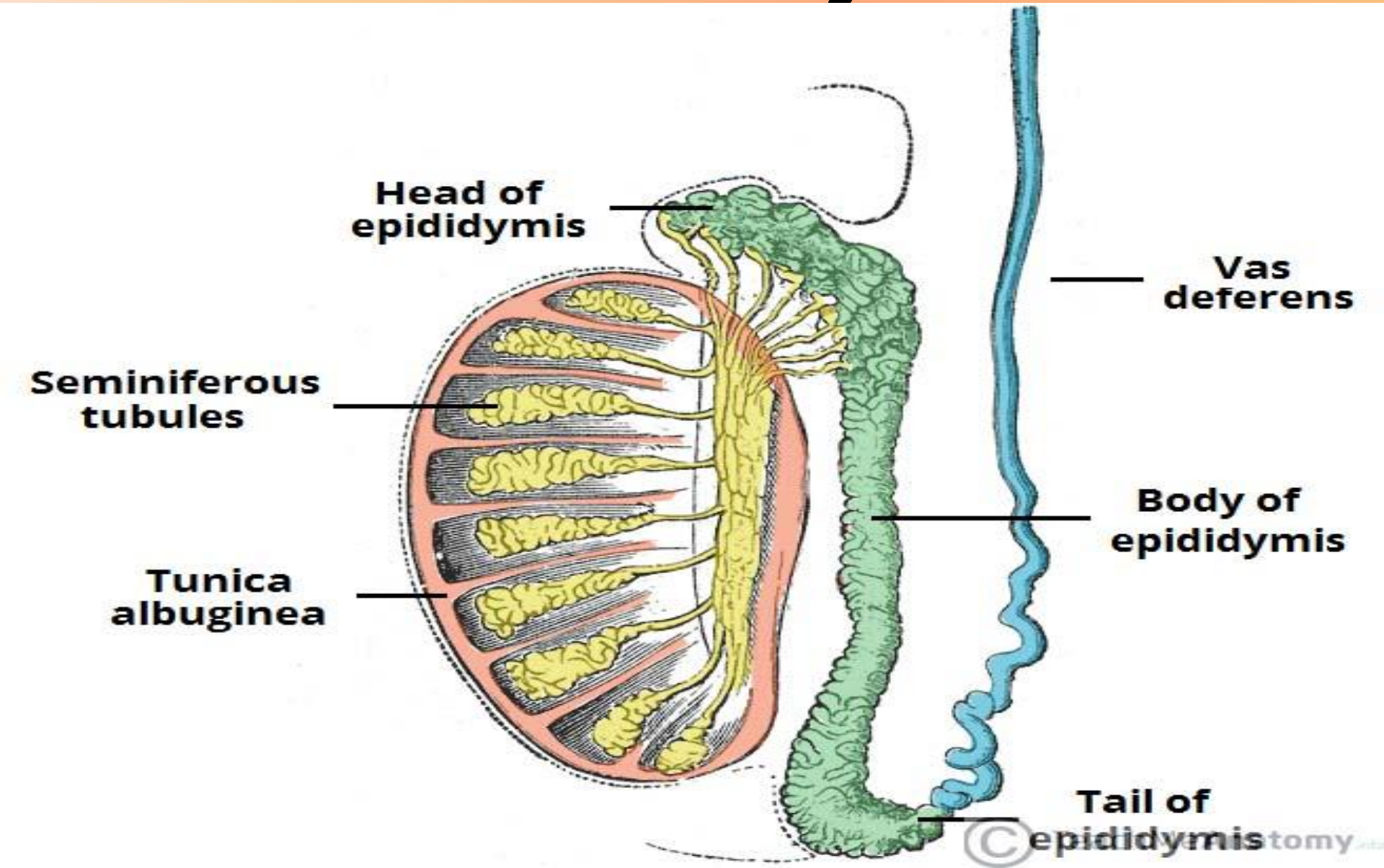
