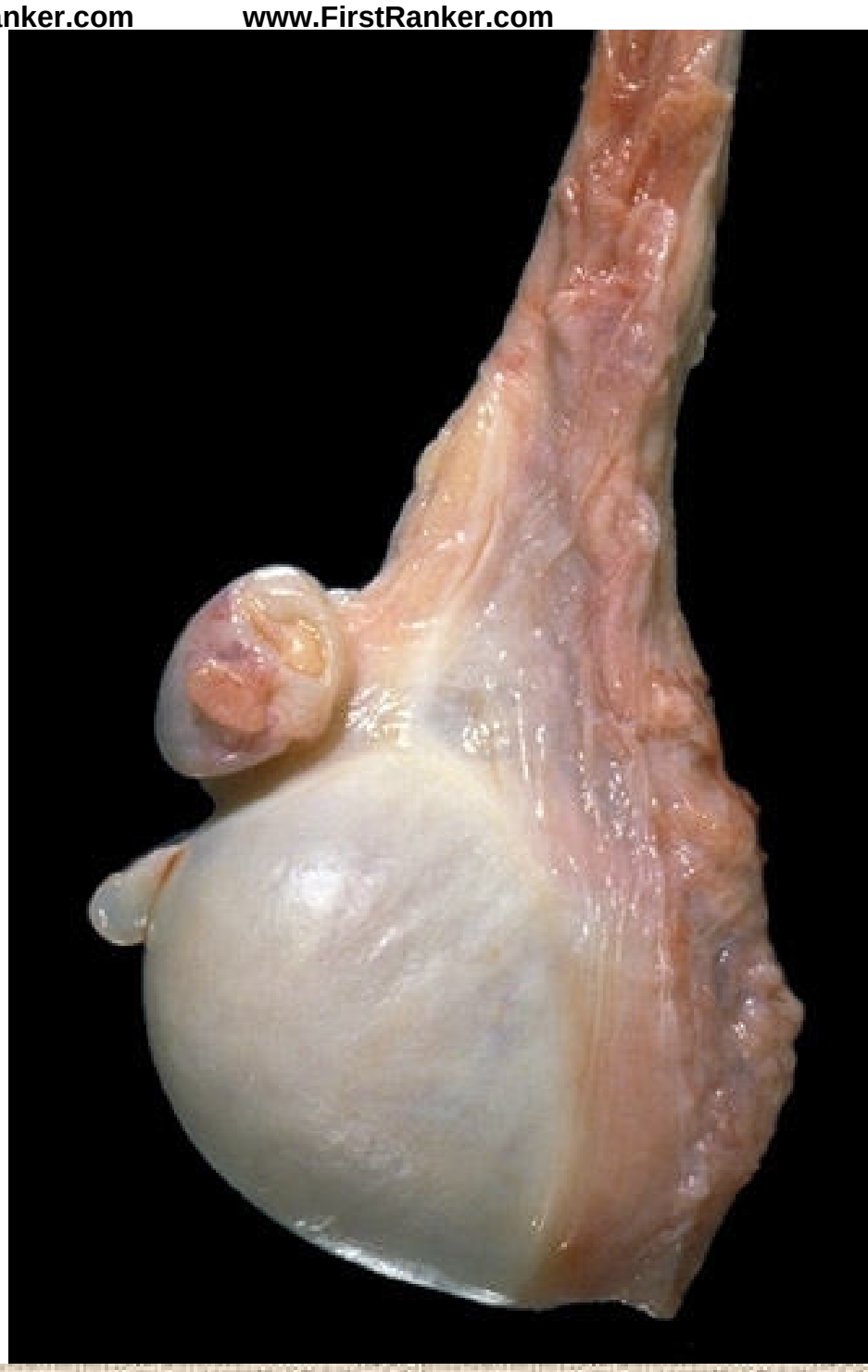
Testicular tumors



Department of Urology

TESTICULAR TUMORS:

- Testicular cancer accounts *for only about 1% of all human neoplasms*.

- Testicular cancer although rare, is the *most common malignancy in men in 15-3 years age group* and accounts for approximatel *23% of all cancers in this group*.

