Testicular tumor

R3 Peerawit Songsiri

TABLE OF CONTENTS

History and epidemiology

History

Manage same protocols as adult : radical orchiectomy + retroperitoneal lymph node dissection

< 1980

1980 - Nowsaday

Prepubertal testis Tumor Registry (PTTR)

- Altered mamagement of testicular tumor in pediatric population

Epidemiology

- 1-2 % of all pediatric tumor
- 0.5 -2 /100,000 in whites, 0.25/100,000 in African-American
- Asia 1.4-fold increased risk of white
- Post puberty
  - 10 times more frequent than boys < 12 years
  - 90-95% are malignant with seminoma or mixed germ cell
- Age :
  - Bimodal distribution (< 3 years and large peak at 15-18 years)

Epidemiology

PTTR

Table 51.1 Primary Testes Tumor Types in 395 Boys Under 12 Years of Age

Tumor Type	Frequency (%)
Yolk sac	62
Teratoma	23
Stromal (unspecified)	4
Epidermoid cyst	3
Juvenile granulosa cell	3
Sertoli cell	3
Leydig cell	1
Gonadoblastoma	1

Metcalfe and colleges

74-87% are benign tumor

43-48% teratoma

15% yolk sac tumor

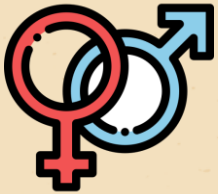
Risk factor

Risk factor

Undescended testis

Familial testicular germ cell

Contralateral testicular germ cell tumor



Gonadal dysgenesis

Risk factor

- Infertility
- Twin-ship
- Testicular atrophy

- Scrotal trauma
- Inguinal hernia
- Mumps orchitis
- Testicular torsion
- Maternal estrogen exposure
- Occupational exposure

Irrelevant

- Obesity
- Vasectomy
- Smoking
- Hydrocele
- Varicocele
- Alcohol
- Circumcision

Cryptorchidism

- 2-5 % of term male infant reduced to 1% at 1 year of age
- Only factor that has level I evidence linking to testicular cancer
- Overall relative risk 4.8
- Boys orchiopexy in older age (>10-12 years) increased risk of testicular cancer
- Should undergo orchiopexy in all children if complete descent not occurred by 12 months of age

Clinical presentation & Diagnosis

Clinical presentation

Fig. 51.9 This 3-year-old child presented with a painless scrotal mass and elevated AFP. He underwent a radical orchiectomy for a yolk sac tumor.

- **Clinical presentation**
  - Nontender scrotal mass (50 -85%)
  - Swollen
  - Precoccious puberty in hormonally active tumor
- **Physical examination**
  - Firm to touch
  - Transillumination : neg
  - Can get above mass
  - Sign of precocious puberty, gynecomastia
- **UA** :Normal urinalysis

Differential diagnosis

- Varicocele
- Spermatocele
- Epididymitis
- Orchitis

Investigation

Recommendations	LE	Strength rating
High-resolution ultrasound (7.5 – 12.5 MHz), preferably a doppler ultrasound, should be performed to confirm the diagnosis.	3	Strong
Alpha-fetoprotein should be determined in prepubertal boys with a testicular tumour before surgery.	2b	Strong

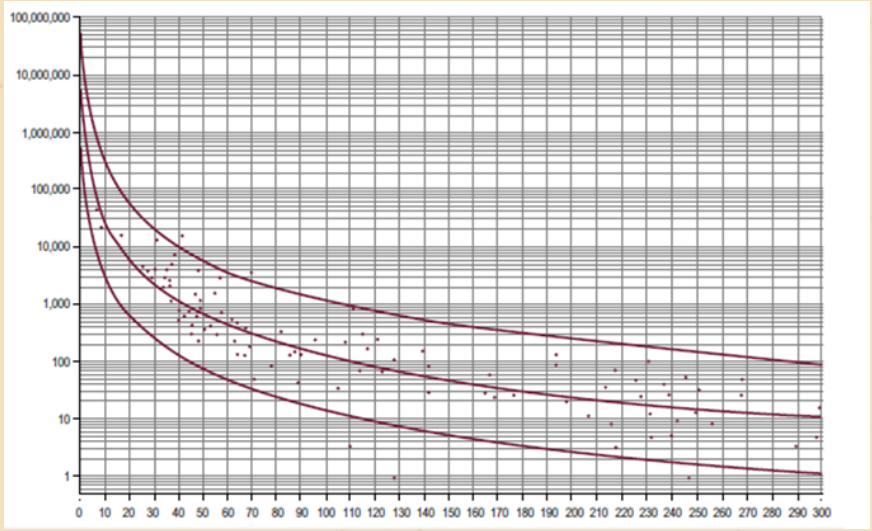
- **Scrotal US**
  - Benign
    - Anechoic cystic lesion
  - Epidermoid / Teratoma
    - Internal calcification
    - Mass with "onsion-skin" (hypo-and hyperechoic lesion)
- **Computed tomography of chest, Abd, pelvis**
  - If malignancy is suspected (most common at lung and retroperitoneum)

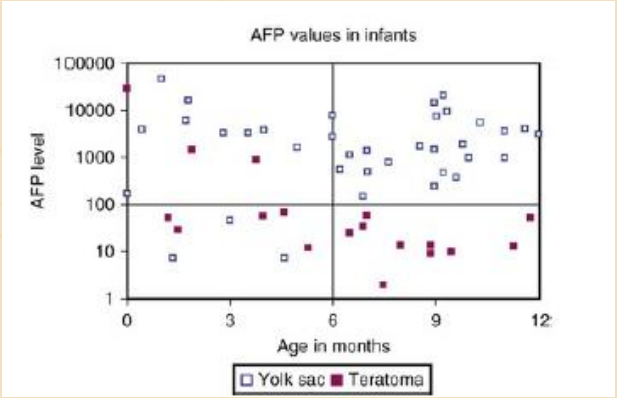
Tumor marker

- **Human chorionic gonadotropin (HCG)**
  - Secrete from seminoma, mixed germ cell tumor, and choriocarcinoma
  - Half-life 24 hours
  - Normally undetectable (<5 IU/L)