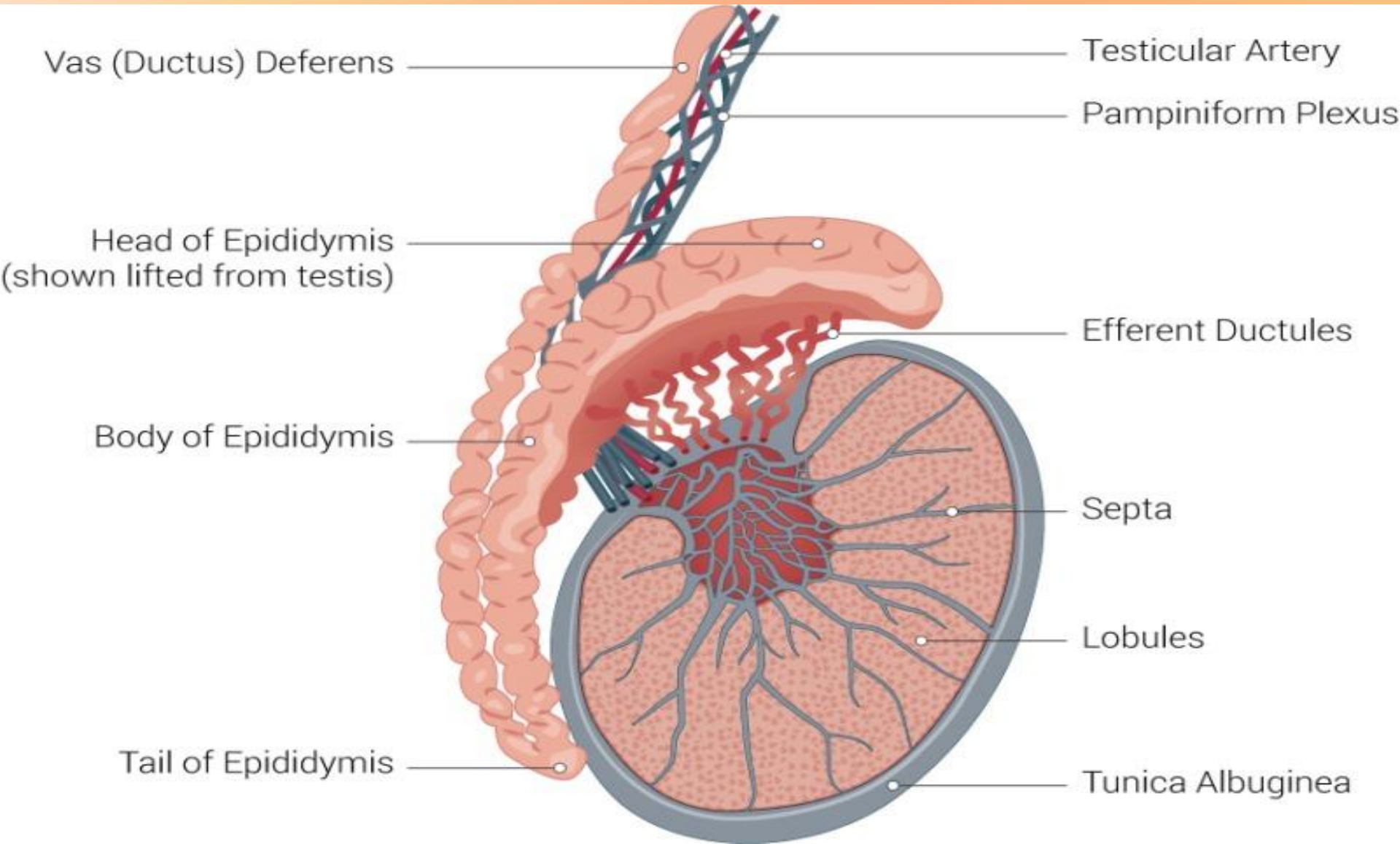
Tumors of the testis