WHO CLASSIFICATION OF TESTICULAR TUMORS:

Germ cell tumors:

Precursor lesions- intratubular malignant germ cell tumor (carcinoma in situ)

Tumors of one histologic type (pure forms)

- Seminoma
  - variant- *seminoma with syncitiotrophoblastic cells*
- Spermatocytic seminoma
  - variant- *spermatocytic seminoma with sarcoma*
- Embryonal carcinoma
- Yolk sac tumor
- Polyembryoma

Trophoblastic tumors- choriocarcinoma

Teratoma

- *Mature teratoma*
  - *Dermoid cyst*
- *Immature teratoma*
- *Teratoma with malignant areas*

Mixed tumors

CLASSIFICATION (CONT...)

Sex cord/ Gonadal Stromal Tumors:

-Pure forms

- Leydig's cell tumor
- Sertoli's cell tumor
  - *large cell calcifying*
  - *lipid rich cell*

-Granulosa cell tumor

- *Adult type granulosa cell tumor*
- *Juvenile type granulosa cell tumor*

-Tumors of thecoma/ fibroma group

-Incompletely diffrentiated sex cord/ gonadal stromal tumors

-Mixed forms.

CLASSIFICATION (CONT...)

-Unclassified forms

-Tumors containing both germ cell and sex cord/ gonadal stromal elements
  -Gonadoblastoma
  -Mixed germ cell- sex cord/ gonadal stromal tumors, unclassified

-Miscellaneous tumors
  -Carcinoid tumors
  -Tumors of ovarian epithelial types.

CLASSIFICATION (CONT...)

-Lymphoid and hematopoietic tumors:
  -Lymphoma
  - Plasmacytoma
  - Leukemia

-Tumors of collecting duct and rete:
  -Adenoma
  -Carcinoma

-Tumors of tunica, epididymis, spermatic cord, supporting structures, and appendices:
  -Adenomatoid tumor
  - Mesothelioma
  - Adenoma
  -Carcinoma
  -Melanotic neuroectodermal tumor.

CLASSIFICATION (CONT...)

-Soft tissue tumors,

-Unclassified tumors, and

-Secondary tumors.

GERM CELL TUMORS- EPIDEMIOLOGY

Low in Africa and Asia.

Life time probability of developing testicular cancer is **0.2%.**

Intermediate in U.S and U.K.

The average annual age adjusted rate is **highest in** Denmark, Norway, Switzerland Germany and New Zealand.

GERM CELL TUMORS- EPIDEMIOLOGY

AGE:

- These neoplasms are the *most common solid tumors of men age 20 - 40 years* and *second most common of men age 15 - 19 years*.

RACIAL FACTORS:

- More common in *white population* than in blacks.

GERM CELL TUMOR- EPIDEMIOLOGY

The evidence for a predominantly genetic influence is not overwhelming.

GENETIC FACTORS:-

The 2 - 3% incidence of bilateral tumors may suggest the potential importance of genetic and (or) congenital factors.

GERM CELL TUMORS- ETIOLOGY

CRYPTORCHIDISM:

7-10% of patients with testicular tumors have prior history of cryptorchidism.

The relative risk of developing a testicular cancer in maldescent testis is 3 to 14 times the normal expected incidence.

5-10% of patients with a history of cryptorchidism develop malignancy in the contralateral normally descended testes.

25% of patients with bilateral cryptorcidism and a history of tetsis cancer develop second GCT.

GERM CELL TUMORS- ETIOLOGY

TRAUMA:

- There is little to suggest a cause and effect relationship in humans.
- Infact trauma in an enlarged testes is an event that prompts medical evaluation

ATROPHY:

- Causative role of atrophy remains speculative.
- nonspecific or mumps associated atrophy of the testis has been suggested as a potential causative factor in testicular cancer.

GERM CELL TUMORS- ETIOLOGY

HORMONES:

Offspring of women exposed to diethylstilbestrol or oral contraceptives has relative risk rate of developing testicular cancer of 2.8 - 5.3%.

Exogenous estrogen administration has also been linked to the induction of leydig's cell tumors.

