

Lecture 1

Testicular Pathology



432 Pathology Team

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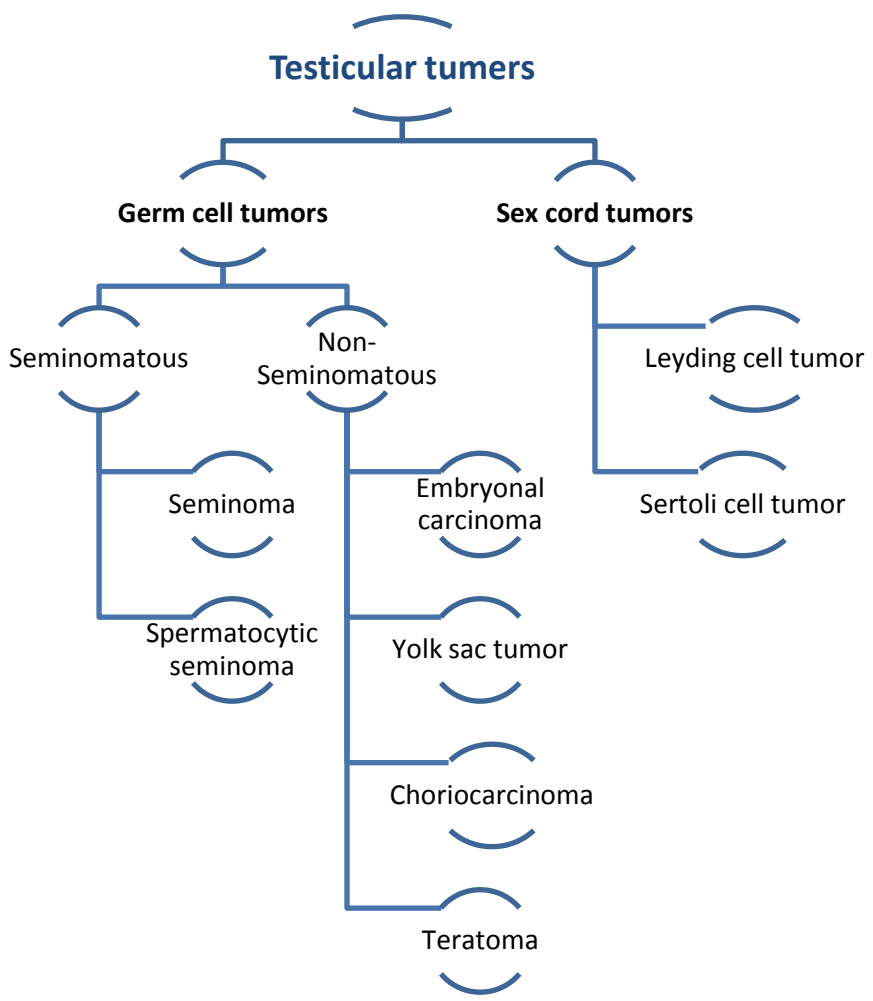
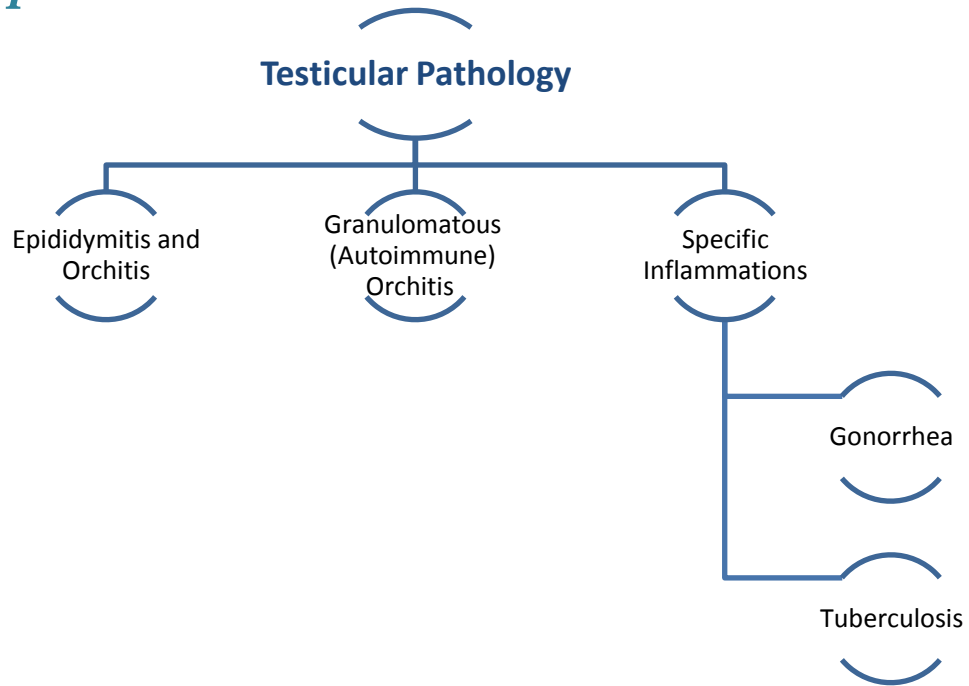
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Reproductive Block



