Testicular Cancer

Osmosis ™

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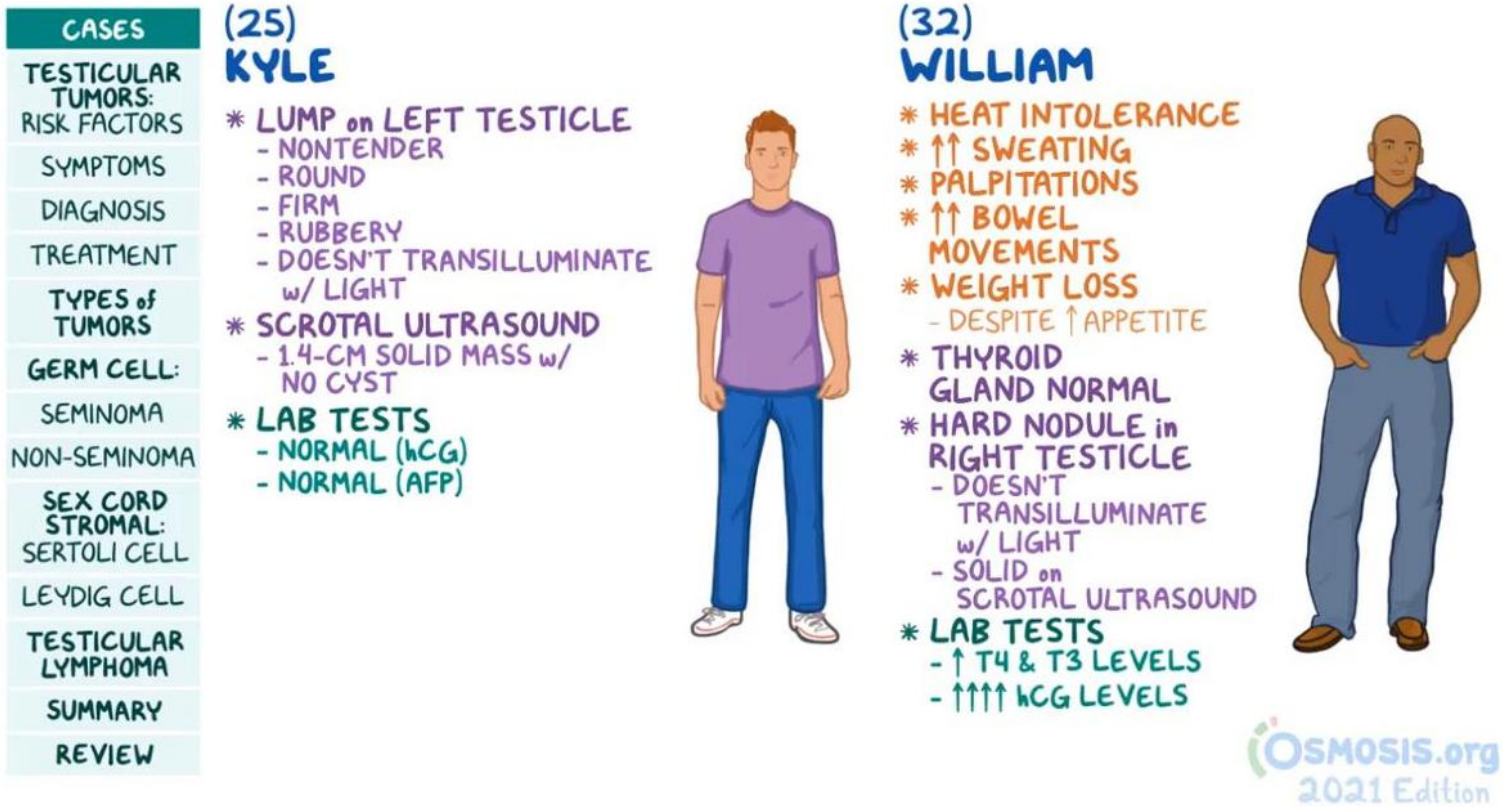
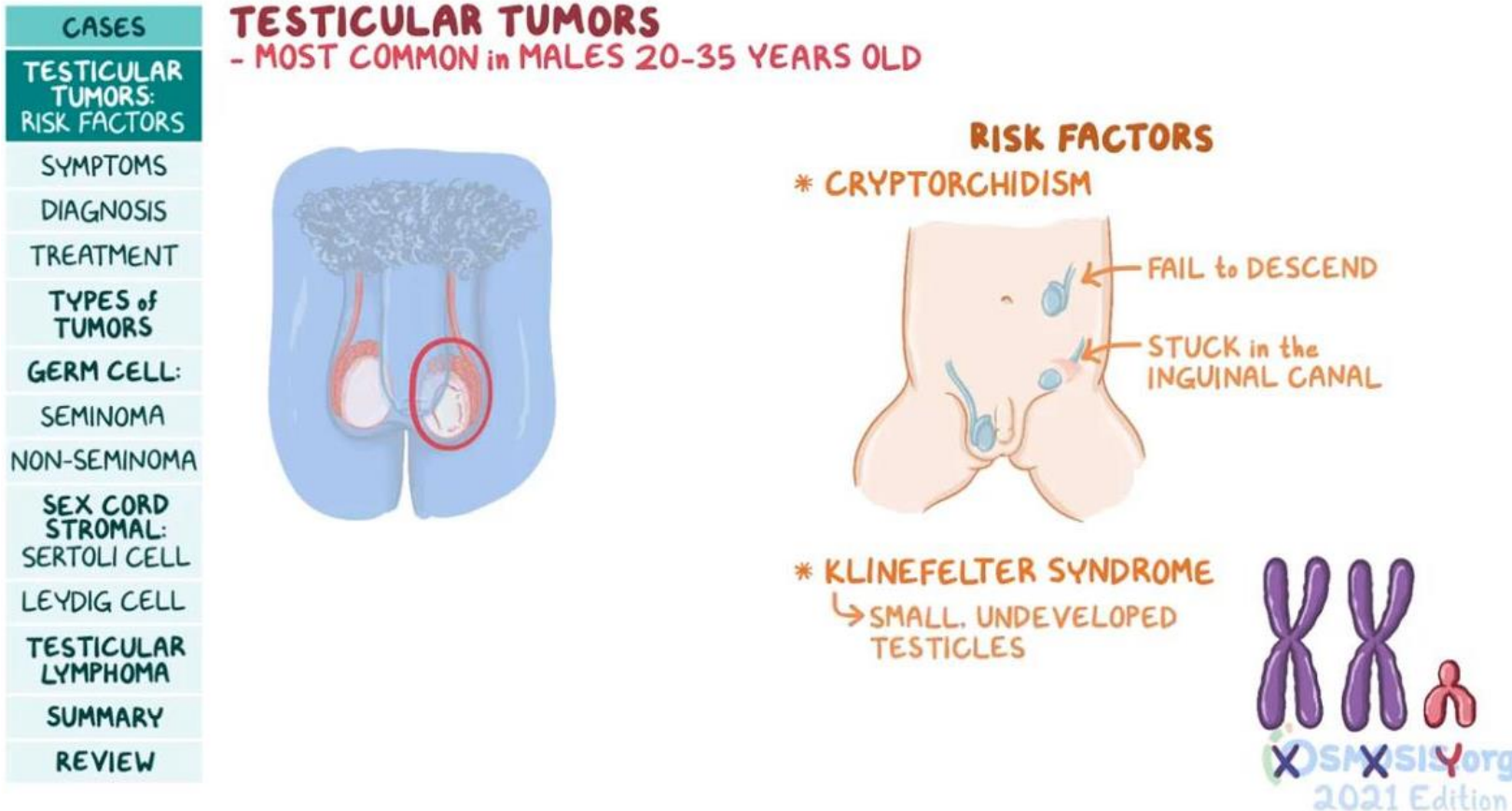
https://www.osmosis.org/learn/Testicular_tumors:_Pathology_review

Learning objectives

1. List the risk factors for testicular cancer
2. Describe the most common presenting signs and symptoms of testicular cancer including advanced disease
3. Describe the significance of tumor markers and imaging in staging testicular cancer
4. Outline the role of chemotherapy, radiation therapy and retroperitoneal lymph node dissection in the management of testicular cancer



25-year-old Kyle comes to the office after palpating a lump on his left testicle while showering this morning.
On physical examination, there is a nontender, round, firm, rubbery mass in the left testicle that does not transilluminate with light. Scrotal ultrasound shows a 1.4-cm solid mass with no cystic components. Laboratory tests reveal normal serum human chorionic gonadotropin or hCG level, and normal α-fetoprotein or AFP level.
Later that day, 32-year-old William comes to the physician's office complaining of heat intolerance, excessive sweating, palpitations, frequent bowel movements and recent weight loss despite increased appetite. His past medical history is insignificant. On examination, the thyroid gland is normal with no signs of goiter or nodules. However, a hard nodule is palpated in the right testicle which does not transilluminate with light and appears solid on scrotal ultrasound. Laboratory studies show increased serum T4 and T3 levels as well as extremely elevated hCG levels. Based on the initial presentation, Kyle and William both have some form of testicular mass.



Okay, now, for your exams, it's important to know that the main risk factors for developing testicular cancer, especially the germ cell variety, include cryptorchidism, which is when the testicles fail to descend to the scrotum or get stuck in the inguinal canal, as well as Klinefelter syndrome, where biological male individuals inherit more than one X chromosome leading to small, undeveloped testicles.