Anatomy


Head of epididymis
Vas deferens
Seminiferous tubules
Body of epididymis
Tunica albuginea
Tail of epididymis

Anatomy


Vas (Ductus) Deferens
Testicular Artery
Pampiniform Plexus
Head of Epididymis
(shown lifted from testis)
Efferent Ductules
Body of Epididymis
Septa
Lobules
Tail of Epididymis
Tunica Albuginea

Anatomy

The testis is composed of **200-300 lobules** of **2-3 seminiferous tubules** lined by cells in different stages of spermatogenesis.

The seminiferous tubules join to form **20-30 straight tubules**, then formed the **rete testis** that give rise to **12-30 efferent ductules**, then the **epididymis** 6 m coiled on the posterior surface of testis.

Finally the **ductus deferens** through the inguinal canal to the abdominal cavity.

Each testis is oval in shape, weight **10-15 g**, the left one is slightly lower than the right, suspended in the scrotum by the spermatic cord.

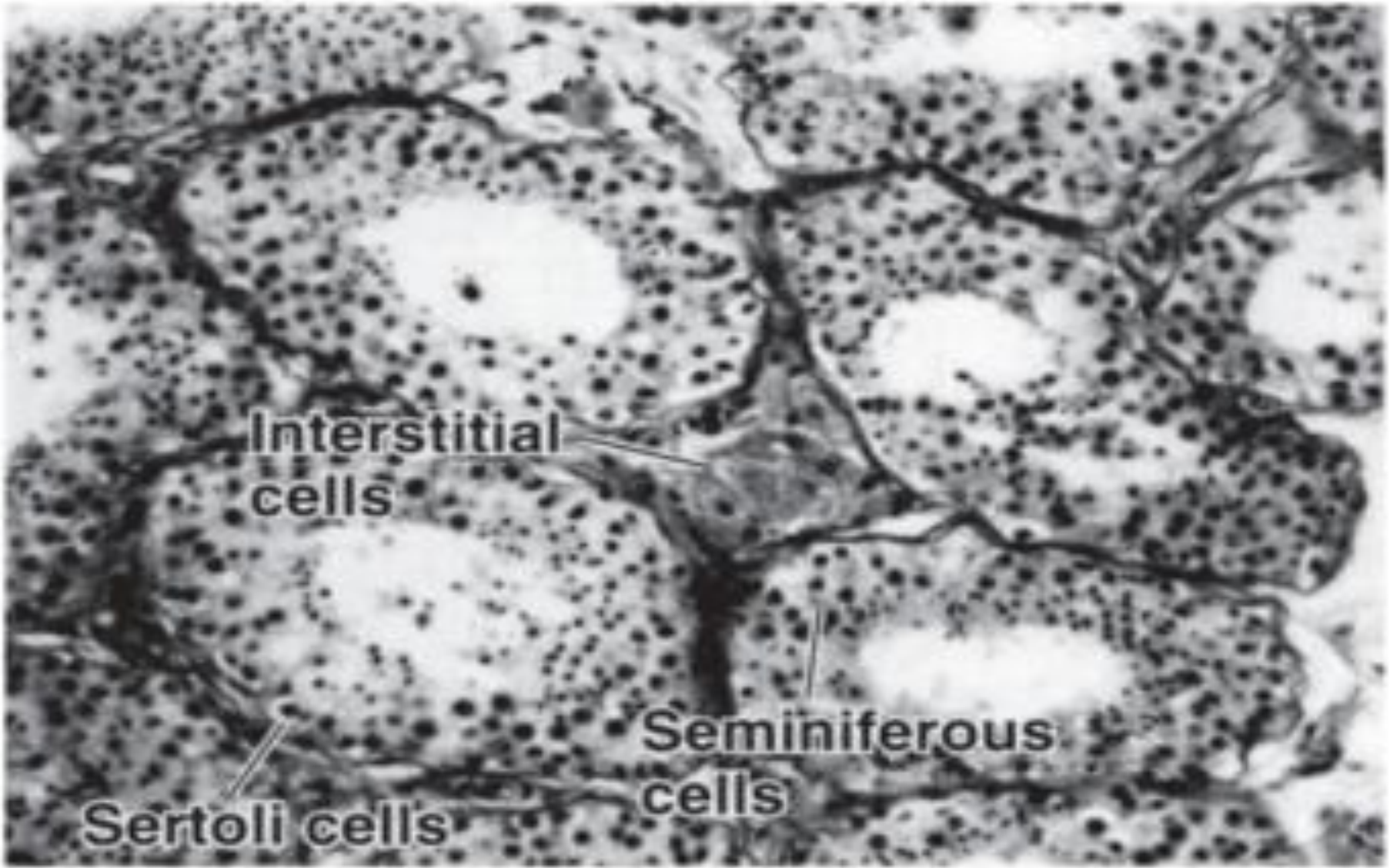
Anatomy

Arterial blood supply: branches of abdominal aorta and collateral from cremastric artery and artery to ductus deferens.

Venous drainage from the right testis to IVC, and from the left testis to left renal vein.

Lymphatic drainage to retroperitoneal lymph: paraaortic, paracaval, and interaortocaval nodes.

Histology



physiology

- The testes have 2 important functions:

1. **Endocrine function**: tetosterone production by Leydig cells
2. **Exocrine function**: Spermatogenesis occurs in the seminiferous tubules with the support of Sertoli cells.

Sertoli cells line the seminiferous tubules and are linked by tight junctions which form the basis for the blood–testis barrier. Sertoli cells foster spermatogenesis and participate in germ cell phagocytosis.

Embryology

- The primitive sex glands appear during the 5th and 6th weeks within the **urogenital ridge** in the abdomen.
- At the 6th week, the gonad consists of a superficial germinal epithelium and an internal blastema.
- During the 7th week, the gonad begins to assume the characteristics of a testis or ovary.
- Genetically, in the presence of a **Y chromosome**, SRY (as known as testis determining factor) induces the d
- The **Wolffian duct** will differentiate into the male duct system, forming the epididymis, vas deferens, seminal vesicles, and ejaculatory ducts, while the Müllerian duct degenerates and forms only the the appendix testis and the prostatic utricle.

Embryology

- The testis later leaves the abdominal cavity and descends into the scrotum. By the 3rd month of fetal life, the testis is located retroperitoneally in the false pelvis. A fibromuscular band (**the gubernaculum**) extends from the lower pole of the testis through the developing muscular layers of the anterior abdominal wall to terminate in the subcutaneous tissue of the scrotal swelling.
- The testis remains at the abdominal end of the inguinal canal until the 7th month. It then passes through the inguinal canal behind (but invaginating) the processus vaginalis. Normally, it reaches the scrotal sac by the end of the 8th month.