Tumor marker

- **Alpha-fetoprotein**
  - Secreted by yolk sac, liver, GI tract
  - Half-life 5.5 days
  - Normal adult < 10ng/ml achieved at 8-10 months
  - Can be elevated in teratoma, but rarely exceed 100 ng/mL





Other

- In mixed histology both AFP and HCG may be elevated
- Precocious puberty and testicular mass work up urinary 17-ketosteroid, serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone

	Testicular tumor	Pituitary lesion
LH	⇩	⇧
FSH	⇩	⇧
Testosterone	⇧	⇧

Staging and classification

Staging

TABLE 40-2

Staging of Testicular Malignant Germ Cell Tumors

Testicular Stage	
I	Limited to testis, completely resected by high inguinal orchiectomy; no clinical, radiologic, or histologic evidence of disease beyond the testis; tumor markers normal after resection
II	Transscrotal orchiectomy; microscopic disease in scrotum or high in spermatic cord; retroperitoneal node involvement (<2 cm) and/or increased tumor markers after resection
III	Gross residual disease, retroperitoneal lymph node involvement (>2 cm), or malignant cells in pleural or peritoneal fluid
IV	Distant metastases involving lung, liver, brain, bone, distant nodes, or other sites

Table 51.2 Children's Oncology Group Staging System for Testicular Cancer

Stage	Features
I	Limited to testis Completely resected by high inguinal orchiectomy No clinical, radiographic, or histologic evidence of disease beyond the testes Patients with normal or unknown tumor markers at diagnosis must have a negative ipsilateral retroperitoneal node sampling to confirm stage 1 disease
II	Trans-scrotal biopsy or orchiectomy Microscopic disease in scrotum or high in spermatic cord (<5 cm from proximal end) Failure of tumor markers to normalize or decrease with an appropriate half-life
III	Retroperitoneal lymph node involvement No visceral or extra-abdominal involvement
IV	Distant metastases

Adapted from Hayes-Lattin B, Nichols CR. Testicular cancer: a prototypic tumor of young adults. Semin Oncol. 2009;36(5):432–438.

Classification

TABLE 40-1

Differences in Distribution of Testicular Tumors Based on Tumor Histology among Study Sites

Tumor Type	*2002 Registry % (N = 395)*	*Pohl % (N = 98)*	*Metcalfe % (N = 51)*	*Ciftci % (N = 51)*
Benign				
Teratoma	23	48	43	18
Epidermoid cyst	3	14	10	6
Leydig cell	1	4	0	6
Sertoli cell	3	3	4	0
Juvenile granulosa cell	3	5	0	N/A
Malignant				
Yolk sac	62	15	8	45
Mixed germ cell	0	0	8	6
Rhabdomyosarcoma	4	Excluded	25	19
Gonadoblastoma	1	2	2	0

N/A, not available.

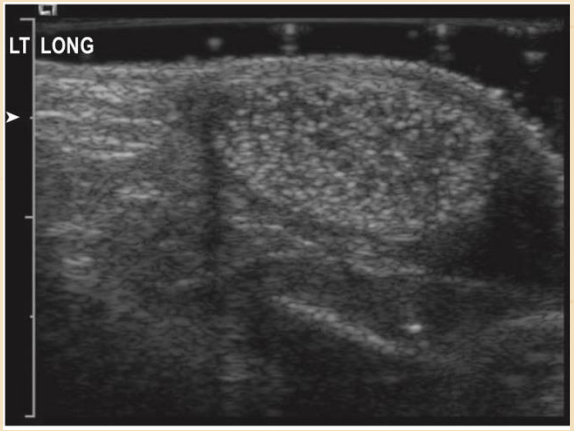
Testicular microlithiasis

- U/S finding that can be seen in conjunction with testicular tumors (15-45%)
- 5% incidentally in healthy young men
- Risk of developing malignancy is not well-studied
- Factor increase risk of malignancy
  - Atrophic/Dystrophic testes
  - Known chromosomal abnormalities
  - Contralateral testicular cancer
  - History of UDT

Need routinely exam and serial scrotal U/S

Carcinoma in situ (CIS)

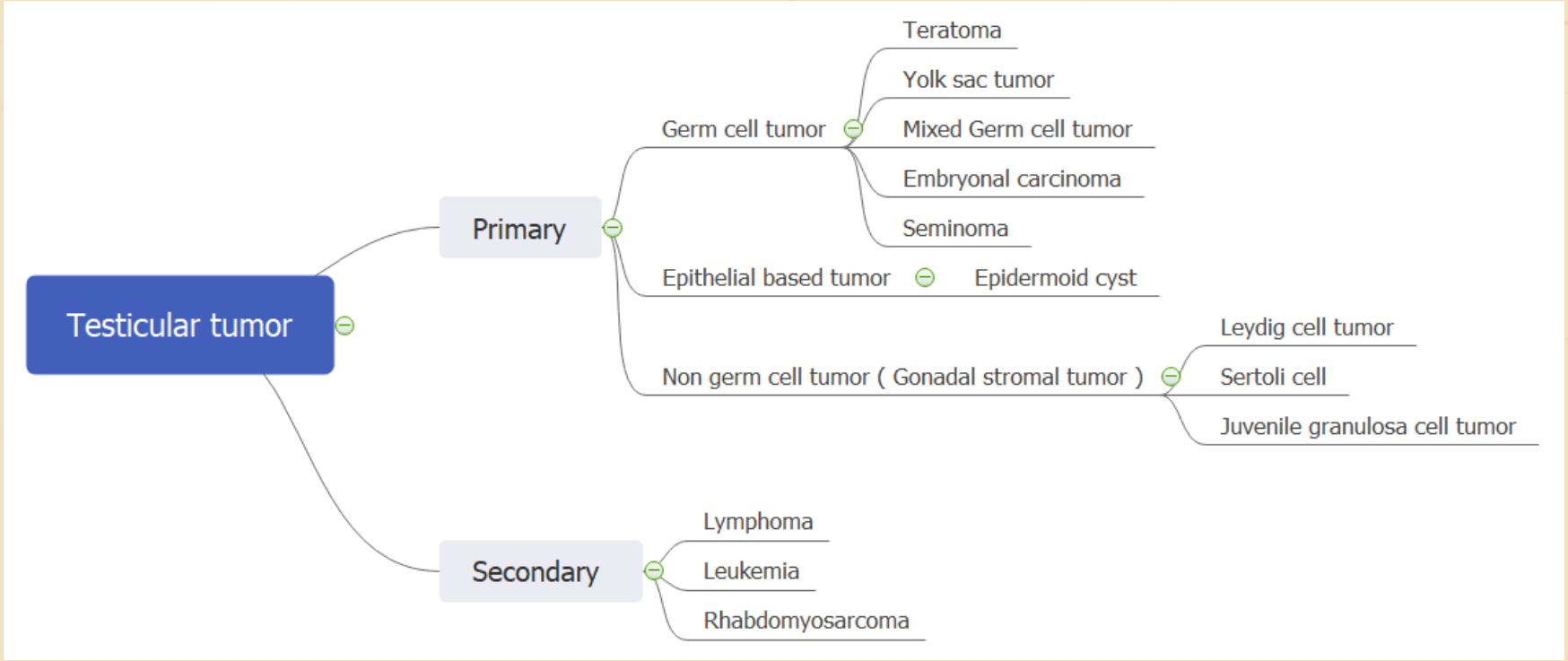
- Premalignant lesion can develop cancer > 50% of testis with CIS
- Testicular microlithiasis associated with ↑ risk of CIS (but not conclusively considered premalignant)
- Prevalence of CIS with history of UDT 2-4%