Histology of Cryptochidism

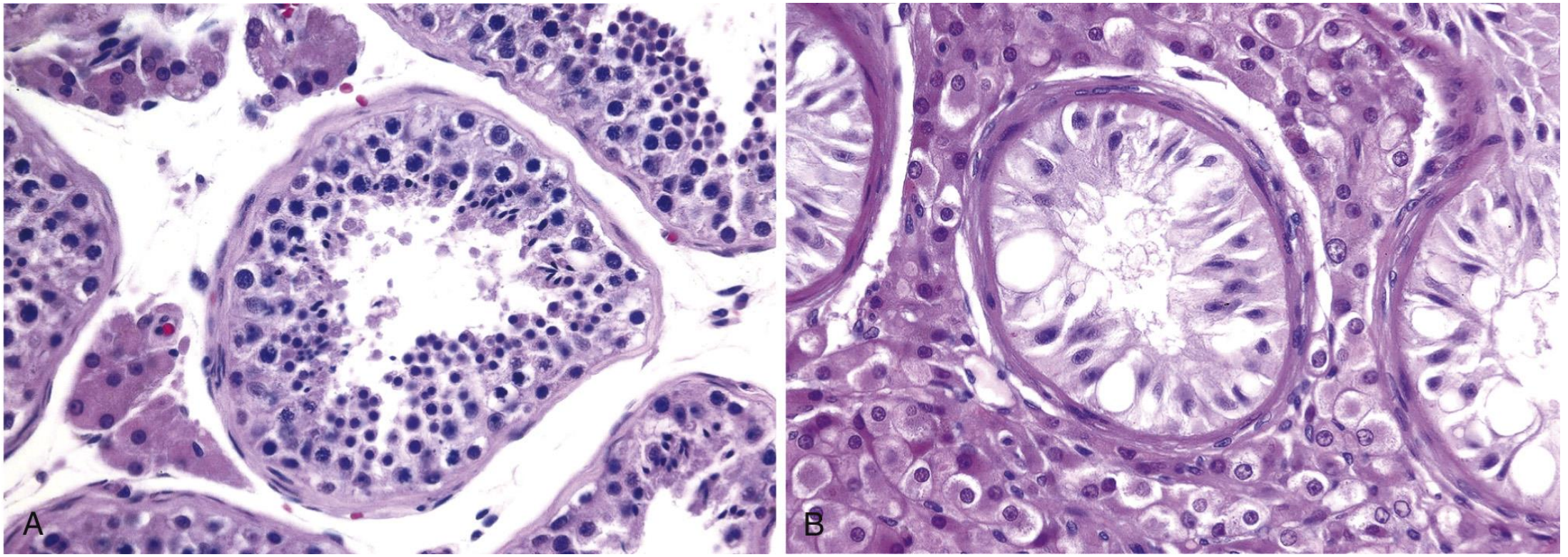
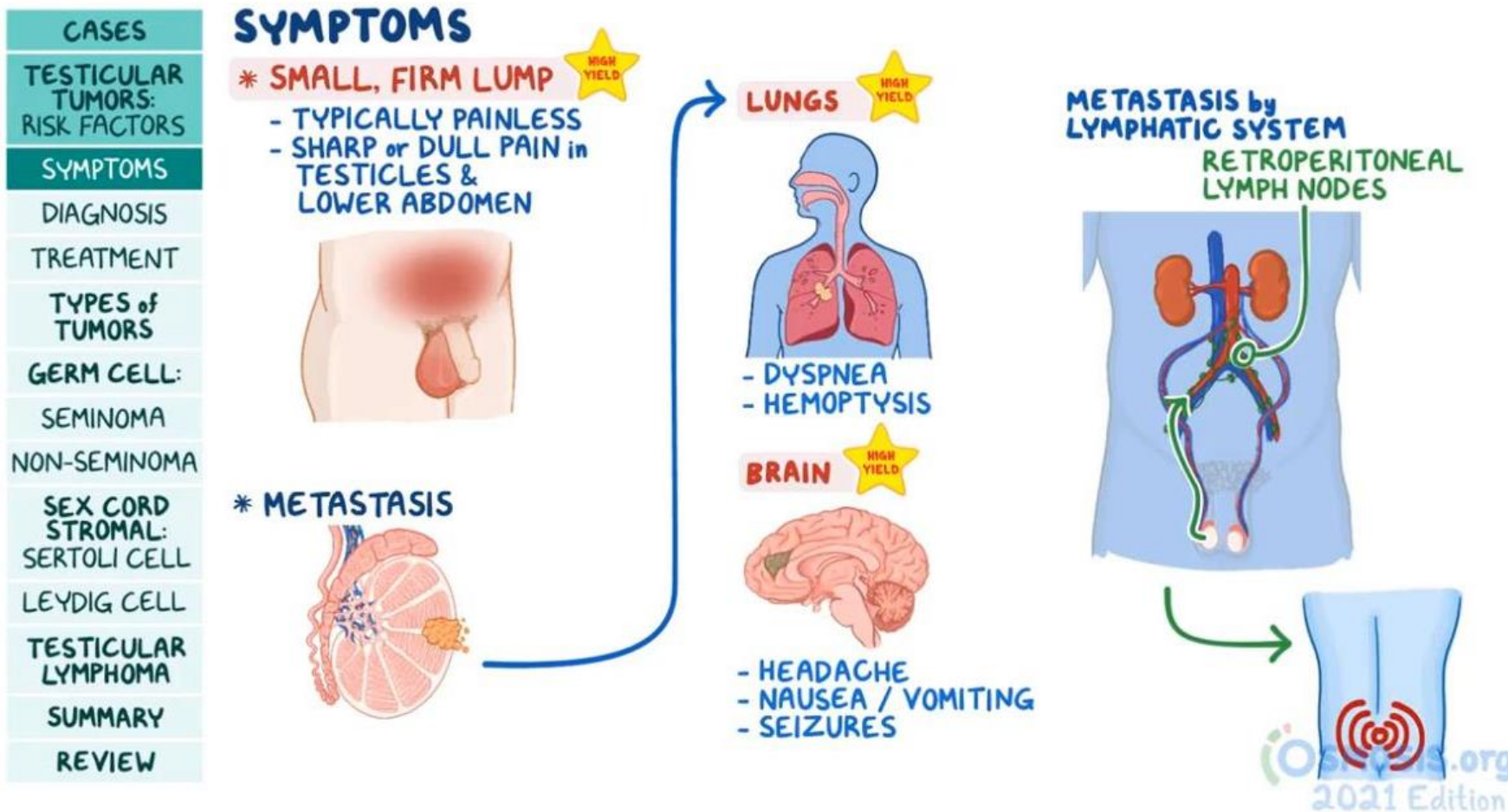
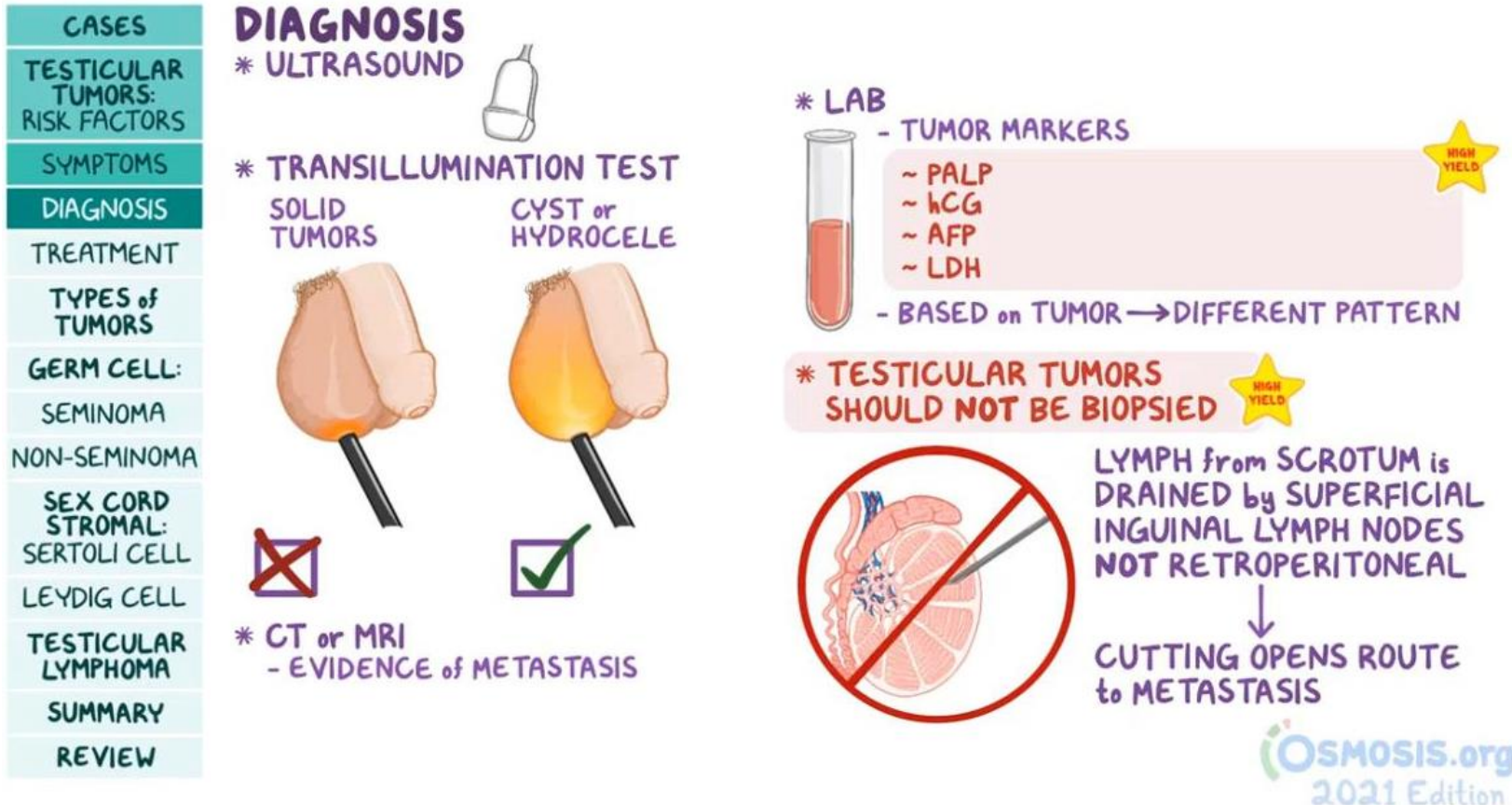


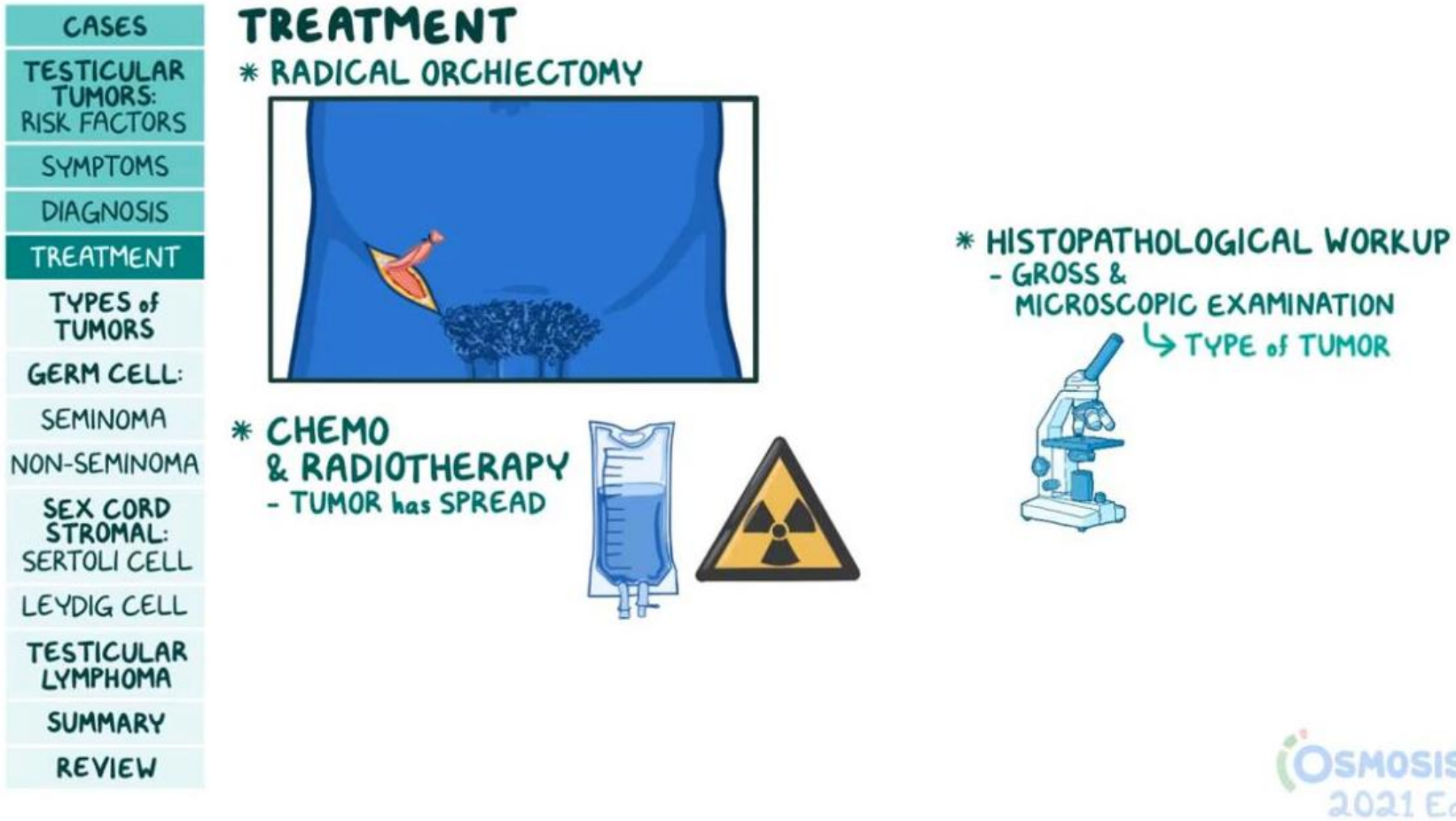
Figure 21.15 Cryptorchidism. (A) Normal testis shows tubules with active spermatogenesis. (B) Cryptorchid testes are small and firm. The histologic changes in the malpositioned testis begin as early as 2 years of age. Early on, **thickening of the basement membrane** of the spermatic tubules is seen Subsequent loss of spermatogonia leaves the tubules with only Sertoli cells. The scarred tubules may appear as dense cords of hyaline connective tissue associated with a concomitant increase in interstitial stroma. Leydig cells are spared and therefore appear relatively prominent. Similar histologic changes may also be seen in the contralateral (descended) testis in males with unilateral cryptorchidism, suggesting that cryptorchidism is a marker of an intrinsic defect in gonadal development.



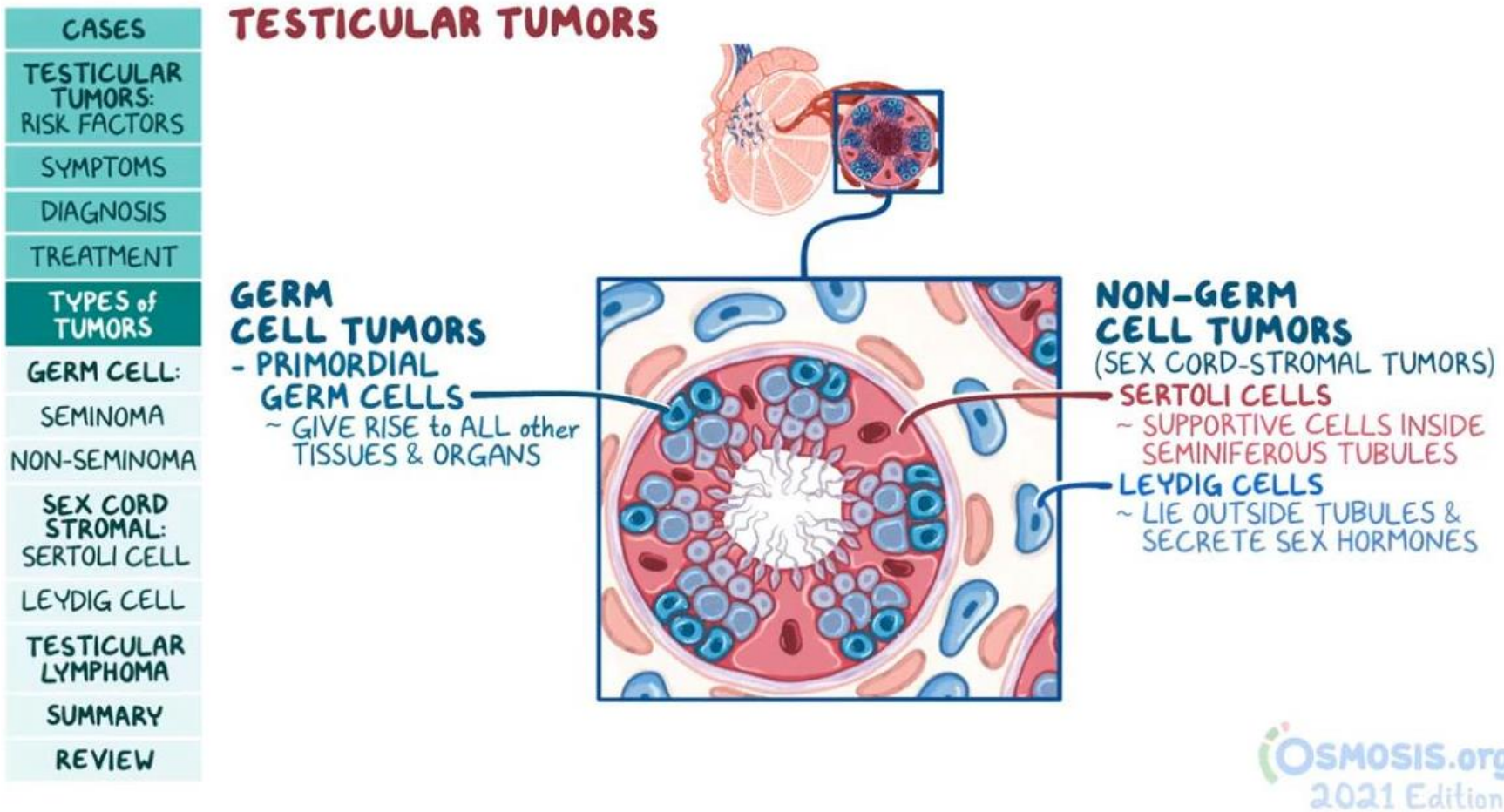
For symptoms, a testicular tumor most often comes up as a small, firm lump that is typically painless, but can sometimes cause a sharp or dull pain in the testicles and lower abdomen. In more severe cases, symptoms may arise from a malignant tumor metastasizing to other organs. This is most commonly hematogenous to the lungs, leading to dyspnea or hemoptysis, which is the coughing of blood, or to the brain, leading to headache, nausea, vomiting or seizures. Another way for the cancer cells to metastasize is by the testicular lymphatic system that drains into retroperitoneal lymph nodes. Metastasis to these lymph nodes leads to symptoms like lower back pain.