Testicular Pathology

Mind Map:



Testicular diseases

1. Epididymitis and Orchitis (inflammation of the testes):

- Inflammatory conditions are generally **more common in the epididymis** than in the testis (**ovary and testicles are very resistance to inflammation**).
- However, some infections, notably **syphilis**, may begin in the testis with secondary involvement of the epididymis (**extremely rare**).
- Epididymitis and possible subsequent orchitis are **commonly related to infections in the urinary tract** (cystitis, urethritis, genitoprostatitis).
- These infections reach the epididymis/testis through either the **vas deference** or the **lymphatics** of the spermatic cord.

Causes of Epididymitis:

- Varies with age:
 - **Children**: **uncommon**, usually associated with a congenital genitourinary abnormality and infection with **Gram -ve rods**.
 - In sexually active men **< 35 years** → **Chlamydia trachomatis** and **Neisseria**
 - **Older than 35 Years** → **E.Coli** and **Pseudomonas**.

Microscopic findings of Epididymitis and Orchitis:

- **Nonspecific acute inflammation** characterized by congestion, edema and infiltration by **lymphocytes, neutrophils and macrophages**.
- Initially involves the interstitial connective tissue → **later** involves tubules → may progress to frank abscess.
- Often followed by **fibrous scarring**.
 - Leydig cells are **not** usually destroyed.

2. Granulomatous (Autoimmune) Orchitis:

- Usually **middle-aged** men, unilateral testicular **mass**.
- Moderately tender but sometimes may present as painless testicular mass; **mimicking a testicular tumor**.
- Although an autoimmune basis is suspected, the cause of these lesions remains **unknown**.
- May be a response to **acid-fast products of disintegrated sperm, post-infectious, or due to trauma or sarcoidosis**
- **Microscopically: granulomas**, restricted within the **spermatic tubules**.

3. Specific Inflammations:

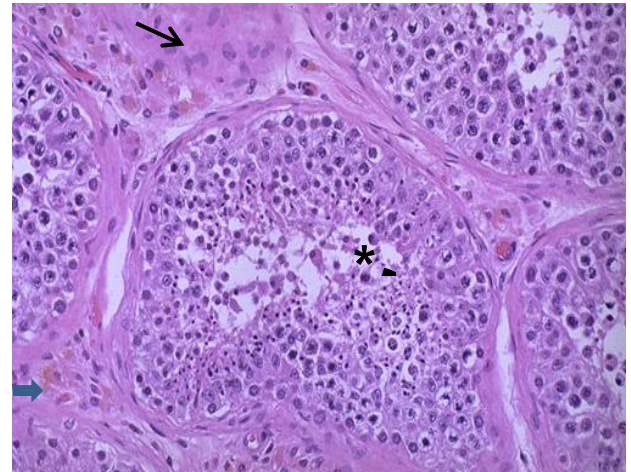
Gonorrhea:

- Extension of infection from the posterior **urethra** → prostate → seminal vesicles → epididymis is the usual course of a neglected gonococcal infection.
- Can lead to frank abscess may spread to testis and can produce a **suppurative orchitis** if not treated.

Tuberculosis:

- Almost invariably **begins in the epididymis** and may spread to the testis.
- In many of these cases, there is associated tuberculous prostatitis and seminal vesiculitis.
- Microscopy: **Caseating Granulomatous inflammation.**

- Pink Leyding cells are seen here in the interstitium (arrow). Note the pale golden brown pigment as well (**bold arrow**). There is active spermatogenesis (*).
- Normal testis shows tubules with active spermatogenesis.