EPIDEMIOLOGY

- **1%** of adult neoplasms and **5%** of urological tumours.
- **5 new cases per 100000 male per year** in the USA.
- At diagnosis, 1-2% are bilateral and 90-95% of cases are germ cell tumours.
- Seminoma is the most common germ cell tumor in bilateral primary testicular tumors, while malignant lymphoma is the most common bilateral tumor of the testis.
- The peak incidence is in the **third decade** of life for non-seminomatous germ cell tumour (NSGCT) and mixed GCT patients, and in the **fourth decade** for seminoma testis (ST) patients.
- In 5% of GCT patients, the primary site is at an extragonadal location.

EPIDEMIOLOGY
RISK FACTORS

- Cryptorchidism.
- Hypospadias.
- Decreased spermatogenesis and impaired fertility.
- Family history of TC.
- The presence of a contralateral testicular tumour.
- Carcinoma insitu.
- More on the right side.
- More in white americans than african americans.
- Higher socioeconomic classes.
- Exogenous estrogen administration to the mother during pregnancy.
- trauma and infection-related testicular atrophy.

Histological classification

The recommended pathological classification based on the 2022 update of the World Health Organization (WHO) pathological classification:

- **1. Germ cell tumours derived from germ cell neoplasia in situ.**
- **2. Germ cell tumours unrelated to germ cell neoplasia in situ.**
- **3. Sex cord stromal tumours of the testis.**
- **4. Tumours of the testicular adnexa.**

Histological classification

- Germ cell tumors:

1. seminoma.
2. non-seminoma

    embryonal cell carcinoma
    yolk sac tumors
    teratoma
    choriocarcinoma
    mixed germ cell tumors

- Sex cord stromal tumours of the testis

    Leydig cell tumour
    Sertoli cell tumours
    Granulosa cell tumours

Seminoma

- May secret hCG … 7%
- Three histologic subtypes:
- stage for stage, there is no prognostic significance to any of these subtypes.

1. **Classic seminoma.** 85%

   Most common in the fourth decade of life.

2. **Anaplastic seminoma.** 5-10%

   Tends to present at a higher stage than the classic variety.

3. **Spermatocytic seminoma.** 1%

   Most case are seen in men above 50 years.

Nonseminoma Germ Cell Tumors Embryonal cell carcinoma

- generally discovered as a small, rounded, but irregular mass invading the tunica vaginalis testis and not infrequently involving contiguous cord structures.

Nonseminoma Germ Cell Tumors yolk sac tumor

- Infantile type of embryonal cell carcinoma.
- Endodermal sinus tumor.
- adenocarcinoma of the infantile testis.
- Orchioblastoma.
- The most common testicular tumor of **infants and children.**
- When seen in adults, it usually occurs in mixed histologic types (40%) and possibly is responsible for AFP production in these tumors.
- Embryoid bodies, a common finding in yolk sac tumors

Nonseminoma Germ Cell Tumors
Choriocarcinoma

- Pure choriocarcinoma is rare (representing only 1% of GCTs, 10% mixed tumors).
- Clinically, choriocarcinomas behave in an aggressive fashion characterized by **early hematogenous spread**. Paradoxically, small intratesticular lesions can be associated with **widespread metastatic disease**.
- Secrets very **high levels of hCG**.

Nonseminoma Germ Cell Tumors Teratoma

- may be seen in both children and adults and represent 5% of GCTs.
- They contain more than one germ cell layer (ectoderm, mesoderm, and endoderm) in various stages of maturation and differentiation.

Embryonal	Yolk sac	Teratoma	Choriocarcinoma
25-35	Infants and children	25-35	20-30
Secretes AFP and β-hCG	Secretes AFP and β-hCG	Does not secrete AFP nor β-hCG	Always secretes β-hCG and never secretes AFP
	Hematogeneous spread		Hematogeneous spread, especially to lungs and liver. No LN involvement (the only one)
Poor response to CTX and RTX	Most common tumor in infants and children		WORST PROGNOSIS

Nonseminoma Germ Cell Tumors Mixed cell type

- up to 25% of all testicular tumors) are teratocarcinomas, which are a combination of teratoma and embryonal cell carcinoma.
- Up to 6% of all testicular tumors are of mixed cell type; seminoma is one of the components.
- Treatment for these mixtures of seminoma and NSGCT is similar to that for NSGCT alone.

Intratubular Germ Cell Neoplasia Carcinoma In Situ

- CIS is widely regarded as the preinvasive precursor of all testicular GCTs except spermatocytic seminoma.
- Controversy exists, however, regarding clinical significance, need for detection, and management of testicular CIS.
- The presence of contralateral atrophy or ultrasonographic microlithiasis in patients with testicular tumors warrants contralateral biopsy. If diagnosed, CIS is usually treated by external beam radiation therapy.
- CIS is usually evenly distributed throughout the testis; therefore, open surgical biopsy (3 mm3) is generally positive in cases where CIS exists
- testicular biopsy remains the "gold standard" for diagnosing CIS.

