University of Kentucky
Department of Urology

Testicular GCT – The Importance of Pubertal Status

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Amanda F. Saltzman MD
Associate Professor, Urology & Pediatrics

Objectives

1. General
2. Age, puberty, STMs
3. Teratoma (pre- vs. post-pubertal)
4. Role of primary RPLND for pre-pubertal patients
5. Surgical management – radical orchiectomy vs. testis-sparing surgery (TSS)

Introduction

- In adults, most testicular masses are malignant
- Orchiectomy is the standard of care for all testicular cancers

- In children, 75% of testicular masses are benign
- Partial orchiectomy is acceptable to minimize removal of gonadal tissue
  - AKA testicular sparing surgery (TSS)

- In pediatrics, COG and NCCN guidance is available → need to know both
  - Pre-pubertal → COG algorithms
  - Post-pubertal → NCCN algorithms

GCTs and Puberty

- Biology is different between younger kids and teens/AYAs
- Differences in:
  - Histology
  - Etiology (field vs focal insult)
  - Chromosomal abnormalities
  - Gene expression profile
  - Incidence
- Thus treatment is often different as well

Age

	Pre-Pubertal	Adolescent/Adult
Malignant potential	70-75% Benign	75% Malignant
Predominant type of malignancy	Pure YST or pure teratoma	Mixed, NSGCT
Metastatic potential	5% at presentation	20-30% at presentation
Teratoma	Common (40%) as pure teratoma, uniformly behaves in a benign manner	Part of a mixed tumor, higher potential for metastatic spread and malignant degeneration

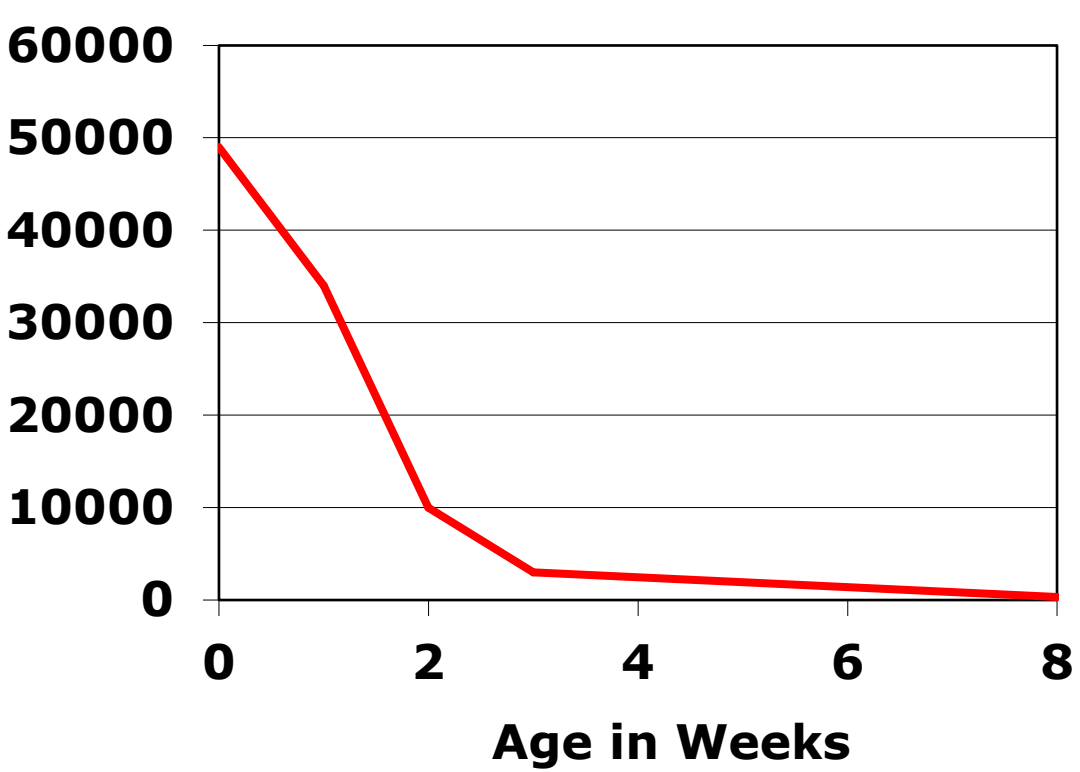
Woo L & Ross JH. "Testicular Tumors in Children and Adolescents." *AUA Update Series* 2019;38:381-9.