CIS in prepubertal testis → Annual testicular exam and US

CIS in postpubertal testis → Biopsy contralateral testis + unilateral orchiectomy → 18-20 Gy radiation if biopsy reveal CIS

Classification



01

Gonadal Stromal Tumors

Sex cord-stromal tumor

- Consist of three subtypes
  1. Leydig cell
  2. Sertoli cell
  3. Juvenile granulosa cell
- 8-11 % of pediatric tumor
- Most are benign

Leydig cell tumor

- Most common non germ cell tumor (NGCTs)
- Peak incidence : 5-9 years
- Tend to benign
- Clinical triad
  1. Unilateral testicular mass (90-93%)
  2. Precocious puberty, gynecomastia (20%)
  3. ↑ 17-ketosteroid levels
- Lab : ↓ LH, ↓ FSH, ↑ testosterone
- Must evaluate for pituitary lesion, CAH
- Treatment
  - Testis-sparing enucleation

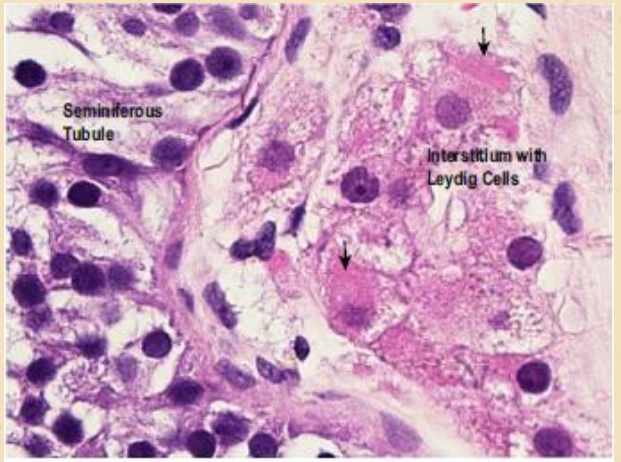


Fig. 51.14 On histologic examination, Reinke crystals (arrows) are pathognomonic for a Leydig cell tumor and are found in up to 40% of these tumors.

Histological : Reinke crystal

Granulosa cell tumor

- Rare in children
- Occur almost in first 6 months of life
- Abnormalities in Y chromosome, associated with ambiguous genitalia
- Tend to benign
- Clinical
  - Neonate with scrotal swelling
  - Normal age-adjusted AFP level
  - US : complex, cystic, multiseptated, hypoechoic mass
- Treatment
  - Testis-sparing enucleation

Sertoli cell tumor

- Rare from of non-GCT
- Median age of presentation 6 month
- Benign in children < 5, 10% malignancy in adult
- 1/3 associated with genetic syndrome, or endocrinopathy eg. Peutz-Jeghers, Carney syndrome
- Clinical
  - Small percentage has gynecomastia
- Treatment
  - Testis-sparing enucleation

Metastatic evaluation with imaging in

1. Older children (> 5 year)
2. Microscopic invasion of spermatic cord
3. Worrisome finding (large tumor, necrosis, vascular invasion, cellular atypia, ↑ mitotic activity)

02

Germ cell tumor

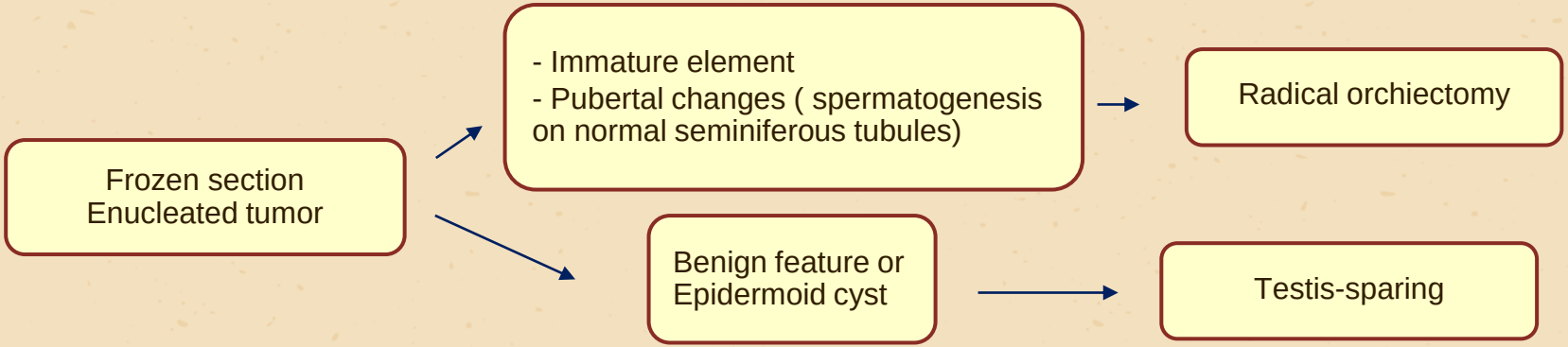
Teratoma

Fig. 51.13 A 4-year-old child was found to have a painless testicular mass. Serum markers were negative. At operation, this well-demarcated tumor was encountered that was amenable to a testis-sparing operation. Frozen analysis was consistent with a benign tumor (teratoma).