Testicular Tumors

- Complex **mixture** of anatomic types.
- **95%** of them originate from germ cells,
 - Age group → 15-30 years, whites > blacks
- Most of **germ cell tumors** are **highly aggressive** cancers.
- Capable of wide, **extensive dissemination** (worst localized tumors in behavior are testicular tumors).
- Current therapy, **most of them can be cured.**
- **Non germinal** tumors are generally **benign.**
- In other organs most of the tumors are benign while in the testicle the reverse is proved; mass lesion in the testicle most likely is malignant.

Classification

1- Germ cell tumors:

a) Seminomatous:

1. Seminoma.
2. Spermatocytic seminoma.

b) Non seminomatous:

3. Embryonal carcinoma.
4. Yolk sac (endodermal Sinus) tumor.
5. Choriocarcinoma.
6. Teratoma.

2- Sex Cord Tumors:

a) Leydig cell tumor

b) Sertoli cell tumor

Predisposing factors:

1. Cryptorchidism: 10% of testicular tumors.
2. Testicular dysgenesis.
3. Genetic factors.

(1) Seminoma (Seminomatous)

- The **most common type of germ cell tumors** (50%)
- Peak incidence in **thirties** (Almost never occur in infants)
- Identical one occurs in the **ovary** (**Dysgerminoma**)

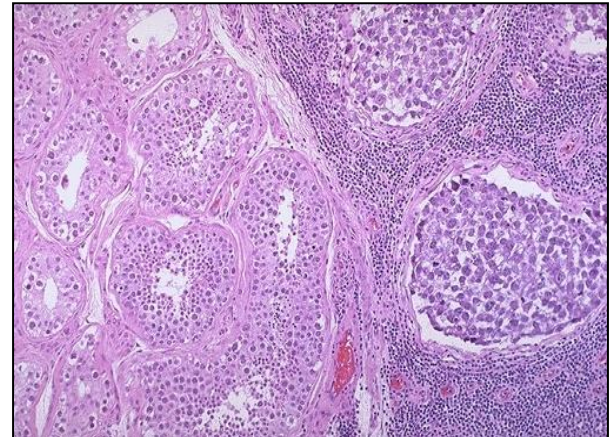
- Bulky masses:
 - Homogenous
 - Gray-white
 - Lobulated cut surface
- Usually **no necrosis or hemorrhage**
- **Usually unilateral mass.**
- In 50% ,the **entire** testis is involved
- Occasionally **extends** to the epididymis, spermatic cord, or scrotal sac.



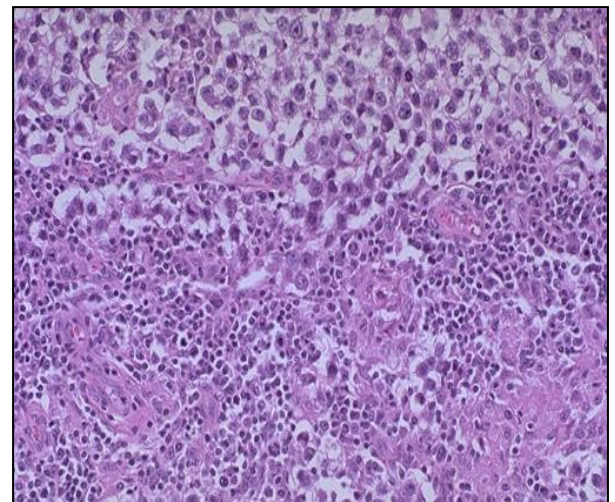
Seminoma of the testis appears as a fairly well-circumscribed, pale, fleshy, homogeneous mass.

Morphology:

- **Microscopically**, sheets of **uniform cells**.
- Lobules separated by delicate **fibrous septa** with many **lymphocytes**.
- Cells are large, round, has distinct cell membrane (in testicular tumors when we see lymphocytes it is most likely seminoma).
- **Large** nucleus with prominent nucleoli.
- Positive for PLAP 'placental alkaline phosphatase' (also, PLAP positive for all germ cell tumors).



- Sometimes we can see granuloma in between.
- Normal spermatogenesis on left, seminoma on right.



