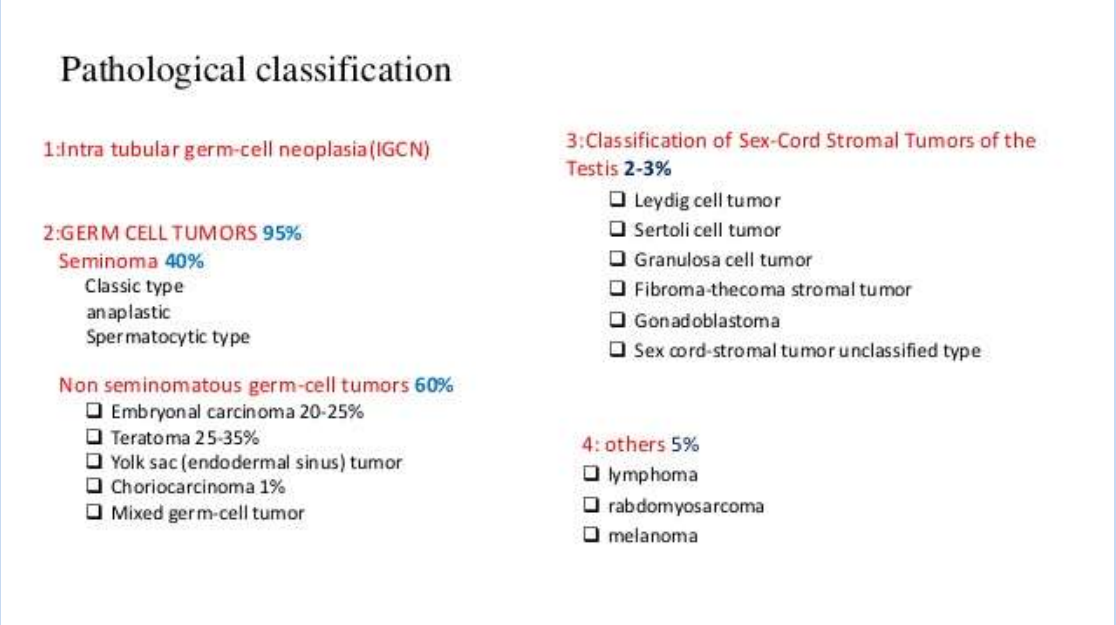
N.B.2:
Tumours of the testicle.



I. Germinal tumours:

1. Seminoma (more differentiated; and, commonest type at middle age).

2. Toti-potential cell tumours (less differentiated).

(a) Teratoma (of mature or immature tissues).
(b) Embryonal carcinoma (a multipotential tumour with multiplicity of morphologic patterns; is highly-malignant though it appears as small discrete greyish-white nodules with areas of haemorrhage).

- If biopsy is done → fungation of the tumour and invasion to the epididymis and spermatic cord.

3. Chorion-carcinoma (a rare red, haemorrhagic, soft and necrotic tumour which shows a variegated cut-surface).

- Though small, it is highly malignant and sends early metastases.
- It produces a hormone → stimulation of the anterior pituitary gland → increased prolactin secretion, Beta HCG strong-positive reaction of **Aschheim Zondek test***, recently pregnancy test in urine or in blood.

II. Interstitial cell tumours:

- *Arise from Leydig cells and start as a small, rounded, yellowish-brown* firm and encapsulated nodule.

Types:

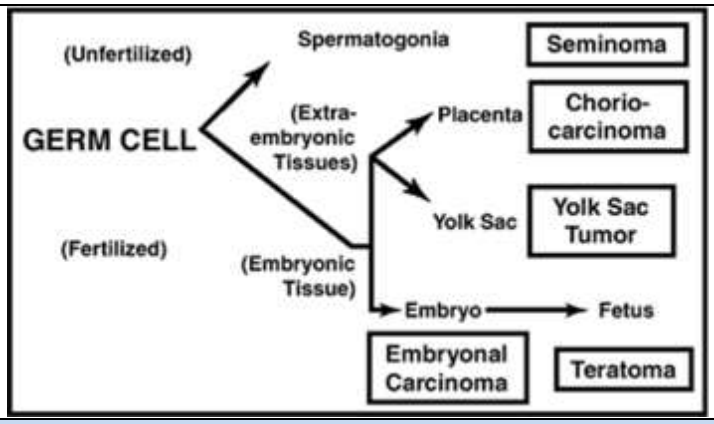
1. Benign.
2. Malignant.

