting in the OR for news.

When the cyst is normal like this, the patient is good to go, otherwise, you have to stage the tumor and dig around lymph nodes and stuff.

Case 2

Name this tumor

External View

Outside looks exactly like last one, but...



MASS. GENERAL HOSPITAL PATHOLOGY DEPT
METRIC 1 2 3 4 5 6 7 8 9 10 11 12 13 14

Internal View

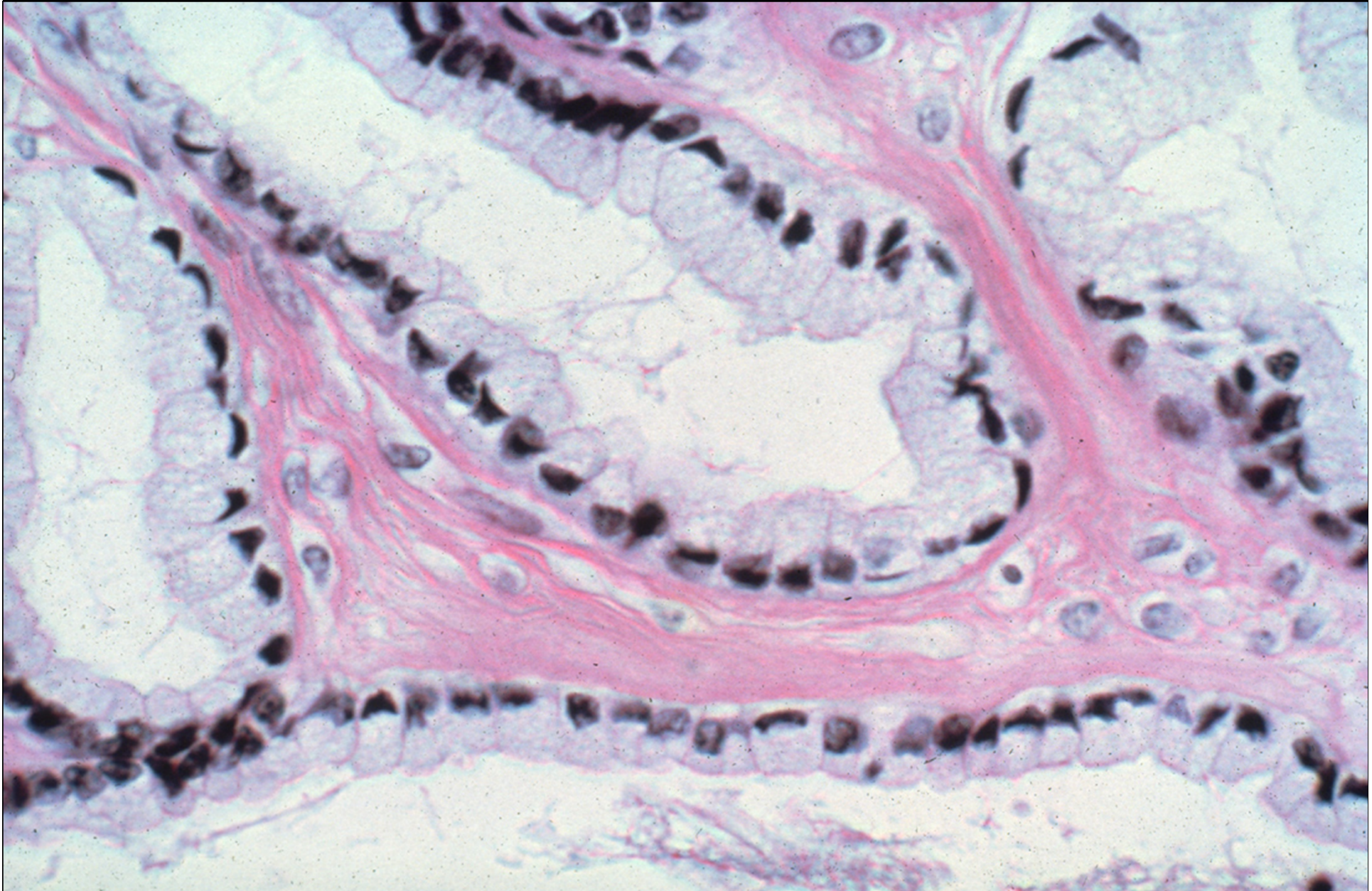
There are hundreds of small cysts (complex cysts)



Complex, multiloculated cyst

normal looking cervix

Lining cells: mucinous, resembling endocervix



Case 2

- Cell type: endocervical = mucinous
- Behavior: Large complex cyst lined by benign cells = cystadenoma
- Final DX: “MUCINOUS CYSTADENOMA”

Mucinous tumors can get pretty large, how large you ask...

Benign ovarian tumors can be very large! I agree

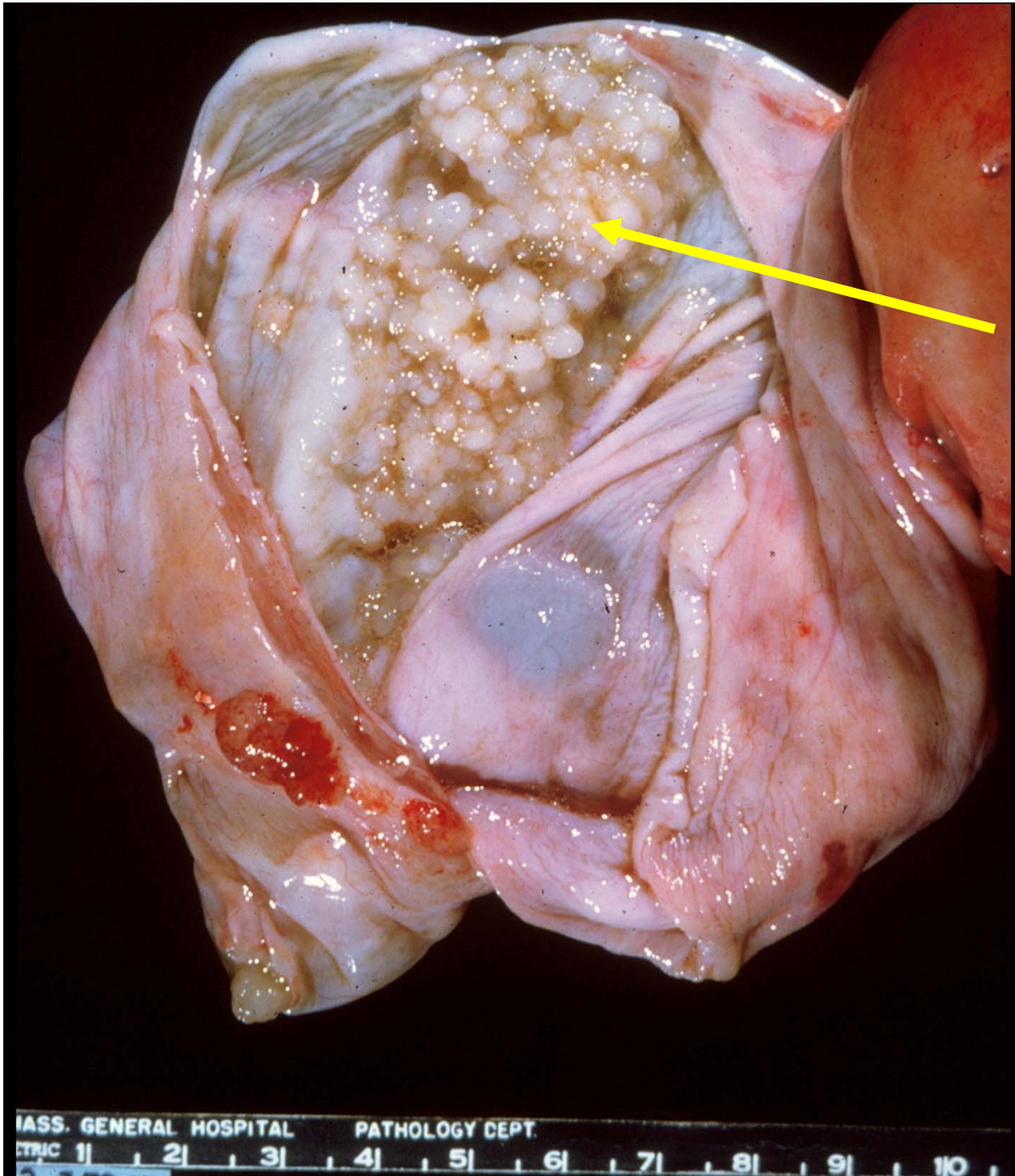


They can be 20, 30 lbs, like pregnant with triplets, I guess. These huge tumors may or may not have many symptoms. There is a lot of room in the abdominal cavity, so they can grow unnoticed for quite a while.

On the outside
looks like the
previous 2...