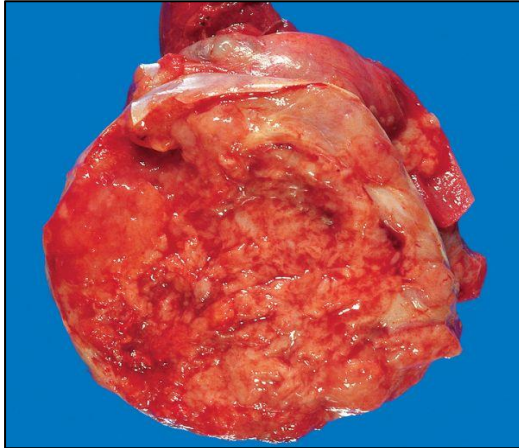
Large cells with distinct cell borders, pale nuclei, prominent nucleoli, and a sparse lymphocytic infiltrate.

(2) Spermatocytic Seminoma (Seminomatous)

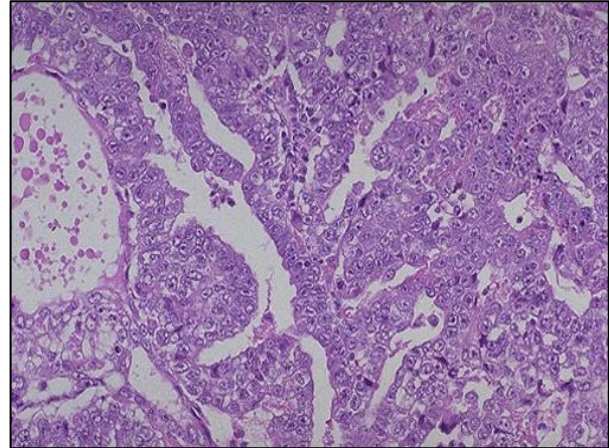
- **Distinctive tumor**, clinically and histologically.
 - 1-2 % of testicular tumors.
 - **Over age 65.**
 - Slow growing tumor, **rarely metastasize it is localized.**
 - **Prognosis is excellent**
- The cells could be large, intermediate or small.

(3) Embryonal Carcinoma (Non seminomatous)

- 20 to 30 year age group.
- **More aggressive** than seminomas.
- Smaller than seminoma.
- Grossly, shows **foci of necrosis and hemorrhage**.
- Microscopically, shows sheets of undifferentiated cells as well as primitive glandular differentiation. Cells grow in **alveolar or tubular** pattern, sometimes with papillary convolutions.
- Could be present with other neoplasm in 45%.



Embryonal carcinoma
Hemorrhagic mass.

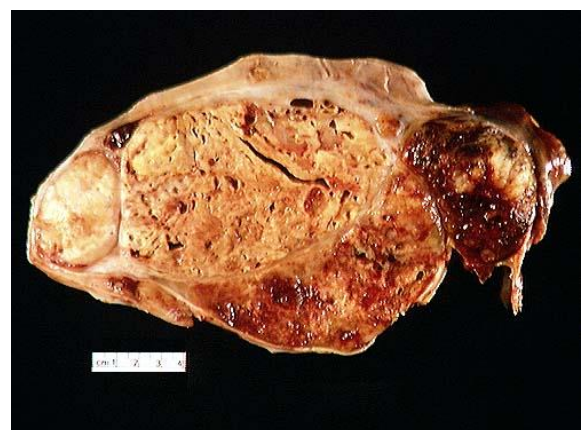


Embryonal carcinoma shows sheets of undifferentiated cells as well as primitive glandular differentiation.

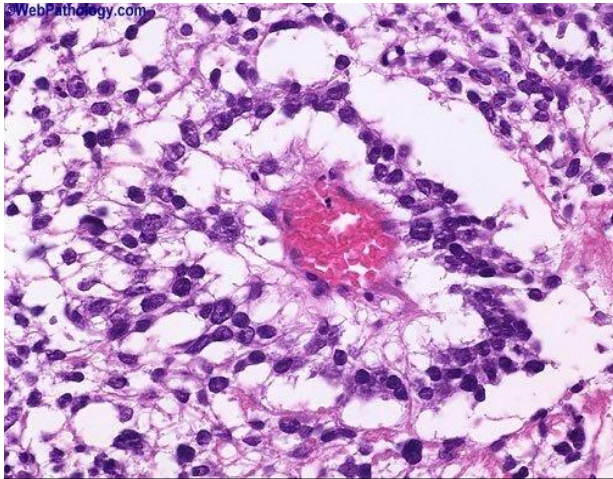
The nuclei are large and hyperchromatic.