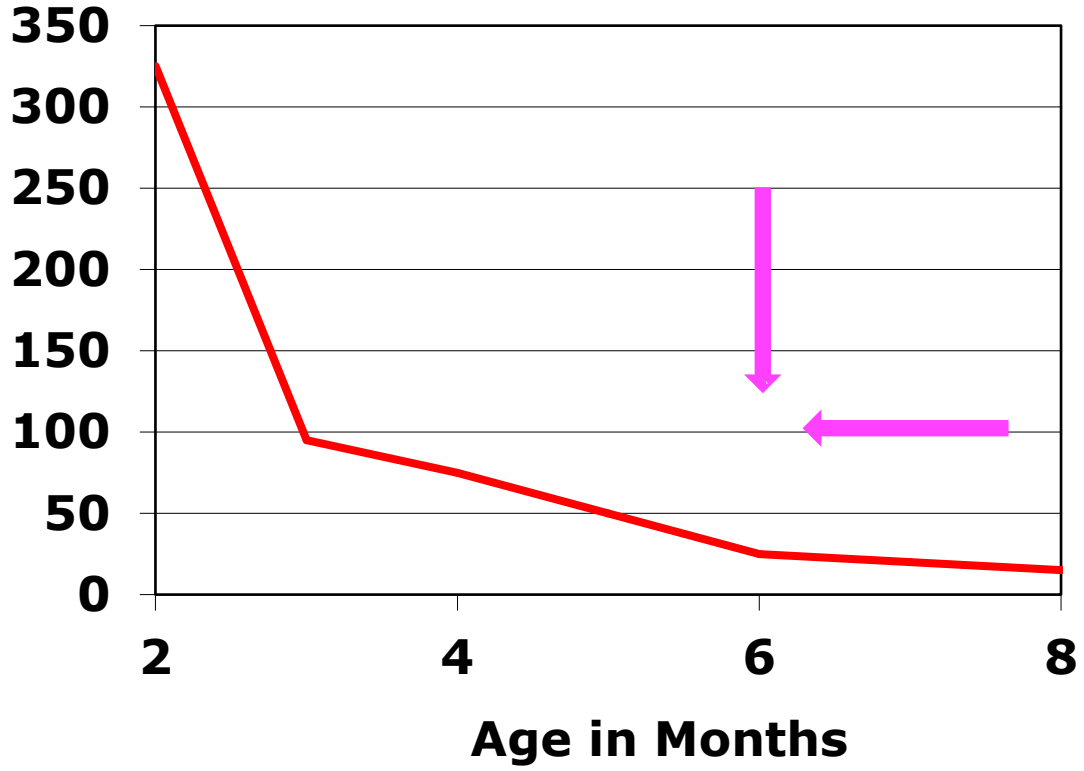
Serum Tumors Markers

- αFP
  - Secreted by 90% of YST, never pure seminoma
  - Secreted by NSGCTs
  - Physiologic elevation in infancy, liver disease; some individuals post-puberty (<20)
- βhCG
  - Elevated with NSGCT (chorio), 20% seminoma
  - Rarely elevated in pre-pubertal patients
  - Elevated with NSGCT (chorio), 20% seminoma, conditions with high LH
- LDH
  - Sign of bulk disease; do not make treatment decisions based on this alone
- Inhibin
- Testosterone
- Estradiol