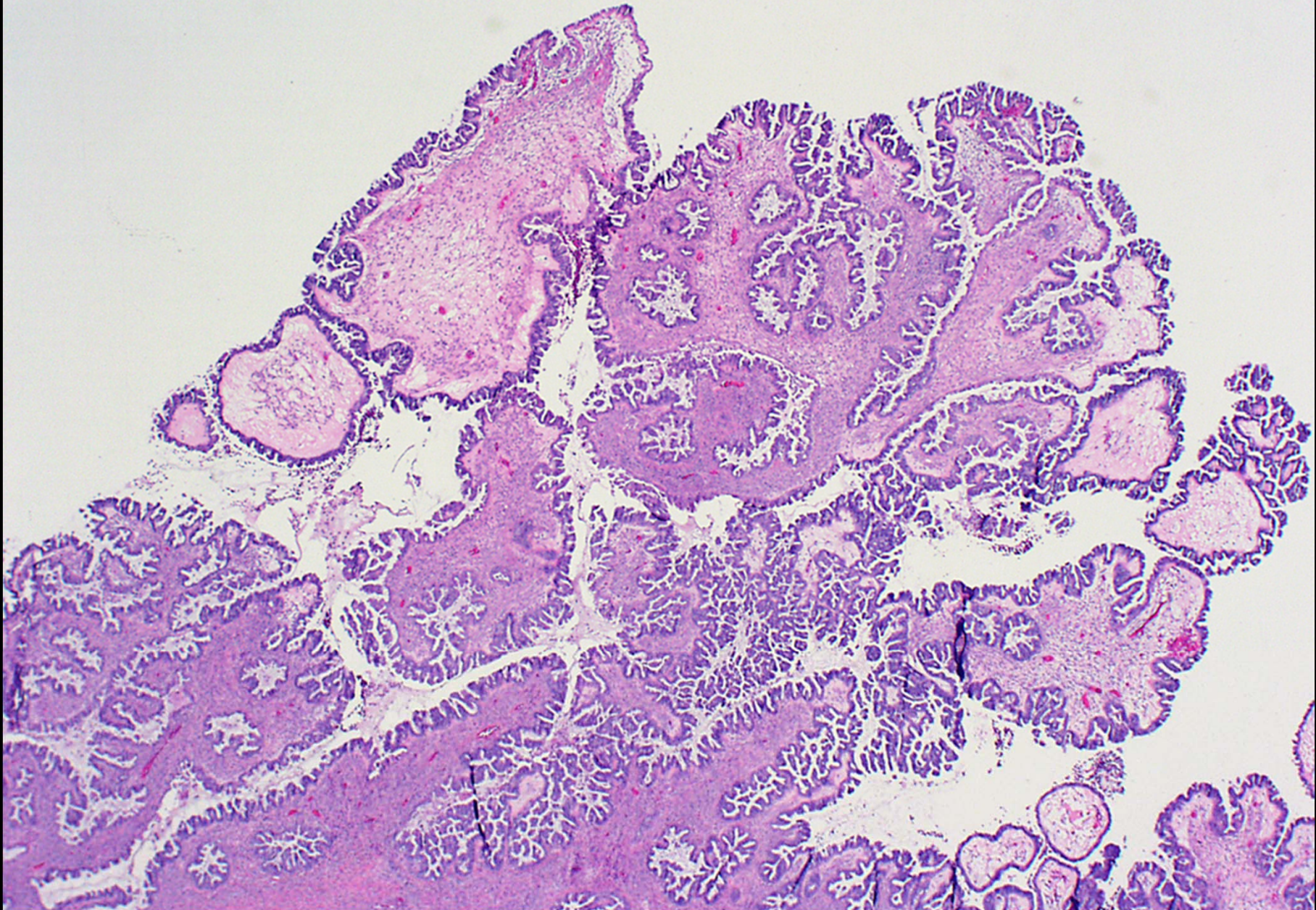
Case 3

Name this tumor



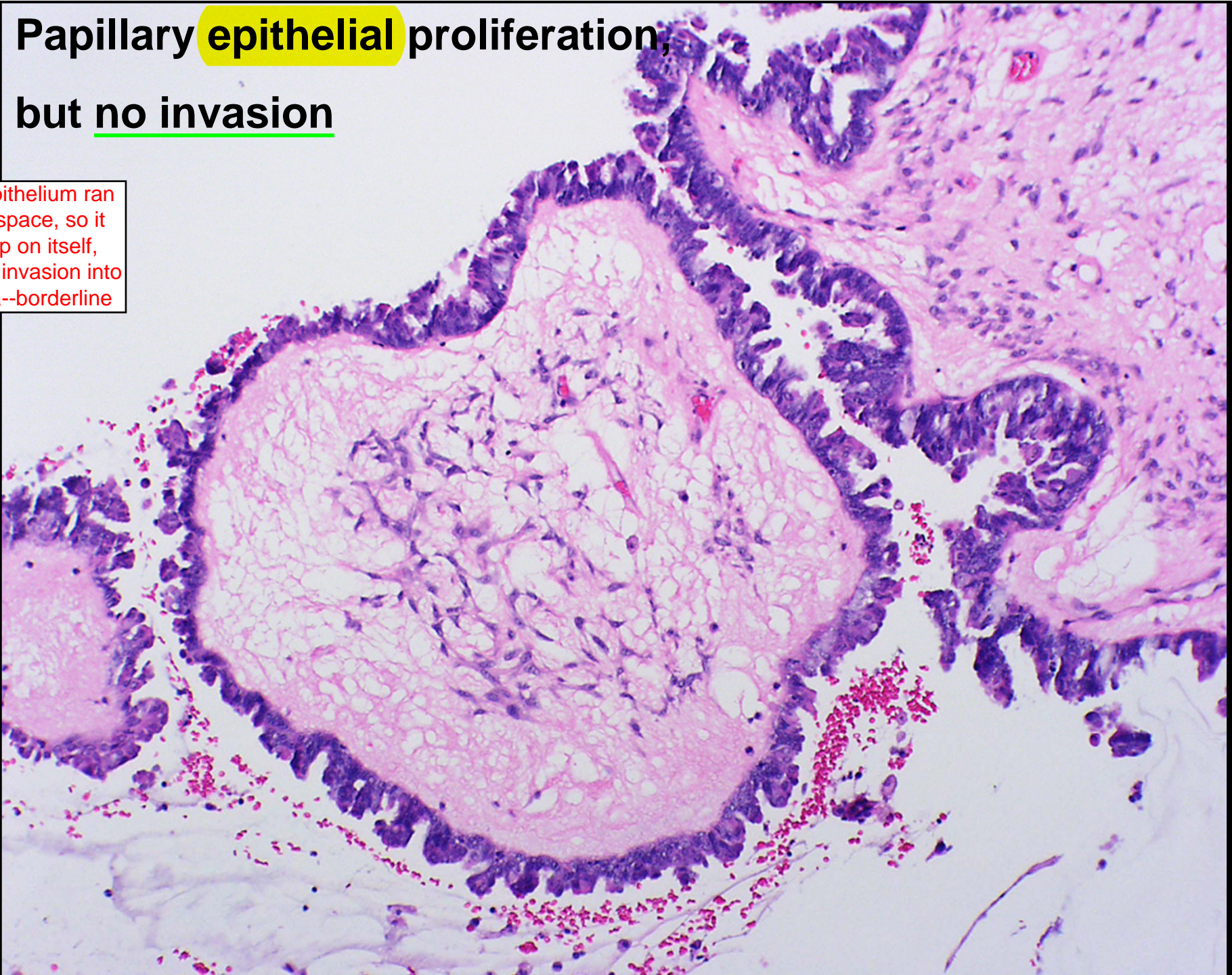
Interior of tumor
Papillary growth
inside cyst

Papillary epithelial proliferation, but no invasion



Papillary epithelial proliferation, but no invasion

The epithelium ran
not of space, so it
piled up on itself,
but no invasion into
stroma--borderline



Case 3

know this

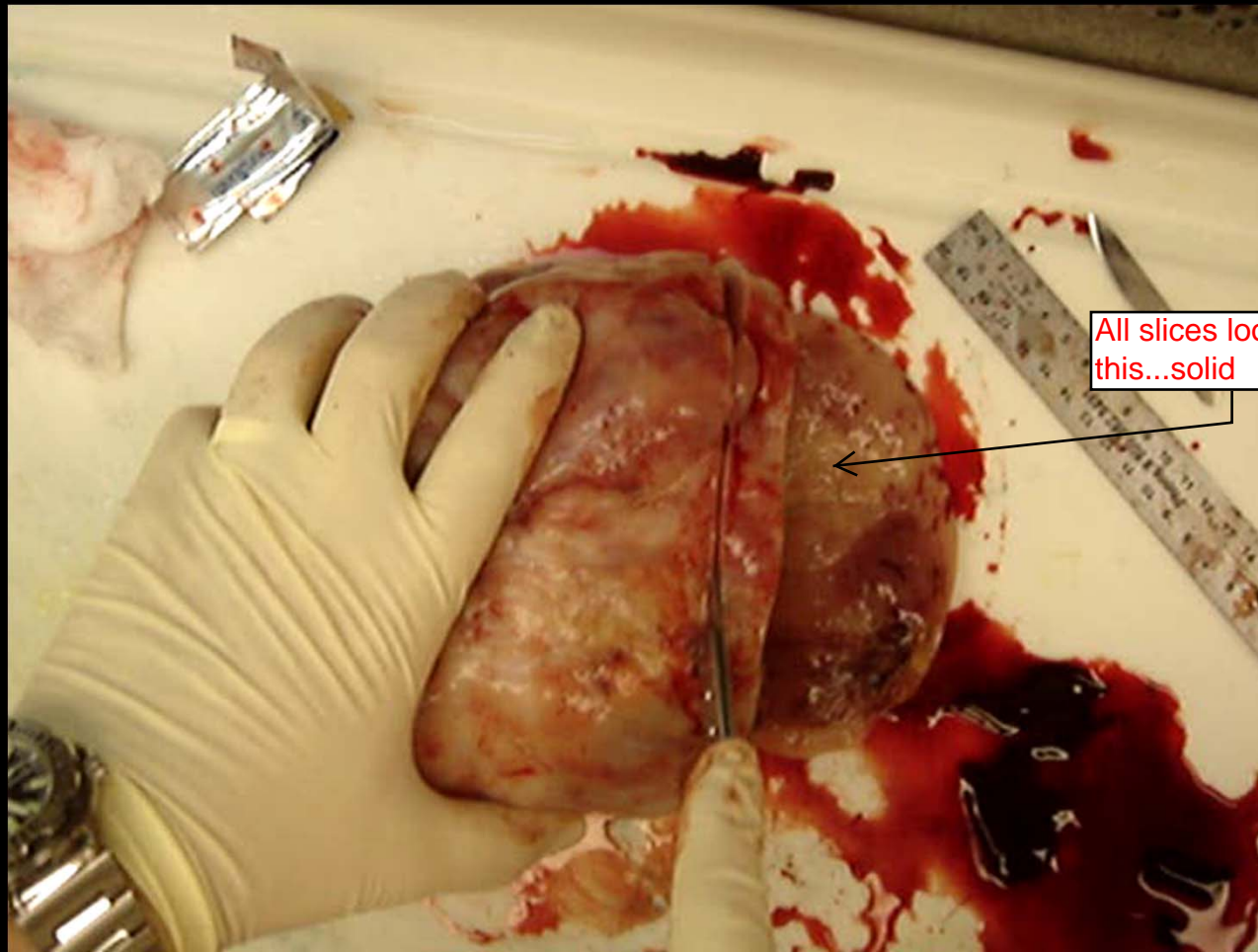
- Cell type: Fallopian tube = serous
- Behavior: **Proliferative but non-invasive growth pattern = borderline**
- Final DX: **“SEROUS BORDERLINE”** (aka serous tumor of low malignant potential)