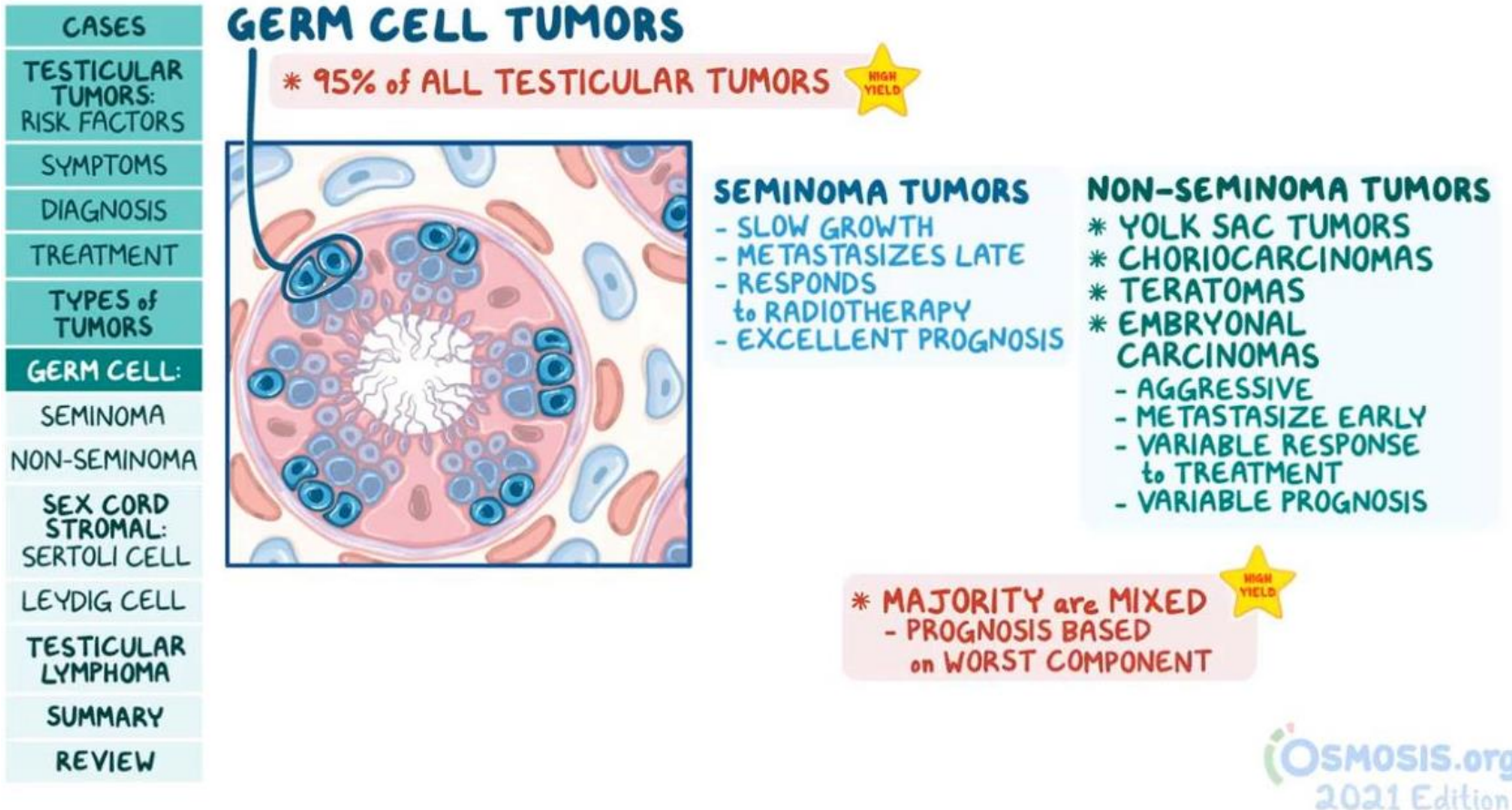
Now, once a lump has been palpated in the testis, diagnosis can be confirmed with an ultrasound.
Also remember that in a transillumination test solid tumors do not transilluminate with light, while hydrocele and cysts do.
Imaging with CT or MRI scan can then be done to look for evidence of metastasis if carcinoma is suspected.
Next, lab tests are used to measure levels of tumor markers like PALP, hCG, and AFP. LDH could also be measured, but it's not very specific. Based on the type of testicular tumor, these markers rise in a different pattern. And that's a popular way for examiners to clue you in a particular type of tumor. Another very high-yield fact that you should absolutely remember is that testicular tumors should not be biopsied. That's because the lymph from the scrotum is drained by the superficial inguinal lymph nodes and not the retroperitoneal ones. So cutting into the scrotum would open an additional route for the cancer cells to escape and metastasize.



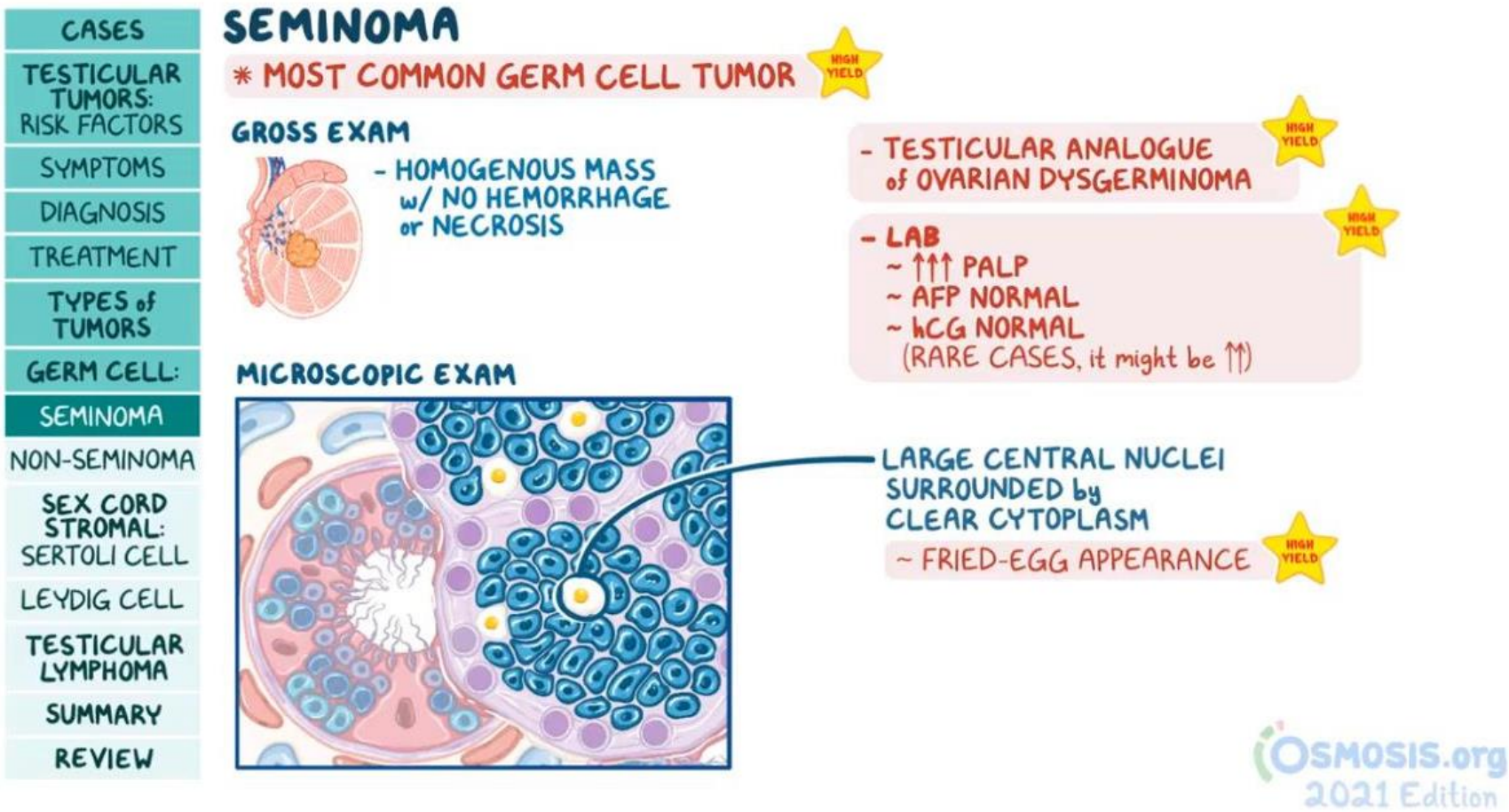
Treatment involves surgical removal of the whole testicle called radical orchiectomy, followed by chemotherapy and radiotherapy if the tumor has spread. After the removal a histopathological work up can be done, involving gross and microscopic examination, to determine the type of the tumor.



Alright, now, there are two types of testicular tumors: germ cell tumors, which derive from primordial germ cells which are the cells that can give rise to all other tissues and organs, and non-germ cell tumors or sex cord-stromal tumors which arise from Sertoli cells, which are supportive cells inside the seminiferous tubules, or Leydig cells which lie outside the tubules and secrete sex hormones.

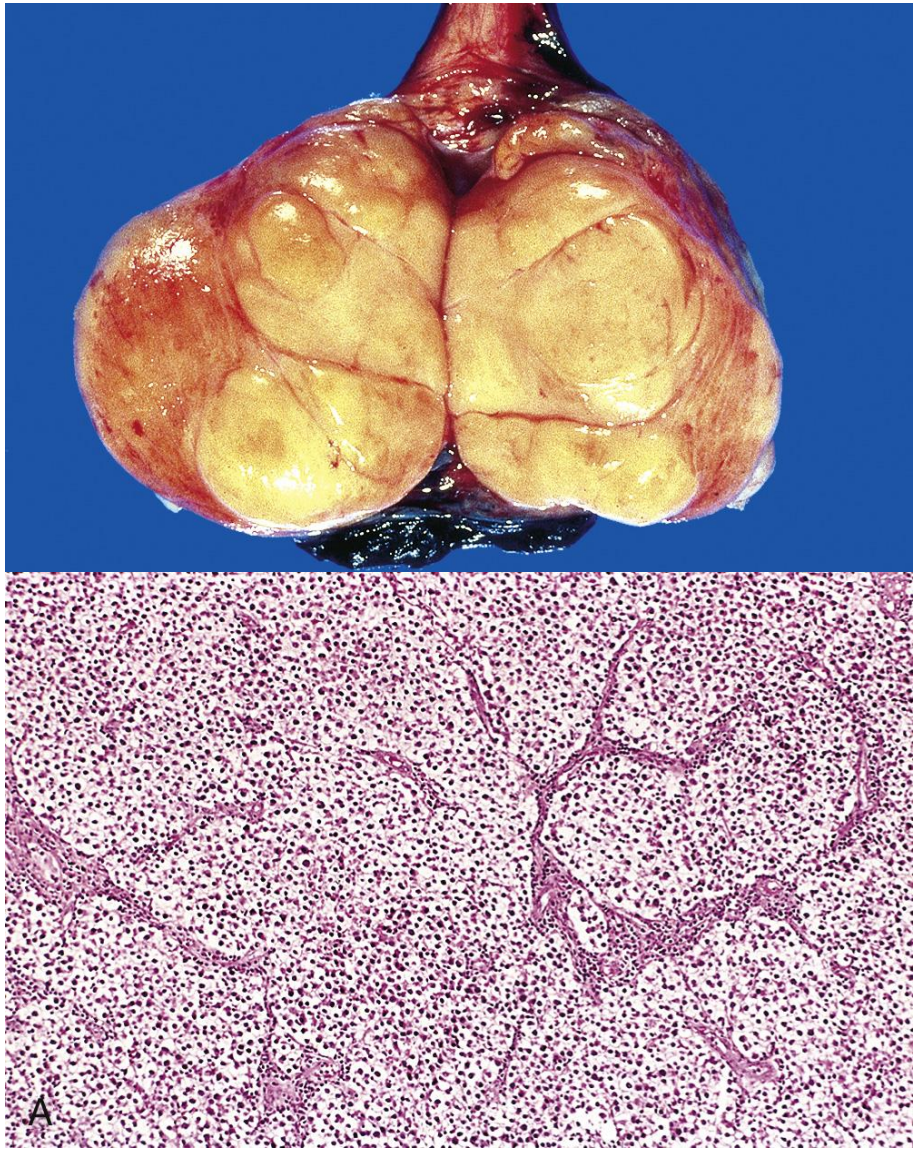


Starting with germ cell tumors, a high-yield fact is that they comprise almost 95% of all testicular tumors.
They can be classified into seminoma tumors, and non-seminoma tumors, which include yolk sac tumors, choriocarcinomas, teratomas and embryonal carcinomas. The reason behind this classification is that a seminoma, in general, has a slow growth, metastasizes late, responds very well to radiotherapy and has an excellent prognosis.
In contrast, non-seminoma tumors are overall more aggressive, metastasize early, have a variable response to treatment and a variable prognosis. However, it’s important to know that the majority of germ cells tumors are mixed and the prognosis is based on the worst component.