Clinical presentation

- painless enlargement of the testis.
- Acute testicular pain is seen in approximately 10% of cases and may be the result of intratesticular hemorrhage or infarction.
- sensation of testicular heaviness.
- symptoms related to metastatic disease. 10%
- Approximately 10% of patients are asymptomatic at presentation, and the tumor may be detected incidentally.

Examination

- A testicular mass or diffuse enlargement is found in most cases. The mass is typically firm and nontender, and the epididymis should be easily separable from it.
- A hydrocele may accompany the testicular tumor.
- Palpation of the abdomen may reveal bulky retroperitoneal disease.
- Gynecomastia is present in 5% of all germ cell tumors but may be present in 30–50% of Sertoli and Leydig cell tumors.

Tumor Markers

- Alpha feto-protein **(AFP)**
- Human chorionic gonadotropin **(hCG)**
- Lactic acid dehydrogenase **(LDH)**

- Other markers: placental alkaline phosphatase **(PLAP)** and γ-glutamyl transpeptidase **(GGT),** and **(CD30)** antigen**.** These markers, however, have not contributed as much to the management of patients as those mentioned previously.

α-fetoprotein	B-hCG	LDH
Normally expressed by early embryo, liver and GIT	Normally produced by placenta	Normally present in smooth muscle cells, cardia, SKM, liver and bones
Expressed by embryonal and yolk sac tumors	Expressed by 100% of choriocarcinomas, 40% of teratomas, and 10% of seminomas	Expressed in seminomas
Elevated AFP suggests non-seminomatous element		Mainly used to determine tumor burden (size). High tumor burden is usually associated with high levels of LDH.
Other causes of increased AFP: liver dysfunction, viral hepatitis, alcohol	Other causes of increased B-hCG: hypogonadism and marijuana	Elevated in serum due to various reasons, so not specific and carries high risk of false positive

Imaging

- Scrotal ultrasonography.
- Scrotal MRI.

- Chest radiographs (posteroanterior and lateral) Vs chest CT scan.

- Computed tomography (CT scan) of the abdomen and pelvis.

- PET/Ctscan.

DIFFERENTIAL DIAGNOSIS

- **Epididymitis or epididymo-orchitis.**
- **Hydrocele .**
- **Spermatocele .**
- **Hematocele .**
- **Granulomatous orchitis (TB).**
- **Syphlitic gumma**
- **Varicocele**

TNM classification of tumors of the testis.

Pathological T (pT)

pT Category	pT Criteria
pTX	Primary tumor cannot be assessed
pT0	No evidence of primary tumor
pTis	Germ cell neoplasia *in situ*
pT1	Tumor limited to testis (including rete testis invasion) without lymphovascular invasion
pT2	Tumor limited to testis (including rete testis invasion) with lymphovascular invasion OR Tumor invading hilar soft tissue or epididymis .
pT3	Tumor directly invades spermatic cord soft tissue with or without lymphovascular invasion
pT4	Tumor invades scrotum with or without lymphovascular invasion

Pathological N (pN)

pN Category	pN Criteria
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis with a lymph node mass 2 cm or smaller in greatest dimension and less than or equal to five nodes positive, none larger than 2 cm in greatest dimension
pN2	Metastasis with a lymph node mass larger than 2 cm but not larger than 5 cm in greatest dimension; or more than five nodes positive, none larger than 5 cm; or evidence of extranodal extension of tumor
pN3	Metastasis with a lymph node mass larger than 5 cm in greatest dimension

Definition of Distant Metastasis (M)

M Category	M Criteria
M0	No distant metastases
M1	Distant metastases
M1a	Non-retroperitoneal nodal or pulmonary metastases
M1b	Non-pulmonary visceral metastases

Definition of Serum Markers (S)

S Category	S Criteria
SX	**Marker studies not available or not performed**
S0	**Marker study levels within normal limits**
S1	**LDH < 1.5 × N* *and hCG (mIU/mL) < 5,000 and AFP (ng/mL) < 1,000***
S2	**LDH 1.5–10 × N* *or hCG (mIU/mL) 5,000 – 50,000 or AFP (ng/mL) 1,000–10,000***
S3	**LDH > 10 × N* *or hCG (mIU/mL) > 50,000 or AFP (ng/mL) > 10,000***