- Most common germ cell tumor in children (40%)
- Most are benign in prepuberty
- Adjacent testis has normal spermatogenesis
- Gross
  - Solid cystic appearance
  - Contains hair, cartilage, muscle, bone, fat
- Histologically
  - 3 layer of ectoderm, endoderm, mesoderm
  - Lipiod reaction

Teratoma : Treatment

- **Before puberty**
  - Testis-sparing surgery
  - No tumor recurrence in ipsilateral or contralateral
  - No radiographic follow is needed
- **After puberty**
  - Radical inguinal orchiectomy
  - Follow AFP for potential recurrence
  - Can be salvage with platinum-based CMT



Epidermoid cyst

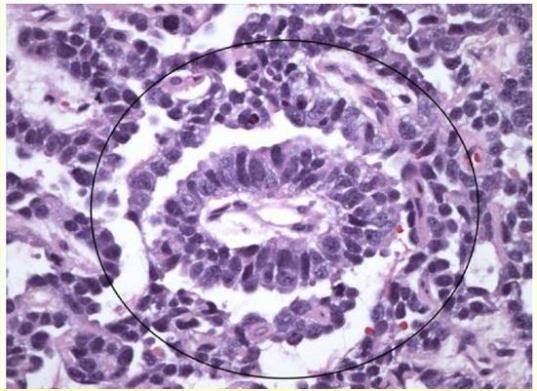
- Benign tumor
- 2-14% of testicular tumor
- Hormonally inactive
- Presentation of tumor
  - smooth, firm, intratesticular mass
  - Consist of cystic structure filled with keratinizing squamous epithelium

- Ultrasound
  - Central hypoechoic mass
  - Echogenic rim
  - Or mixed internal echogenicity

Yolk sac tumor (YST)

- Also called endodermal sinus tumor, embryonal adenocarcinomas, orchioblastoma, Teillum tumor
- Incidence 8-15%
- Most occur in boys < 2 year, but rare in first 6 months of life
- PTTR of American academy of pediatric
  - 84.5% localized stage I
  - 15.5% metastasis (most common site is lungs)
- ↑ AFP level

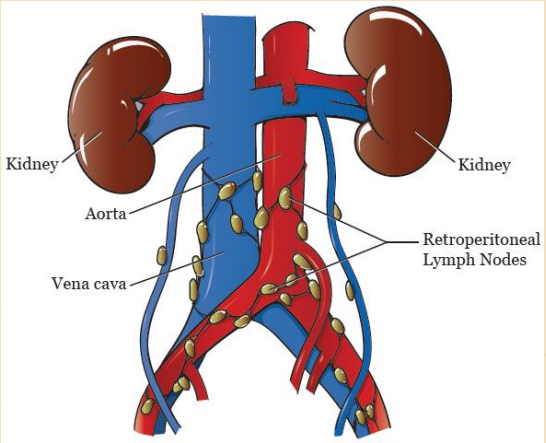
- **Histology**
  - Firm and yellow, white to gray
  - Schiller-Duval bodies, + AFP and placenta-like alkaline phosphatase



Yolk sac tumor (YST)

- **Treatment**
  - Standard radical orchiectomy
  - 5-year survival 99%

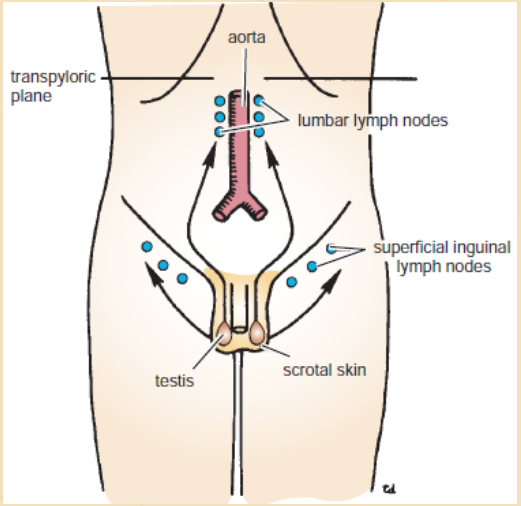
- **Stage I (tumor limited to testis)**
  - Radical inguinal orchiectomy
  - Tumor marker monthly, CXR q 2 month for 2 years
  - Abdominopelvic CT or MRI q 3 month for 1 year , q 6 month in 2nd year
  - After 2 year if normal follow up 6 month – yearly



RPLND

- Recommend in unknown or normal tumor marker at diagnosis
- To confirm stage I
- Used less often due to 85% is stage I, high complication rate, recurrence (20%) can be savage with CMT

Yolk sac tumor (YST)



- **Stage II**
  - Radical orchiectomy
  - Combination of CMT
    - Cisplatin or carboplatin + Etoposide+ Bleomycin

RPLND in case of

- Persistent retroperitoneal mass
- Elevated AFP after CMT

Yolk sac tumor (YST)

- **Stage III**
  - Enlarged retroperitoneal spread (LN > 4 cm)
- **Stage IV**
  - Metastases beyond retroperitoneum or any viscera

Management

- Radical orchiectomy
- CMT -> same protocol of stage II + RPLND

Mixed germ cell tumor

- 20% of pediatric/adolescent germ cell tumor
- Up to 80% are confined to the testis at presentation
- Foci of choriocarcinoma : poor prognosis
- Management
  - Follow adult guideline