Features

- In children → androgen-formation → sexual precocity.
- In adults → androgen + oestrogen → feminizing trait and gynaecomastia.

N.B.3:

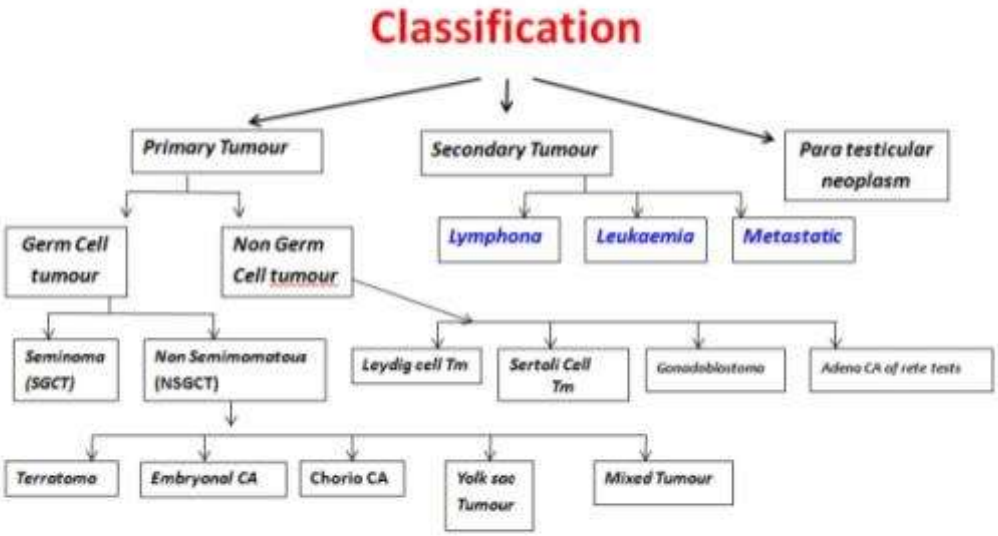
- *Malignant tumours of the testicle are usually characterized by:*
  1. *Some overlap between the various forms.*
  2. *Early metastases in lymph nodes.*
  3. *Blood-spread to lungs, liver and other viscera.*