***N indicates the upper limit of normal for the LDH assay.**

Table 81–3. STAGE GROUPING FOR TESTIS CANCER ACCORDING TO THE AJCC STAGING SYSTEM

Stage Grouping	T	N	M	S
Stage 0	pTis	N0	M0	S0
Stage I	T1–T4	N0	M0	SX
Ia	T1	N0	M0	S0
Ib	T2	N0	M0	S0
	T3	N0	M0	S0
	T4	N0	M0	S0
Is	Any T	N0	M0	S1–S3
Stage II	Any T	Any N	M0	SX
IIa	Any T	N1	M0	S0
	Any T	N1	M0	S1
IIb	Any T	N2	M0	S0
	Any T	N2	M0	S1
IIc	Any T	N3	M0	S0
	Any T	N3	M0	S1
Stage III	Any T	Any N	M1	SX
IIIa	Any T	Any N	M1	S0
	Any T	Any N	M1	S1
IIIb	Any T	Any N	M0	S2
	Any T	Any N	M1	S2
IIIc	Any T	Any N	M0	S3
	Any T	Any N	M1a	S3
	Any T	Any N	M1b	Any S

AJCC, American Joint Committee on Cancer; TNM, tumor, nodes, metastasis.
Data from Vogelzang NJ, Scardino PT, Shipley WU, Coffey DS (eds): Genitourinary Oncology. Philadelphia, Lippincott, Williams & Wilkins, 1999.

TREATMENT

- Inguinal radical orchidectomy including division of the spermatic cord at the internal inguinal ring. It is the standard of care.
- Testis-sparing surgery: may be considered with caution.
- Scrotal approaches and open testicular biopsies should be avoided.
- Insertion of testicular prosthesis.
- Contralateral biopsy has been advocated to exclude CIS.

TREATMENT

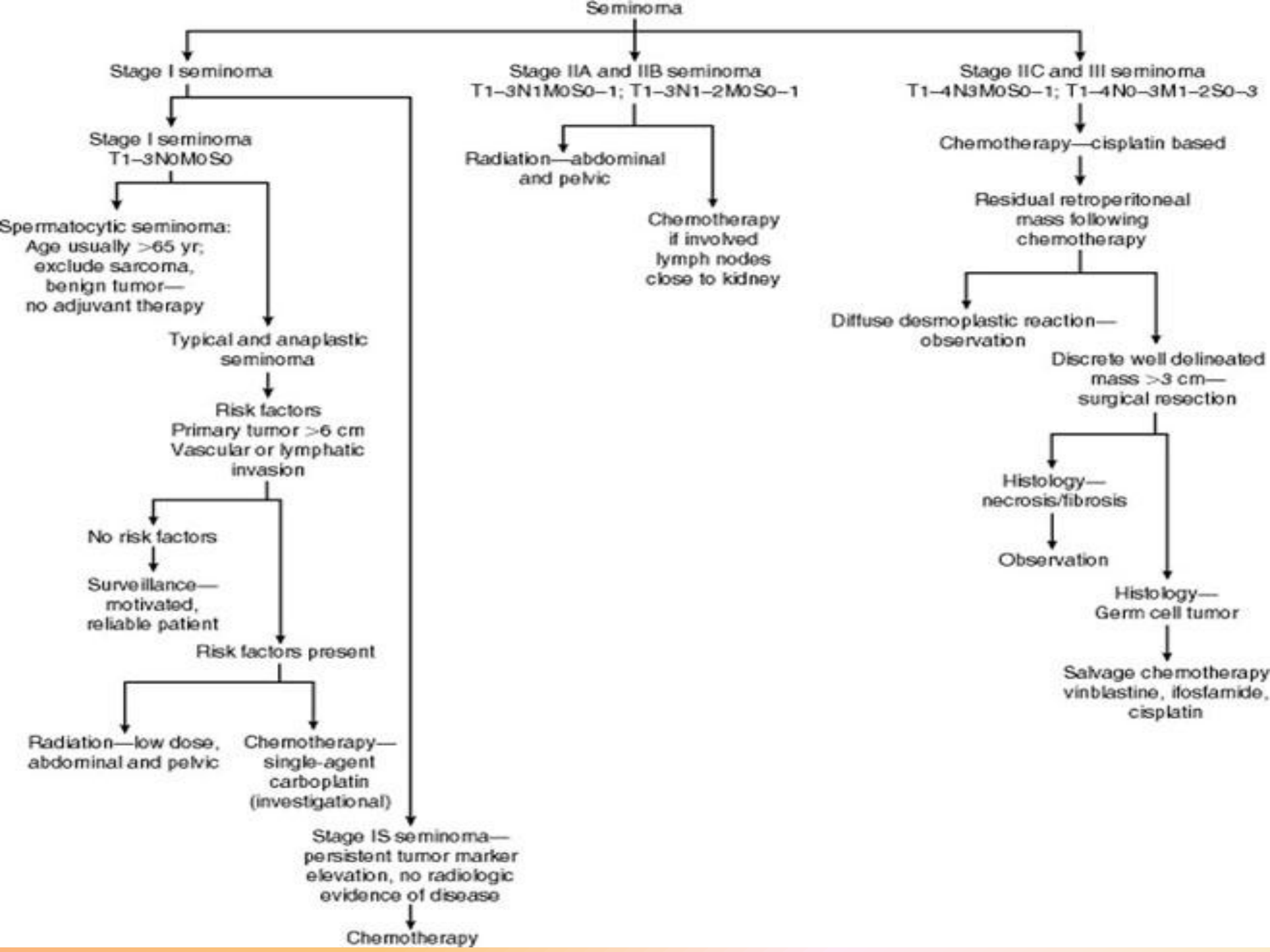
- CONCERNS:

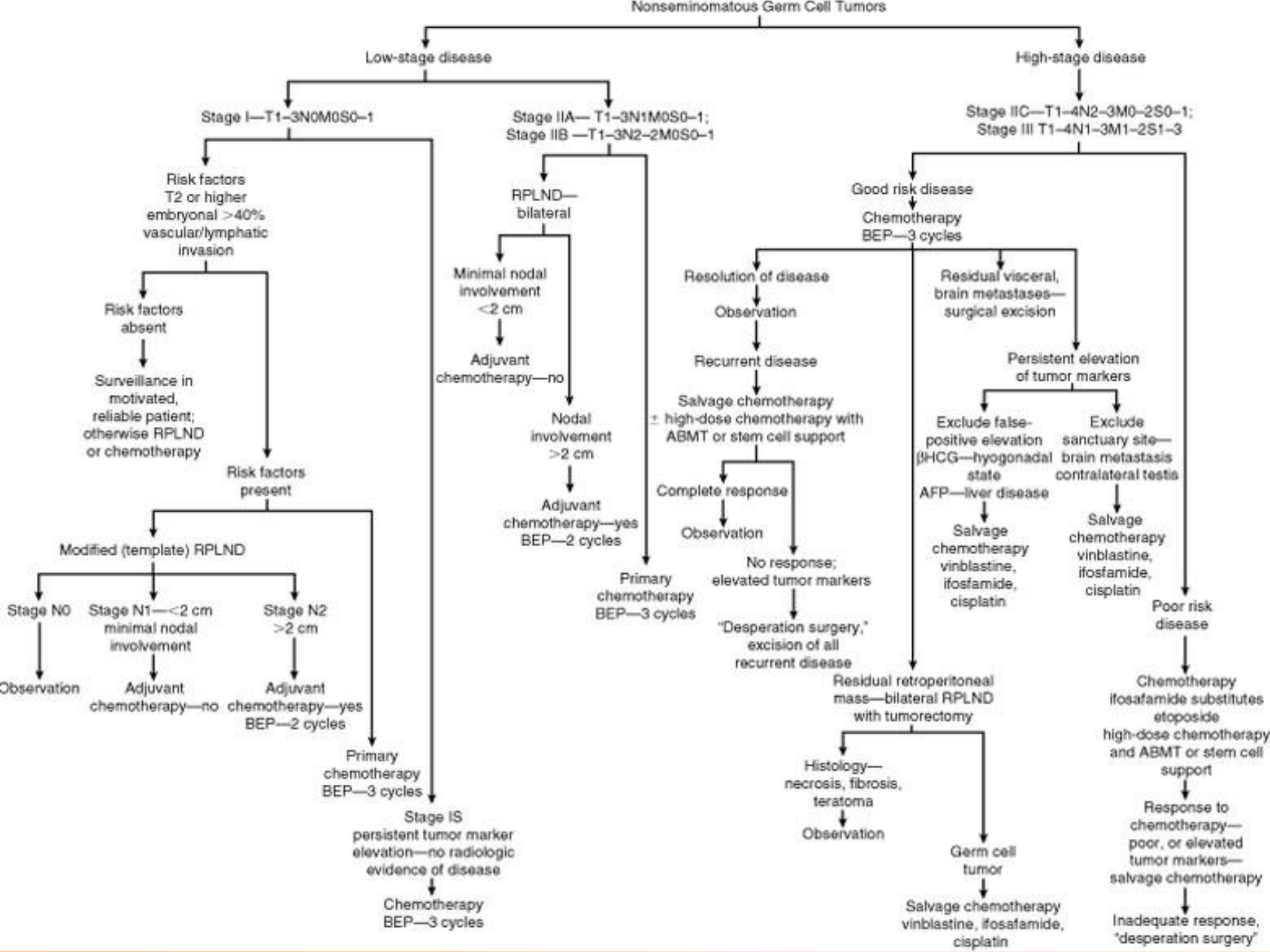
- **1. APPEARANCE.**
- **2. FERTILITY.**
- **3. SEXUAL FUNCTION.**

TREATMENT

- **SEMINOMA:**
- surveillance
- radiotherapy
- chemotherapy.

- **NON-SEMINOMA:**
- Surveillance.
- Nerve-sparing RPLND.
- Retroperitoneal lymph node dissection (RPLND).
- Chemotherapy.