GERM CELL TUMOR- CLINICAL MANIFESTATIONS:

The usual presentation of a testicular tumor is *a nodule or painless swelling in one gonad.*

On rare occasions, infertility *is the presenting complaint.*

30-40% may complain of a dull ache or heavy sensation *in the lower abdomen, anal area, or scrotum.*

In 10%, acute pain *is the presenting complain.*

GERM CELL TUMORS- CLINICAL MANIFESTATIONS

In 10% of patients, the presenting manifestation may be due to metastasis:-

A neck mass

- Supraclavicular lymph node metastasis.

Gastrointestinal disturbances

- Retroduodenal metastasis

Lumbar back pain

- Involving psoas muscle or nerve roots

Bone pain

- Skeletal metastasis

Central and peripheral nervous system manifestations

- Cerebral, spinal cord, or peripheral root involvement

Unilateral or bilateral lower extremity

- Iliac or caval obstruction.

GERM CELL TUMORS- PHYSICAL EXAMINATION

BIMANUAL EXAMINATION:

Beginning with the normal contralateral testis.

Any firm, hard, or fixed area should be considered suspicious.

Testicular tumors tend to remain ovoid, being limited by the tough investing tunica albuginea.

A hydrocele may be present and increases the difficulty of palpation.

GERM CELL TUMOR-

Scrotal Sonography:

USGof the scrotum is basically an extension of the physical examination.

Any hypoechoic area within the tunica albuginea is markedly suspicious for testicular cancer.

In patients with a diagnosis of EGCT, ultrasound of the testis is mandatory to be certain that one is not dealing with a primary GCT.

GERM CELL TUMORS- IMAGING STUDIES

Chest Radiography:

- Postero-anterior and lateral chest radiographs: Metastatic workup

Chest CT:

- Indicated in patients with abnormal X-ray scans.

GERM CELL TUMORS- IMAGING

- Abdominal CT:
- Most effective means to identify retroperitoneal lymph node involvement.
- Excellent for visualization of kidney, ureters, retro-crural space in the para-aortic region.
- However cannot sufficiently distinguish between fibrosis, teratoma, and malignancy by size criteria alone.

GERM CELL TUMORS

IMAGING

- MRI:
- Testicular tumors are hypointense on T2 weighted images, and show brisk and early enhancement after I.V Gadolinium.
- PET:
- To detect radiographic abnormalities after chemotherapy.
- Neither PET nor CT has the ability to detect microscopic nodal disease.

GERM CELL TUMORS

TUMOR MARKERS

- Applied to body fluid and tissue sections.
- Oncofetal substances: associated with embryonic development (AFP, HCG),
- Cellular enzymes: LDH, PLAP.
- Capable of detecting small tumor burdens (105 cells) that are not detectable by currently available imaging techniques.

GERM CELL TUMORS

TUMOR MARKERS

- AFP:
- Not produced by pure choriocarcinoma or pure seminoma.
- HCG:
- Choriocarcinoma (all patients),
- Embryonal carcinoma (40-60%),
- Pure seminoma (5-10%).

GERM CELL TUMORS

TUMOR MARKERS

LDH:

- Has low specificity.
- There is a direct relationship between tumor burden and LDH levels.

PLAP:

- Raised in 40% of patients with advanced disease.

GGTP:

- Raised in one third of patients with active seminoma.

CD30:

- possible marker for embryonal carcinoma.

STAGING

- RADICAL INGUINAL ORCHIDECTOMY(HIGH TYPE)
- TESTIS SPARING SURGERY- Highly controversial

GERM CELL TUMORS : STAGING

The American Joint Committee on Cancer staging for GCTs:

Primary Tumor (T):

pTx: primary tumor *cannot be assessed.*

pT0: *no evidence* of primary tumor

pTis: *intratubular germ cell neoplasia.*

pT1: *tumor limited to the testis and epididymis and no vascular or lymphatic invasion.*

pT2: tumor limited to the testis and epididymis with *vascular or lymphatic invasion* or tumor extending through the tunica albuginea with *involvement of tunica vaginalis.*

pT3: tumor *invades the spermatic cord* with or without vascular/ lymphatic invasion.

pT4: tumor *invades the scrotum.*

GERM CELL TUMORS : STAGING

Regional lymph nodes (N)	Nx: regional lymph nodes *cannot be assessed.*	N0: *no regional lymph node* metastasis.	N1: lymph node mass *2cm or less* in greatest dimension or *multiple lymph node masses, none more than 2cm* in greatest dimension.	N2: lymph node mass *more than 2cm but not more than 5 cm* in greatest dimension, or multiple lymph node masses, anyone mass greater than 2 cm but not more than 5 cm in greatest dimension.	N3: lymph node mass *more than 5cm* in greatest dimension.