(4) Yolk Sac Tumor (Non seminomatous)

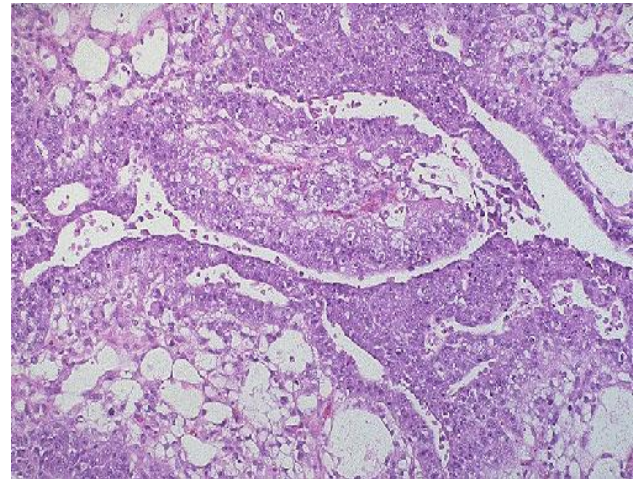
- Also known as **Endodermal sinus tumor**.
- The **most common tumor in infant** and children up to 3 years of age.
- Has a very good prognosis.
- Non encapsulated, homogenous, mucinous appearance.
- **Microscopically**: structures resemble endodermal sinuses
 - **Schiller-Duval** bodies
 - Hyaline – pink globules
 - AFP positive α -fetoprotein



Mixed germ cell **tumor** of testes, with embryonal carcinoma, **yolk sac tumor**



Schiller-Duval body is a structure seen in yolk sac tumor. It consists of a central vessel surrounded by tumor cells – the whole structure being contained in a cystic space often lined by flattened tumor cells.



An endodermal sinus tumor (yolk sac tumor) of the testis is shown composed of primitive germ cells that form glomeruloid or embryonal-like structures. These tumors are most frequent in children, but overall they are rare.

(5) Choriocarcinoma (Non seminomatous)

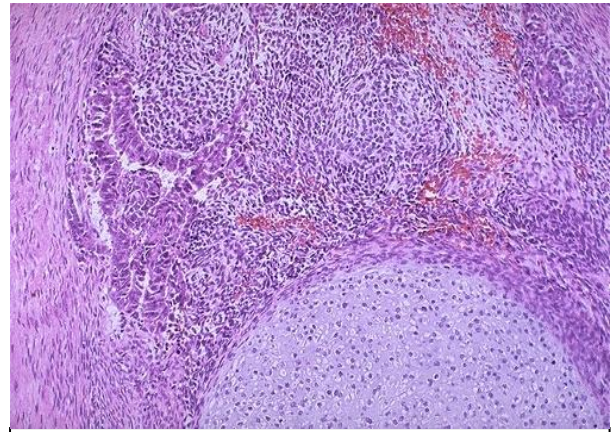
- Highly malignant tumor
- Cytotrophoblastic and syncytiotrophoblastic cells
- Small lesions
- HCG positive "human chorionic gonadotropin"

(6) Teratoma (Non seminomatous)

- Various cellular or organoid components.
- Any age, infancy to adult life.
- **Mature forms are common in infants and children.**
- Adult forms are rare.
- As a component with other type in 45%.
- Usually large 5 -10 cm
- Heterogeneous appearance
- Hemorrhage and necrosis indicate embryonal component
- **Composed of heterogenous collection of cells** or organoid structures
- Neural tissue, cartilage, squamous epithelium, glandular components....
- Germ cell tumors could arise from teratoma
- **In children ,mature teratomas behave benign**
- In **post pubertal** male, all teratomas **regarded malignant** and capable of metastasis, regardless of **whether the elements are mature or not.**



A small testicular carcinoma is shown here. There is a mixture of bluish cartilage with red and white tumor tissue. This neoplasm microscopically contained mainly teratoma, but areas of embryonal carcinoma were also present.