Seminoma

- Rare in children
- Most common tumor in uncorrected abdominal UDT

- Treatment
  - Radical orchiectomy + retroperitoneal radiation
  - Follow adult guideline

Embryonal carcinoma

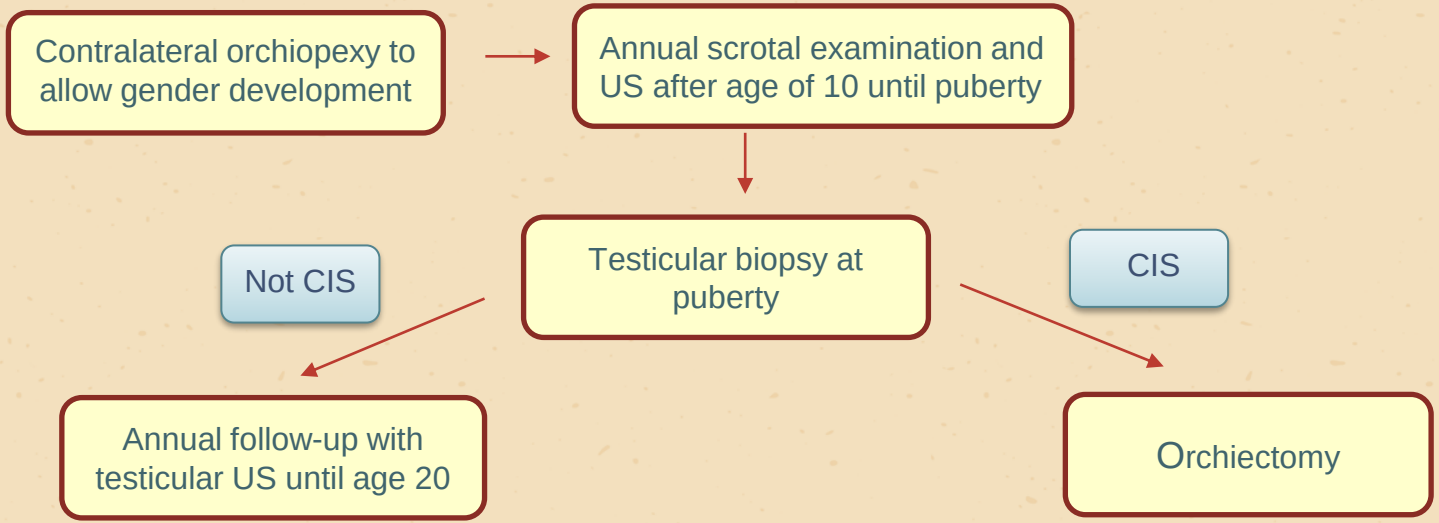
- Common germ cell tumor after puberty
- 10% are pure embryonal tumor
- Histology
  - Distinctive sheets, glands and papillary structure
  - Primitive epithelial cells with crowded pleomorphic nuclei
  - Poor diff : CD30+, OCT3+, c-KIT negative
- Treatment
  - Orchiectomy
  - Postoperative CMT and close follow up in high risk tumor
    - Tumor composed of > 80% embryonal cell carcinoma or AFP >10,000 mg/ml, vessel invasion, stage T2 or greater

Gonadoblastoma

- Classically seen in mixed gonadal dysgenesis (45,X/46,XY)
- Related to presence of testis-specific protein-Y-encoded gene (TSPY)
- Female with complete androgen insensitivity syndrome(CAIS) with intraabdominal testis
- Small, bilateral 30% of cases, malignant in 10%, histology resemble seminoma
- Gonad of origin
    - 20% dysgenetic testis
    - 26% streak gonad
    - 54% undifferentiated gonad

Gonadoblastoma

- Treatment
  - Traditionally : bilateral gonadectomy due to risk of degeneration into invasive seminoma
  - Currently : debate of timing and need for gonadectomy



Choriocarcinoma

- Rarest of gonadal germ cell tumor (0.3% of testicular tumor)
- Increase level of beta-HCG
- Clinical
  - Precocious puberty
  - Gynecomastia
  - Hyperthyroid
- Histological
  - Syncytiotrophoblastic cells with mononucleated cells around foci of hemorrhage
  - Beta-HCG and placental lactogen stain positive

03

Miscellanous tumor

Rhabdomyosacrcoma

- Technically a paratesticular tumor
- Most frequent tumor of paratesticular origin (4-25% of scrotal masses)
- Arise from testicular tunic, epididymis, or spermatic cord
- Peak between 3-4 months and 15-19 years of age
- Infant tumor more indolent than adolescent age group (90% vs 63% failure-free survival)
- Prognosis improve due to introduction of vincristine, dactinomycin, cyclophosphamide (VAC)
- Most common subtype is embryonal rhabdomyosarcoma (97%)

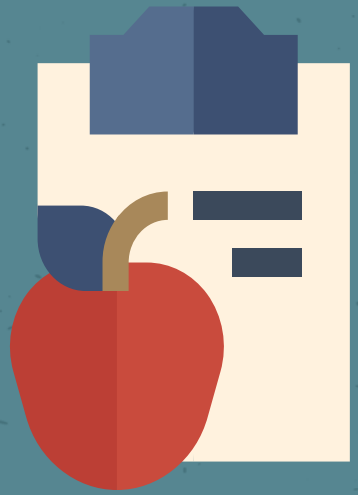
Rhabdomyosacrcoma

- Investigation
  - U/S : paratesticular location, hyperechoic. Heterogenous, solid mass
  - CT or MRI of retroperitoneum for staging purposes (30-40% have micrometastasis to retroperitoneum)
  - Metastasis work up : chest CT, LFT, bone scan, bone marrow biopsy
- Histology
  - Small round blue cells
- Treatment
  - Radical inguinal orchiectomy
  - RPLND recommended in
    - Patient > 10 years
    - < 10 years with radiological evidence