GERM CELL TUMOR STAGING:

Distant metastasis (M)

M0: *no evidence* of distant metastasis.

M1: *non regional nodal or pulmonary* metastasis.

M2: *nonpulmonary* visceral metastasis.

GERM CELL TUMOR STAGING:

Serum tumor markers (S)

	LDH	hCG (mIU/ml)	AFP (ng/ml)
S0	≤ N	≤ N	≤ N
S1	<1.5 x N	< 5000	< 1000
S2	1.5-10 N	5000 - 50000	1000-10,000
S3	> 10 N	>50,000	> 10,000

PROGNOSIS

SEMINOMA

Good Prognosis:

- Any primary site
- No pulmonary or visceral metastasis
- AFP: Normal;
- hCG: Any value
- LDH: Any value

Intermediate prognosis:

- Any primary site
- Nonpulmonary visceral metastasis
- AFP: Normal;
- hCG: Any value
- LDH: Any value

Poor prognosis:

No patients classified as poor prognosis

PROGNOSIS

NONSEMINOMA

Good Prognosis:

- Testis or retroperitoneal primary
- No pulmonary or visceral metastasis
- AFP<1000ng/ml; hCG<5000IU/L; LDH<1.5times upper limit.

Intermediate prognosis:

- Testis or retroperitoneal primary,
- No nonpulmonary visceral metastasis
- Any of: AFP1000-10,000ng/ml; hCG5000-50,000IU/L; LDH1.5-10 times upper limit

Poor prognosis:

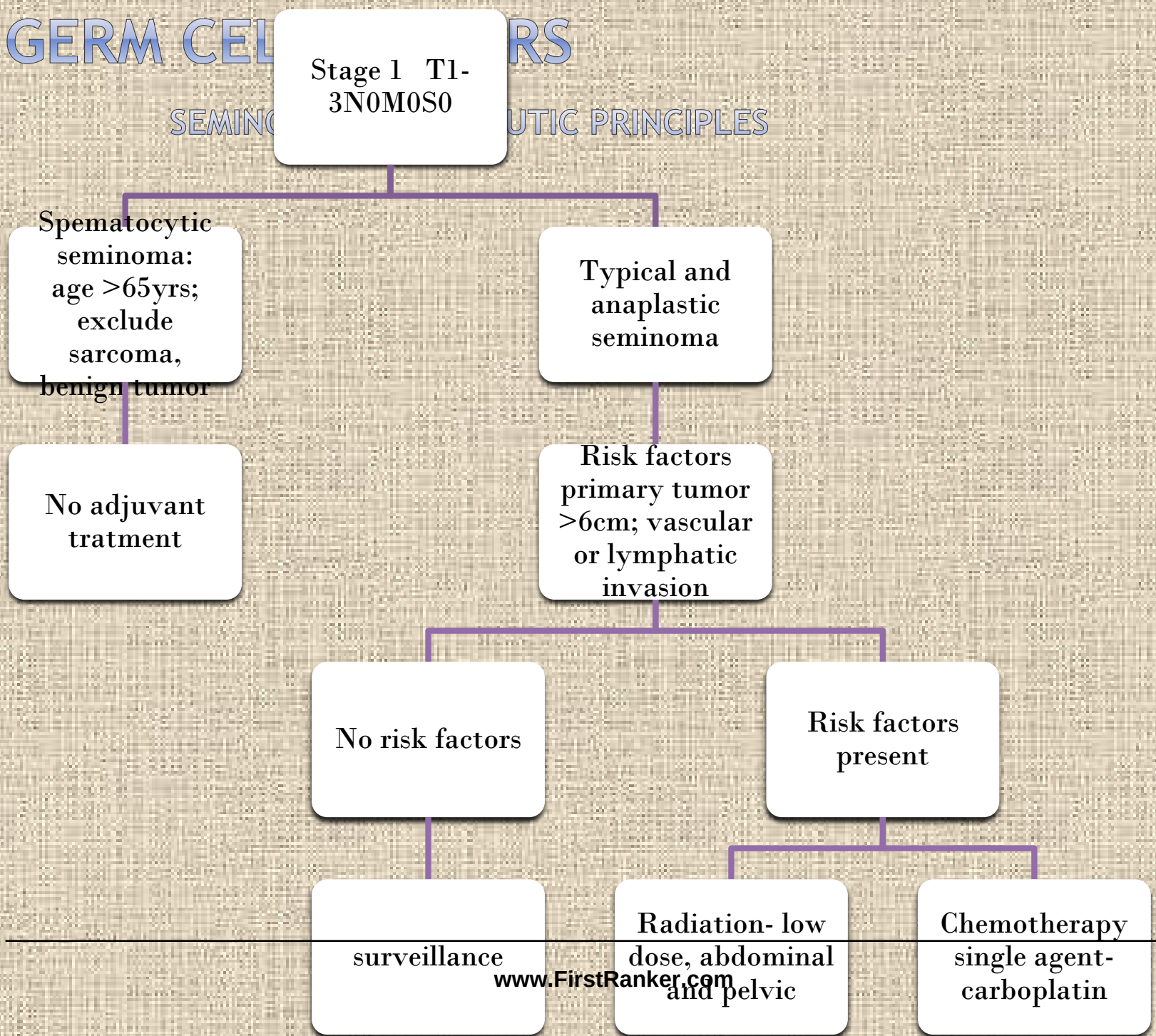
Any of the following criteria:

- Mediastinal primary
- Nonpulmonary visceral metastasis
- AFP>10,000ng/ml; hCG>50,000IU/L; LDH>10 times upper limit.

TREATMENT

GERM CEL RS

SEMINO UTIC PRINCIPLES



GERM CELL TUMORS

SEMINOMA: STAGE 1

- Radiation therapy:
- Today most centers administer 25Gy to para-aortic nodes only.
- This has a 5 year survival in excess of 95%.
- Primary Chemotherapy:
- Single agent carboplatin compare favorably with adjuvant radiation therapy.
- 2 courses of carboplatin were associated with no relapse and favorable toxicity profile.

GERM CELL TUMORS

SEMINOMA: STAGE 1

Surveillance:

Appropriate for patients with:

1. tumors smaller than 6 cm,
2. absence of vascular invasion, and
3. normal hCG levels.

in motivated and reliable patients.

GERM CELL TUMORS

SEMINOMA: STAGE IIA AND IIB

Stage IIA and IIB seminoma

- Radiation- abdominal and pelvic
- Chemotherapy- if lymph nodes close to kidney

GERM CELL TUMORS

SEMINOMA: STAGE IIA AND IIB

Radiation therapy:

N1 disease receive *30 Gy*, and N2 disease receive *35 Gy*.

Patients with stage II seminoma have 5 year *survival rates of 70% to 92%*.

Chemotherapy:

Irradiation to kidney is avoided- parenchyma is sensitive.

So, chemotherapy is preferred in this region.

GERM CELL TUMORS

SEMINOMA: STAGE IIC AND III

Stage IIC and III seminoma

Chemotherapy- cisplatin based

Residual retroperitoneal mass following chemotherapy

Diffuse desmoplastic reaction- observation

Descrete well deliniated mass>3cm

Surgical resection

Histology- necrosis/fibrosis

Histology- germ cell tumor

observation

Salvage chemotherapy

GERM CELL TUMORS

SEMINOMA: STAGE IIC AND III

Cisplatin based chemotherapy:

>90% of patients achieve a complete response.

Residual masses are resected if on CT scan:

-if they are well delineated,

-distinct from surrounding structures, and

-diameter is larger than 3 cm.

NON-SEMINOMATOUS GERM CELL TUMORS

STAGE 1: TREATMENT PRINCIPLES.