Okay, so seminoma is the most common type of germ cell tumor. For your exams, remember that gross examination of this tumor typically shows a homogenous mass with no hemorrhage or necrosis. On microscopic examination, tumor cells are large with central nuclei surrounded by clear cytoplasm. A key word for that is a “fried-egg appearance”. Another high-yield thing to know is that this is the testicular analogue of ovarian dysgerminoma. Now, lab tests may show increased PALP levels, however, remember that AFP levels are always normal. hCG is usually also normal, but in rare cases, it might be increased.

Gross and histopathology of Seminoma



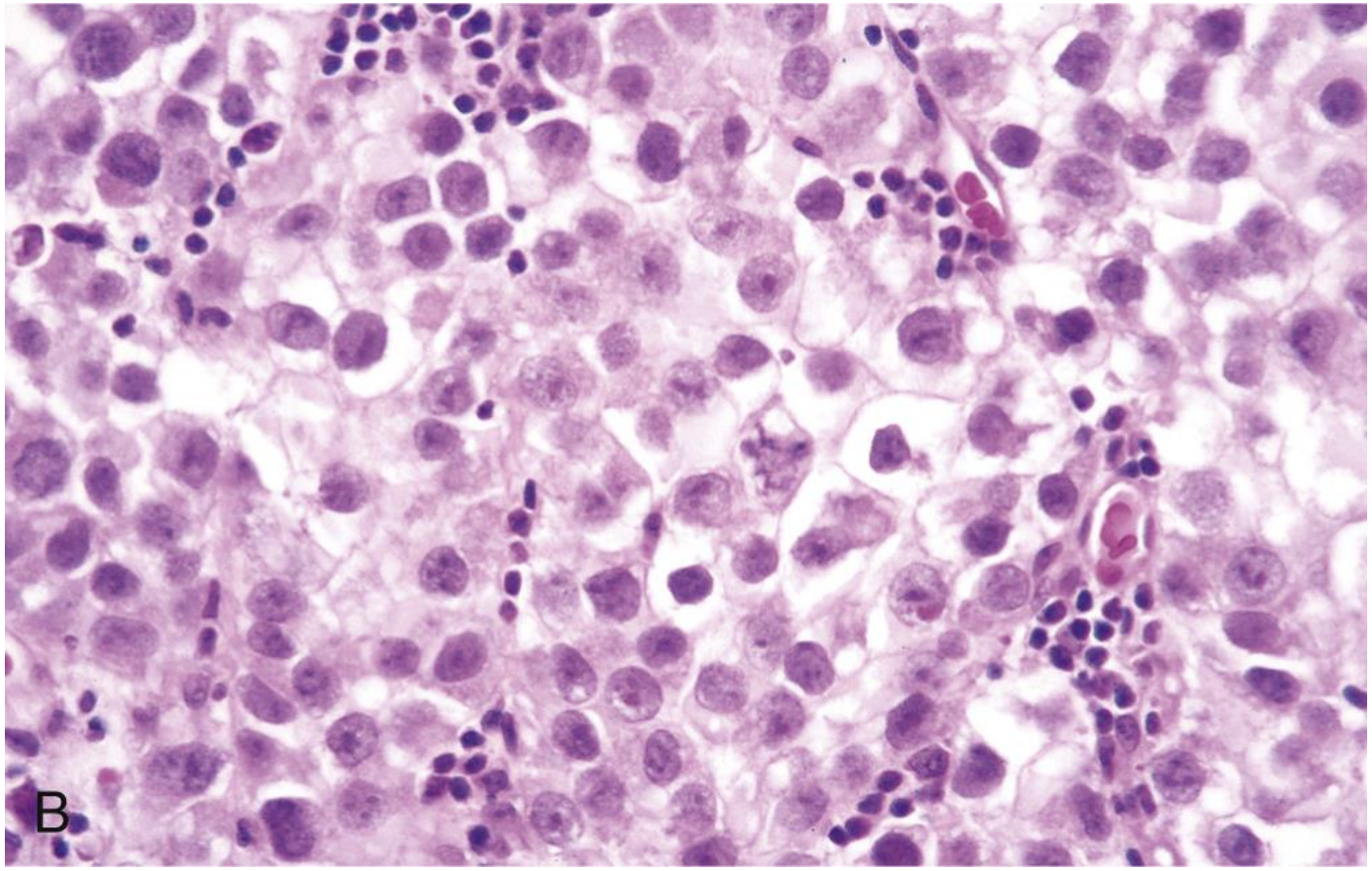
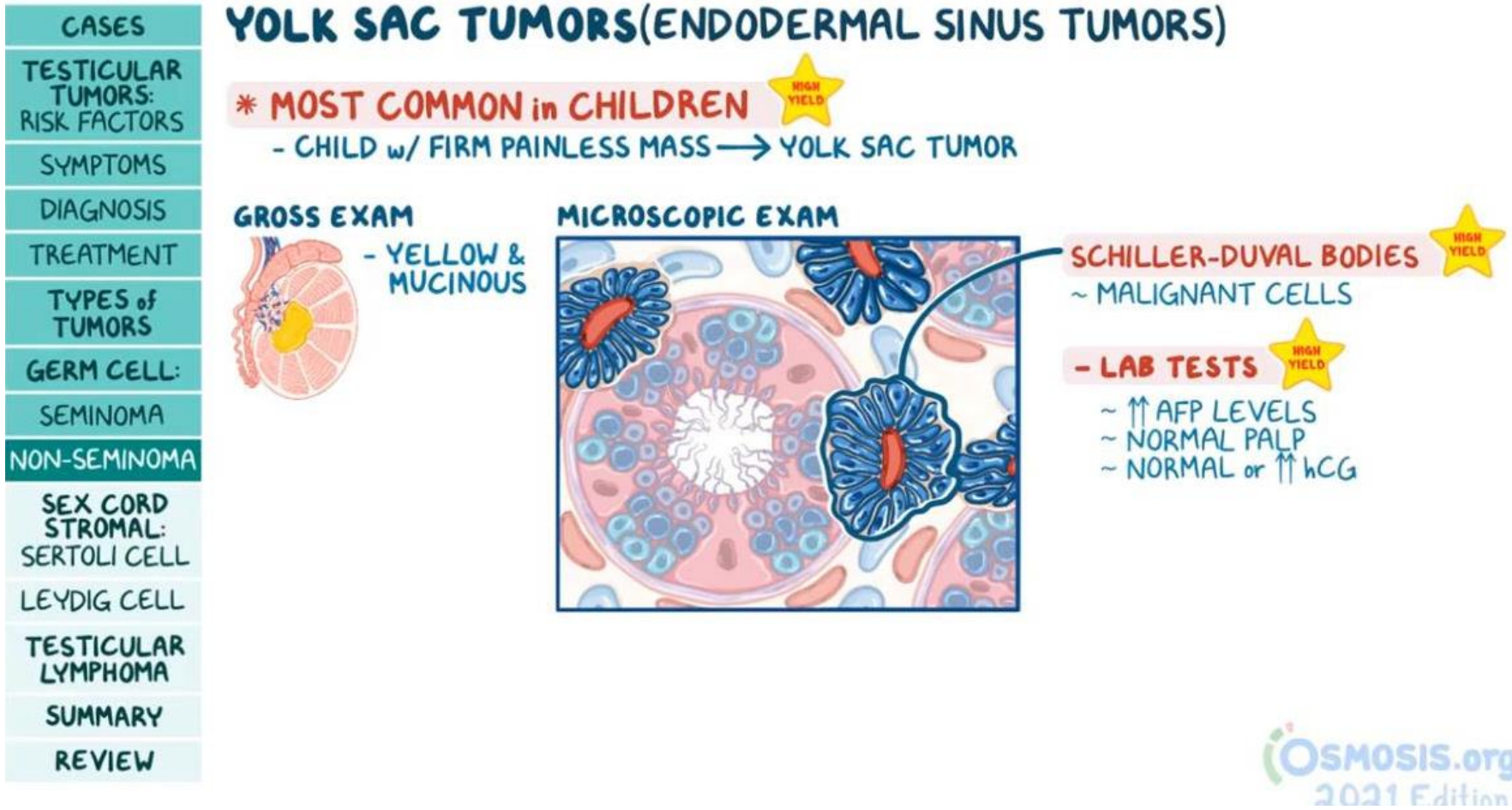


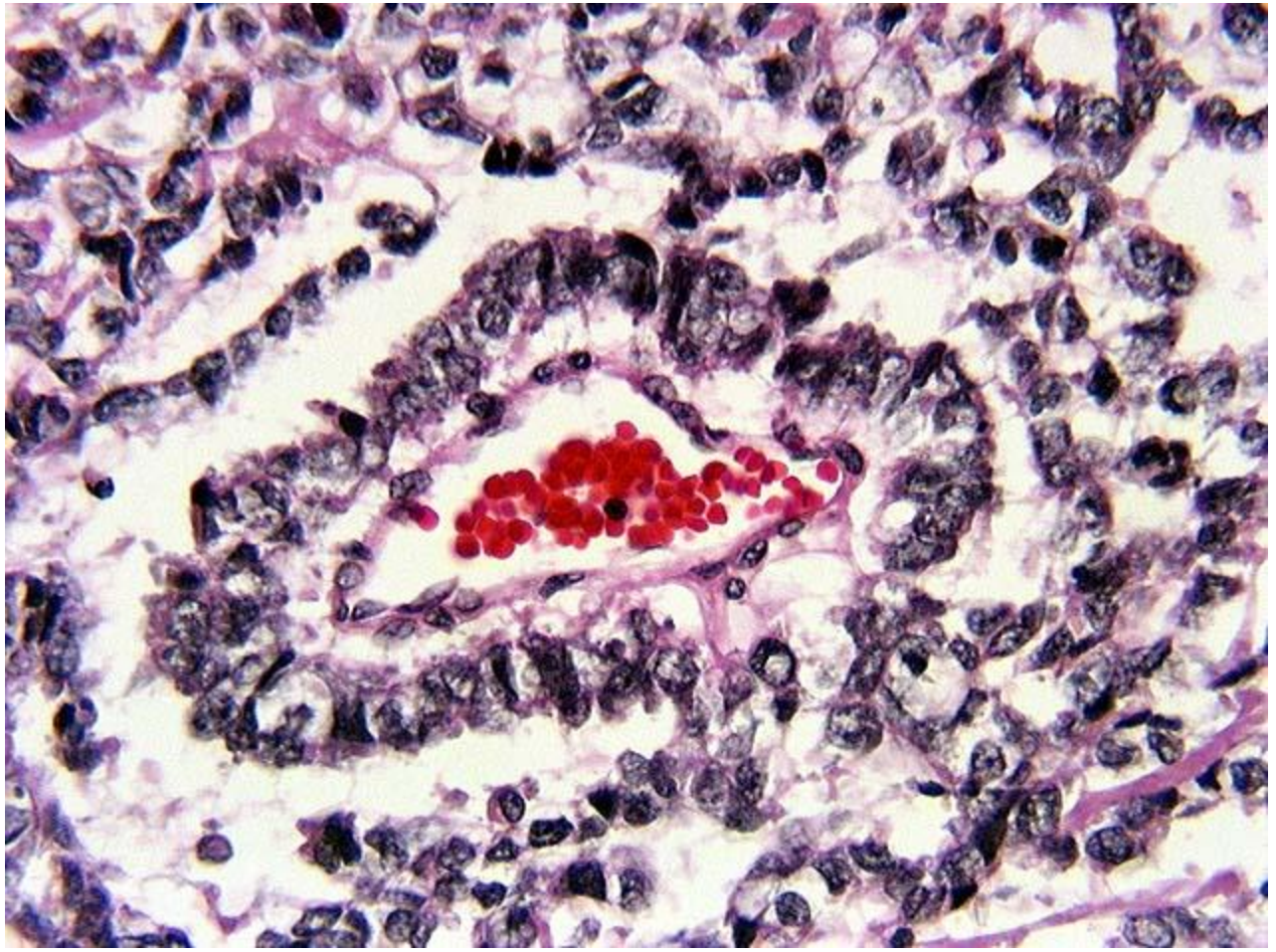
Figure 21.19 (A) Seminoma of the testis, appearing as a well-circumscribed, pale, fleshy, homogeneous mass on cut surface. (B) Low magnification shows sheets of pale tumor cells divided into poorly demarcated lobules by delicate septa containing reactive lymphocytes. (C) High magnification reveals large cells with distinct cell borders, pale nuclei, prominent nucleoli, and abundant cytoplasm.