} Stromal tumors

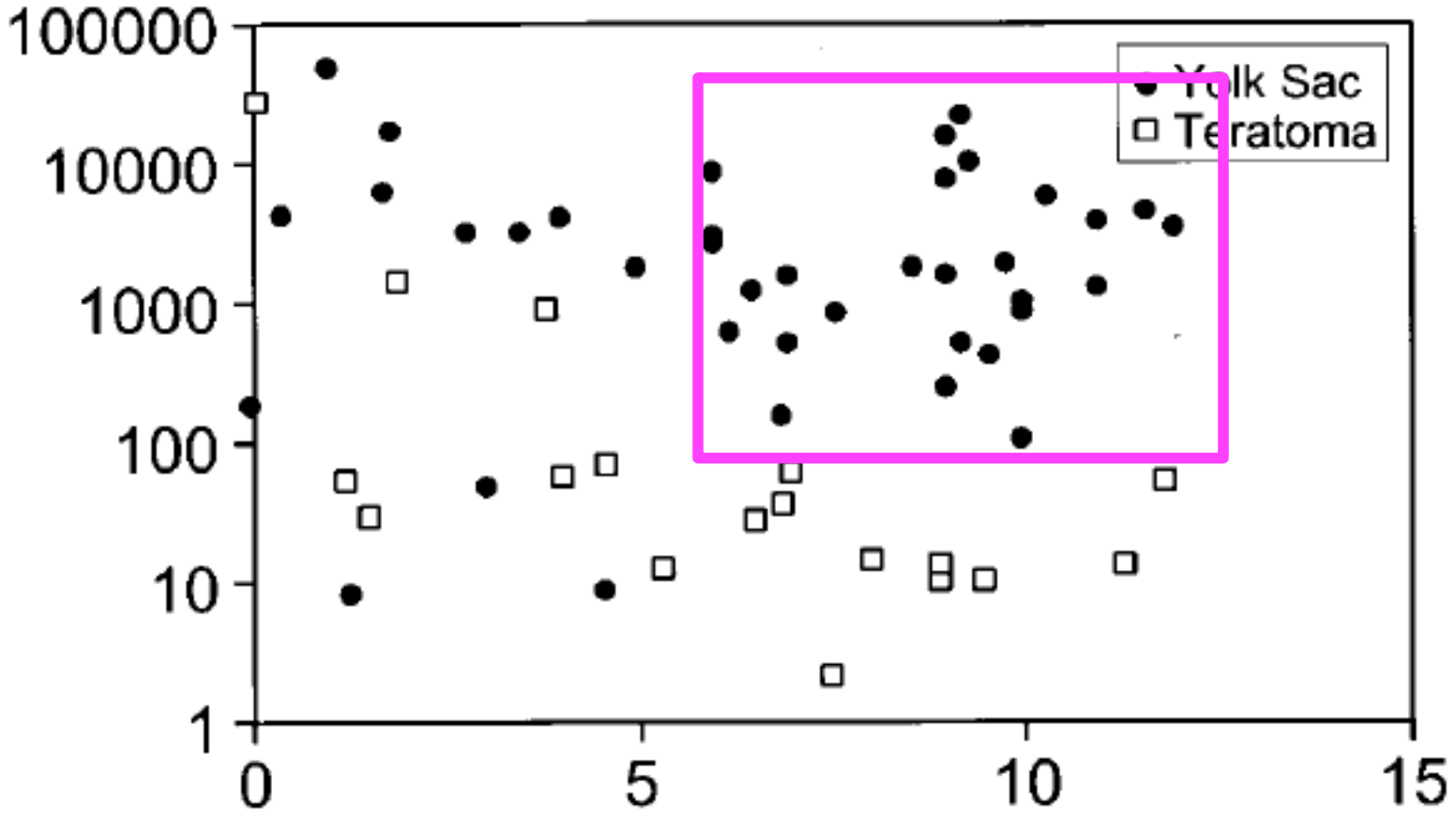
αFP - Neonates





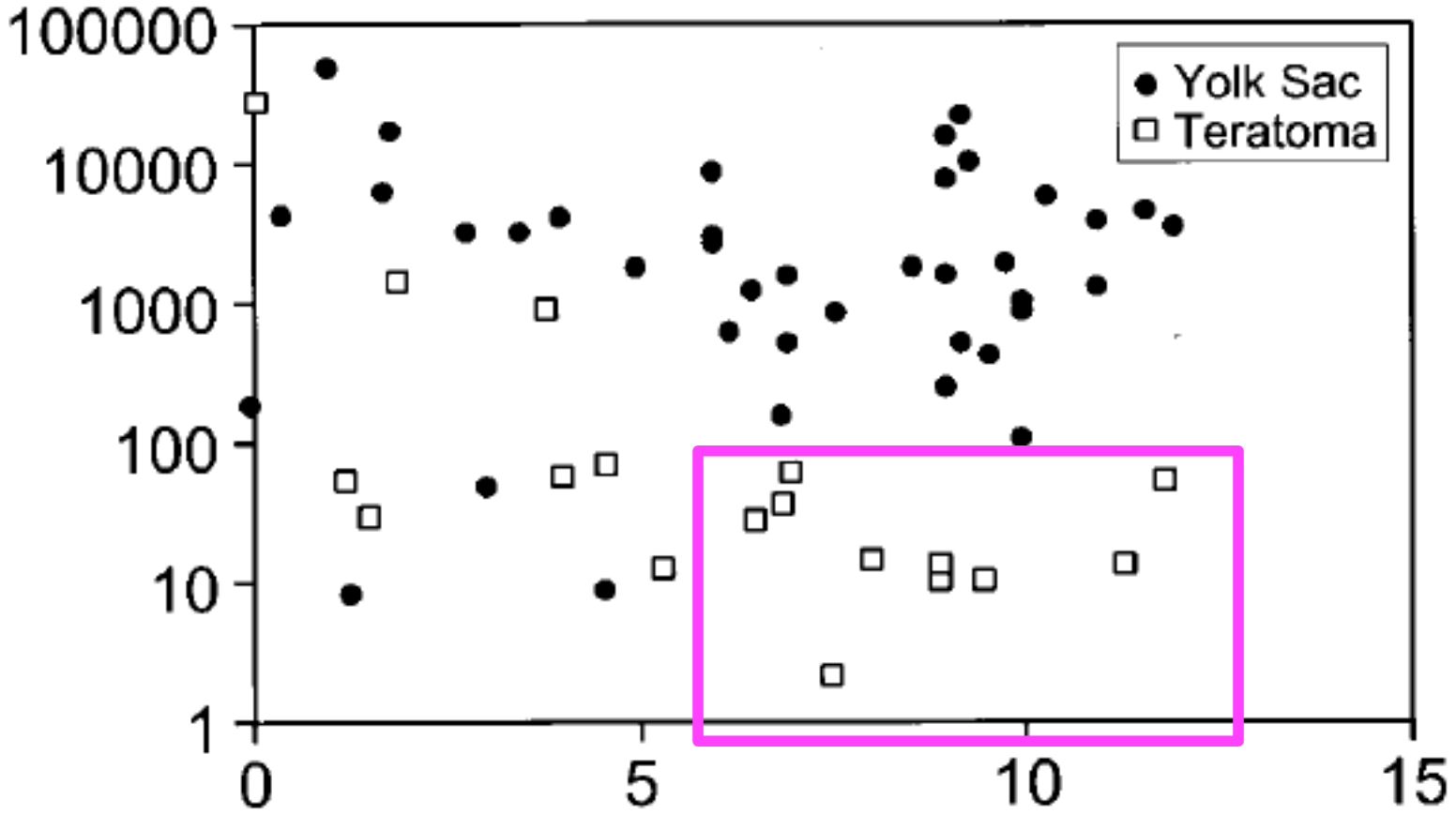
Ross JH, Rybicki L, Kay R. *J Urol* 2002;168:1675-9.

Infants with Testis Masses



After age >6mos, all YST had αFP>100

Infants with Testis Masses



After age >6mos, all teratoma had αFP<100

Teratoma

- Can be found at any age
  - Commonly pure and mature in pre-pubertal patients
- Behavior depends on age/pubertal status of patient
  - Benign in pre-pubertal (focal insult, no GCNIS)
  - Mets and malignant degeneration in post-pubertal (field effect, with GCNIS)
- Surgical management depends on pubertal status and tumor markers
  - Cannot differentiate pathology on preoperative imaging

Grady RW, Ross JH, Kay R. *J Urol 1997*;158:1191-1192.