Case 4

Name this tumor

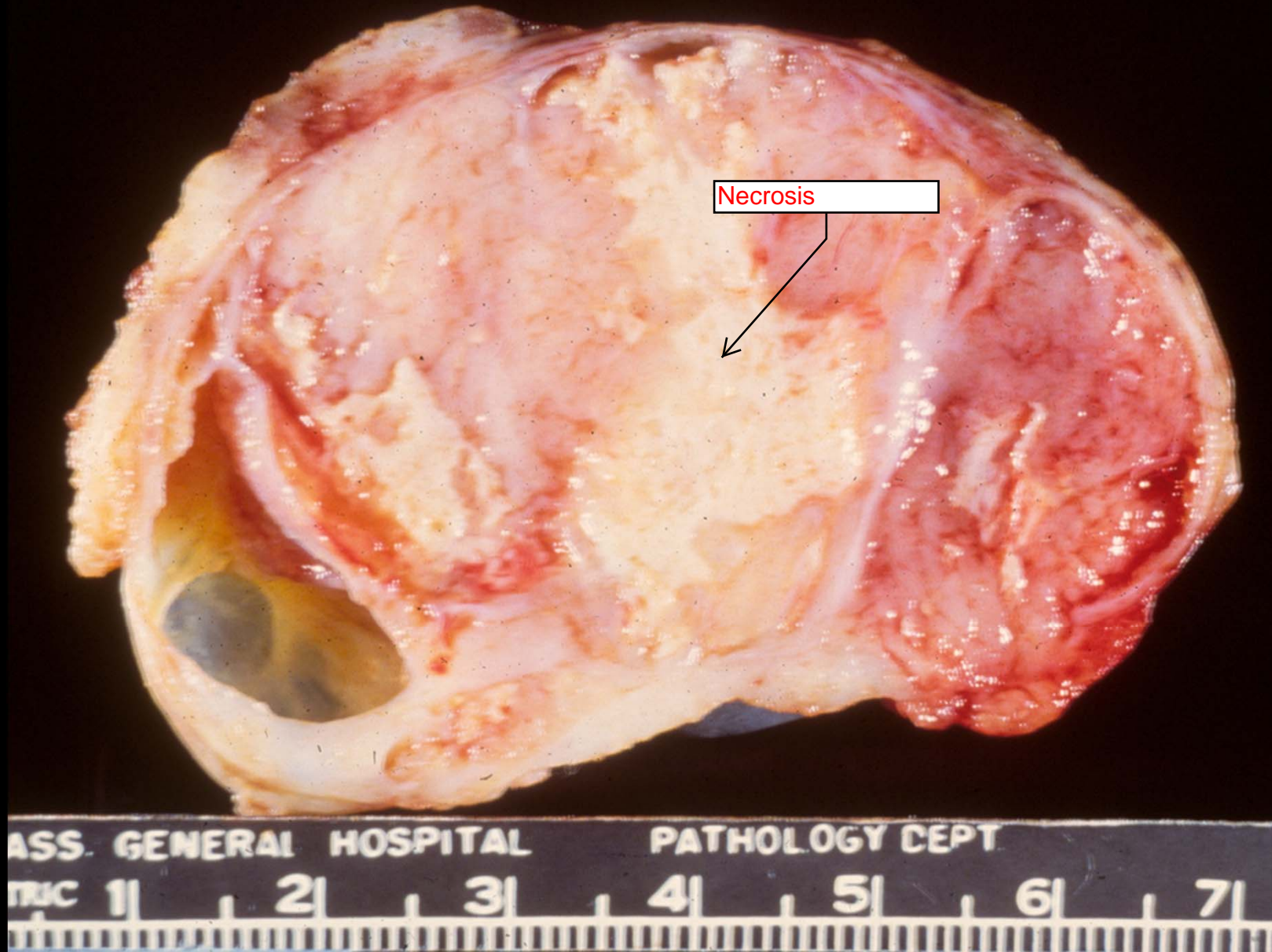
Case 4

Video #2

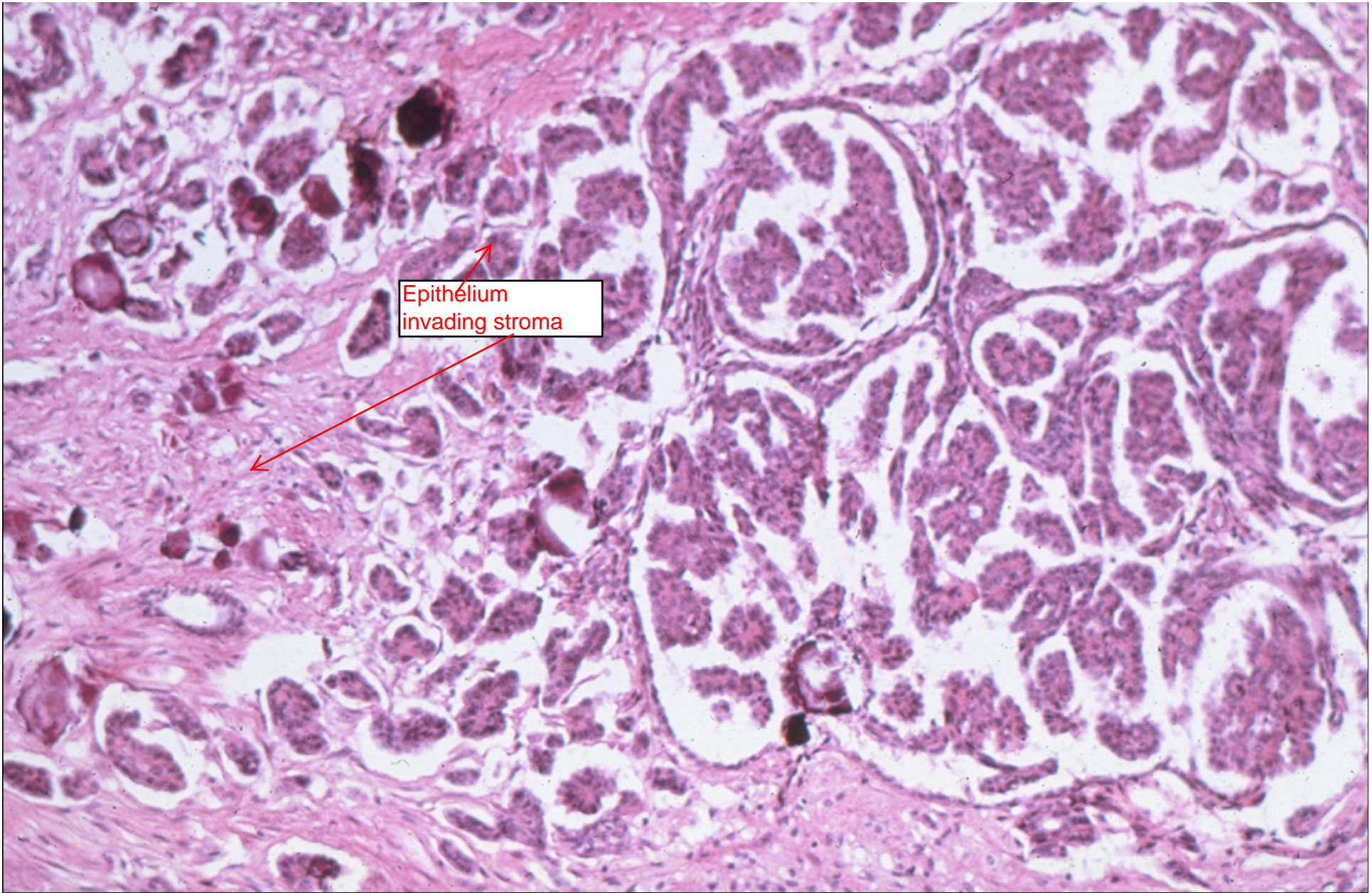


<http://www.youtube.com/user/ProfBentley#p/u/2/YkyFuibx4rs>

Internal View



Mostly solid with necrosis

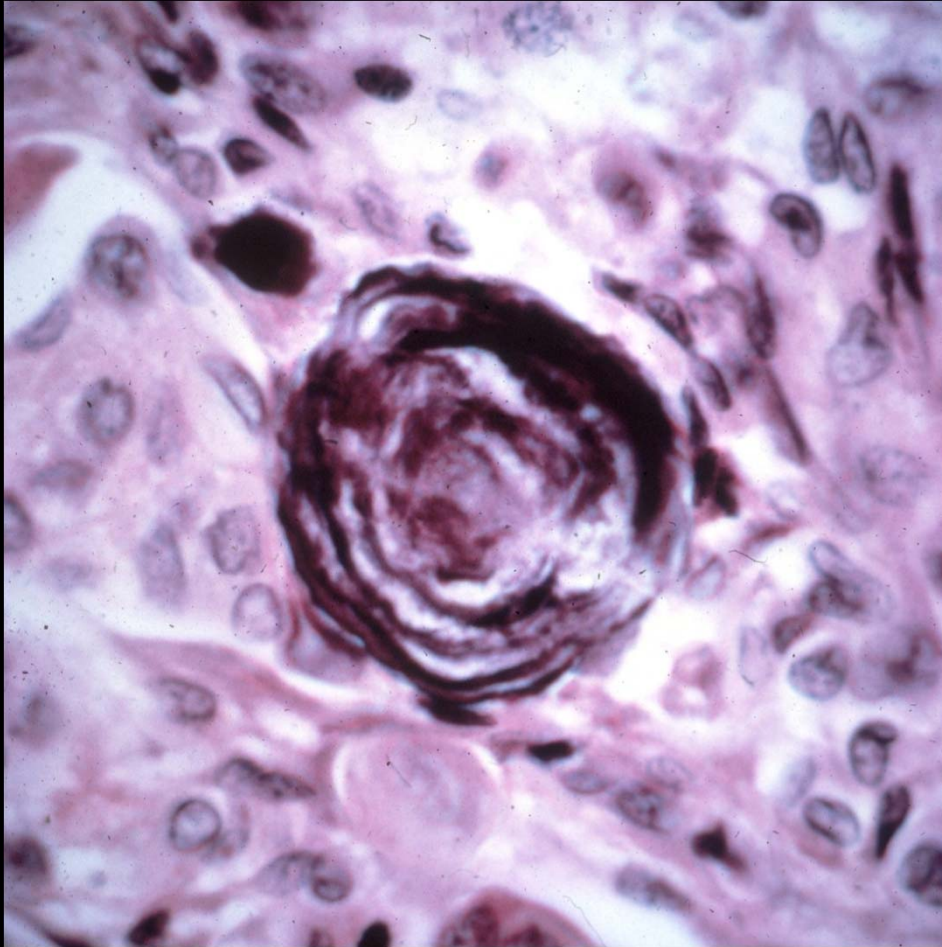


Epithelium
invading stroma

Stromal invasion

Prominent in serous ovarian tumor, but
not specific

Psammoma Bodies



- Concentrically laminated calcifications
- Strongly associated with ovarian serous neoplasms

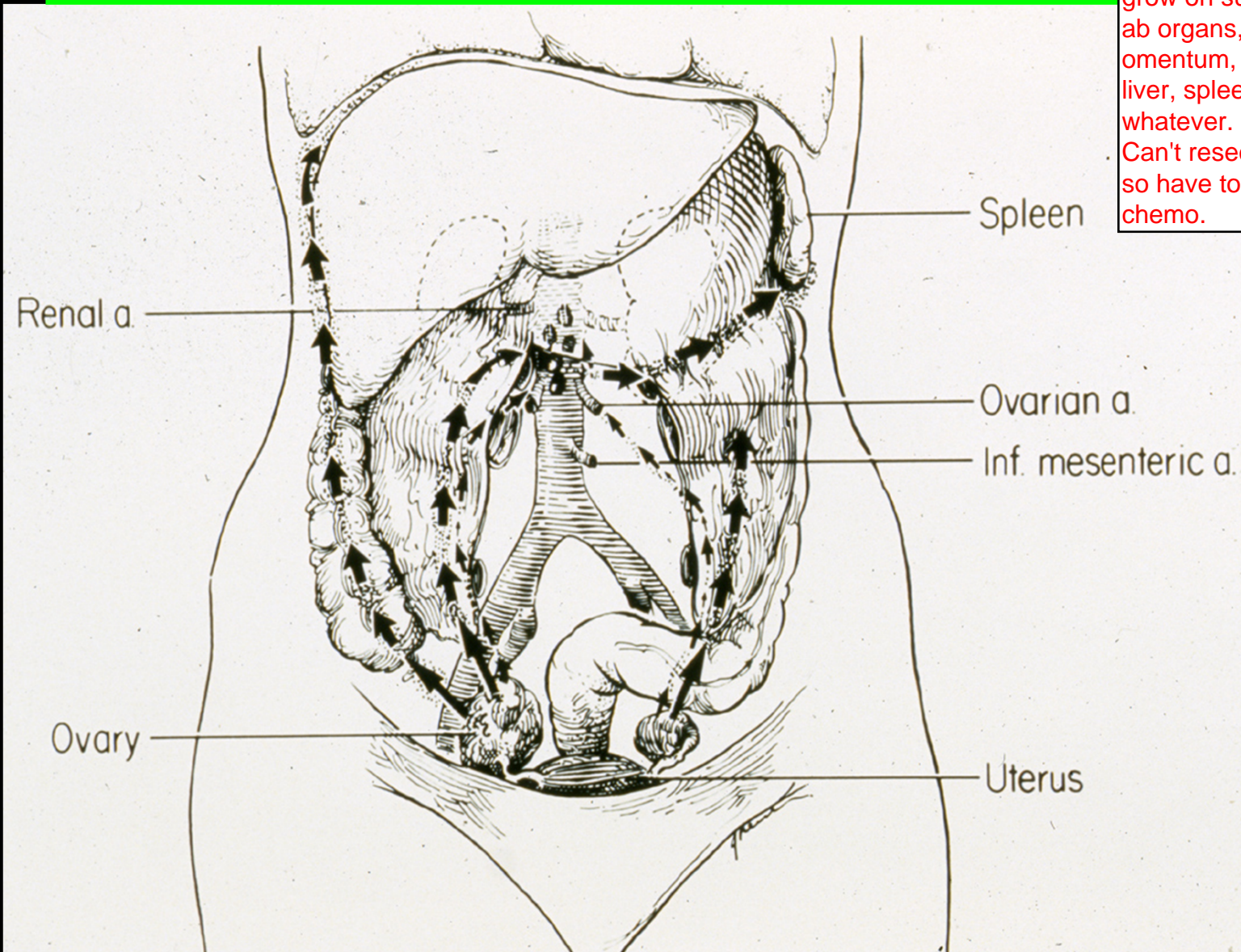
Case 4

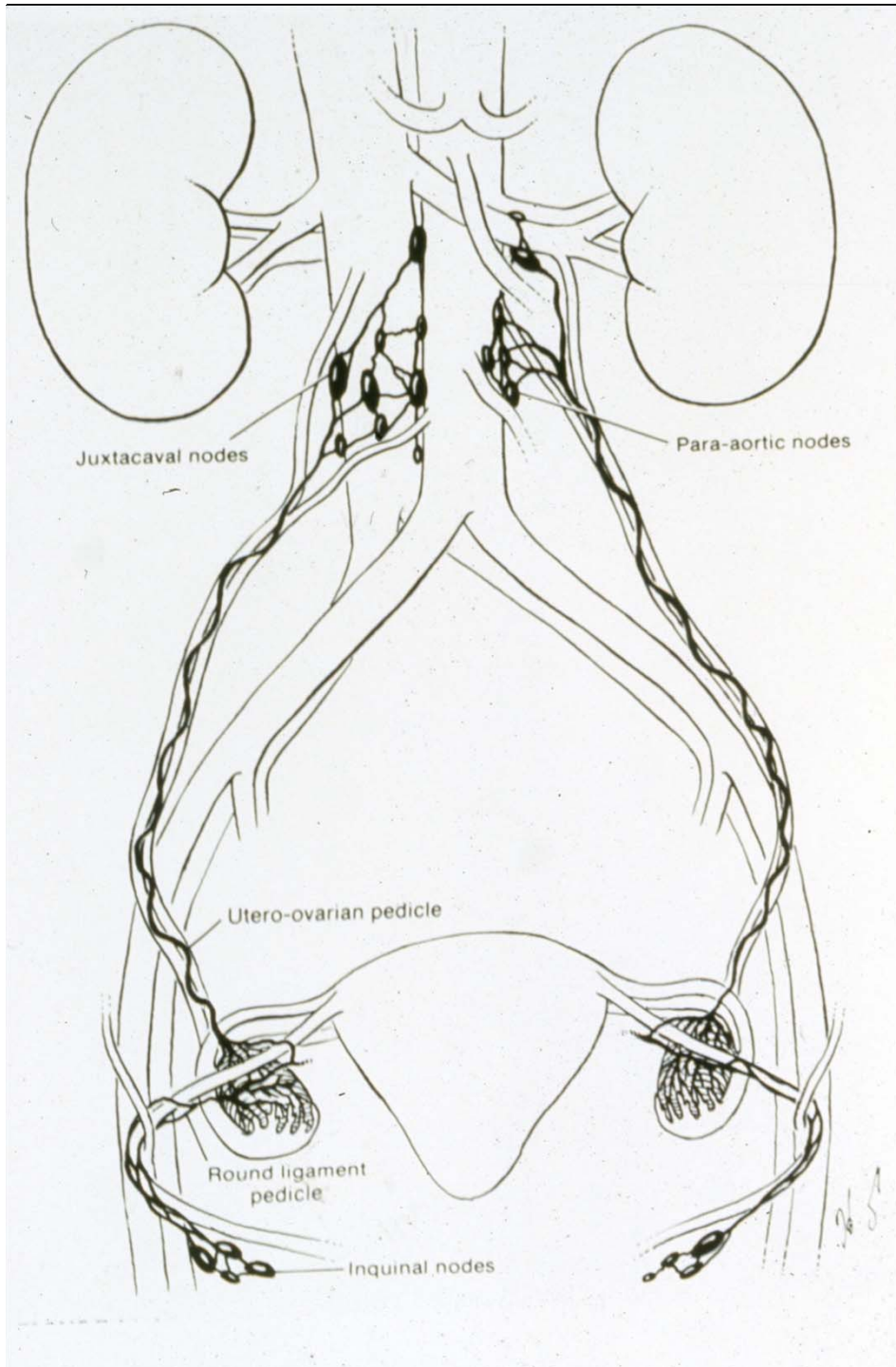
- Cell type: fallopian tube = serous
- Behavior: Large solid mass lined by anaplastic cells invading stroma = adenocarcinoma.
- Final DX: “SEROUS ADENOCARCINOMA”
(aka serous papillary adenocarcinoma, or if largely cystic, cystadenocarcinoma)

Don't worry about
cystic/papillary
adenocarcinoma.
They are treated
the same way.