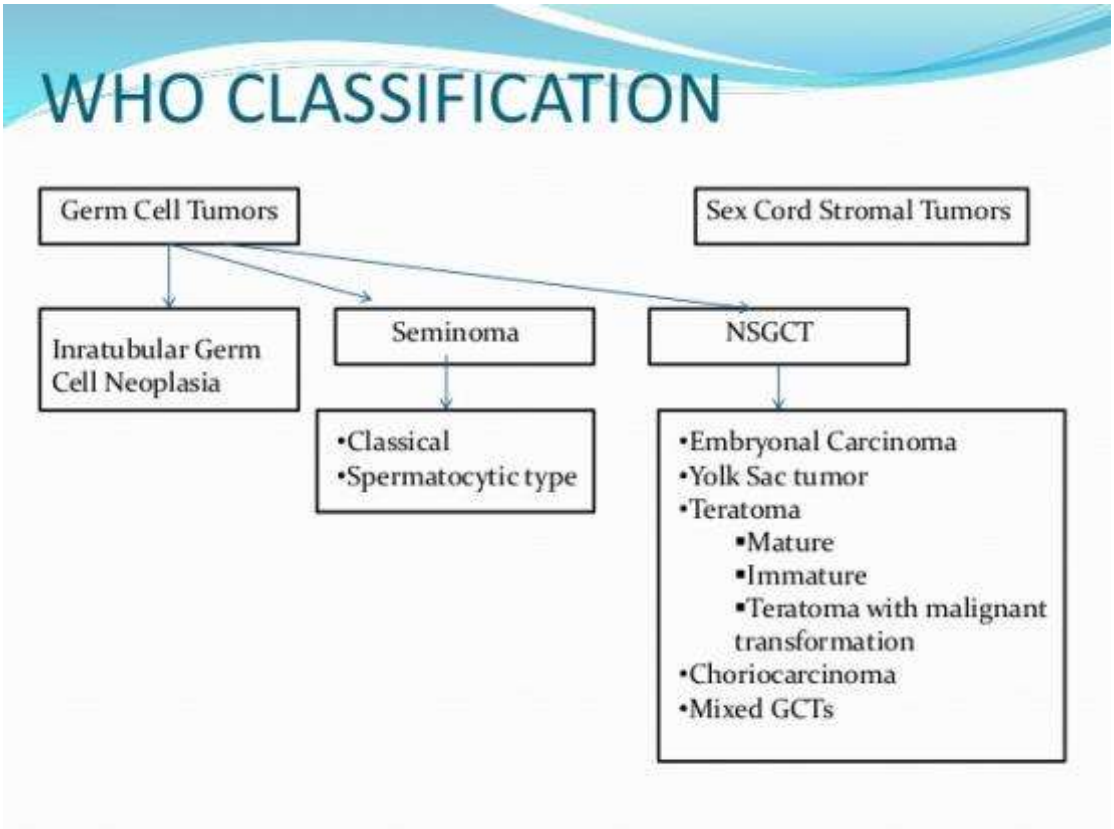


- ***The Aschheim-Zondek Test for Pregnancy (historical pregnancy test)**
- Many different methods have been devised for the early detection of pregnancy.
- From the time of the Ancient Egyptians, inspection of the urine has been a popular place to start.
- However, it was not until the discovery of hormones in the early twentieth century that the development of truly reliable pregnancy tests occurred.
- Prior to 1978, when the first home pregnancy tests became available in the United States, pregnancy testing was done in hospital laboratories using various methods, one of them being the Aschheim-Zondek, or A-Z test.
- The A-Z test is a product of research into human reproduction carried out in the early twentieth century.
- Developed by German gynecologists Selmar Aschheim and Bernhard Zondek in 1927, the A-Z test was one of the first bioassays developed to detect early pregnancy.
- Armed with new information about chemical messengers called hormones, Aschheim and Zondek identified the anterior pituitary gland as an endocrine gland that performs important roles in ovarian function. It is now known that a family of hormones called **gonadotropins** is essential to control of the ovarian and uterine cycles and to sexual maturation.
- During the menstrual cycle, an increase in gonadotropin levels causes a mature ovarian follicle to release its egg and develop into a corpus luteum.
- In 1903 Ludwig Fraenkel became the first to describe the human corpus luteum, a glandular mass found in the ovaries of a female during menstruation that has important endocrine functions.
- Fraenkel also named the hormone progesterone, which the corpus luteum secretes in addition to estrogen. These hormones support the endometrium and suppress release of gonadotropin in order to prevent the maturation of other ovarian follicles.
- If the egg is not fertilized, the corpus luteum dissociates and the endometrium sloughs off.
- Conversely, if the egg is fertilized, it implants itself and secretes the hormone associated with modern early pregnancy detection— human chorionic gonadotropin (hCG)—which signals the corpus luteum to continue secretion of progesterone and estrogen in order to prevent the endometrium from sloughing off.
- Remarkably, although Aschheim and Zondek developed the A-Z test in 1927, hCG itself was not discovered until the 1950s.
- This landmark in the history of pregnancy tests simply operated under the assumption

that a substance **present only in the urine of pregnant women** could be used to elicit some sort of measurable response in other, nonhuman organisms.