Pre-Pubertal Testis Tumor Registry

- AAP Section of Urology from 1980-1996
  - Age <12y; mean follow up 37 mos
  - Managed with radical or partial orchiectomy

- n=392
  - 62% with YST
  - 23% teratoma (n=92)

- Of those with teratoma:
  - Median age 13 mos
  - 0 patients with mets at diagnosis or during follow up
  - All elevations in αFP in infants <12mos old*

Grady RW, Ross JH, Kay R. *J Urol 1997*;158:1191-1192.
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Pre-Pubertal Tumors → More Likely to be Benign?

- When prior study came out, this conflicted with institutional reports of benign tumors being more common than YST
- 98 patients from 4 major pediatric institutions

Category	Pathology	Frequency
Malignant	YST	15%
Benign	Teratoma mature immature	48% 44% 4%
	Epidermoid cyst	14%
	Stromal tumors granulosa cell Sertoli cell mixed	13% 5% 4% 1%
	Other	9%

Pohl H, *et al. J Urol* 2004 ; 172 (6 pt 1):2370-2

Pre-Pubertal Tumors → More Likely to be Benign?

- Vast majority of pre-pubertal testis tumors are benign, not malignant
  - Prior registry likely biased by lower submission of benign cases to a tumor registry

- Given high prevalence of benign pathology → TSS should be considered standard
  - Orchiectomy should be reserved for patients with elevated AFP or tumors known to be malignant (i.e. by frozen section)

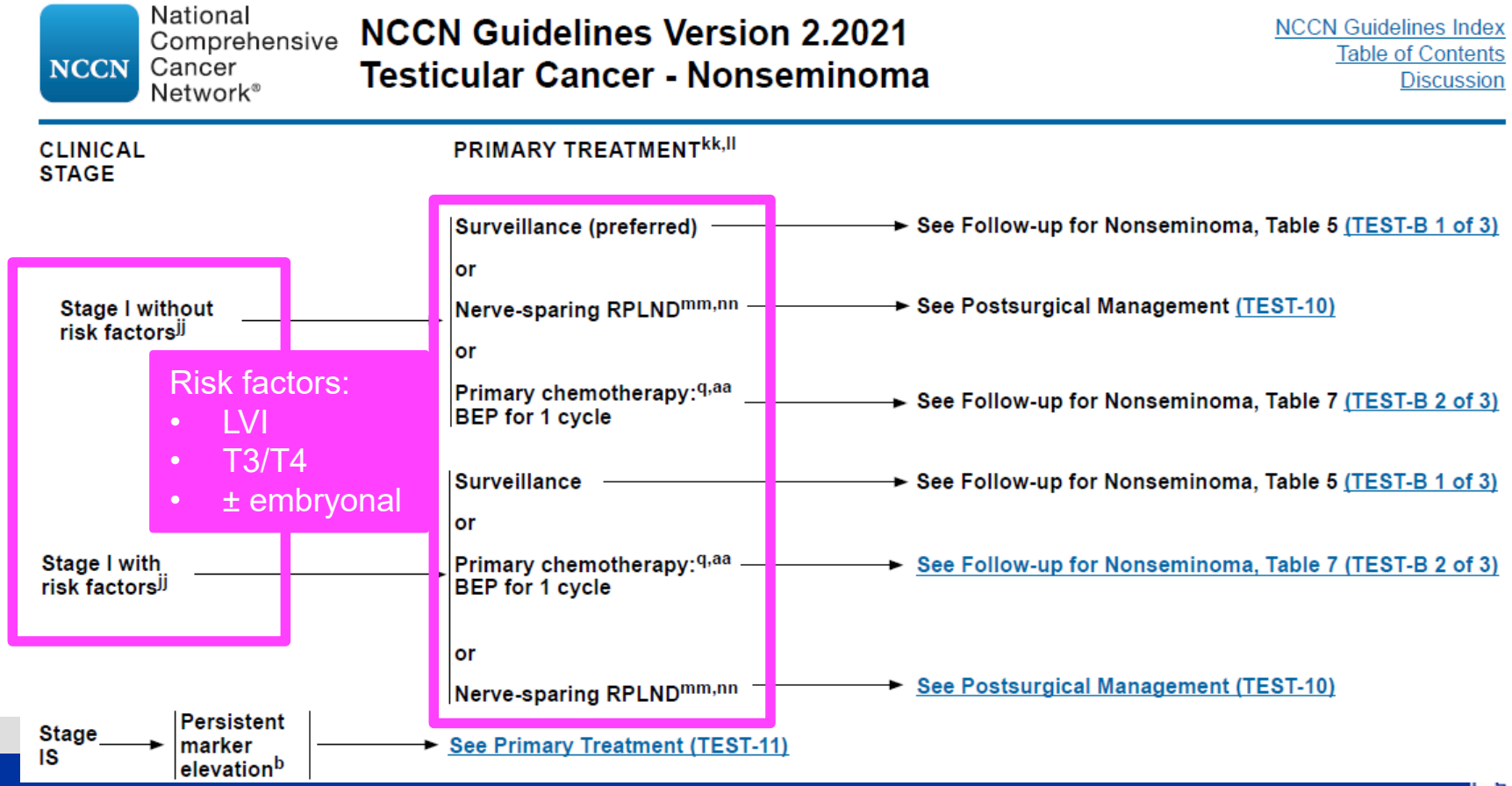
Pre-Pubertal Immature Teratoma

- Most teratomas are mature → benign
  - Excision
  - No follow up

- Rarely immature
  - Complete excision usually curative
  - No large series has reported recurrence or mets
    - Mets in single case report
    - Malignant transformation → mets limited to 2 case reports
  - May consider follow up, but no adjuvant therapy indicated