Ovarian Cancer: Peritoneal Spread Common

Unfortunately, most ovarian cancer caught late, after peritoneal spread. The tumor likes to grow on surface of ab organs, omentum, gutters, liver, spleen, whatever. Can't resect this, so have to go chemo.





Ovarian Cancer: Patterns of Lymph Node Spread

Can go to lymph
nodes

Borderline Tumors

Distinct Biologic Behavior

Borderline Tumors can spread to peritoneal surface and lymph nodes, but they are not invasive even with metastasis.

- Do not show destructive stromal invasion, even in metastatic implants or in lymph nodes
- Slow growing, indolent tumors
- Unresponsive to chemotherapy

Prognosis: 5 year survival

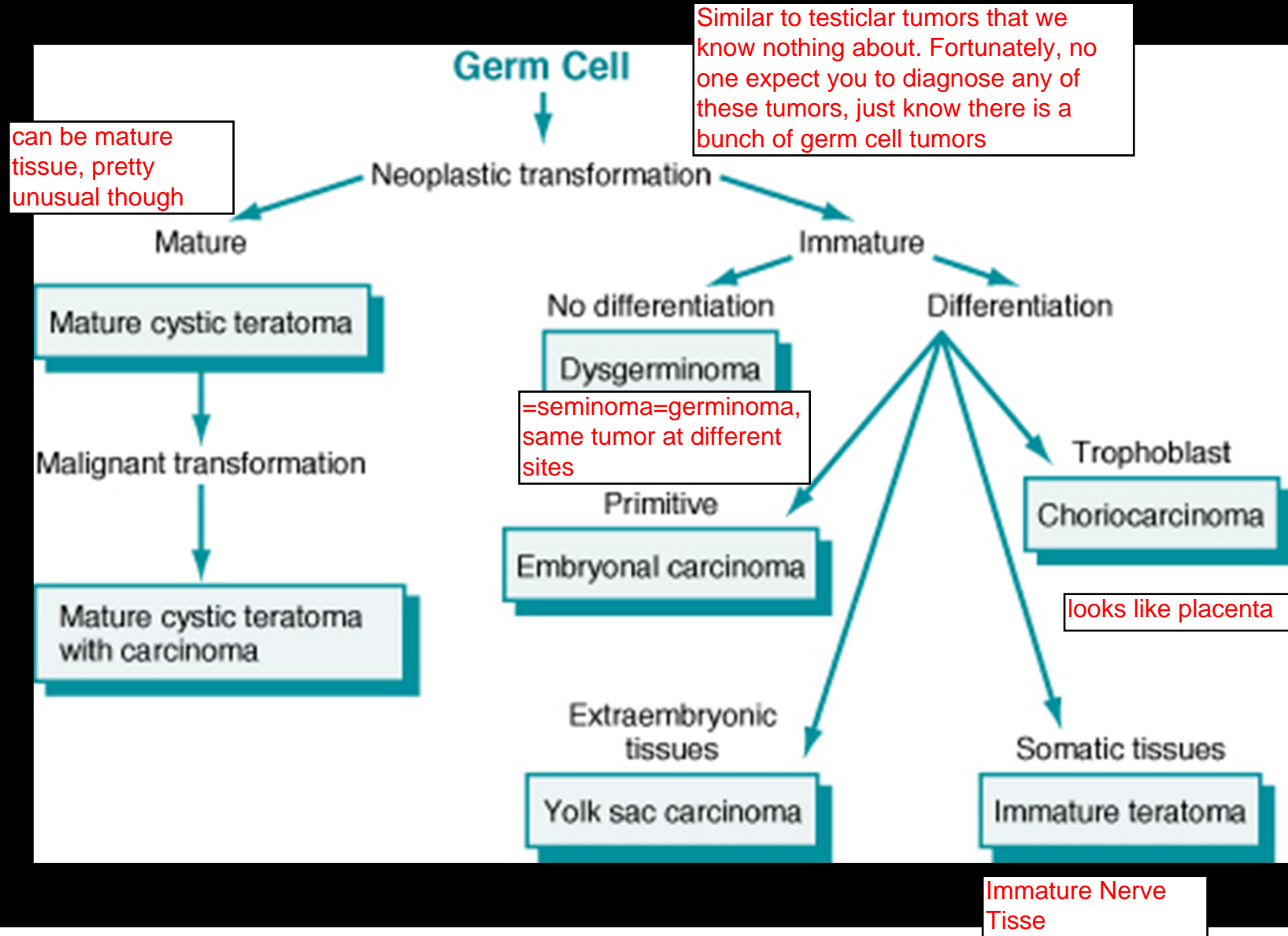
- **Confined to ovary:**
 - **Borderline: 99%** Can cut out ovary and cure patient
 - **Carcinoma: 70%**
- **Spread beyond ovary:**
 - **Borderline: 80-90%** Even with spread, prognosis pretty good.
 - **Carcinoma: 10%**

Chemo has no role because tumor is so slow growing. Prognosis measured in multiple years. Usually can take out the ovary and patient be cured. Even if the tumor has spread into the peritoneal cavity, prognosis is still good.

Here is a typical natural history of borderline tumors: found tumor, took it out. 5 years later, tumor came back. Repeat surgery. Eventually, patient suffers from the complication of the surgery and dies. Small number of tumor eventually progress to adenocarcinoma, but this is uncommon. Patient is more likely to die from complication of surgery than from borderline tumors.

Germ Cell Tumors

Derivation of Germ Cell Tumors



Germ Cell Tumors

most contains skin and hair, hence dermoid

Mature cystic teratoma (Dermoid Cyst)

- Common: 15-20% of all ovarian tumors
- Occur in young women and even children
- Form large cyst lined by full differentiated skin, including hair
- Can contain any other somatic tissue in the body
 - Brain, cartilage, bone, teeth, GI tract, bronchus most common

These structures can be very well formed, story about finding a fully formed foot in the teratoma.

Dermoid Cyst

Video #3

Warning: It is very, very gross. Advise you to take a deep breath before watching.

When you cut it open, liquid with waxy stuff oozes out. there is a ball of hair inside. The sebaceous gland, like on regular skin secrete waxy stuff, but it has nowhere to go, so it accumulates.

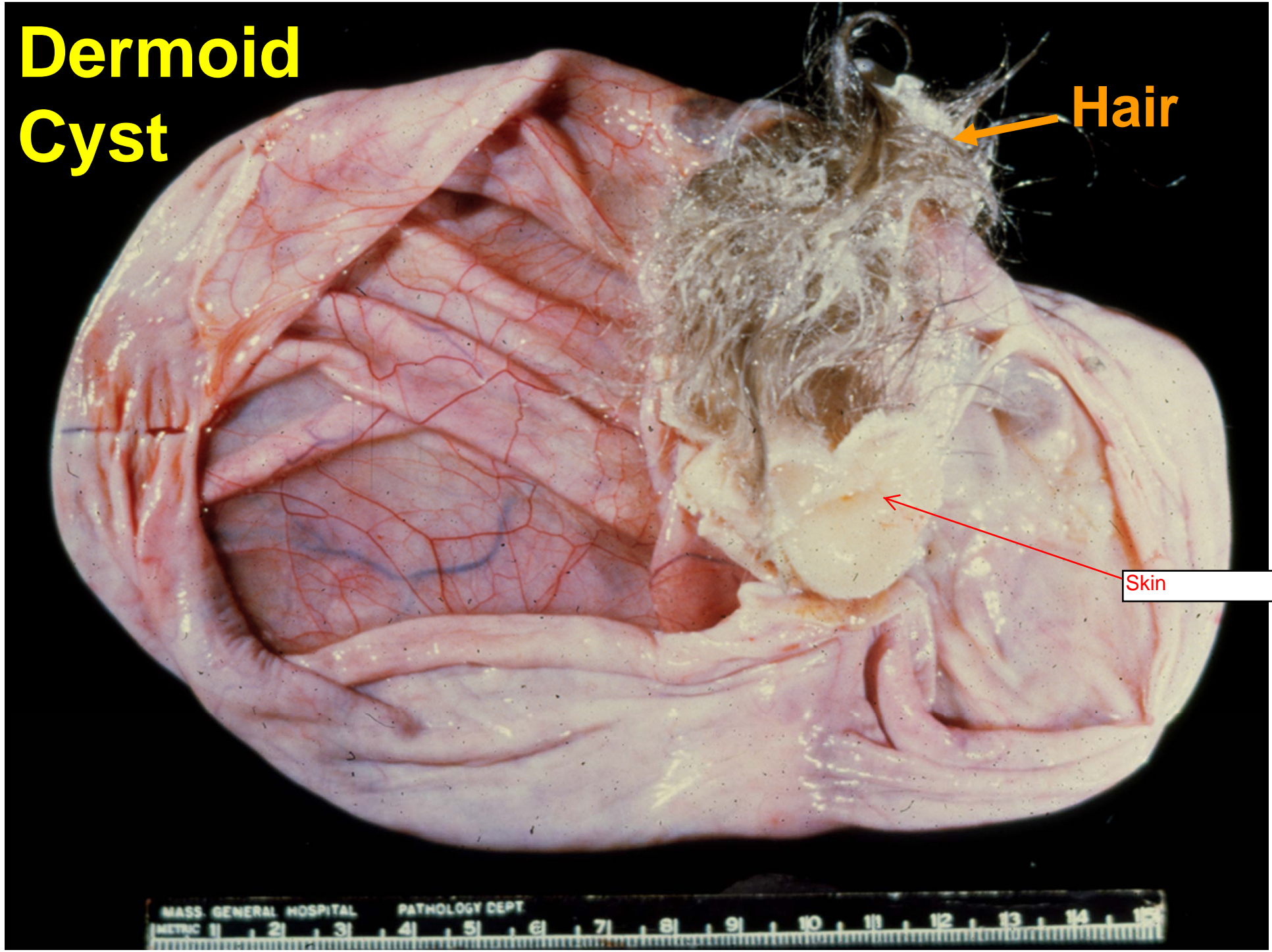
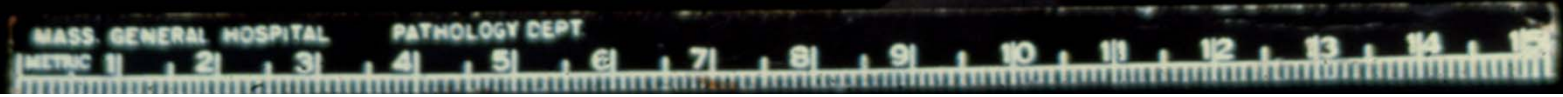