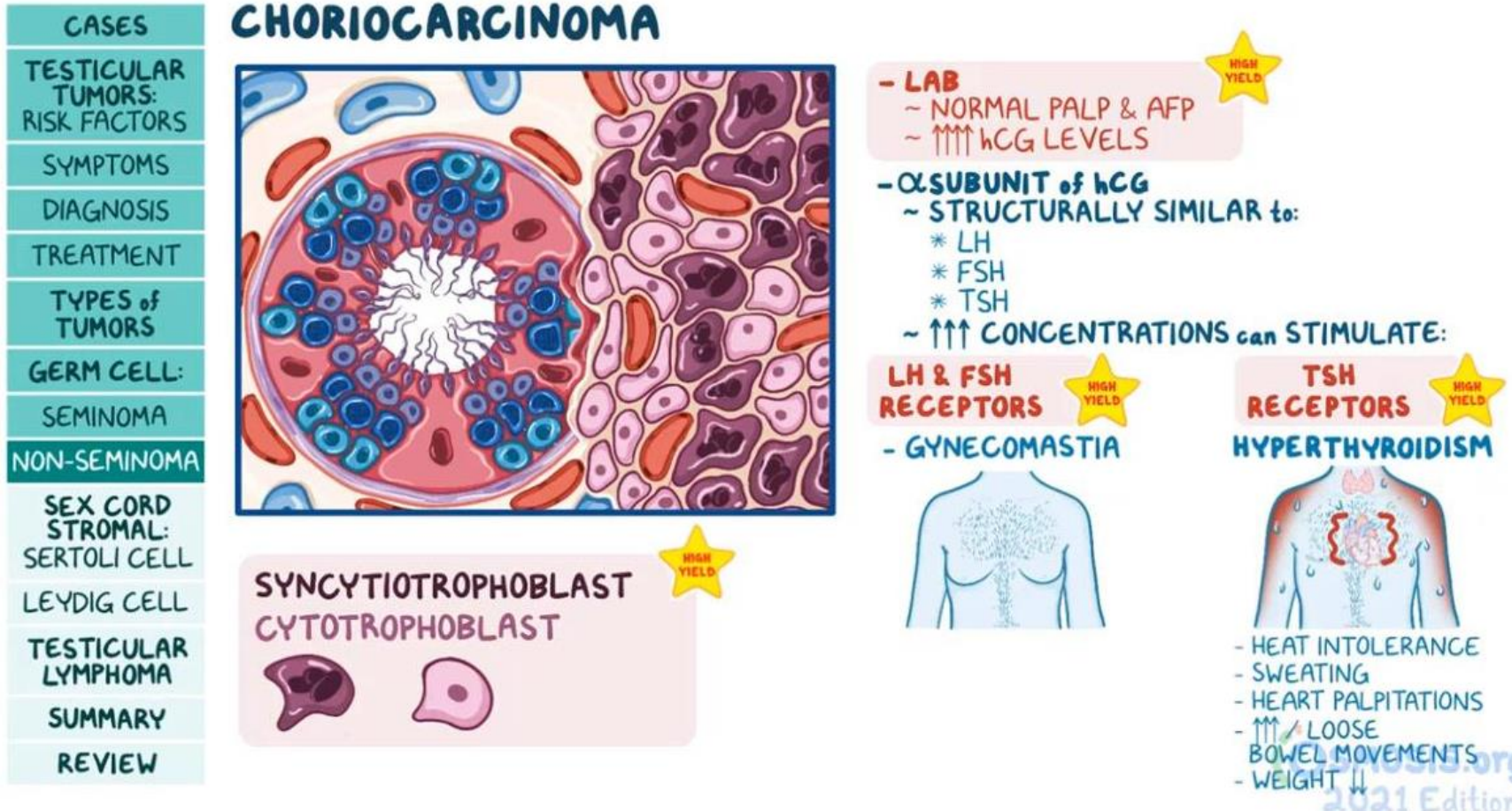
Moving on to non-seminomatous tumors, let's start with yolk sac tumors, also known as endodermal sinus tumors. What's high-yield here is that these are the most common testicular tumor in children. So, if a test question is about a child, particularly younger than 3 years old, with a firm, painless testicular mass, think of yolk sac tumor at the top of your differentials. On gross examination, this type of tumor is typically yellow and mucinous. A key thing to keep in mind is that, under the microscope they form glomeruloid structures or Schiller-Duval bodies, which are rings of malignant cells around the central blood vessel. Lab tests classically show elevated AFP levels, with normal PALP and normal or increased hCG.

yolk sac tumors (aka endodermal sinus tumors)

: Glomeruloid structures or Schiller-Duval bodies



https://path.upmc.edu/cases/case152/images/micro10.jpg



Next, there's choriocarcinoma. Under the microscope these tumors contain two types of large cells, cytotrophoblasts with central nuclei and pale cytoplasm, and syncytiotrophoblasts that have multiple nuclei and darker cytoplasm. For your test, remember that lab tests will show normal PALP and AFP, but extremely elevated hCG levels. Now, the alpha subunit of hCG is structurally similar to luteinizing hormone or LH for short, follicle stimulating hormone or FSH for short and thyroid-stimulating hormone or TSH for short. So, in very high concentrations, it can go and stimulate LH and FSH receptors in the breast, resulting in gynecomastia or TSH receptors, causing symptoms of hyperthyroidism, like heat intolerance, sweating, palpitations, frequent or loose bowel movements and weight loss. So if a question describes a male with gynecomastia or hyperthyroidism, hCG levels over the roof and a testicular lump, it's most probably choriocarcinoma.

Histology of Choriocarcinoma

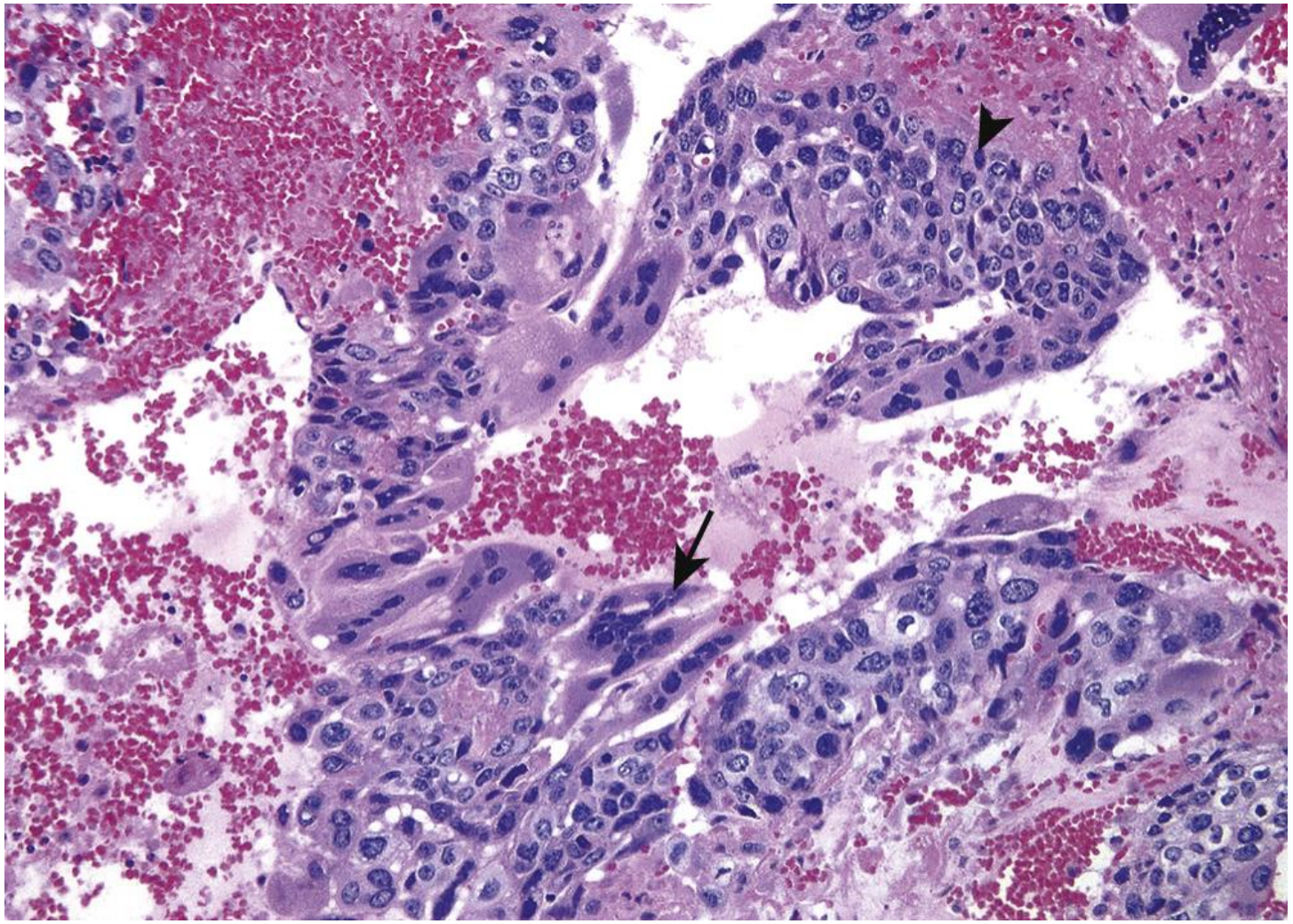
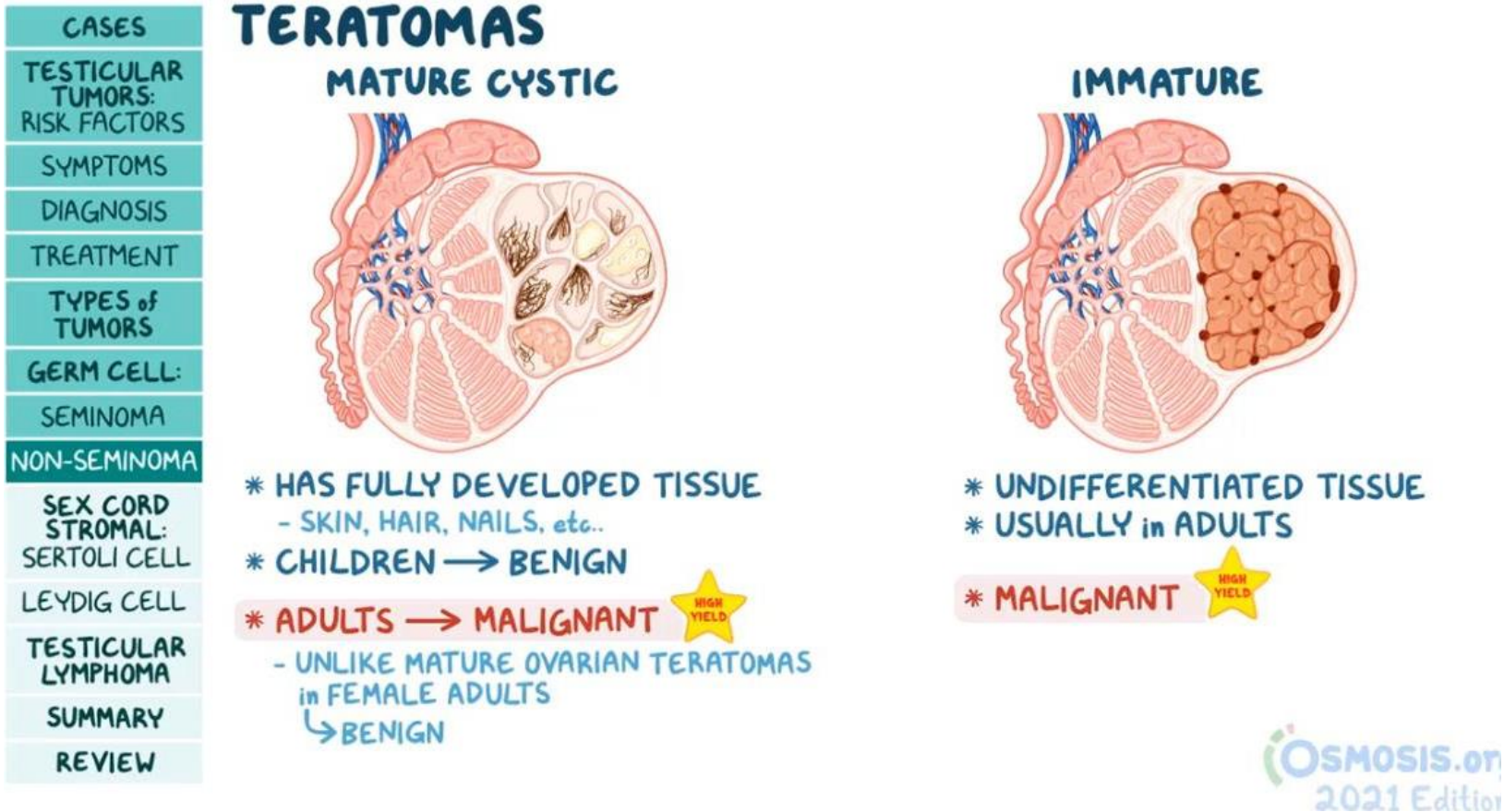


Figure 21.23Choriocarcinoma. Both cytotrophoblastic cells *(arrowhead)* with central nuclei and syncytiotrophoblastic cells *(arrow)* with multiple dark nuclei embedded in eosinophilic cytoplasm are present. Hemorrhage and necrosis are seen in the upper right field.