Post-Pubertal Teratoma May Involve RPLND

- Post-pubertal → stage and treat like an adult → NCCN
  - Teratoma is universally malignant NSGCT in this group



Primary RPLND

- Adjuvant therapy after orchiectomy (± chemotherapy)
- In COG algorithms for pre-pubertal patients, there is no real role
  - Nodal involvement → assume mets → prefer systemic chemotherapy
- Per COG, LNs are "classed" based on size
  - <1cm = negative → surveillance
  - >2cm = mets → systemic chemotherapy
  - 1-2cm = indeterminate → close interval scan in 4-6 weeks
    - If same/growing, consider excisional biopsy vs. assume mets
    - "Biopsy…by excision of suspicious nodes only without formal RPLND"

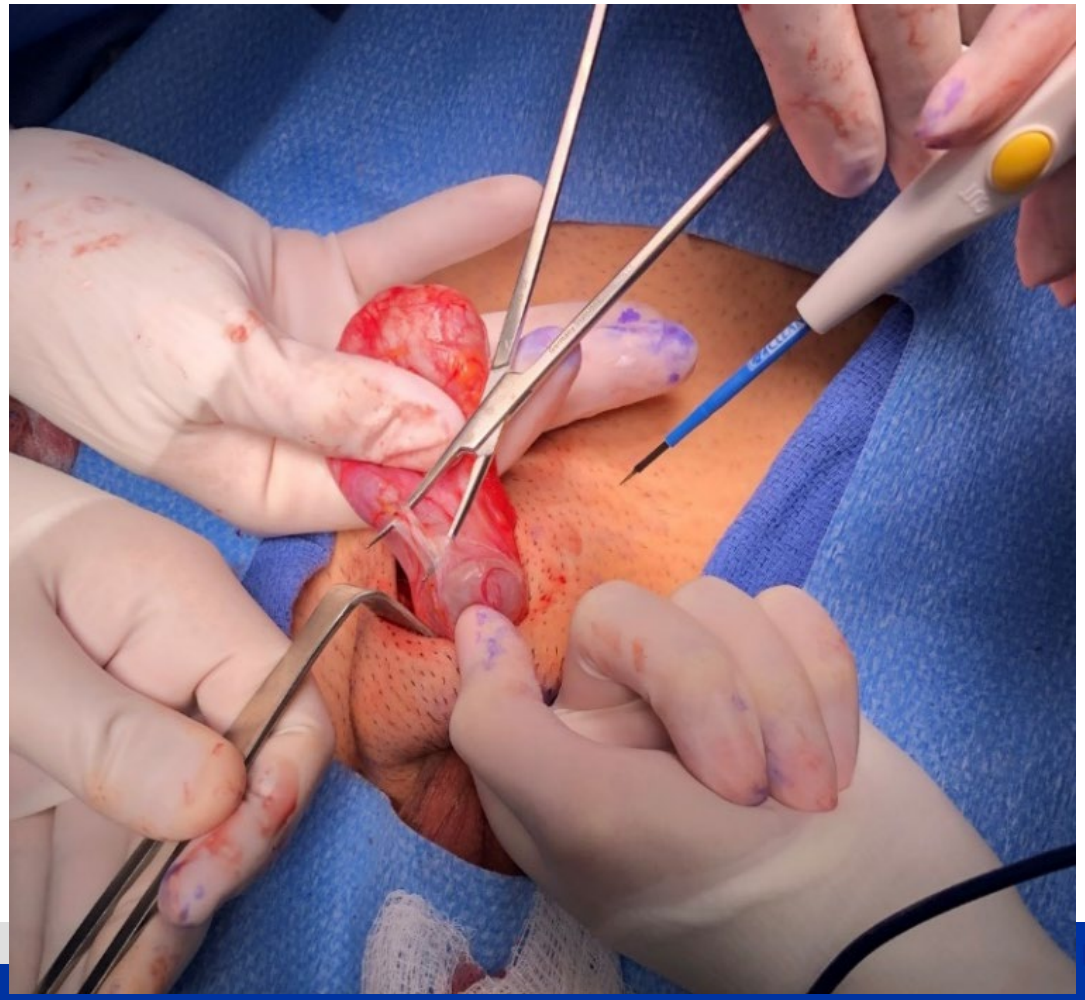
Partial vs. Radial Orchiectomy

- Always ***inguinal*** approach
  - Pre-pubertal with age-appropriate/normal STMs → TSS
  - Post-pubertal independent of STMs → radical orchiectomy
    - Minimize risk of local recurrence
    - <2cm, 10-15% chance of malignancy
- Some exceptions:
  - Pre-pubertal patient with elevated STMs* → radical
  - Post-pubertal patient with:
    - B tumors
    - Solitary testis
    - Mass <2cm with normal STMs