Seminoma
Stage I seminoma
Stage IIA and IIB seminoma
T1–3N1M0S0–1; T1–3N1–2M0S0–1
Stage IIC and III seminoma
T1–4N3M0S0–1; T1–4N0–3M1–2S0–3
Stage I seminoma
T1–3N0M0S0
Radiation—abdominal and pelvic
Chemotherapy if involved lymph nodes close to kidney
Chemotherapy—cisplatin based
Residual retroperitoneal mass following chemotherapy
Spermatocytic seminoma: Age usually >65 yr; exclude sarcoma, benign tumor—no adjuvant therapy
Typical and anaplastic seminoma
Diffuse desmoplastic reaction—observation
Discrete well delineated mass >3 cm—surgical resection
Risk factors
Primary tumor >6 cm
Vascular or lymphatic invasion
Histology—necrosis/fibrosis
Observation
No risk factors
Surveillance—motivated, reliable patient
Risk factors present
Histology—Germ cell tumor
Salvage chemotherapy vinblastine, ifosfamide, cisplatin
Radiation—low dose, abdominal and pelvic
Chemotherapy—single-agent carboplatin (investigational)
Stage IS seminoma—persistent tumor marker elevation, no radiologic evidence of disease
Chemotherapy


Nonseminomatous Germ Cell Tumors
Low-stage disease
High-stage disease
Stage I—T1–3N0M0S0–1
Stage IIA— T1–3N1M0S0–1;
Stage IIB —T1–3N2–2M0S0–1
Stage IIC—T1–4N2–3M0–2S0–1;
Stage III T1–4N1–3M1–2S1–3
Risk factors
T2 or higher
embryonal >40%
vascular/lymphatic
invasion
Risk factors
absent
Surveillance in
motivated,
reliable patient;
otherwise RPLND
or chemotherapy
Risk factors
present
Modified (template) RPLND
Stage N0
Observation
Stage N1—<2 cm
minimal nodal
involvement
Adjuvant
chemotherapy—no
Stage N2
>2 cm
Adjuvant
chemotherapy—yes
BEP—2 cycles
Primary
chemotherapy
BEP—3 cycles
Stage IS
persistent tumor marker
elevation—no radiologic
evidence of disease
Chemotherapy
BEP—3 cycles
RPLND—
bilateral
Minimal nodal
involvement
<2 cm
Adjuvant
chemotherapy—no
Nodal
involvement
>2 cm
Adjuvant
chemotherapy—yes
BEP—2 cycles
Primary
chemotherapy
BEP—3 cycles
Good risk disease
Chemotherapy
BEP—3 cycles
Resolution of disease
Observation
Recurrent disease
Salvage chemotherapy
± high-dose chemotherapy with
ABMT or stem cell support
Complete response
Observation
No response;
elevated tumor markers
"Desperation surgery,"
excision of all
recurrent disease
Residual visceral,
brain metastases—
surgical excision
Persistent elevation
of tumor markers
Exclude false-
positive elevation
βHCG—hyogonadal
state
AFP—liver disease
Salvage
chemotherapy
vinblastine,
ifosfamide,
cisplatin
Exclude
sanctuary site—
brain metastasis
contralateral testis
Salvage
chemotherapy
vinblastine,
ifosfamide,
cisplatin
Residual retroperitoneal
mass—bilateral RPLND
with tumorectomy
Histology—
necrosis, fibrosis,
teratoma
Observation
Germ cell
tumor
Salvage chemotherapy
vinblastine, ifosfamide,
cisplatin
Poor risk
disease
Chemotherapy
ifosfamide substitutes
etoposide
high-dose chemotherapy
and ABMT or stem cell
support
Response to
chemotherapy—
poor, or elevated
tumor markers—
salvage chemotherapy
Inadequate response,
"desperation surgery"

Prognosis

- Survival in testicular cancer has improved dramatically over the past several years, reflecting the continuing improvement and refinement in combination chemotherapy.

- For seminoma treated by orchiectomy and radiotherapy, the 5-year disease-free survival rate is 98% for stage I and 92–94% for stage IIA .

- Survival in patients with NSGCTs treated by orchiectomy and RPLND for stage I disease ranges from 96% to 100%.

SECONDARY TUMORS OF THE TESTIS

- Secondary tumors of the testis are rare.
- Three categories are considered:
- **Lymphoma:** the most common testicular tumor in a patient older than 50 years and is the most common secondary neoplasm of the testis, accounting for 5% of all testicular tumors. The most common bilateral testicular cancer.
- **Leukemia:** The testis is a common site of relapse for children with acute lymphocytic leukemia.
- **metastatic tumors:** Metastasis to the testis is rare. The most common primary site is the prostate, followed by the lung, gastrointestinal tract, melanoma, and kidney

THANK YOU