Another type of germ cell tumors are teratomas. There are actually two types of teratomas. The first is mature teratoma that has fully developed tissue inside, like skin, hair, nails etc. It usually appears in children and is typically benign. But, what's high-yield is that when it appears in adults, it tends to be malignant. This is unlike mature ovarian teratomas in female adults, which tend to be benign. The other type is immature teratoma which has undifferentiated tissue, usually appears in adults and also tends to be malignant.

Gross and histopathology of teratoma

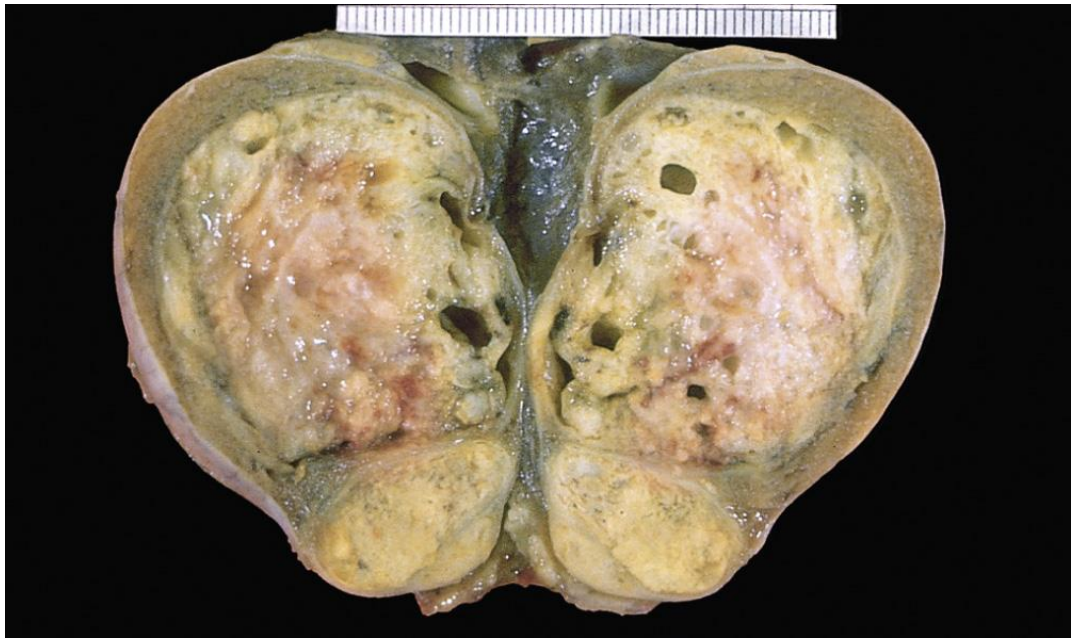


Figure 21.24Teratoma of testis. The variegated cut surface with cysts reflects the presence of multiple tissue types.

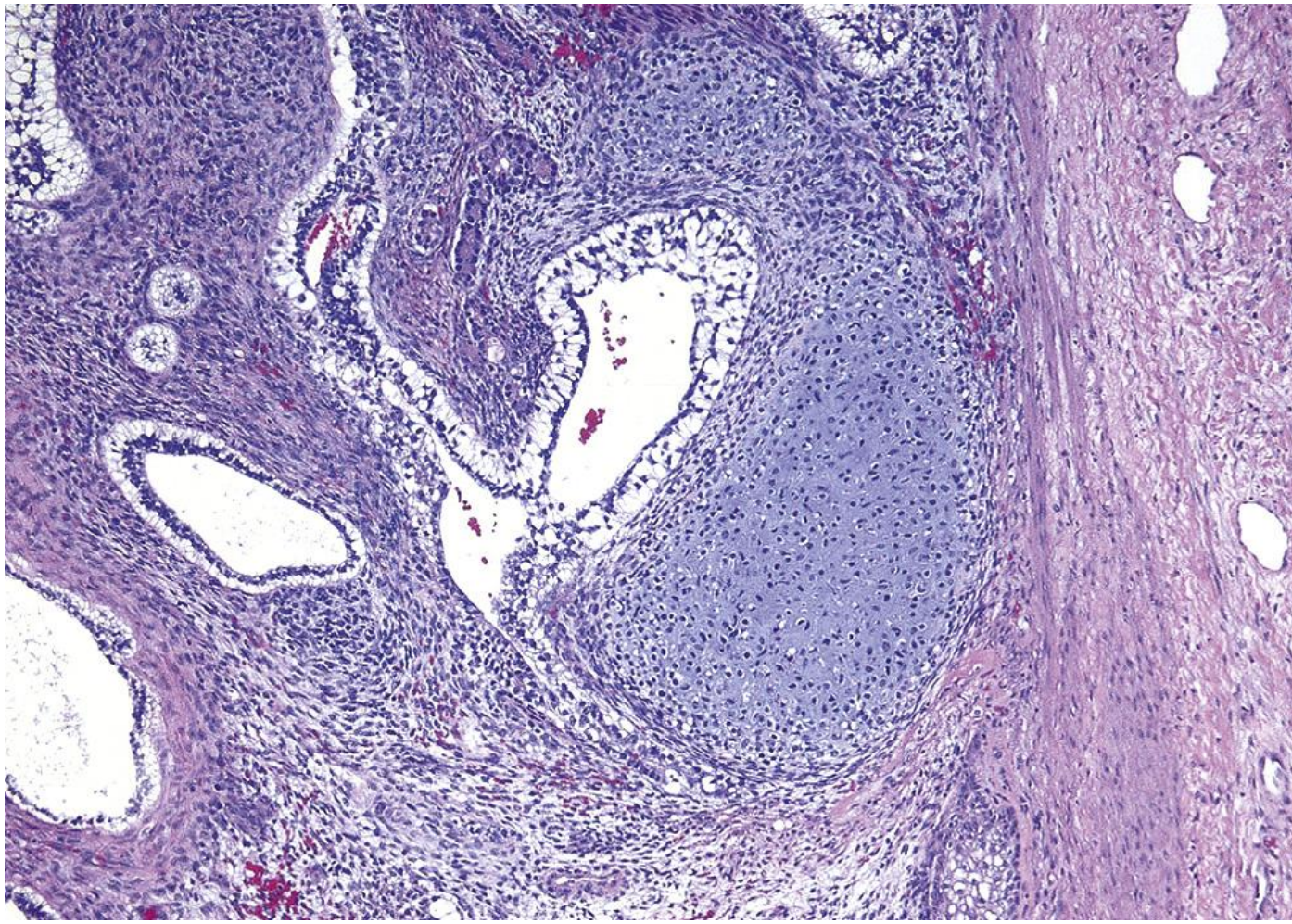
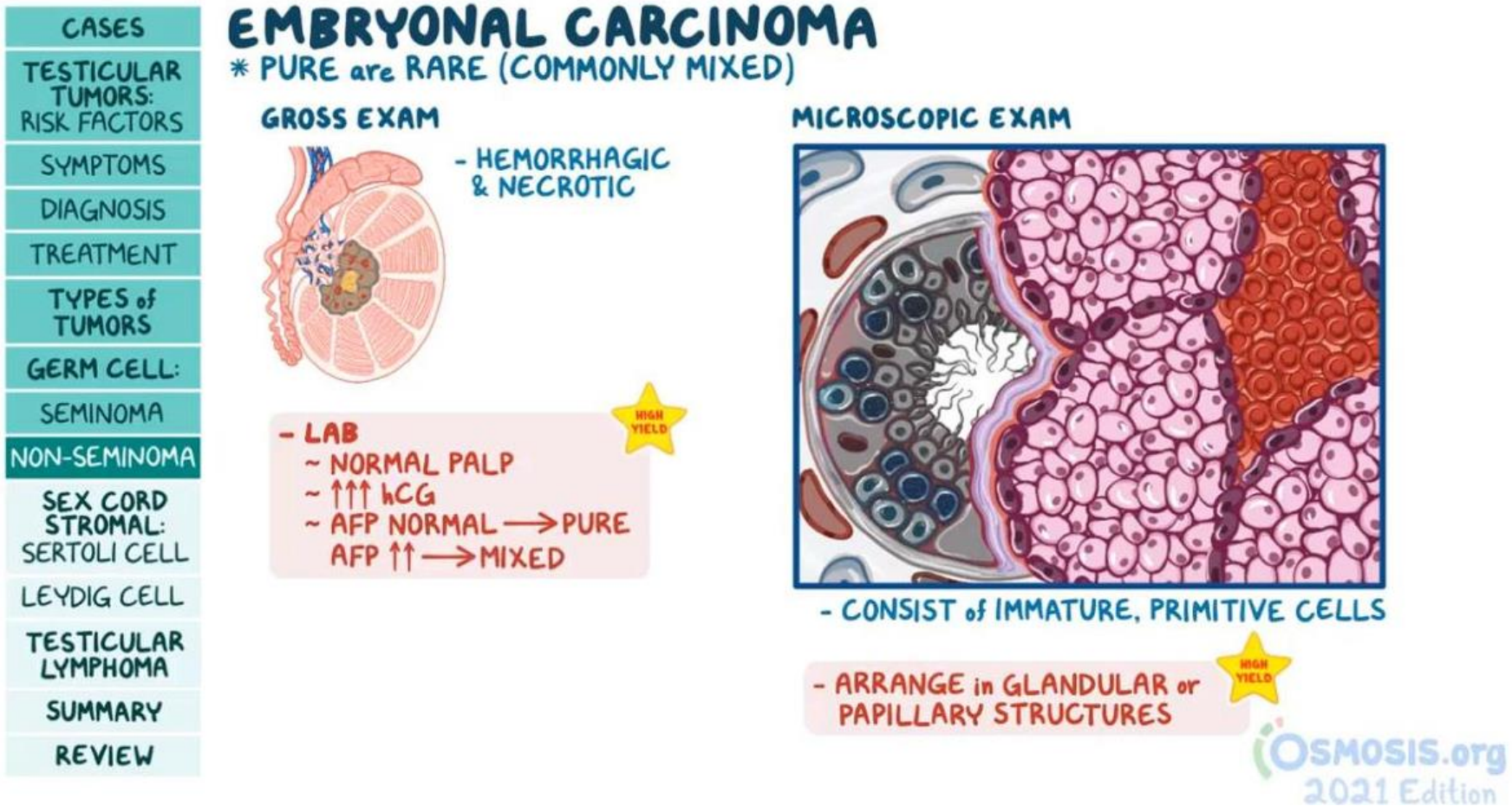


Figure 21.25. Teratoma of the testis, consisting of a disorganized collection of glands, cartilage, smooth muscle, and immature stroma.



Finally, there's embryonal carcinoma. Pure embryonal carcinomas are rare, but are very commonly mixed with other types of germ cell tumors. On gross examination, they are usually hemorrhagic and necrotic. Under the microscope, they consist of immature, primitive cells which tend to arrange in glandular or papillary structures. And that's actually a frequently tested fact! Lab tests may show normal PALP levels, elevated hCG levels, while AFP is normal in pure embryonal carcinomas, but may be elevated when mixed.