Stage 1

Risk factors: T2 or higher, embryonal>40%, vascular/lymphatic invasion.

Stage 1S

Risk factors absent	Risk factors present	Chemotherapy BEP 3 cycles
surveillance	Modified RPLND	Primary chemotherapy BEP 3 cycles

Stage N0	Stage N1	Stage N2
observation	observation	Adjuvant chemotherapy BEP 2 cycles

NONSEMINOMATOUS GERM CELL TUMORS

STAGE 1: TREATMENT PRINCIPLES

Retro-peritoneal lymph node dissection:

- Capable of eradicating resectable disease in the majority of N1-N2 tumors.
- 5 year survival for stage 1 is *95%.*
- *5-10% experience relapse:* high cure rates with chemotherapy.

Modified (template) RPLND:

- Complete dissection in the most likely area, and modification in less likely area.
- *Ejaculation* is preserved in 100%, and *fertility* noted in 75% of patients.

NONSEMINOMATOUS GERM CELL TUMORS

STAGE 1: TREATMENT PRINCIPLES

Primary radiation therapy:

- 5 year survival for stage 1: 80-95% when chemotherapy is used to treat relapses.
- Relapse rate after radiation therapy: 24%.

The main objections to radiation therapy:

- Inaccuracy of clinical staging,
- Lack of survival data,
- Prior radiation makes it difficult for future surgical or pharmacological intervention, and
- Risk of second malignancy: 18% in 25 years.

NONSEMINOMATOUS GERM CELL TUMORS

STAGE 1: TREATMENT PRINCIPLES

Prognostic factors for clinical stage 1 tumors:

- Invasion of testicular veins,
- Invasion of lymphatics,
- Absence of yolk sac elements,
- presence of embryonal cell carcinoma, and
- Angiogenesis: *factor VIII stain* positive.

NONSEMINOMATOUS GERM CELL TUMORS

STAGE 1: TREATMENT PRINCIPLES

Surveillance:

Surveillance is indicated in stage 1 disease:-

- without any risk factors for relapse,
- in motivated patients, and
- who fully understands the risk of failure to comply.

NONSEMINOMATOUS GERM CELL TUMORS

STAGE 1: TREATMENT PRINCIPLES

- Surveillance protocol:
- Physical examination, chest radiographs, and tumor markers: monthly for 1st year, every 2 months for second year, and every 3-6 months thereafter.
- CT abd: every 2-3 months for the first 2 years, and every 6 months thereafter.
- Finally, surveillance is necessary for minimum of 5 years, possibly 10 years after orchiectomy.

NONSEMINOMATOUS GERM CELL TUMORS

STAGE 1: TREATMENT PRINCIPLES

Primary chemotherapy:

2 cycles of bleomycin, cisplatin, and etoposide are used.