At the bottom is a focus of cartilage. Above this is a primitive mesenchymal stroma and to the left a focus of primitive cells most characteristic for embryonal carcinoma. This is embryonal carcinoma mixed with teratoma.

Clinical Features of Testicular tumors:

- **Biopsy** of a testicular tumour is associated with **a risk** of tumour spillage (**A biopsy should not be performed, as it raises the risk of spreading**).
- The standard management of solid tumours is radical orchiectomy.
- Lymphatic spread is common.
- **Retroperitoneal and para-aortic nodes are first to be involved.**
- Hematogenous spread to Lung, liver, Brain, and bones.

Summary from Robbins

Testicular Tumors

- Testicular tumors are the most common cause of painless testicular enlargement. They occur with increased frequency in association with undescended testis and with testicular dysgenesis.
- Germ cells are the source of 95% of testicular tumors, and the remainder arises from Sertoli or Leydig cells. Germ cell tumors may be composed of a single histologic pattern (60% of cases) or mixed patterns (40%).
- The most common “pure” histologic patterns of germ cell tumors are seminoma, embryonal carcinoma, yolk sac tumors, choriocarcinoma, and teratoma. Mixed tumors contain more than one element, most commonly embryonal carcinoma, teratoma, and yolk sac tumor.
- Clinically, testicular germ cell tumors can be divided into two groups: seminomas and nonseminomatous tumors. Seminomas remain confined to the testis for a long time and spread mainly to para-aortic nodes—distant spread is rare. Non-seminomatous tumors tend to spread earlier, by both lymphatics and blood vessels.
- HCG is produced by syncytiotrophoblasts and is always elevated in patients with choriocarcinomas and those with seminomas containing syncytiotrophoblasts. AFP is elevated when there is a yolk sac tumor component.

Summary

Germ Cell Tumors

(1) Seminomatous

	Seminoma	Spermatocytic seminoma
Gross	Homogenous and lobulated cut surface	-
Microscopic	Uniform cell with lymphocytes and Large nucleus with prominent nucleoli	-
Tumor marker	PLAP	-
	Most common- peak incidence in 30s	Over age 65- Good prognosis - rarely metastasize

(2) Non-seminomatous

	Embryonal carcinoma	Yolk sac tumor	Choriocarcinoma	Teratoma
Gross	Foci of necrosis and Hemorrhage	Homogenous mucinous appearance	Small lesions	Heterogeneous appearance
Microscopic	Undifferentiated cells and primitive glandular differentiation	1.Schiller-duval bodies 2. Hyaline- pink granules	Cytotrophoblastic and syncytiotroblstic cells	Heterogeneous collection of cells or organoid structure
Tumor marker	-	AFP	HCG	-
	20-30 yrs age group could present with other neoplasm	Most common in infants and children up to 3 yrs	Highly malignant	Children -Benign (mature) Adults - Malignant

Questions

1/ A 20-year-old man presents with dysuria, urgency, and urethral discharge. Physical examination shows suppurative urethritis, with redness and swelling at the urethral meatus. Which of the following is the most likely etiology of urethritis in this patient?

- (A) *Borrelia recurrentis*
- (B) *E. Coli*
- (C) *Haemophilus ducreyi*
- (D) *Neisseria gonorrhoeae*

2/ An 8-year-old boy is brought to the physician because his parents noticed a mass on his left testicle. Physical examination reveals a solid mass that cannot be transilluminated, and biopsy shows a haphazard arrangement of benign differentiated tissues, including squamous epithelium, glandular epithelium, cartilage, and neural tissue. The left testicle was removed surgically, and the patient is symptom free 5 years later. Which of the following is the most likely diagnosis?

- (A) Embryonal carcinoma
- (B) Mature teratoma
- (C) Mixed germ cell tumor
- (D) Teratocarcinoma

3/ A 2-year-old boy is brought to the physician because his parents noticed a mass on his right testicle. Physical examination confirms the parents' observation. An orchiectomy is performed. Microscopic examination of the surgical specimen shows neoplastic cells forming glomeruloid Schiller-Duval bodies. Which of the following serum markers is most useful for monitoring the recurrence of tumor in this patient?

- (A) CA-125
- (B) Estrogen
- (C) α -Fetoprotein
- (D) Human chorionic gonadotropin

Answers:

- 1- D
- 2- B
- 3- C

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