- Specifically, the Aschheim-Zondek test calls for the injection of a woman's urine into an immature female mouse.
- It was correctly hypothesized that if a woman is pregnant, the young mouse will go into heat despite its young age.
- Ultimately, the Friedman test would use rabbits rather than mice, eliciting the popular symbol of rabbit-killing to describe pregnancy testing as the rabbit would have to be sacrificed in order to identify the presence or absence of a corpus luteum.
- The test further evolved in efficiency in the 1950s with the use of **toads** rather than mice or rabbits, as these egg-laying organisms do not have to be sacrificed in order to confirm a positive or negative test result.
- The technical process of the A-Z test is more complex than it first appears.
- A suitable mouse for use in an A-Z test needs to be three to five weeks in age and weigh between six and ten grams.
- For each pregnancy test, three to five of these infant mice are necessary, as some of them will die before the end of the test.
- After a urine specimen is collected from the female, it is tested for acidity and made basic.
- Afterward, one or two drops of tricresol are often added in order to preserve the sample, and the urine is filtered if cloudy in appearance.
- Subsequently, 3 mL of the urine sample is injected subcutaneously into each mouse three times per day for three days.
- Two days after the last injection, all of the mice are sacrificed and the ovaries are examined macroscopically.
- The presence of the human gonadotropin hormone in the urine sample is indicated by several characteristic changes in the mice.
- The A-Z test is said to be positive if the ovaries are enlarged (two to three times normal size) with red dots visible (due to hemorrhage into the follicles) or if luteinization occurs and several corpora lutea are visible.
- A corpus luteum can be identified macroscopically as a small yellow dot on the ovaries.
- If the uterus appears enlarged with no changes in the ovaries, the test is negative.
- The uterus becomes enlarged because of other hormones present in the urine, not because of hCG.
- However, if the first reaction is observed but the organism displays other features of heat, such as cornification of the vagina, the test is repeated with a second urine sample.
- The A-Z test was impressively reliable.
- After the first 2,000 A-Z tests were performed, the test was estimated to have a 98.9% success rate (with seventeen errors being false negatives and five being false positives), according to "Aschheim-Zondek Test for Pregnancy—
- Its Present Status." Nevertheless, the A-Z test was destined to become obsolete, with the introduction in **1960 of an immunoassay for pregnancy testing.**
- This was a more convenient test that did not require animal sacrifice.
- The A-Z test was also used to test for other conditions such as ectopic pregnancy, Hydatidiform mole, chorion-Epithelioma, incomplete abortion and testicular tumors, which also produce human chorionic gonadotropin.
- Although the A-Z test is no longer used, it was an important step in the development of modern pregnancy test kits.


Classification
Primary Tumour
Secondary Tumour
Para testicular neoplasm
Germ Cell tumour
Non Germ Cell tumour
Lymphona
Leukaemia
Metastatic
Seminoma (SGCT)
Non Seminomatous (NSGCT)
Leydig cell Tm
Sertoli Cell Tm
Gonadoblastoma
Adeno CA of rete tests
Terratoma
Embryonal CA
Chorio CA
Yolk sac Tumour
Mixed Tumour


WHO CLASSIFICATION
Germ Cell Tumors
Sex Cord Stromal Tumors
Inratubular Germ Cell Neoplasia
Seminoma
NSGCT
•Classical
•Spermatocytic type
•Embryonal Carcinoma
•Yolk Sac tumor
•Teratoma
▪Mature
▪Immature
▪Teratoma with malignant transformation
•Choriocarcinoma
•Mixed GCTs