http://www.youtube.com/user/ProfBentley#p/u/1/Djv0IS96_gI

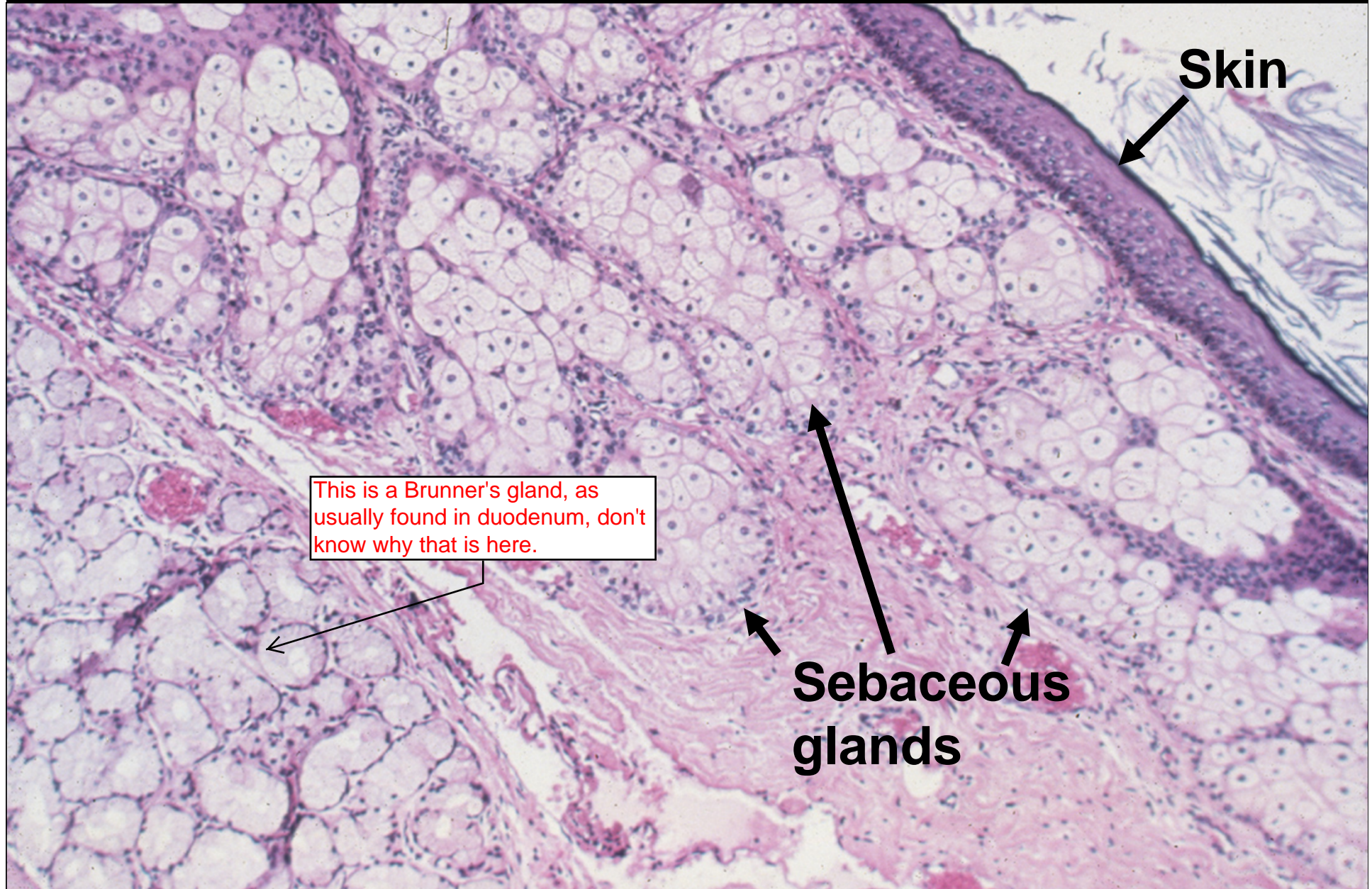
Dermoid Cyst

Hair

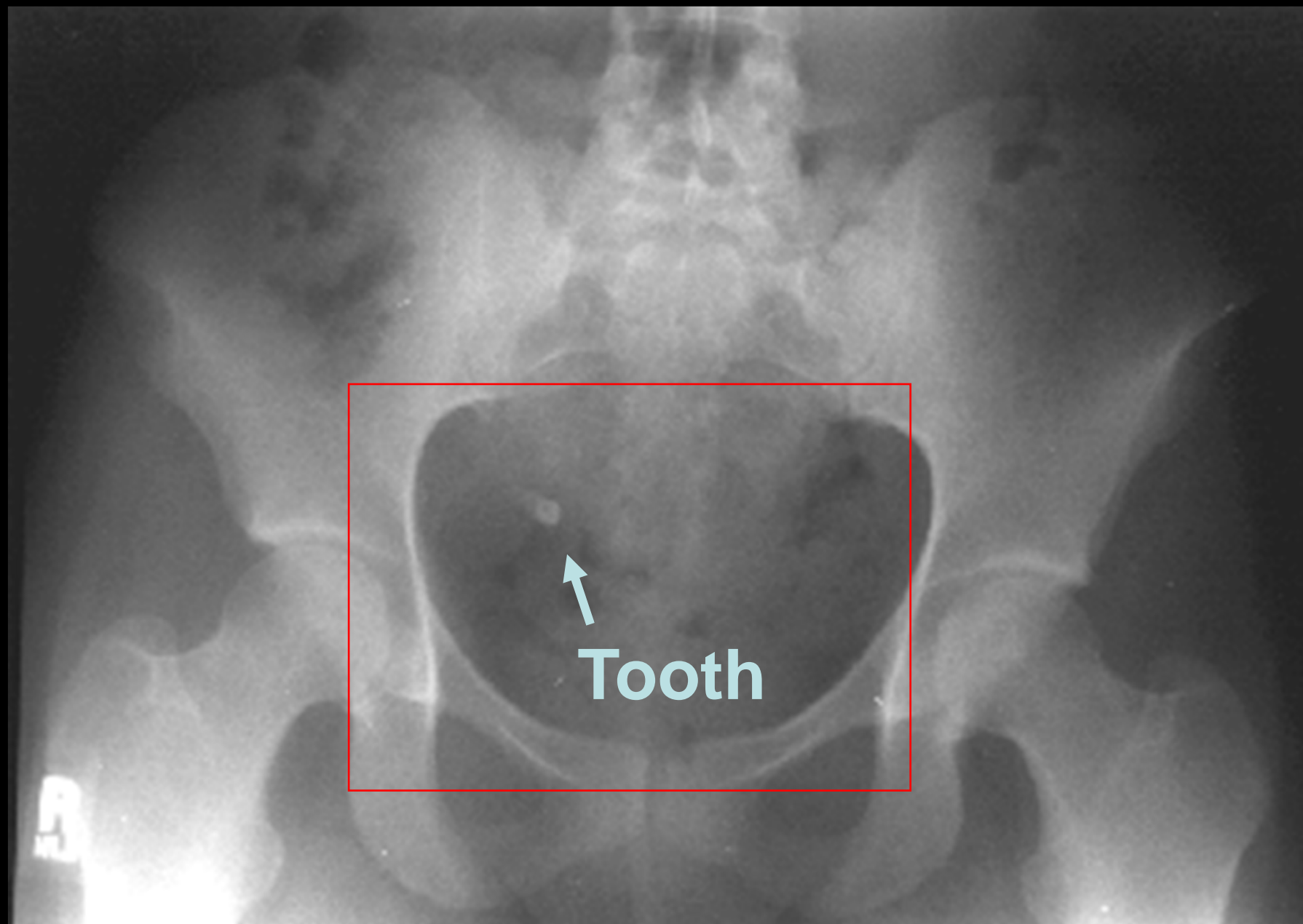
Skin



Dermoid Cyst



Dermoid Cyst



Germ Cell Tumors

Monodermal teratoma hence, mono

- Overgrowth a single mature tissue type
- Can develop any of the diseases that would normally occur in that tissue
 - “Struma Ovarii” (thyroid tissue)

People loves this. Medical mysteries.

Story: Patient has hyperthyroidism, but still does after thyroid is taken out!!! Why? There is another part of the gland somewhere else.

Q: is there blood supply to these tumors?

A: yeah.

Sex Cord Stromal Tumors

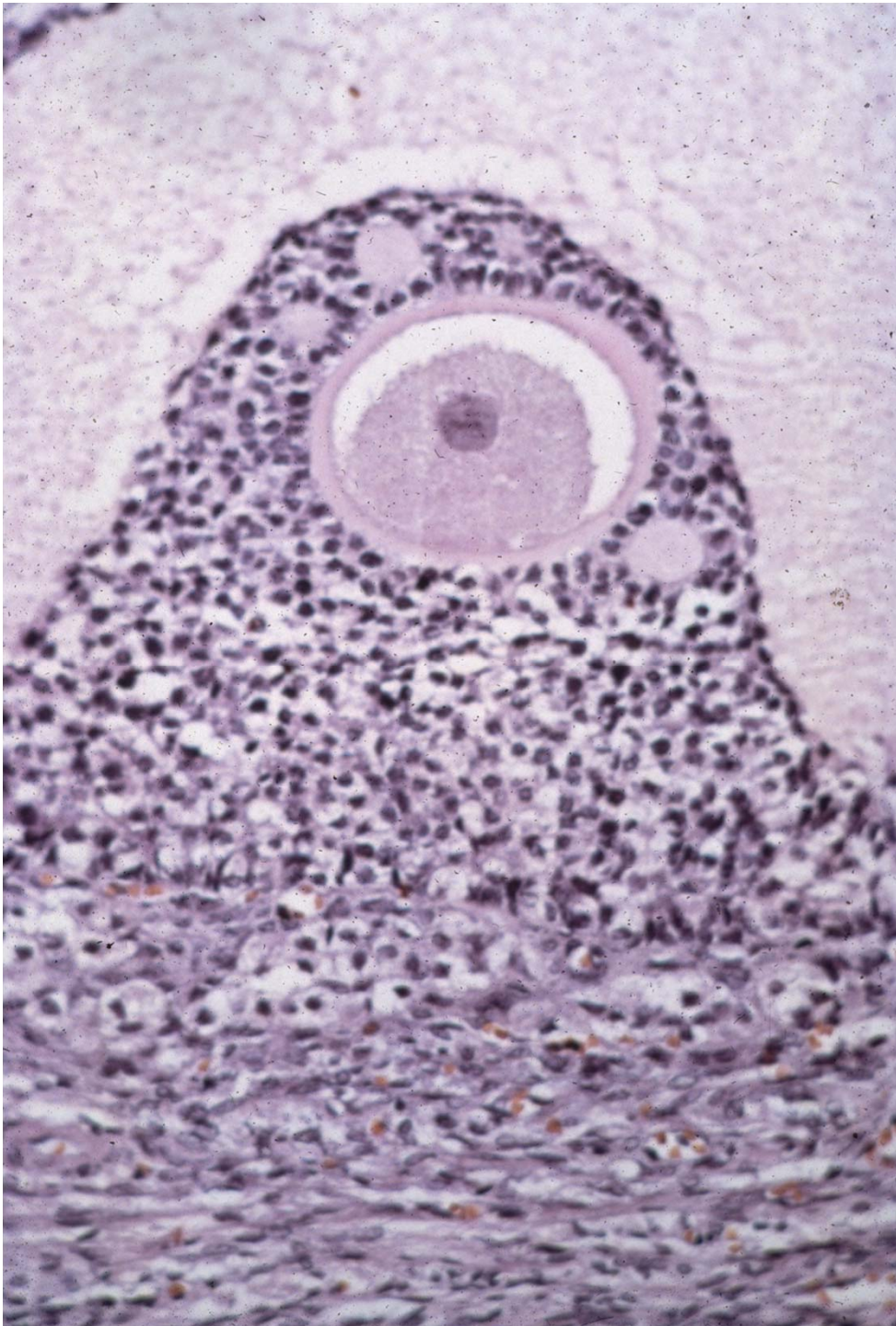
Talking about cells that support the oocytes

Sex Cord/Stromal Tumors

- Granulosa Cells
 - Granulosa cell tumors
 - Sertoli-Leydig cell tumors

Can decide to be male and be Sertoli-Leydig cells.

- Thecal cells
 - Thecoma and fibroma



Sex Cord Stromal Tumors

- **Fibroma/thecoma: most common, benign**

- **Granulosa cell tumors**
 - Can secrete large amounts of estrogen
 - Increased rate of endometrial, breast CA
 - Premature puberty

most common malignancy in Stromal tumors

That's why we care.

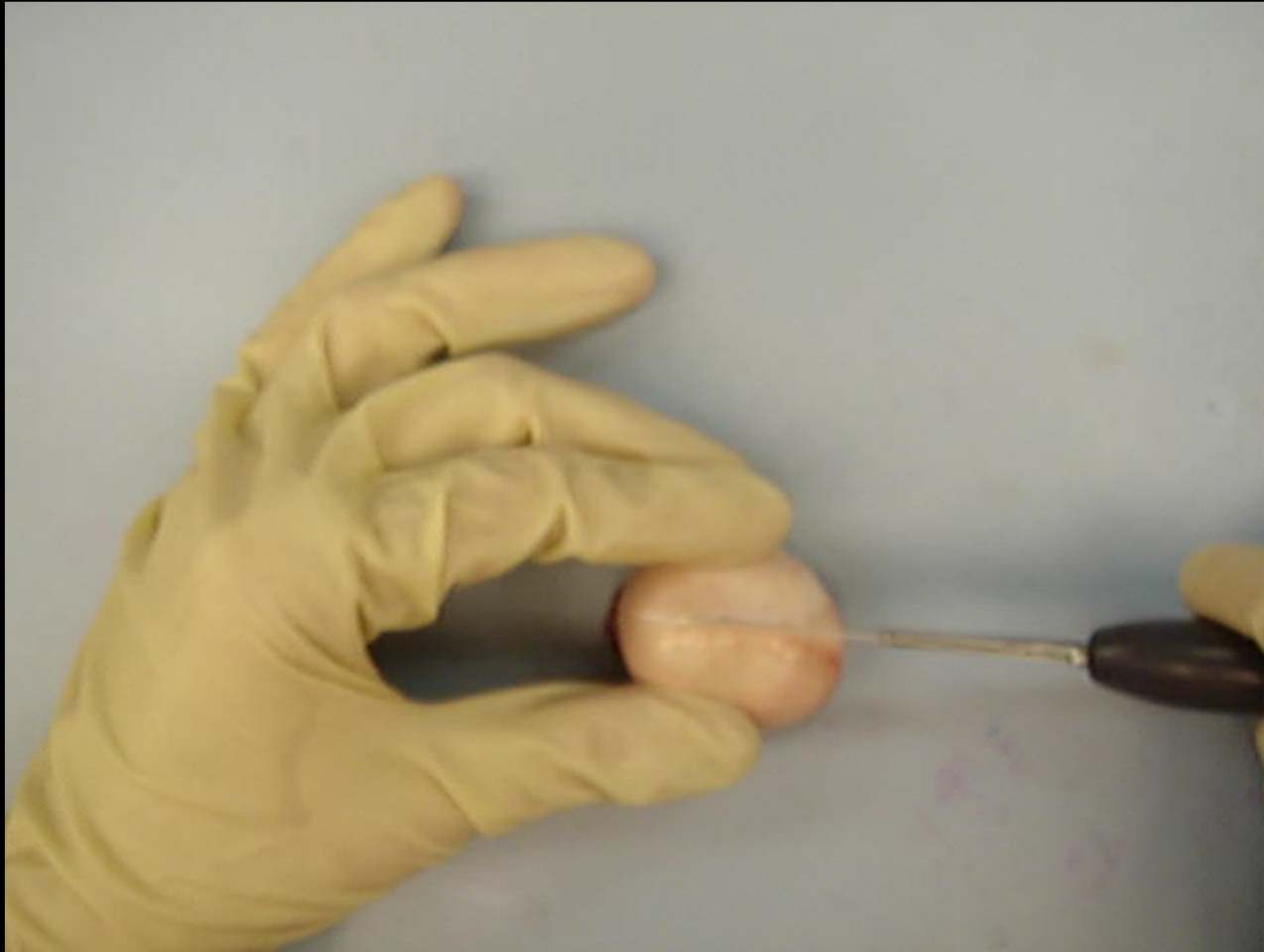
- **Sertoli-Leydig cell tumors**
 - Recapitulates testis
 - Secretes testosterone
 - Masculinizing