→ TSS

TSS – Technical Pearls

1. Be prepared to convert to radical orchiectomy if needed
   - Inguinal incision
   - High control of cord



TSS – Technical Pearls

1. Be prepared to convert to radical orchiectomy if needed
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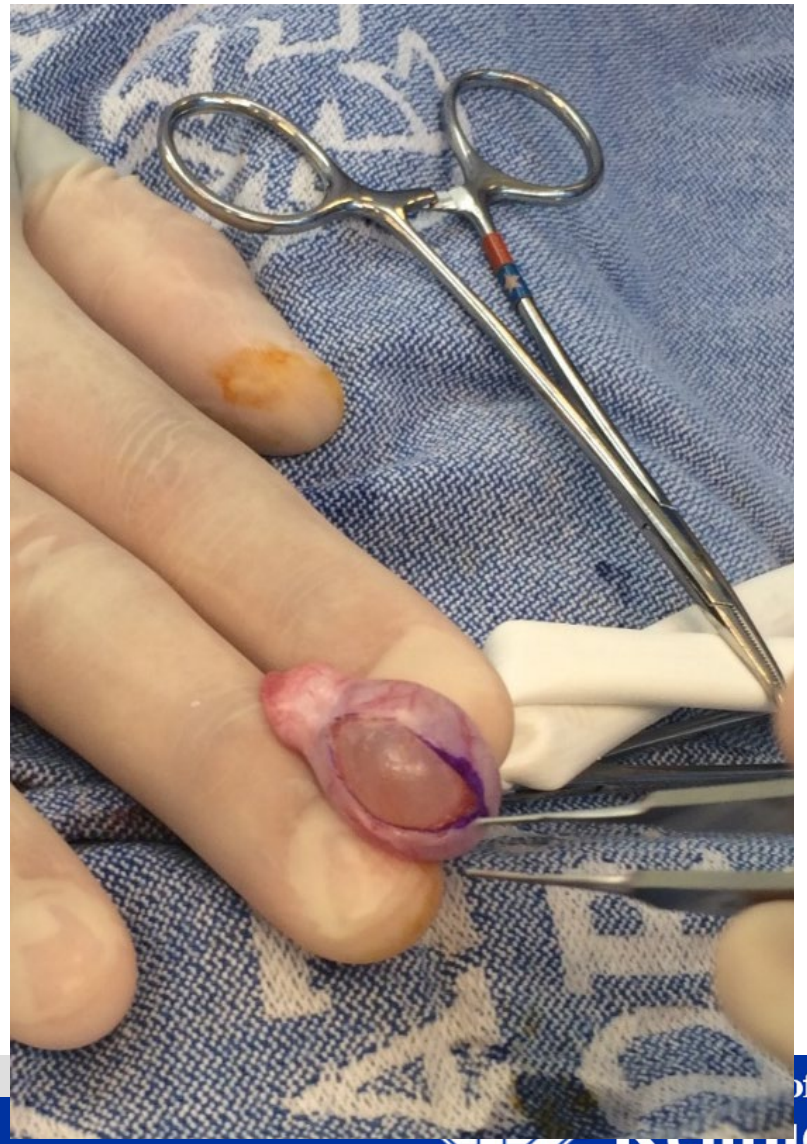
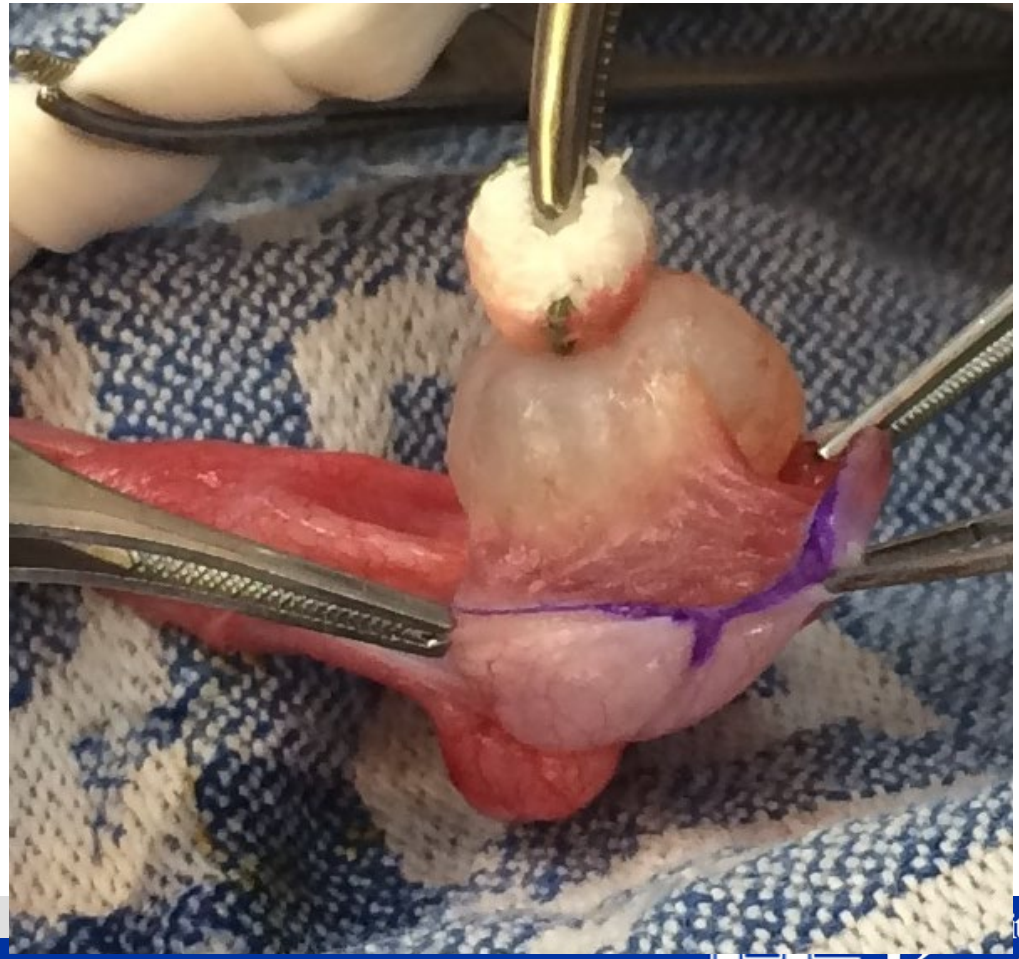
   - High control of cord
2. Intraoperative US