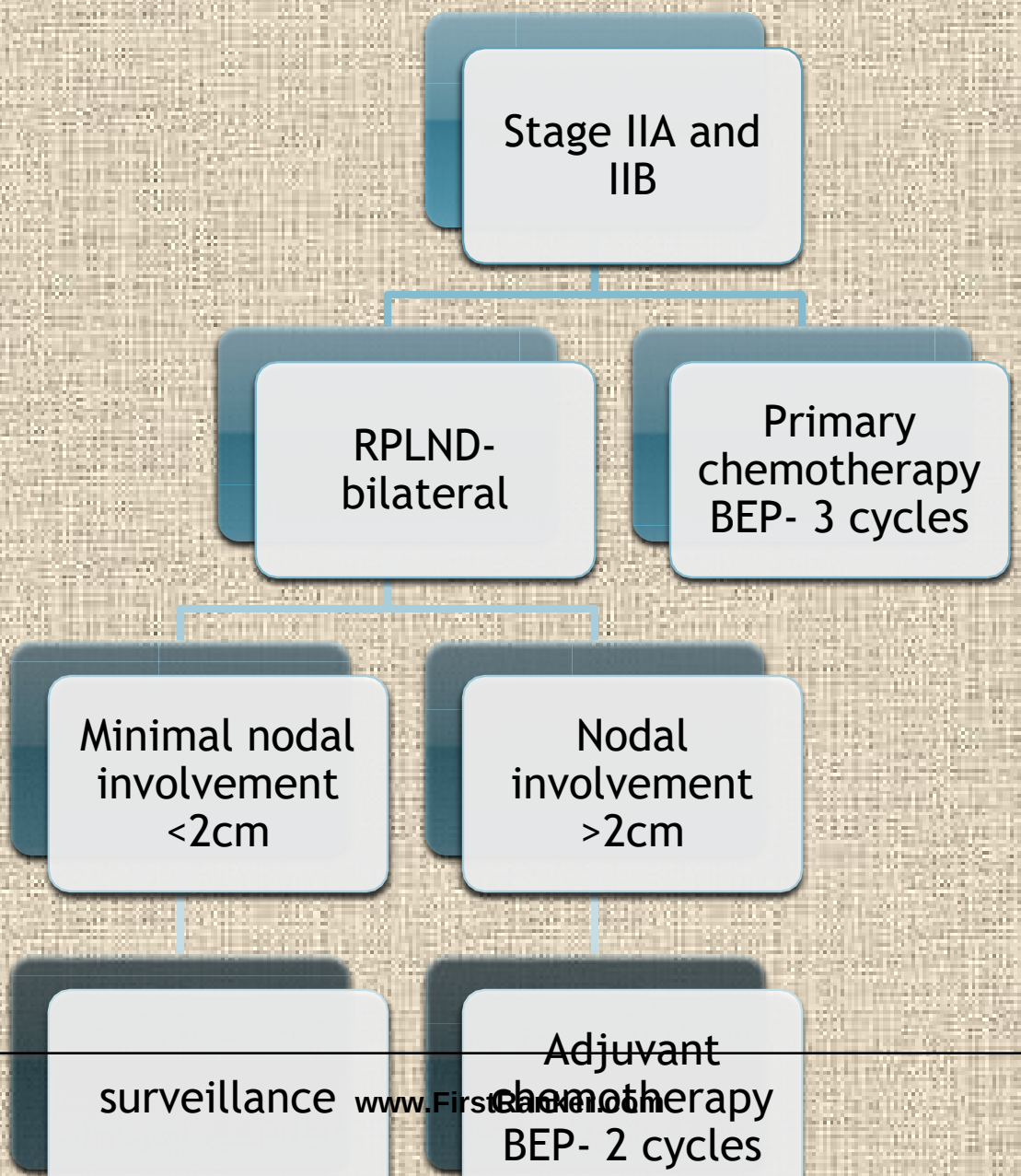
5 year survival: *95%-100%*.

Added advantage of treating *metastatic disease outside the retroperitoneum*.

Suitable for centers *where expertise for RPLND are not available*.

NONSEMINOMATOUS GERM CELL TUMORS

STAGE IIA AND IIB: TREATMENT PRINCIPLES



NONSEMINOMATOUS GERM CELL TUMORS

STAGE IIA AND IIB: TREATMENT PRINCIPLES

RPLND:

A complete bilateral lymphadenectomy is recommended.

- Patients with minimal retroperitoneal disease on RPLND: *careful follow-up.*
- Patients with more extensive disease on RPLND: *two cycles of adjuvant chemotherapy.*