because of the androgen secretion

Fibroma

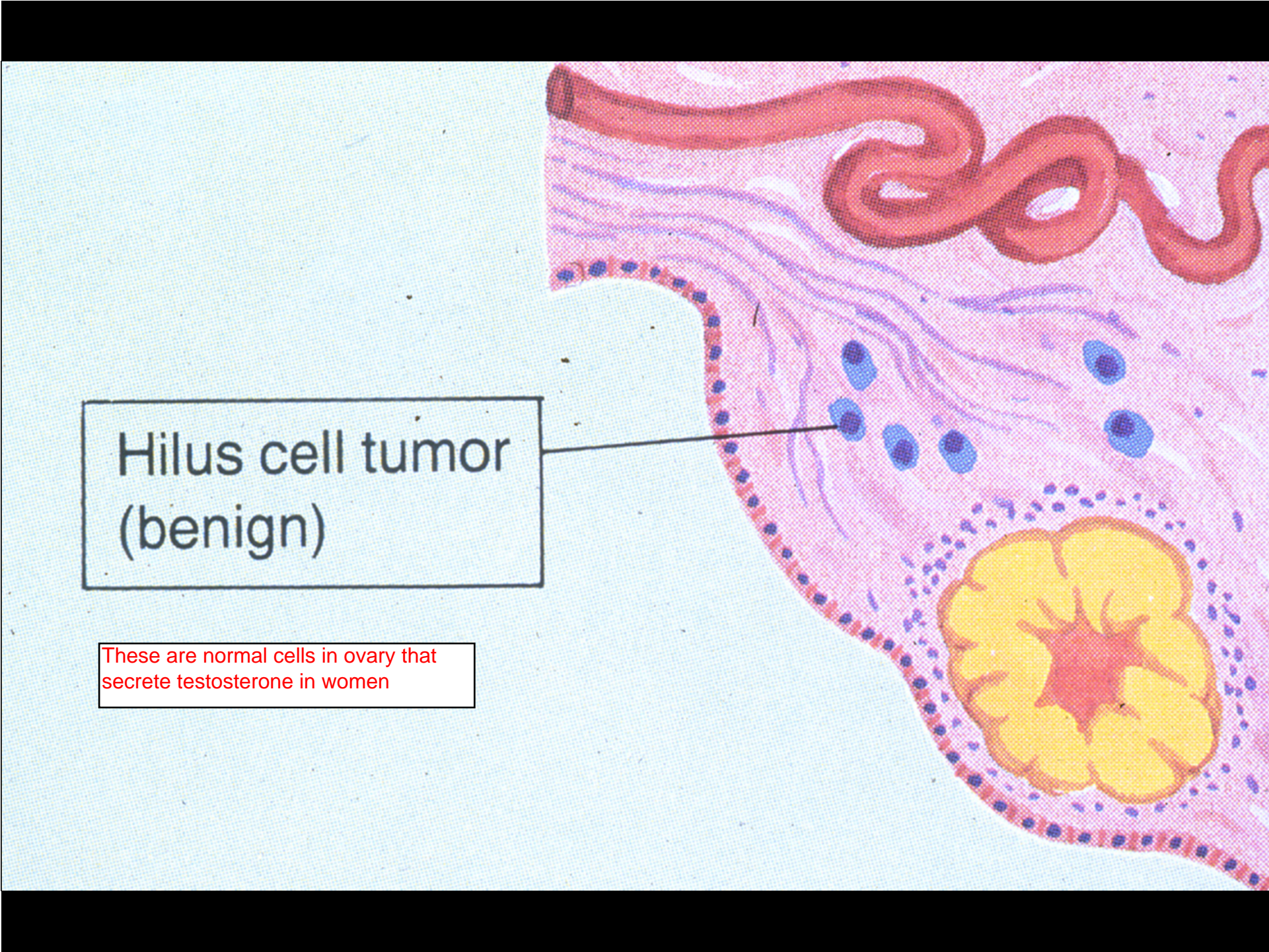
Video #4

Very hard to cut
into. Almost pure
collagen.



Almost rock-hard!

<http://www.youtube.com/user/ProfBentley#p/a>



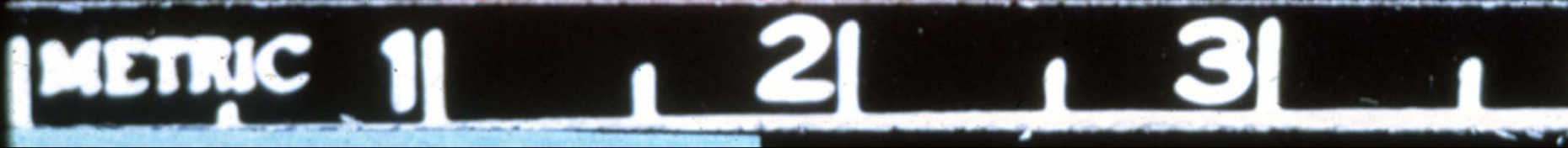
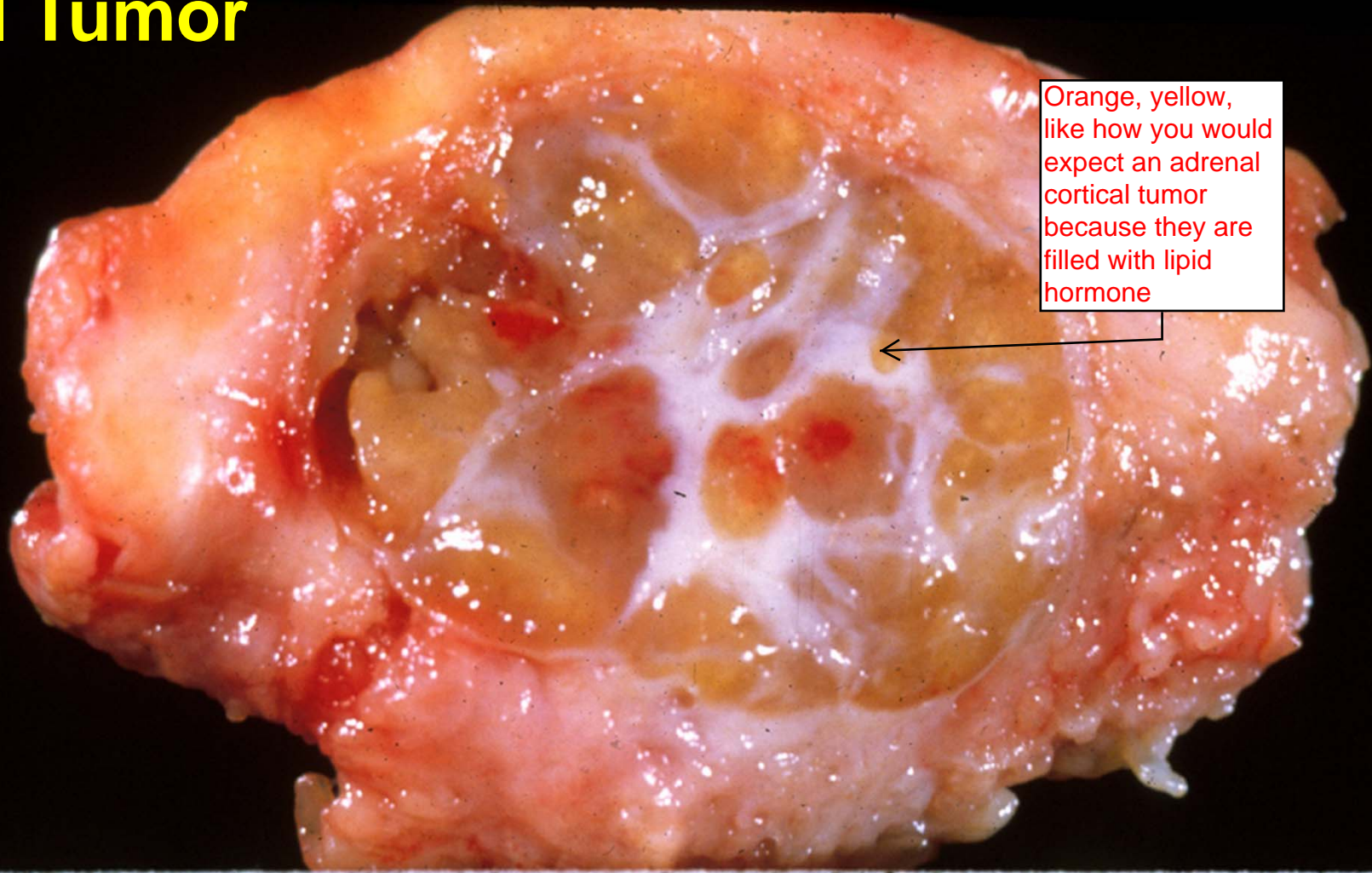
Hilus cell tumor
(benign)

These are normal cells in ovary that
secrete testosterone in women

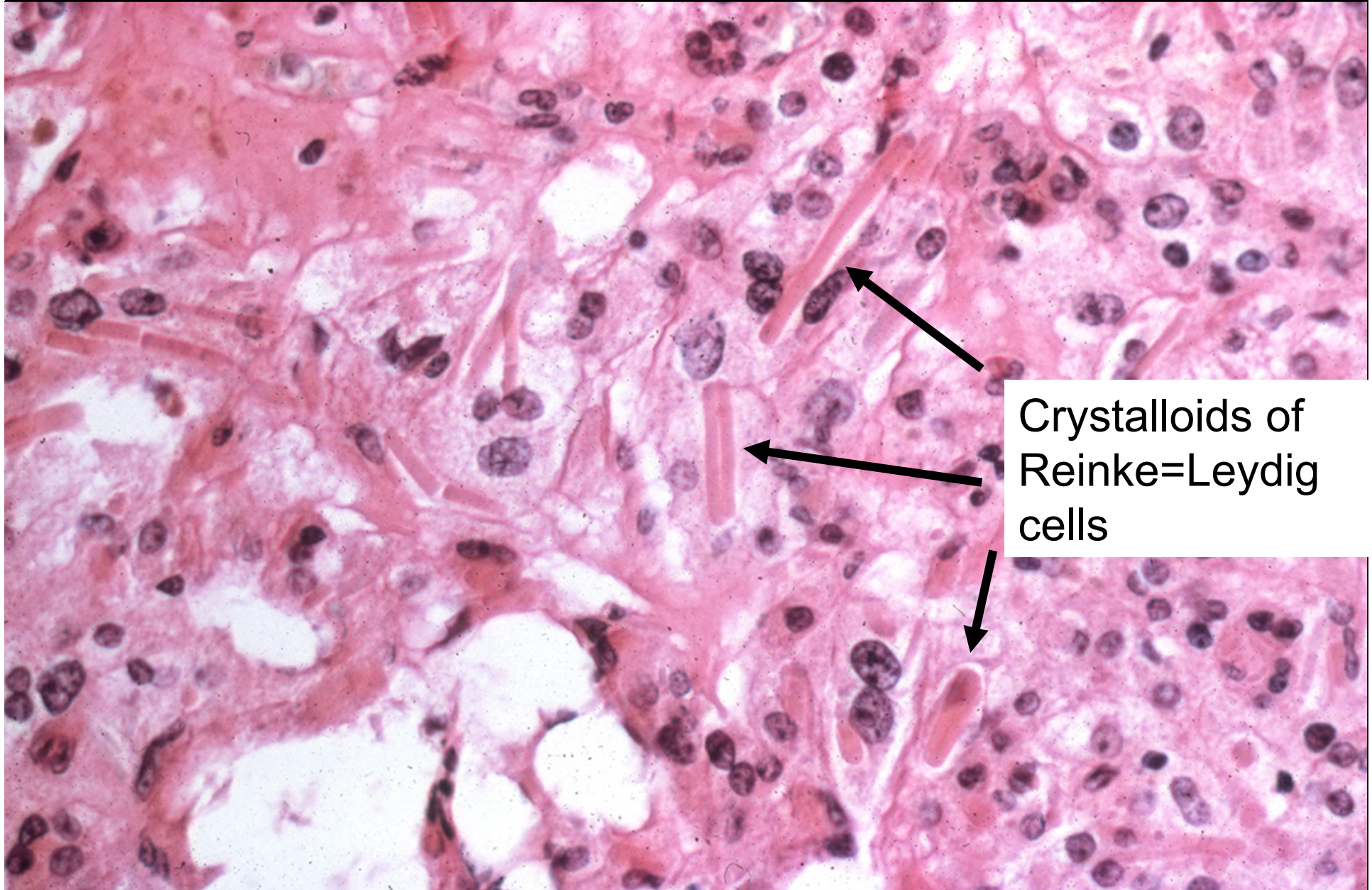
Hilar (Leydig) Cell Tumor

Can present in many interesting, unusual ways

Orange, yellow, like how you would expect an adrenal cortical tumor because they are filled with lipid hormone



Hilar Cell Tumor



Crystalloids of
Reinke=Leydig
cells

Tumor Markers

Useful for work up

- CA-125: Serous tumors

Nonspecific, usually anything that causes inflammation causes CA-125 elevation, endometriosis, etc.