Microscopic picture of yolk sac tumour

- Various histologic patterns
- Reticular / microcystic:
  - Most common and characteristic pattern
  - Loose network of anastomosing channels that focally expand to form variably sized cysts; these spaces are lined by primitive tumor cells with varying amounts of clear, glycogenated cytoplasm, occasionally containing lipid
  - Microcysts may contain eosinophilic hyaline globules and amorphous, eosinophilic acellular basement membrane material
  - Loose, hypocellular and myxoid stroma
- Endodermal sinus:
  - Contain Schiller-Duval sinuses or bodies - tubulopapillary sinusoidal structures with central vascular core and cuboidal to columnar epithelial-like cell lining
    - Diagnostic of entity when present
    - Seen in only 20% of tumors
- Other patterns (**Histopathology 2012;60:1023**):
  - **Polyvesicular vitelline**: prominent cysts lined by flattened to columnar cells within a variably cellular stroma, occasionally with eccentric constriction (resembling the division of the primary yolk sac vesicle)
  - **Solid: sheet-like arrangement** of cells with large nuclei and well defined borders; cells may have abundant clear cytoplasm or may be more blastema-like with smaller cells and scant cytoplasm
  - **Hepatoid:** scattered small clusters or cords of large polygonal cells with abundant eosinophilic cytoplasm and prominent nucleoli, separated by thin fibrous bands
  - **Intestinal:** primitive cells forming glands separated by stroma; lined by mucinous columnar cells, goblet cells and rarely, Paneth cells
  - **Endometrioid:** glandular pattern resembling conventional or secretory **endometrial endometrioid carcinoma** (subnuclear and sometimes supranuclear vacuoles resembling secretory endometrium)
  - **Parietal:** extracellular deposits of basement membrane material, usually within reticular foci and surrounding groups of tumor cells
  - **Festoon:** undulating ribbons, occasionally with a drape-like arrangement
  - **Tubular**

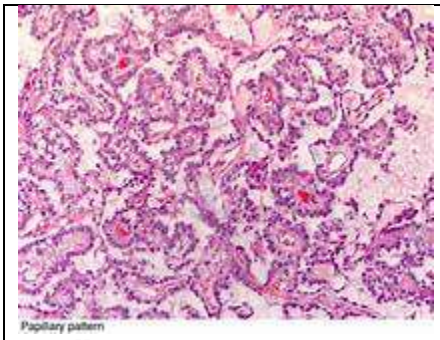
- **Papillary**

Positive stains

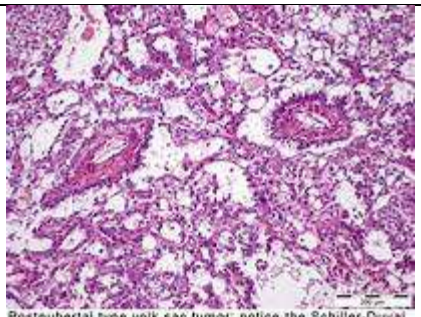
- AFP (gold standard, patchy expression), glypican 3 (less specific but stronger expression), SALL4 (Arch Pathol Lab Med 2014;138:351)
- AE1/3
- In areas with:
  - Hepatic differentiation: HepPar1 (Int J Gynecol Pathol 2014;33:365)
  - Intestinal differentiation: CDX2, villin
  - Foregut derived epithelium: TTF1

Negative stains

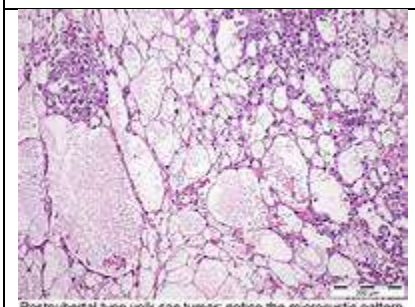
- OCT3/4, SOX2, D2-40, CD117, PLAP, CD30, b-HCG