Gross and histopathology of Embryonal Carcinoma

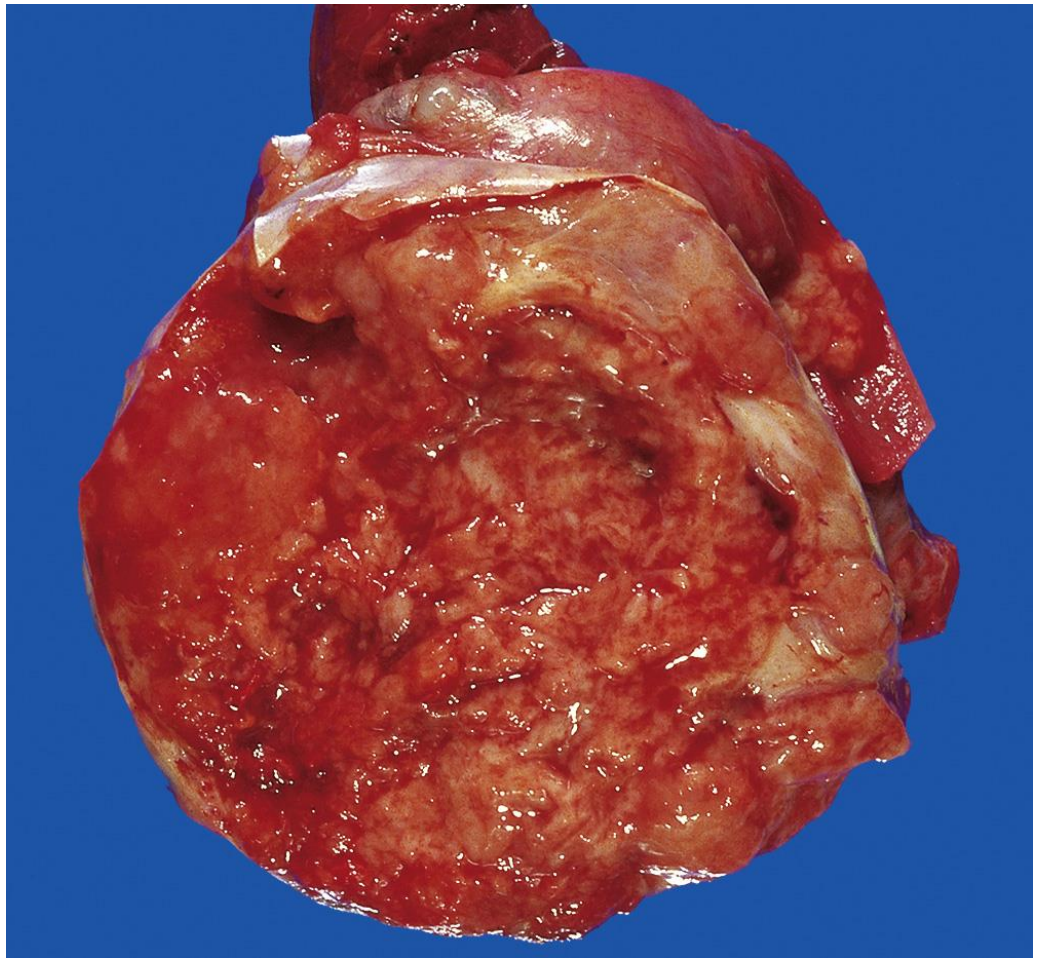


Figure 21.21 Embryonal carcinoma. In contrast to the seminoma embryonal carcinoma often produces a hemorrhagic mass.

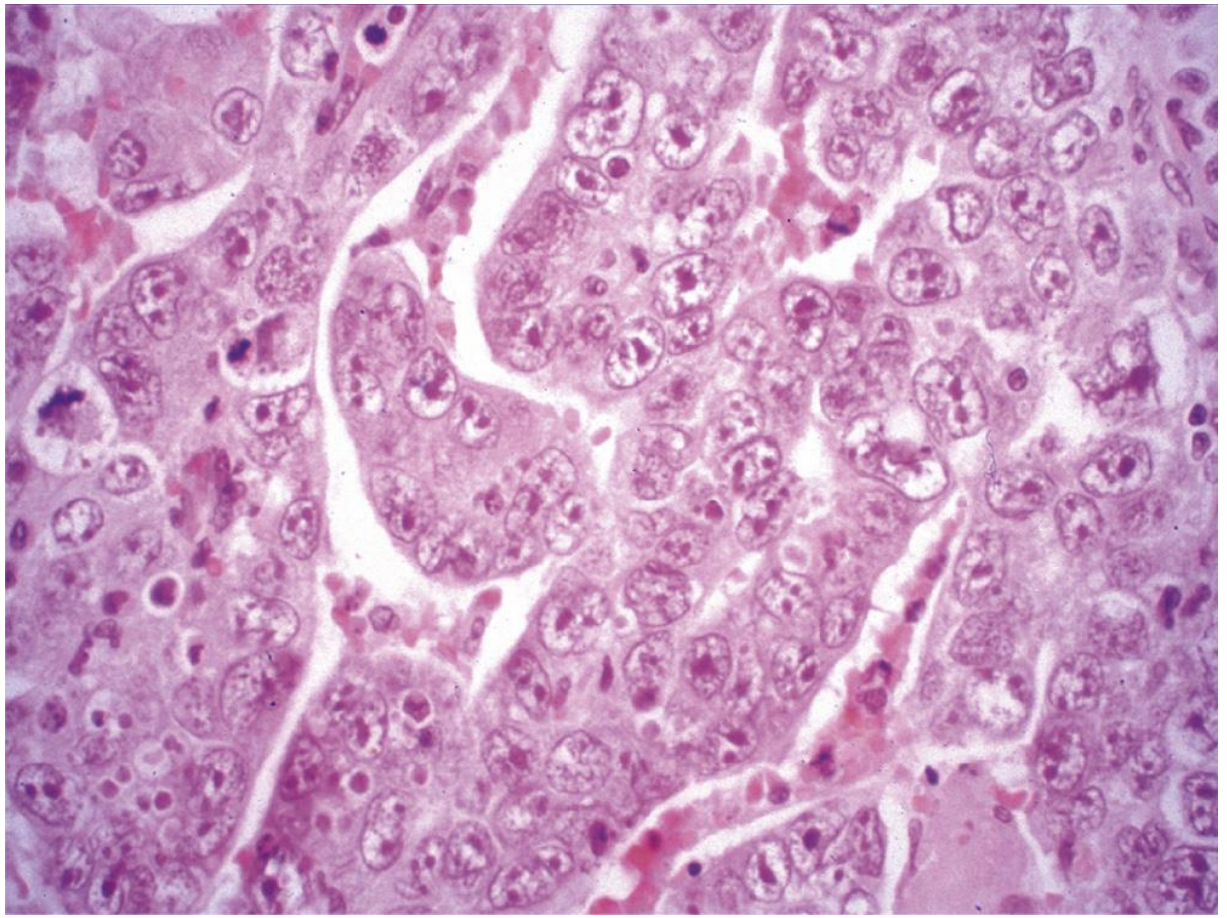
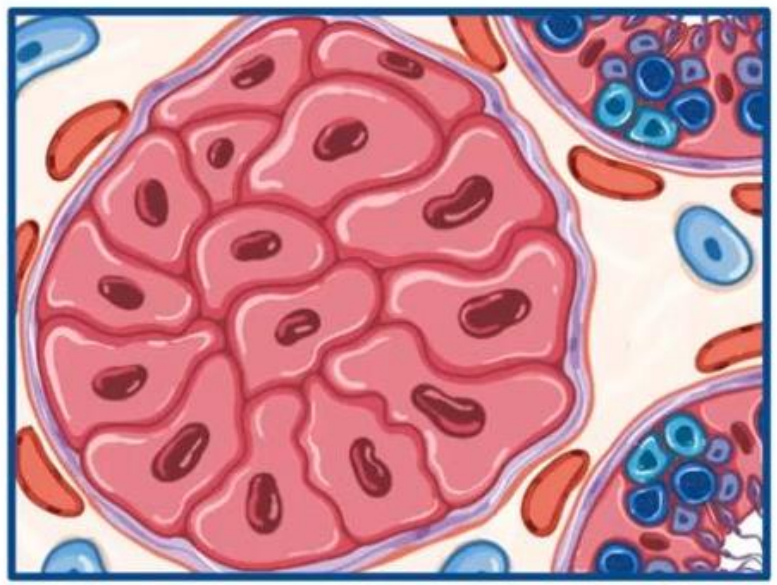


Figure 21.22Embryonal carcinoma composed of cells with large, hyperchromatic nuclei arranged in sheets and poorly formed glands.

CASES
TESTICULAR TUMORS: RISK FACTORS
SYMPTOMS
DIAGNOSIS
TREATMENT
TYPES of TUMORS
GERM CELL:
SEMINOMA
NON-SEMINOMA
SEX CORD STROMAL: SERTOLI CELL
LEYDIG CELL
TESTICULAR LYMPHOMA
SUMMARY
REVIEW

SEX CORD STROMAL TUMORS

* 5% of TESTICULAR TUMORS
* TYPICALLY BENIGN
* SERTOLI CELL TUMORS & LEYDIG CELL TUMORS
  - RARE
  - DON'T PRODUCE ANY HORMONES (HIGH YIELD)



- ORIGINATE INSIDE the SEMINIFEROUS TUBULES (HIGH YIELD)

Alright now that we've looked at the germ cell tumors, let's shift gears and go over the sex cord stromal tumors. These comprise the remaining 5% of testicular tumors, are typically benign, and include Sertoli cell tumors and Leydig cell tumors. Sertoli cell testicular tumors are rare, and don't produce any hormones. For your test, what you need to know is that, under the microscope, Sertoli tumor cells originate inside the seminiferous tubules.

Gross and Histopathology of Sertoli cell tumor

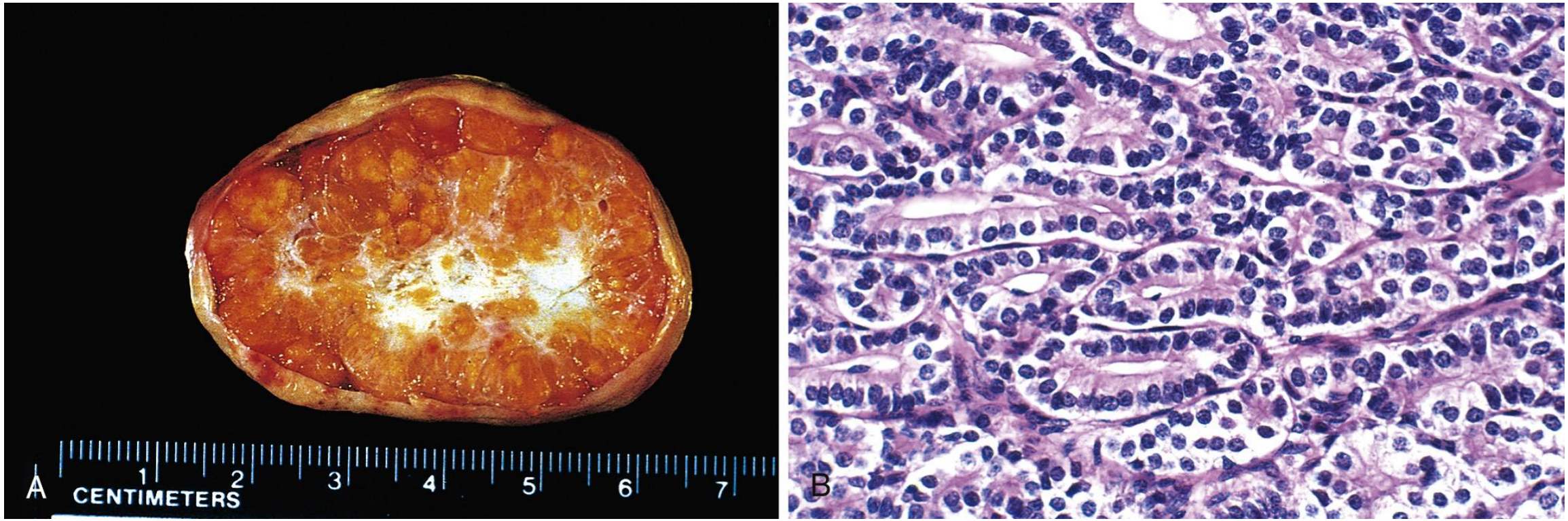
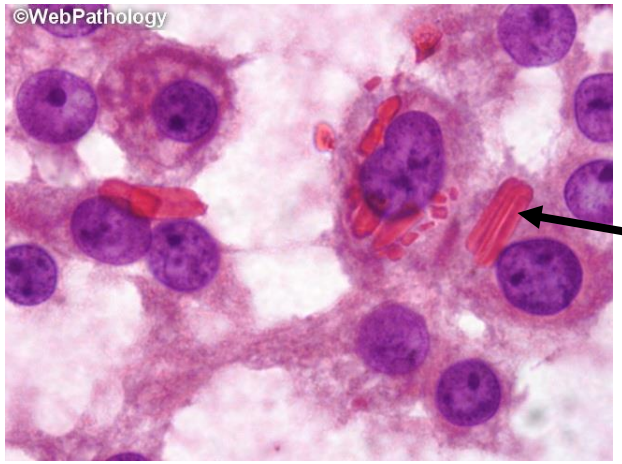
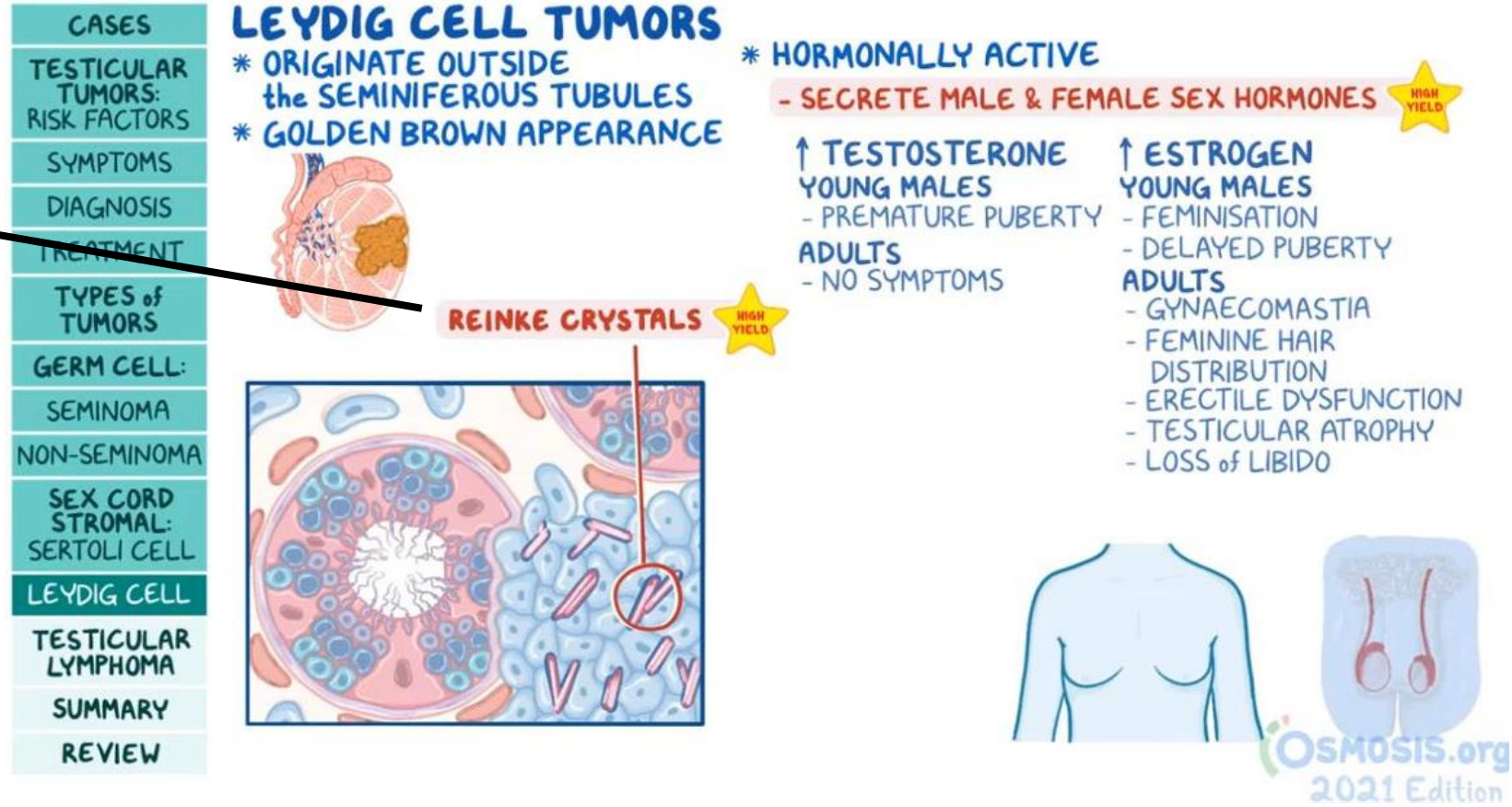