TSS – Technical Pearls

1. Be prepared to convert to radical orchiectomy if needed
   - Inguinal incision
   - High control of cord
2. Intraoperative US
3. Frozen section
   - High correlation with final pathology (99%)
   - May guide intraoperative decision-making



TSS – Technical Pearls

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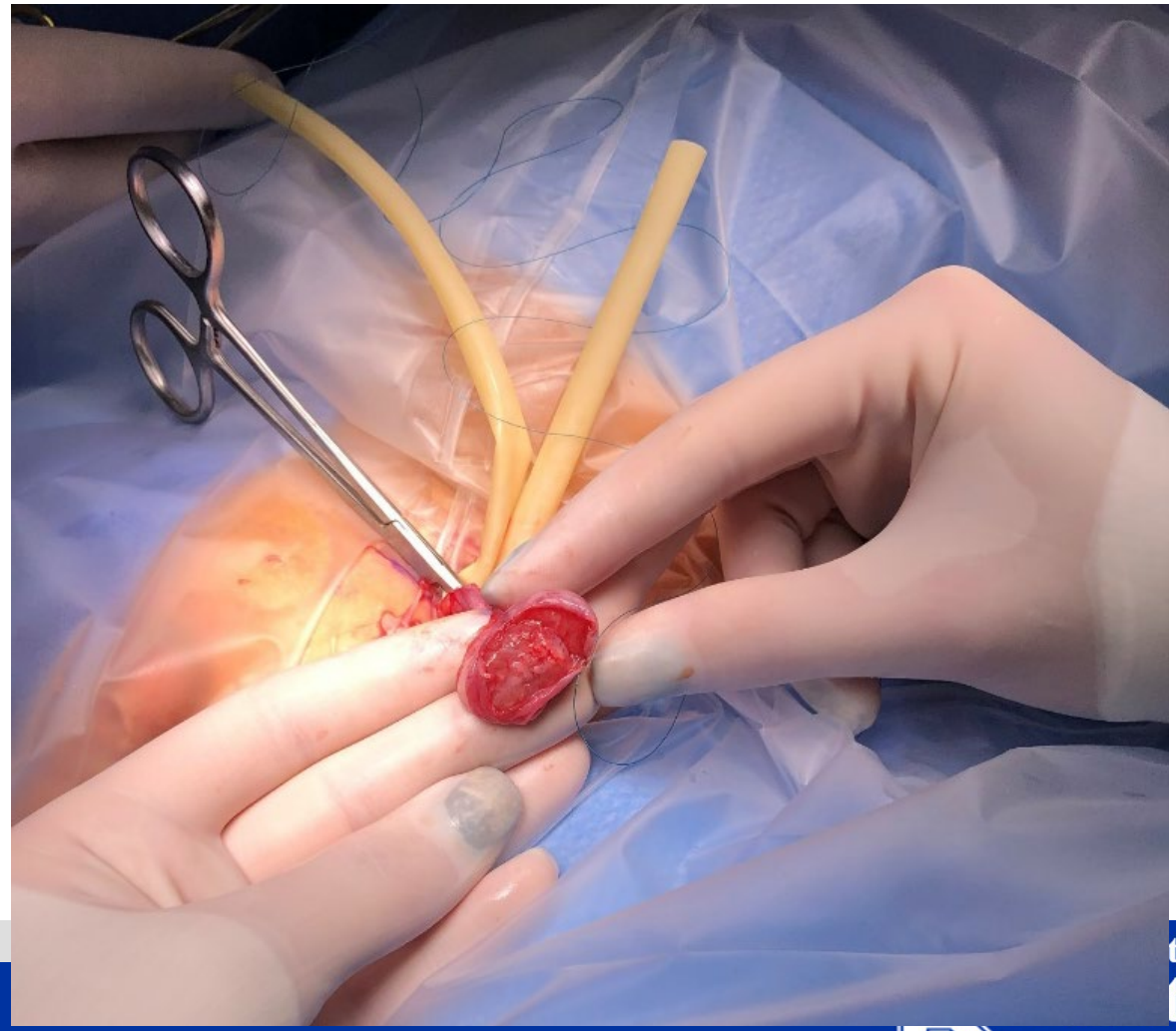
4. Sample adjacent tissue*
   - Surrounding GCNIS?
   - Pubertal status