**Avoid biopsy (may lead to contamination of operative field)

Lymphoma and leukemia

- ALL is common cause of prepubertal testicular mass
- U/S scrotal in first diagnosis leukemia/lymphoma
  - Homogenous hypoechoic mass
- Biopsy in case of newly enlarged testis after CMT for additional CMT
- Clinical
  - 25% - widespread systemic involvement
  - 25% - Ann Arbor stage II (involvement of lymph node below diaphragm)
  - 50% - Ann Arbor stage I (confined to testis)



Operative Treatment

Management algorithms

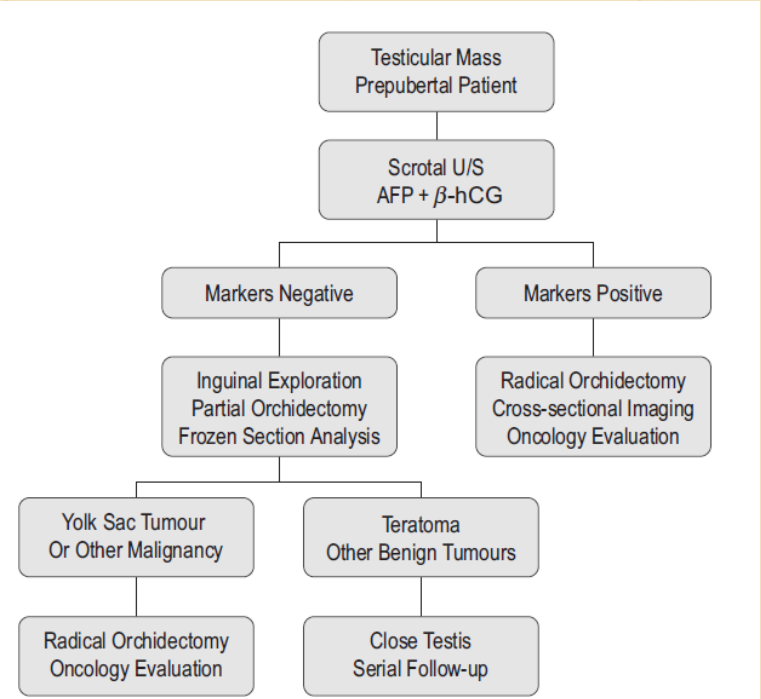


Fig. 51.8 This algorithm depicts management of the prepubertal male with a testicular mass that is suspicious for cancer.

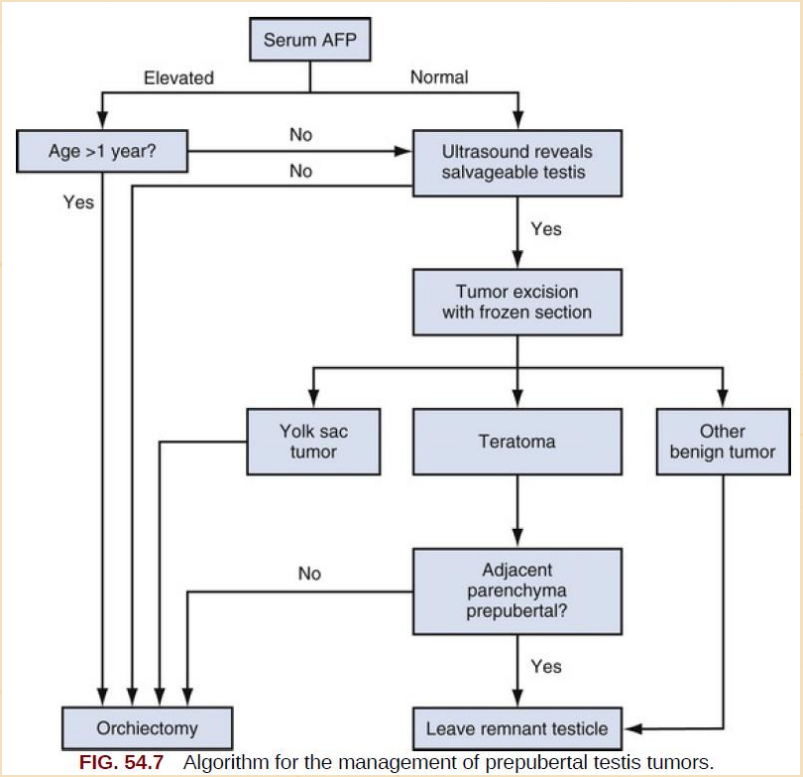
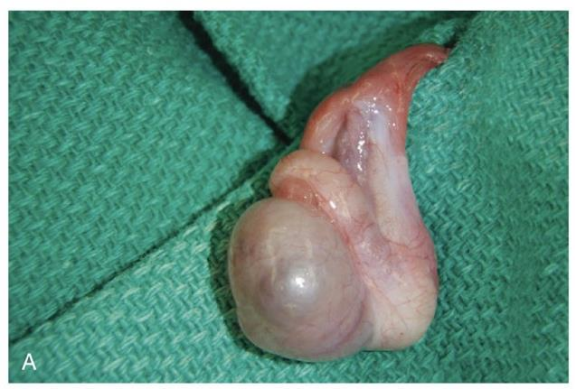


FIG. 54.7 Algorithm for the management of prepubertal testis tumors.