- **Not useful for screening** (often elevated in benign conditions) but can be **useful in following pts with known cancers.**

However, it is good for monitoring tumor recurrence.

- Alpha fetoprotein (AFP): **Yolk sac** variant of germ cell tumors

- HCG: **Choriocarcinoma**

Q: What about PSA?

A: Well only prostate secrete PSA, not the case w/ CA-125. CA-125 not just secreted by ovary. PSA isn't too specific either, but it is better than CA-125.

Ovary: Metastatic Tumors

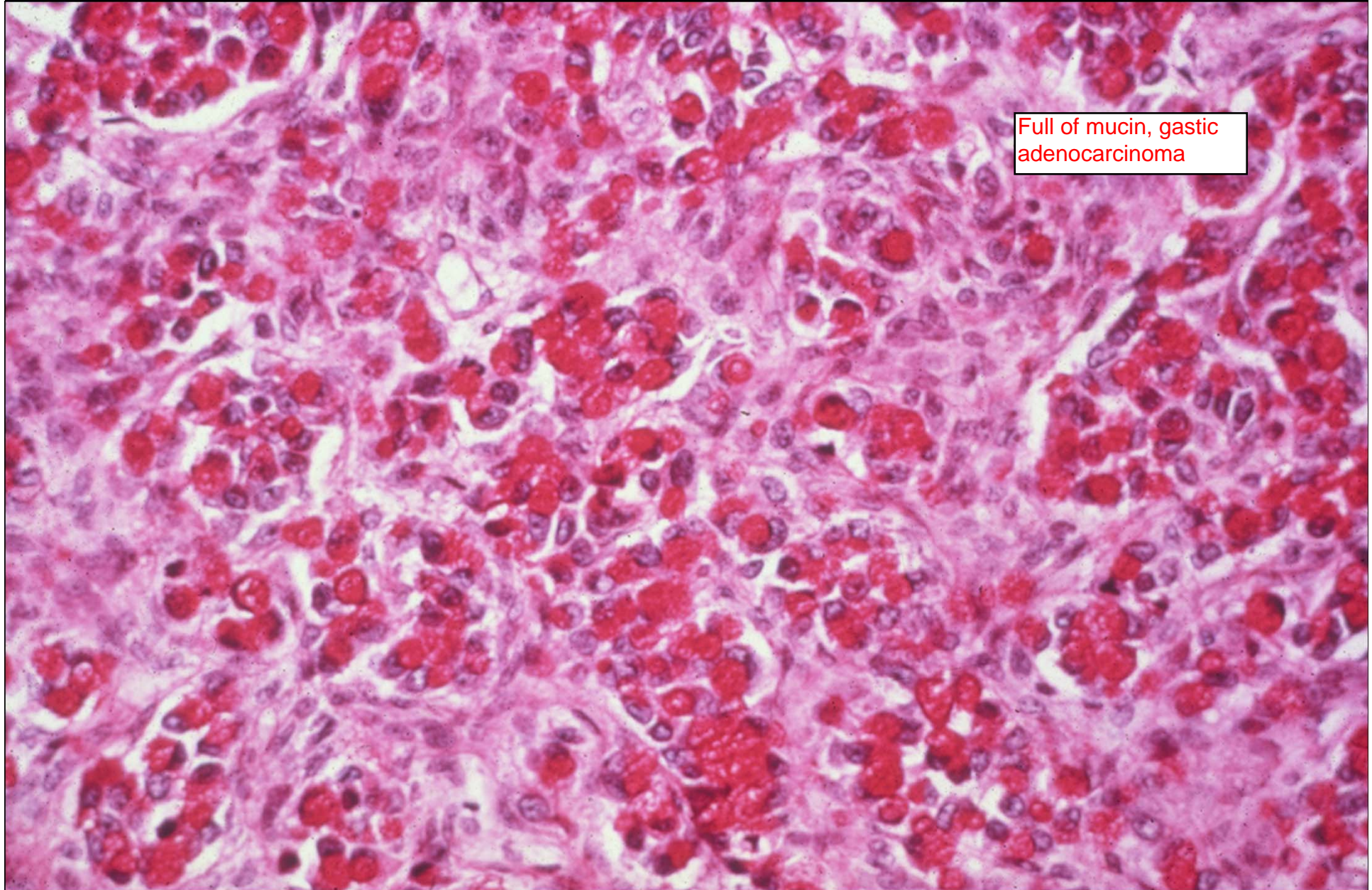
- Colon, stomach, breast commonly spread to ovary.
- Can be very large, mimicking ovarian primary
- Ovarian metastasis can present before primary tumor is evident, especially with gastric cancers.
- AKA: “Krukenberg tumor”

Interesting fact



This dude thought he found a new tumor, turned out it was stomach metastasis. Now Krukenberg tumor= metastatic adenocarcinoma. Poor guy, people won't stop rubbing it in.

Krukenberg Tumor: Mucin Stain



Full of mucin, gastic adenocarcinoma

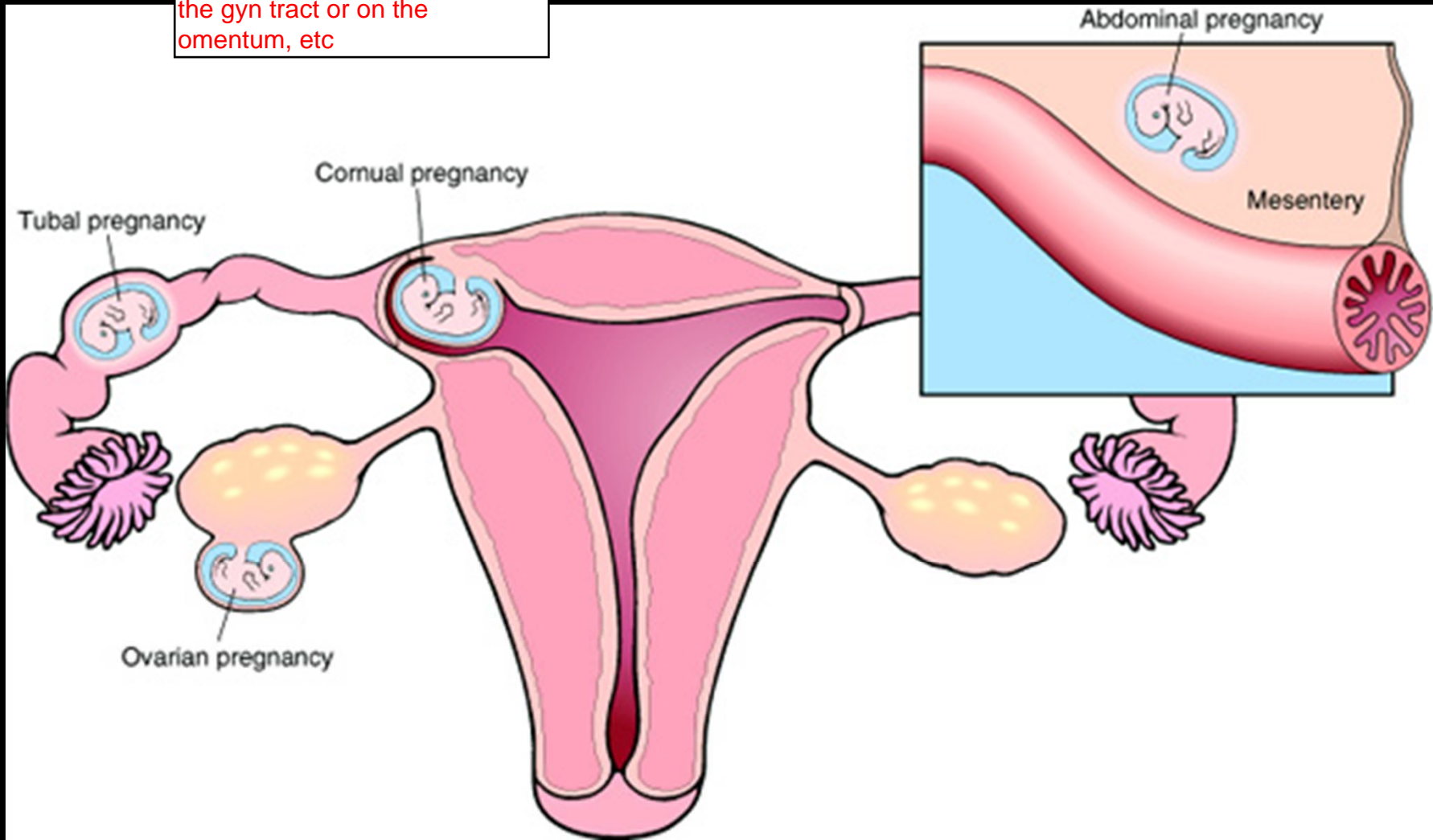
Diseases of Pregnancy

Diseases of Pregnancy

- Infectious (covered elsewhere)
- Ectopic Pregnancy
 - **Implantation of embryo anywhere other than endometrium**
 - 1% of gestations are ectopic
 - Most (90%) are tubal
 - Other sites: ovaries, peritoneum
 - **Rupture/bleeding is major complication**

can die from this very easily

Can be in any weird place, in the gyn tract or on the omentum, etc



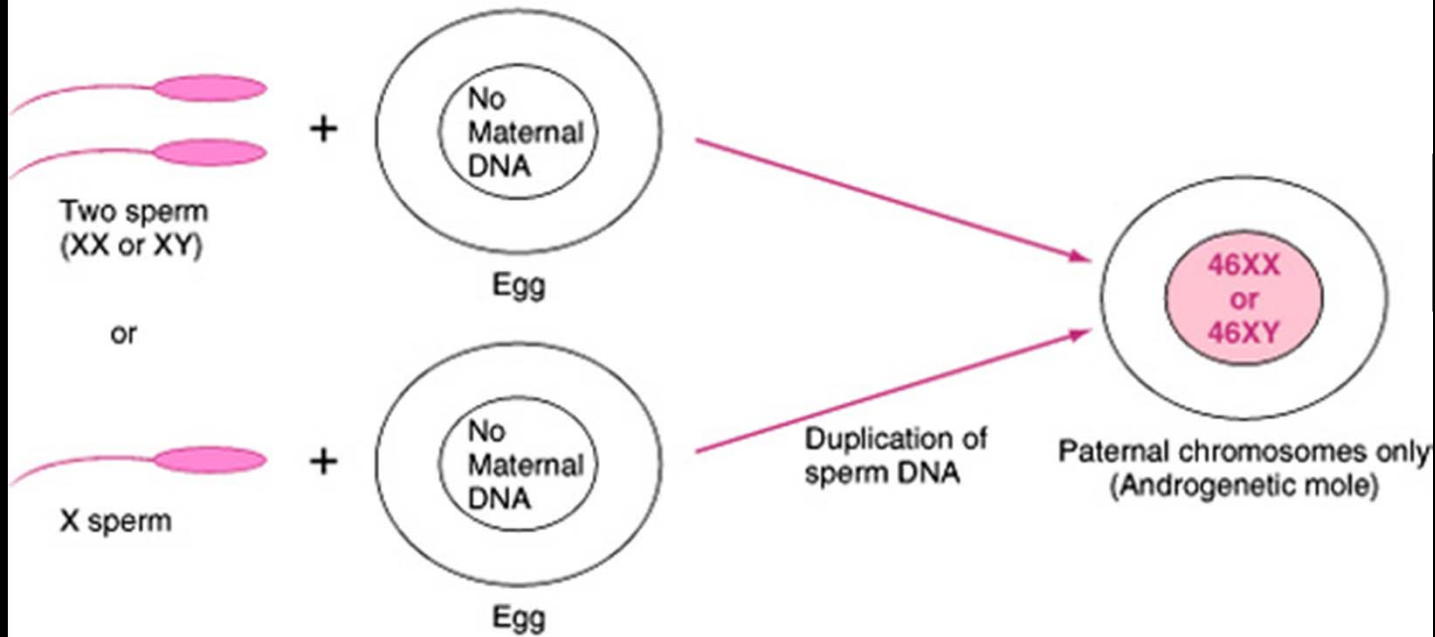
Gestational Trophoblastic Dz

Neoplasms from placenta

- Hydatidiform Mole
 - Benign neoplasm of the chorionic villi
 - Can **persist or invade.** but not metastasizes
- Two types:
 - Complete Mole: 2 copies paternal DNA
 - Partial Mole: 2 copies paternal, 1 copy maternal DNA (triploid)
- Incidence 1:2000 in US
 - Much higher in Asia

not a good thing,
because of genetic
imprinting

COMPLETE MOLE



All dad DNA, no fetus. If it were, we'll have human cloning.