*peri-/post-pubertal patients

Controversy – Cold Ischemia

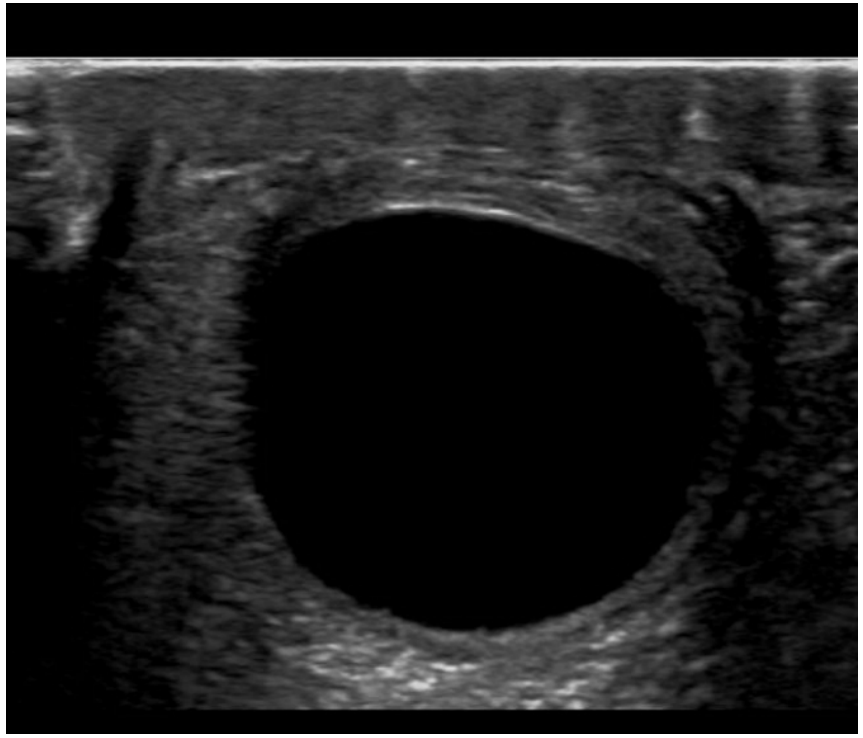
- Icing testis during TSS to minimize ischemia-reperfusion injury
- Used in initial reports by German Testicular Cancer Study Group[1]
  - Ischemic testis placed in crushed ice during frozen section review
  - To preserve Sertoli cells, which show damage after 30 mins warm ischemia
- Studied in prepubertal rat models comparing warm vs. cold ischemia for 30 mins[2]
  - No difference in testosterone levels at puberty
  - No difference in sperm counts at puberty
  - More histologic differences in cold ischemia group at puberty

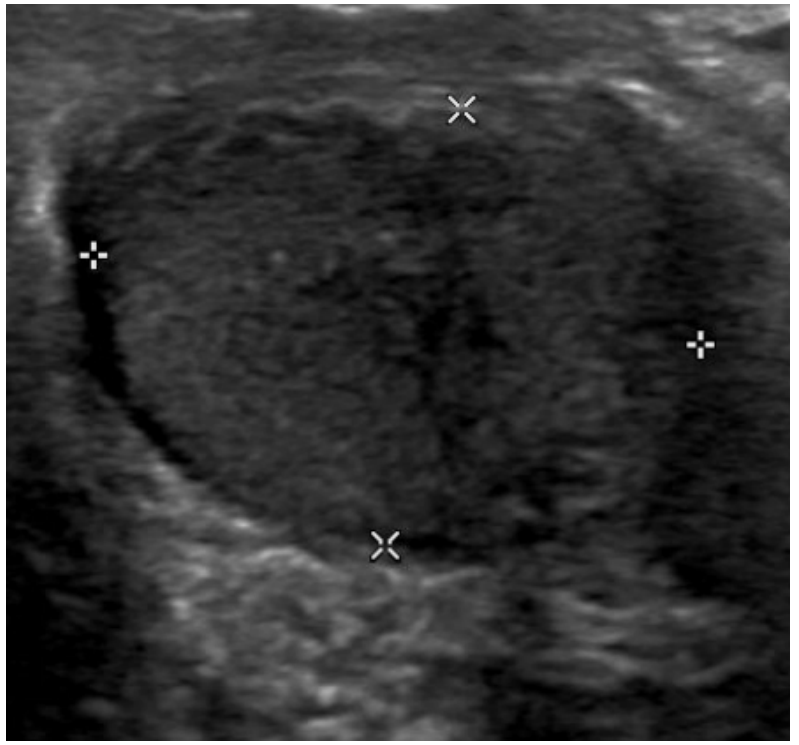
[1] Heidenreich A, *et al.* *J Urol* 2001;166(6):2161-5.
[2] McNamara ER, *et al.* *J Ped Urol* 2014;10(4):593-7.

Controversy – Cord Occlusion

- Helps with hemostasis
  - Only needed when enucleating
- Decrease seeding/spillage?
  - No evidence that this occurs
  - No evidence that this affects oncologic outcomes
  - Probably more related to molecular changes than manipulation alone
- Try to minimize occlusion to balance hemostasis with maximal perfusion of remaining parenchyma

Pre- and Post-op Appearance





Conclusions

- ***Pubertal status*** of patient is critical!
  - Pre-pubertal → COG guidelines
  - Post-pubertal → adult guidelines
- Remember physiologic elevations of αFP in infants
- RPLND is (generally) ***not*** indicated in pre-pubertal patients
- ***Inguinal*** approach for oncologic surgery on testis
- TSS is the gold standard for pre-pubertal patients
  - Be ready → radical orchiectomy
  - Use intraoperative frozen section

amanda.saltzman@uky.edu
504-444-1443

@UKYurology @UKYPedsUro @PedsUroOnc @urosaltyMD

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