01

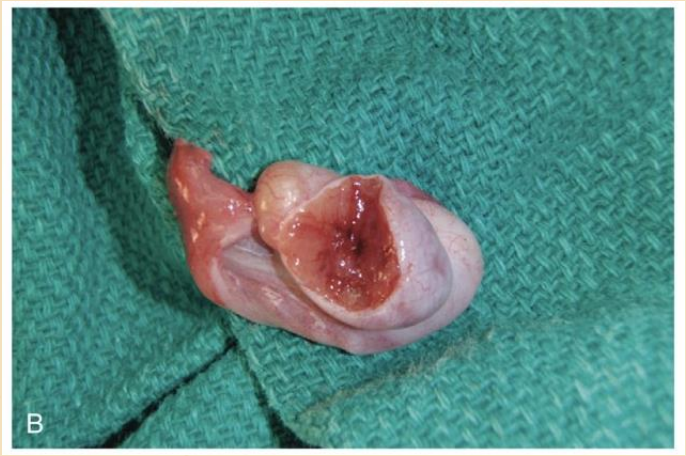
Testis-sparing surgery

Testis-sparing surgery



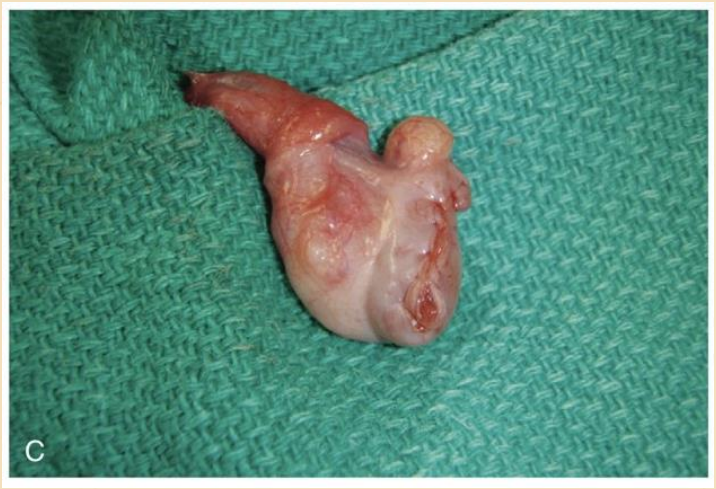
- Inguinal incision
- External oblique aponeurosis is open to level of internal ring
- Cremasteric fiber is dissected from cord structure to allow circumferential control of cord
- Testis is delivered through inguinal incision

Testis-sparing surgery



- Tunica vaginalis is opened directly over mass
- Excision biopsy of mass is performed without violate tumor capsule
- Frozen section evaluate

Testis-sparing surgery



- If benign -> tunica vaginalis is closed with fine absorbable suture, and replaced in the scrotum
- If malignancy -> radical orchiectomy

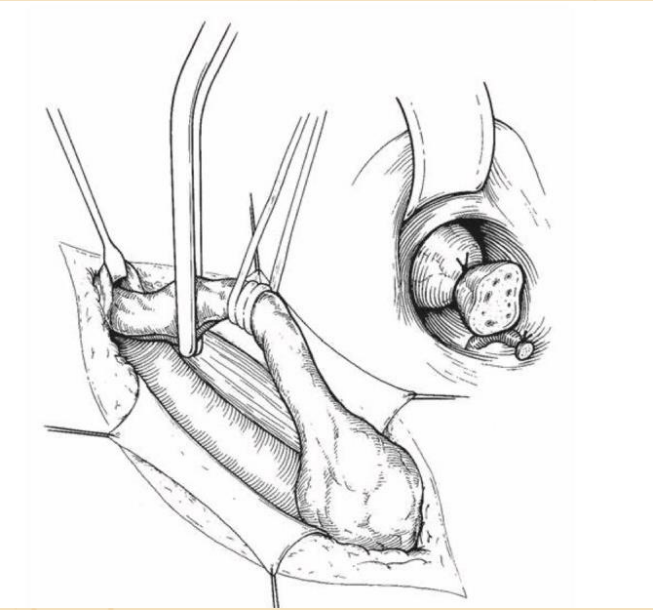
Testis-sparing surgery

- Normal tissue adjacent to tumor must sent for pathologist to exclude pubertal change
- 90% of adult testicular tumor are associated with intratubular germ cell neoplasia (ITGCN) in surrounding parenchyma
- ITGCN are precursors for germ cell tumor, if left in situ may cause recurrent of tumor

02

Radical inguinal orchiectomy and retroperitoneal lymph node dissection

Radical inguinal orchiectomy



- Standard inguinal incision
- Open external ring back to level of the internal ring
- Dissect cremasteric fiber until fully mobilized of cord
- Cord is clamped and divided at level of internal ring
- Stump is suture and ligate
- Dissect testis from scrotum and divided from gubernaculum
- Excision tumor and close wound

Retroperitoneal lymph node dissection (RLPND)

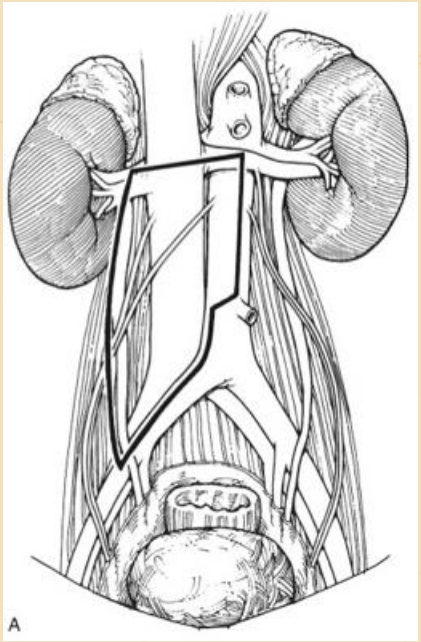
- Current pediatric testicular tumor protocol do not include RLPND
- Indication
  - COG advice RLPND for all children > 10 years suspected paratesticular tumor to avoid failure in the retroperitoneum an burden of second-line therapy

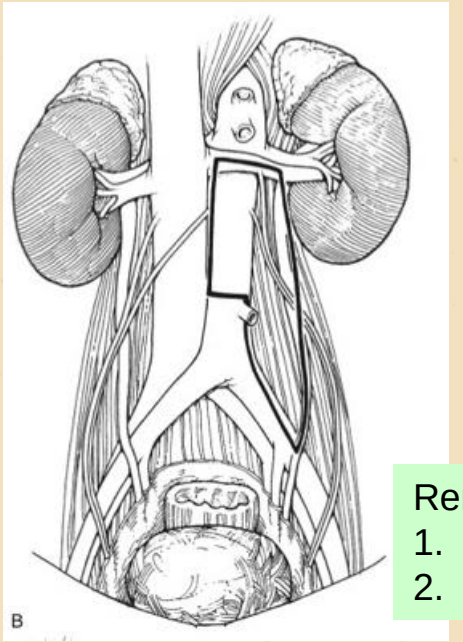
Retroperitoneal lymph node dissection (RLPND)