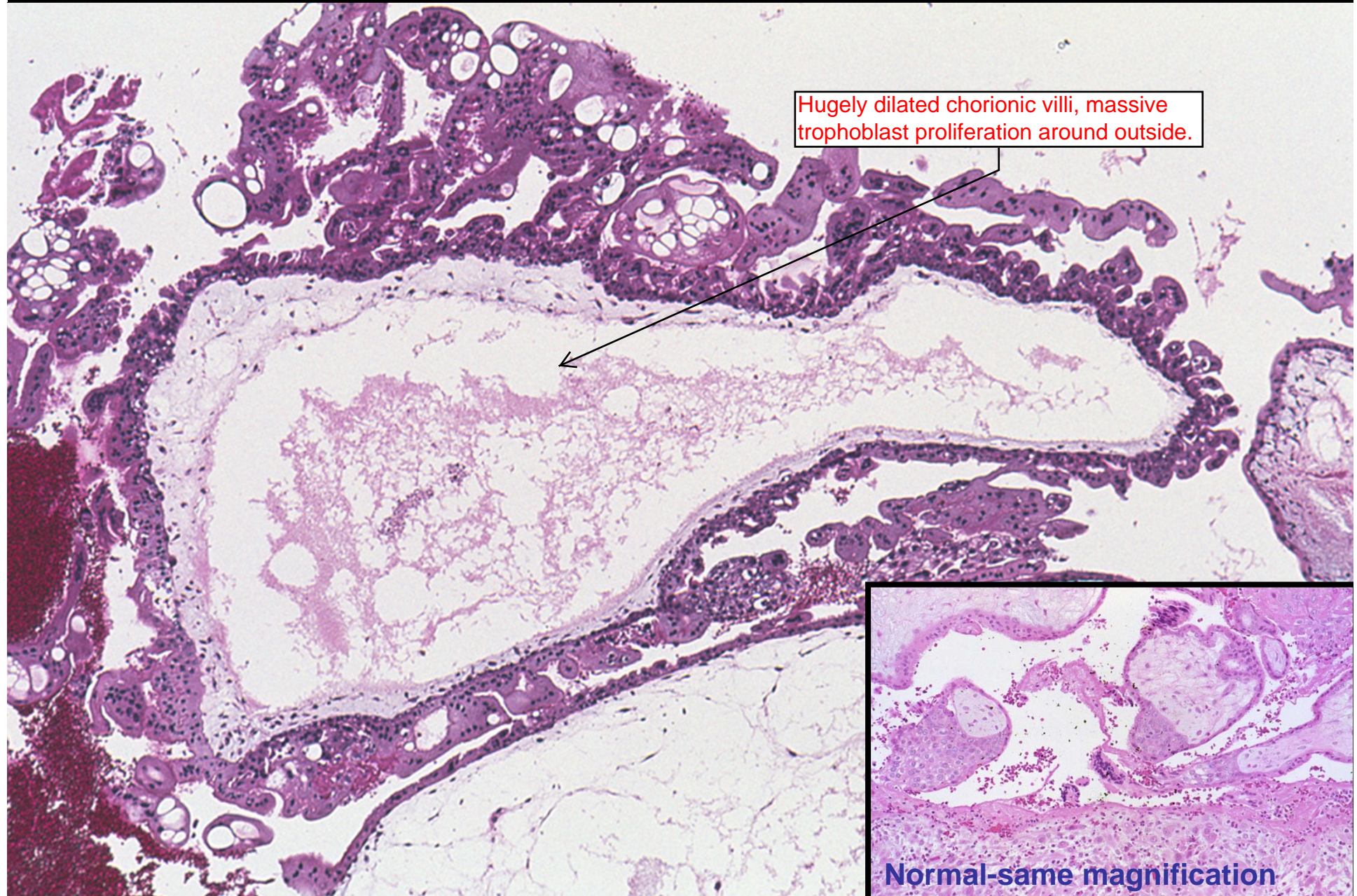
Pathogenesis of Molar Gestations

PARTIAL MOLE



Triploid

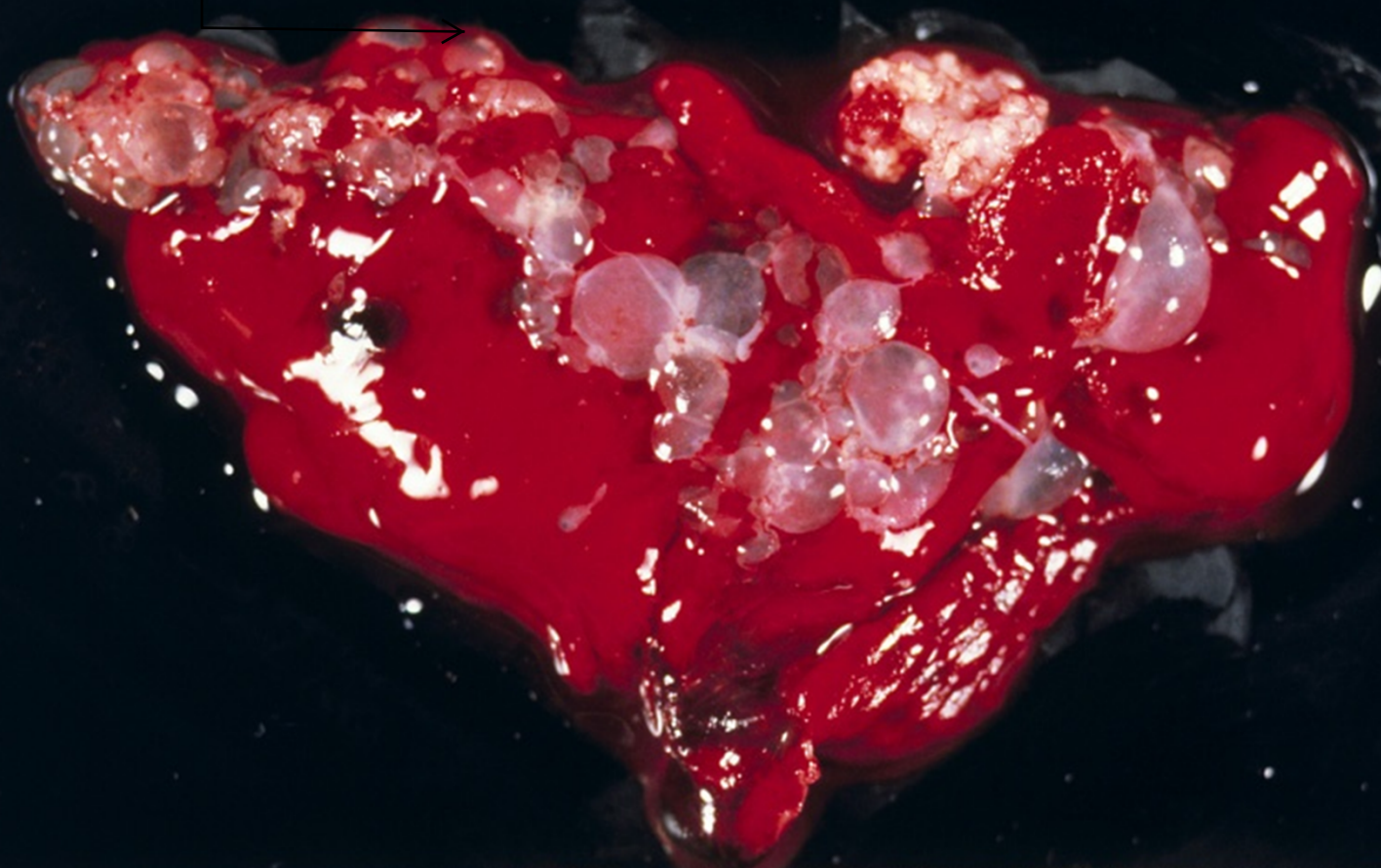
Complete Mole



Complete Mole

Chorionic villi are usually so small that you can't see with naked eye. These are not normal when they are grape-like

This happens during pregnancy. Instead of the cute fetus we saw on ultrasound, these women have these moles. May be bleeding or exaggerated pregnancy reactions, e.g. nausea because of the skyrocketing HCG secreted by the trophoblast.



Gestational Choriocarcinoma

Really bad tumor of chorionic villi

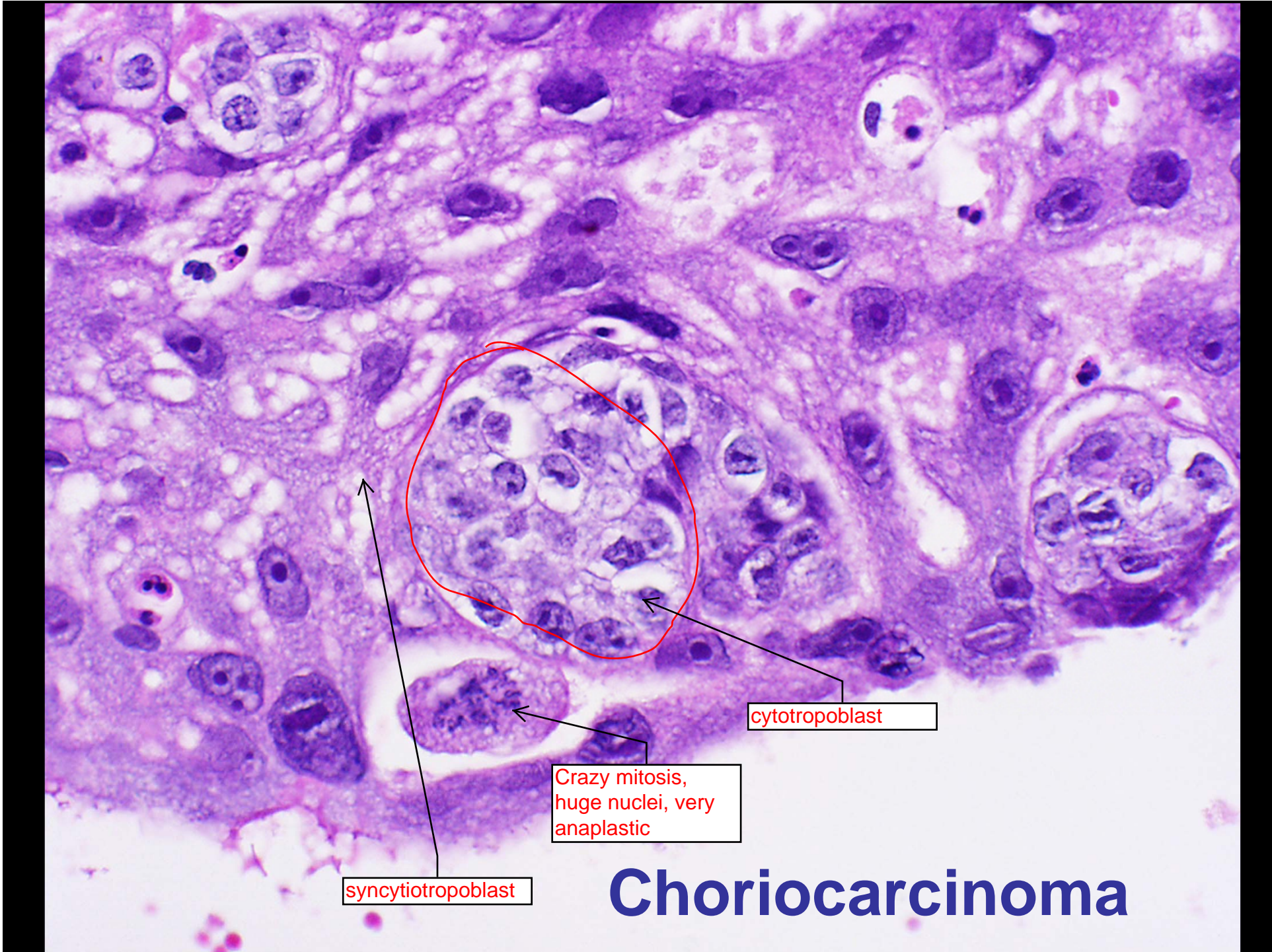
- **Very aggressive** malignancy of **trophoblast**
- **>90% metastatic at presentation**
 - Lung, brain
- **1/30,000 pregnancies in US**
 - 10 fold higher in Asia

relatively
uncommon in US

Gestational Choriocarcinoma

- **Greatly increased risk with mole**
 - 50% of have history of mole
 - 25% spontaneous abortion
 - 25% normal pregnancy
- **Secrete beta-HCG: Tumor marker**

Very good marker
for detecting this
tumor



syncytiotrophoblast

Crazy mitosis,
huge nuclei, very
anaplastic

cytotrophoblast

Choriocarcinoma

Gestational Choriocarcinoma


Though aggressive, very curable. Almost 100% even with wide metastasis.

- Chemotherapy extremely effective

- Near 100% cure rate That's nice.

- **Unique to uterine choriocarcinoma arising after pregnancy—chorioCA in ovary, testis or other sites has poor response to chemotherapy.**

Just the pregnancy related uterine choriocarcinoma



Summary

- Described common diseases of fallopian tube, especially pelvic inflammatory disease.
- Described the main categories of ovarian neoplasms
- Compared the incidence and mortality rates for ovarian cancer vs. other gyn cancers.
- Listed the commonly occurring epithelial neoplasms in the ovary
- Predicted the behavior of benign, borderline, and malignant ovarian epithelial neoplasms
- Classified the common forms of gestational trophoblastic disease

THE END