NONSEMINOMATOUS GERM CELL TUMORS

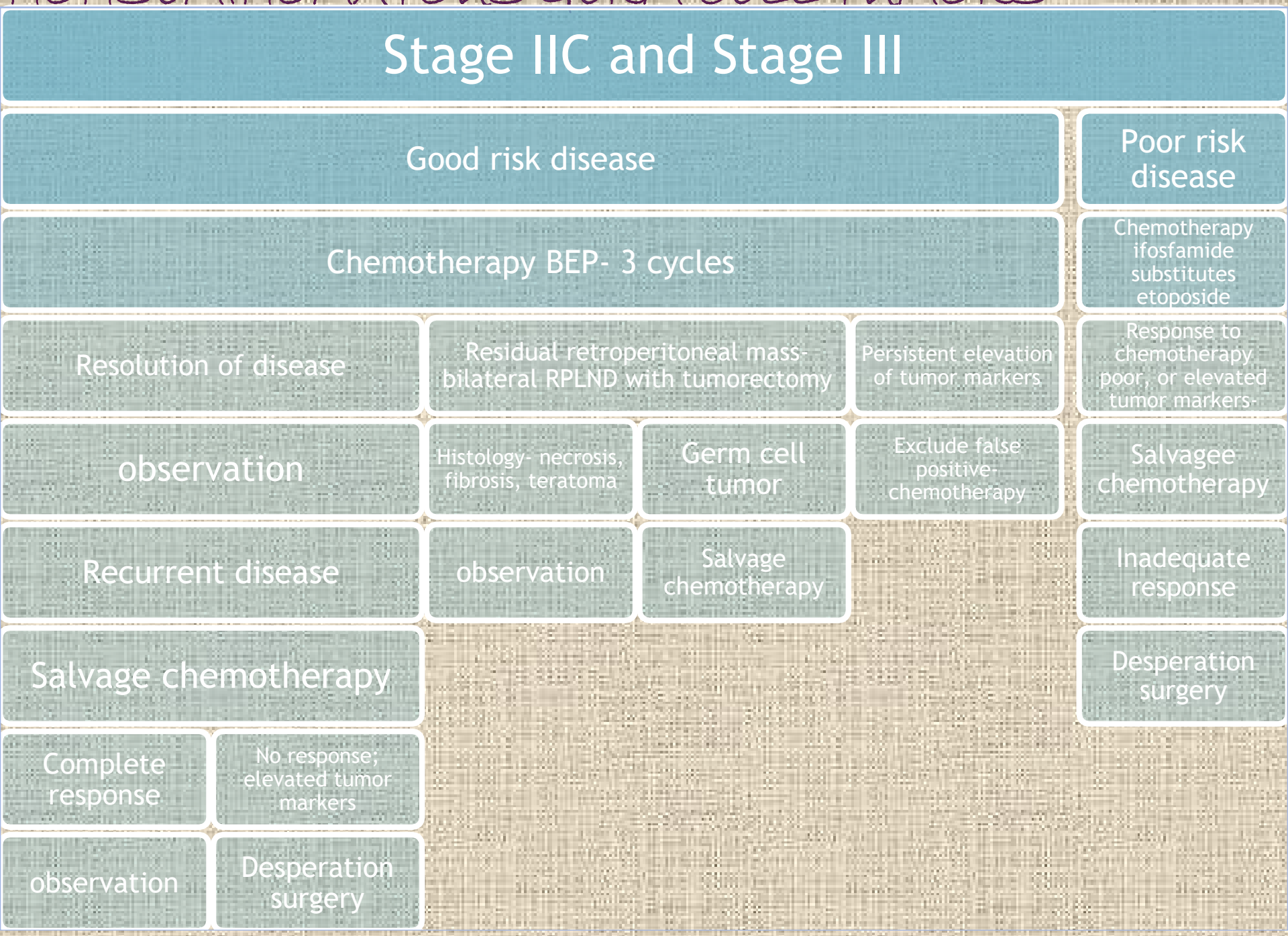
STAGE IIA AND IIB: TREATMENT PRINCIPLES

Primary chemotherapy:

- If nodes are larger than 3 cm on CT.
- Avoids ejaculatory failure.

Disadvantages: azoospermia, secondary malignancy.

17% of stage IIa patients and 39% of stage IIb patients require RPLND after chemotherapy for relapse.



NONSEMINOMATOUS GERM CELL TUMORS

STAGE IIC AND III: TREATMENT PRINCIPLES

Contraindication to adjunctive surgery in patients after chemotherapy: The presence of elevated levels of tumor markers.

Salvage Chemotherapy:

- residual cancer that has been resected after chemotherapy,
- who do not respond to traditional courses of induction therapy.

NONSEMINOMATOUS GERM CELL TUMORS

STAGE IIC AND III: TREATMENT PRINCIPLES

Patients who failed initial chemotherapy regimens:

Ifosfamide in combination with vinblastine and cisplatin.

Patients who failed 1st and 2nd line therapy:

Autologous bone marrow transplant or stem cell support with high dose chemotherapy regimens.