- Midline abdominal incision
  - Right side lesion
    - Remove lymphatic in interaortocaval, precaval, and rt paracaval distribution
  - Left side lesion
    - Left paraortic and preaortic lymphatic
  - Important to preserve contralateral sympathetic for emission and ejaculation

Retroperitoneal lymph node dissection

Remove lymphatic in
1. Interaortocaval
2. Precaval
3. Right paracaval

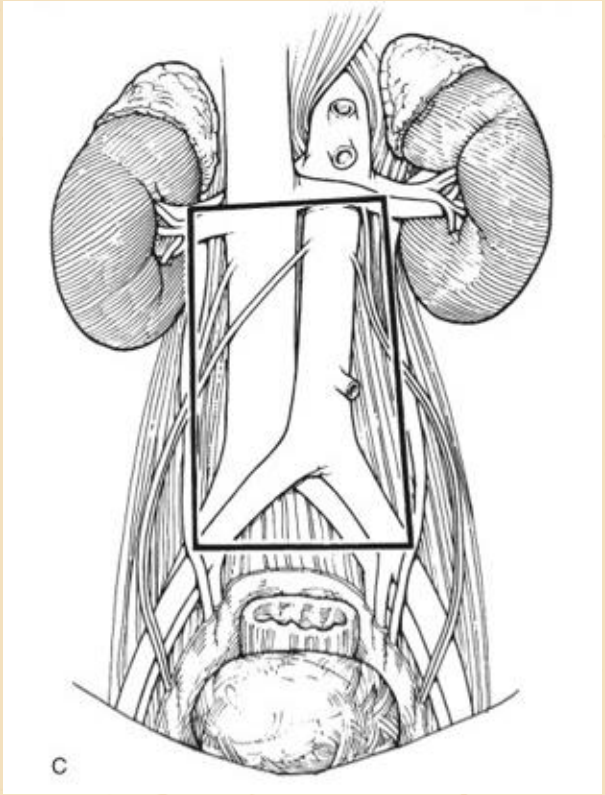




Remove lymphatic in
1. Left paraortic
2. Preaortic lymphatic

Retroperitoneal lymph node dissection

- Bilateral dissection
  - Finding viable tumor outside template distribution
  - Advanced-stage
  - High volume disease



Chemotherapeutic strategies & Survival in maligant germ cell tumor

Survival in malignant Germ cell tumor

- Prior to effective CMT
- Malignant germ cell tumors (MGCT) 3 year survival rate 15-20% with surgery and radiation

CMT : Cisplatin, etoposide, bleomycin

TABLE 40-3

Standard Treatment for Children Younger Than 15 Years with Testicular Germ Cell Tumors by Histology and Stage

Histology	*Stage*	*Treatment*	*Overall Survival (6-Year)*
Mature teratoma	Localized	Surgery + observation	100%
Immature teratoma	Localized	Surgery + observation	100%
MGCT	Stage I	Surgery + observation	100%
	Stage II-IV*	Surgery + PEB	94%

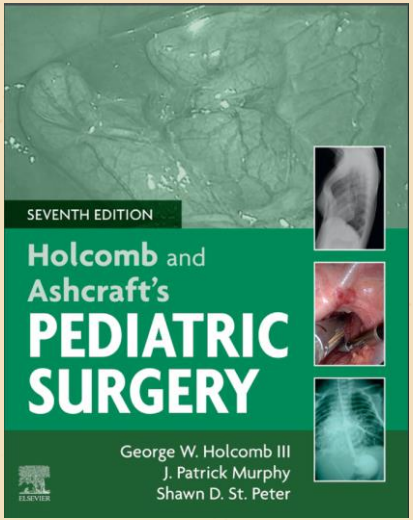
*Patients greater than 15 years old with stage IV testicular tumors should be discussed in a multidisciplinary oncology group for more intensive therapy.

MGCT, malignant germ cell tumors; PEB, cisplatin, etoposide, and bleomycin.

Children's Oncology Group (COG)

	Definition	Management
Low risk	Stage I immature teratoma and MGCT of the testis	Surgery + close follow-up
Intermediate risk	Stage II-IV gonadal tumors	Surgery + cisplatin, etoposide, and bleomycin

References


SEVENTH EDITION
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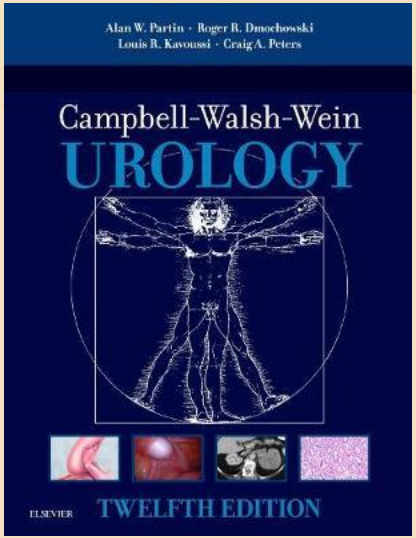
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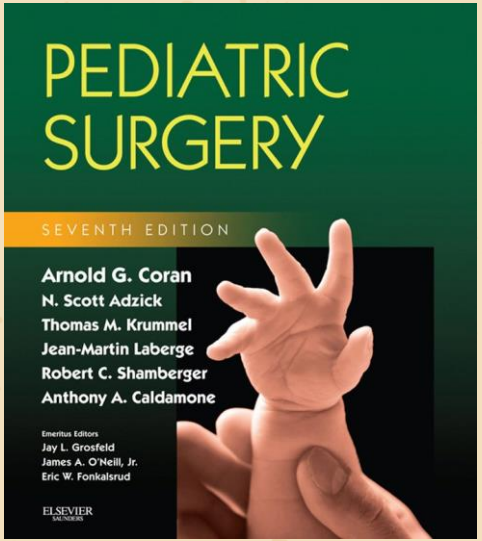
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THANKS!

Do you have any questions?