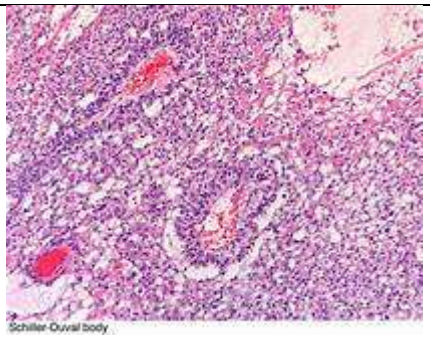
Papillary type



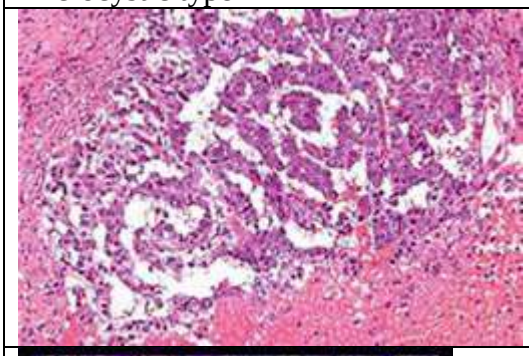
Schiller Duval bodies

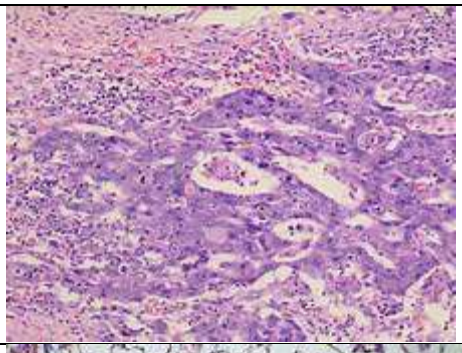


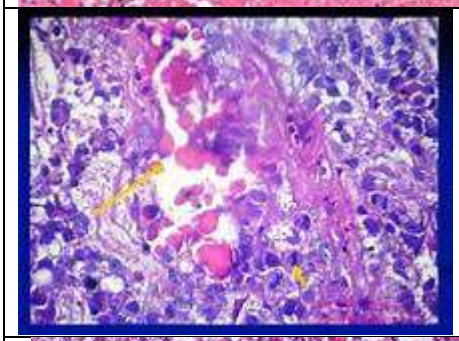
Microcystic type

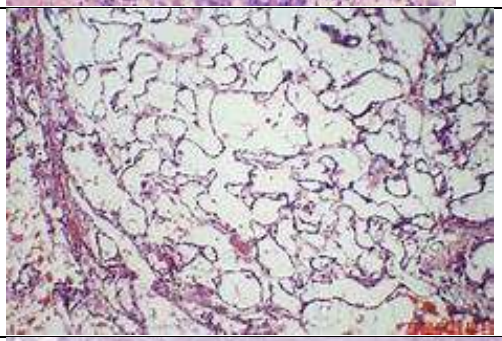


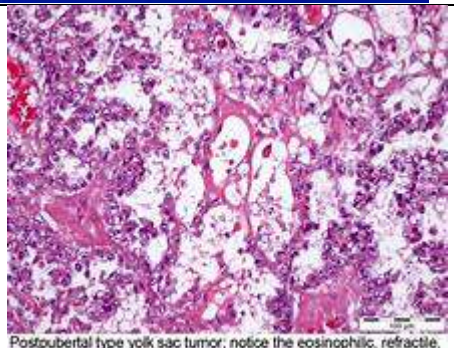
Schiller Duval bodies

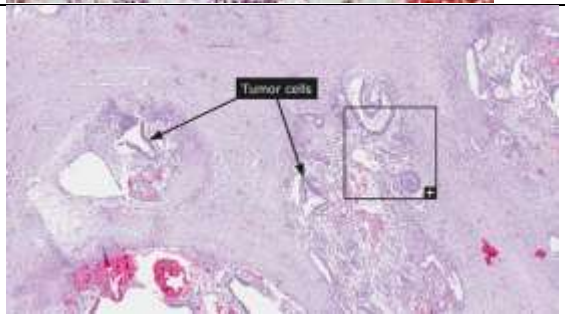


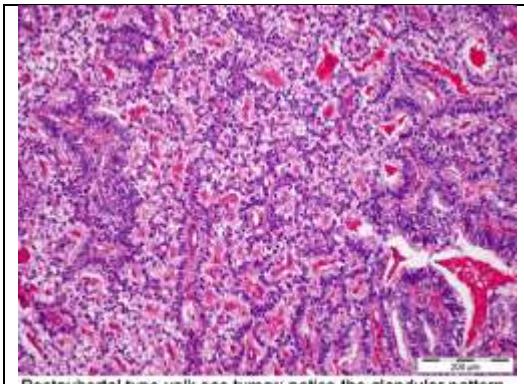












Postpubertal type yolk sac tumor; notice the glandular pattern, formed by packed anastomosing / branching glands