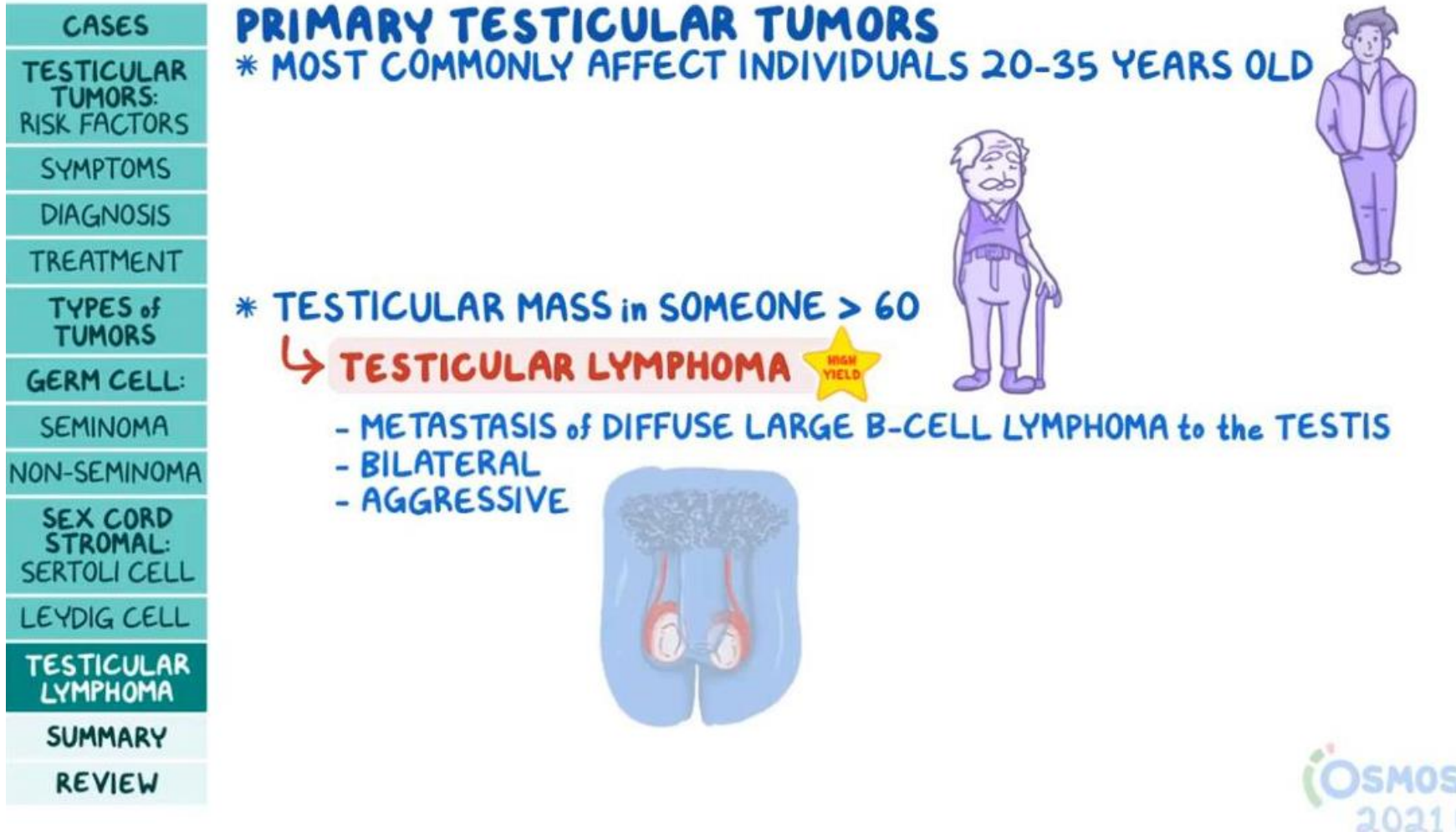
Figure 22.45. Sertoli cell tumor. (A) Gross photograph illustrating characteristic golden-yellow appearance of the tumor. (B) Photomicrograph showing well-differentiated Sertoli cell tubules. Microscopically, a range of differentiation is seen. Well-differentiated tumors show tubules composed of Sertoli cells or Leydig cells interspersed with stroma (Fig. 22.45B). Not shown: The intermediate forms show only immature tubules and large eosinophilic Leydig cells. The poorly differentiated tumors have a sarcomatous pattern with a disorderly disposition of epithelial cell cords. Leydig cells may be absent. Heterologous elements, such as mucinous glands, bone, and cartilage, may be present in some tumors.



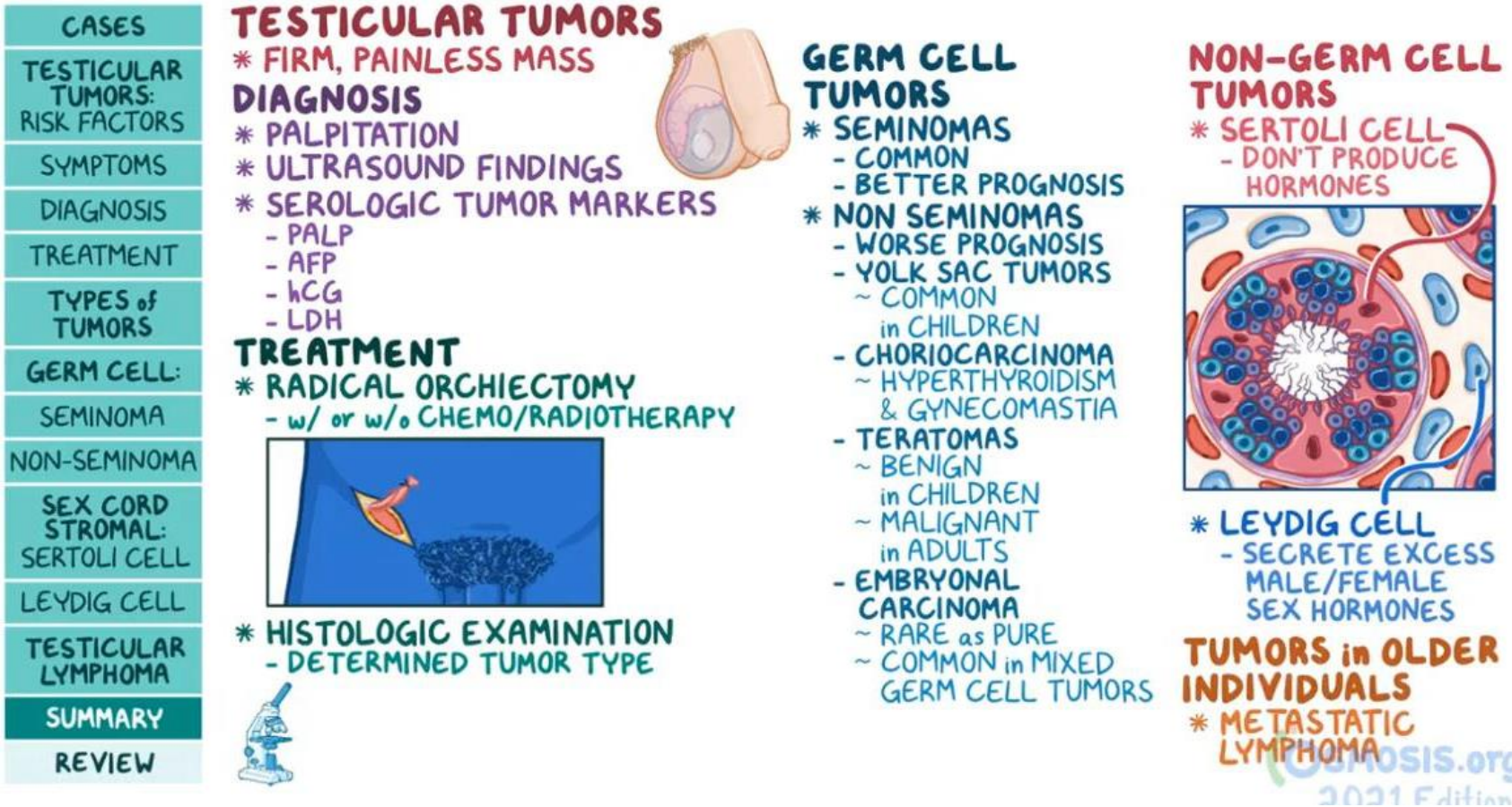
https://www.webpathology.com/image.asp?n=5&Case=38 This touch prep was prepared from the freshly cut tumor surface (same case as previous image). The smear was alcohol-fixed and stained with H&E. Several intact and fragmented Reinke's crystalloids are present. Reinke's crystalloids are seen in 30-40% of Leydig cell tumors.



For Leydig cell tumors, on the other hand, a high-yield fact is that tumor cells originate outside the seminiferous tubules and classically have a golden brown appearance grossly. On histology, they contain Reinke crystals, which are pink, rod like crystals inside their cytoplasm. Another important thing to remember is that these tumors can be hormonally active, meaning they could secrete both male and female sex hormones. Excess male sex hormones, like testosterone, can cause premature puberty in young males, while in adults they usually cause no symptoms. Excess female sex hormones, like estrogen, can cause feminisation and delayed puberty in young biologically male individuals. In adults they can cause gynaecomastia, feminine hair distribution, erectile dysfunction, testicular atrophy and loss of libido or sexual drive.



Okay, before we wrap up, remember that all these primary testicular tumors most commonly affect individuals aged between 20 and 35 years old. If the test question mentions a testicular mass in someone older than 60, think of testicular lymphoma. This typically arises from the metastasis of diffuse large B-cell lymphoma to the testis. It can be bilateral and is often aggressive.



All right, as a quick recap, most testicular tumors present as a firm, painless testicular mass. Diagnosis is made primarily with palpation, ultrasound findings, and determination of serologic tumor markers, including PALP, AFP, hCG and LDH. Treatment is radical orchiectomy, with or without chemo- or radiotherapy, after which histologic examination can be performed to determine the tumor type. The majority of testicular tumors are germ cell tumors and can be classified into seminomas, which are the common one and have a better prognosis and non-seminomas, which have a worse prognosis. Non-seminomas include yolk sac tumors, which are the most common type in children, choriocarcinomas, which are associated with hyperthyroidism and gynecomastia, teratomas, which are usually benign in children and malignant in adults, and embryonal carcinomas, which are rare as pure carcinomas but a common element of mixed germ cell tumors. Non germ cell testicular tumors come from the Sertoli cells, which don't produce hormones or the Leydig cells which can secrete excess male and female sex hormones. Finally, testicular tumors in older individuals are usually metastatic lymphomas.

Alright, back to our cases. Kyle presented with a nontender, round, firm, rubbery mass in the left testicle, which didn't transilluminate and appeared solid on ultrasound. This is a classical presentation of a testicular tumor.
Lab tests showed normal AFP and hCG, which is usually the case in seminomas. This was confirmed in the pathology report after radical orchiectomy, which revealed a homogenous mass with no hemorrhage or necrosis and cells with a "fried-egg appearance". On the other hand, William came in with symptoms of hyperthyroidism, extremely elevated hCG levels, and a testicular lump, which all make us suspicious of a choriocarcinoma. He also underwent radical orchiectomy, after which microscopic examination of the tumor confirmed the presence of cytotrophoblasts and syncytiotrophoblasts.