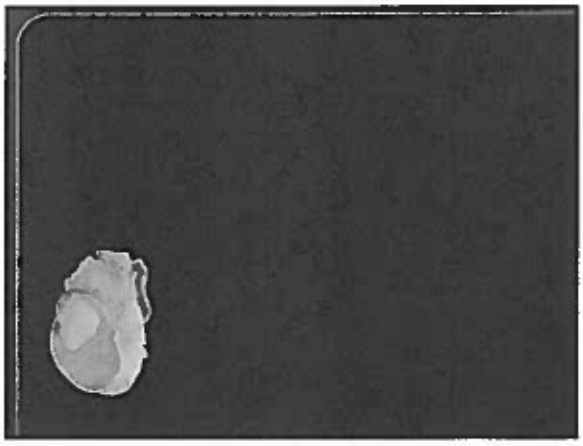


Testicular cancer

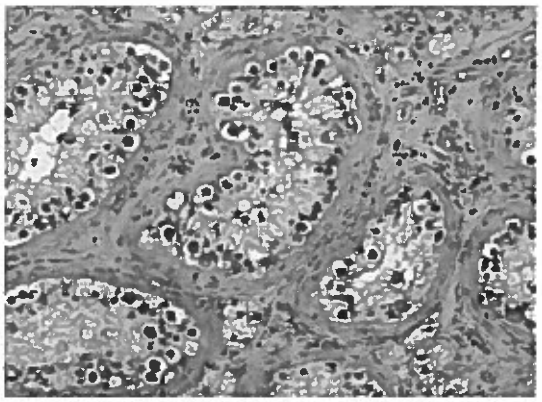
- 1% of malignant neoplasm in males
- Most common malignancy in age 15-44
- Rising incidence in most northern developed countries
- Highest incidences in Switzerland and Scandinavian countries
- Important racial variations in incidence
- Estimated new cases and deaths from testicular cancer in the United States in 2011:
  - New cases: 8,290.
  - Deaths: 350.

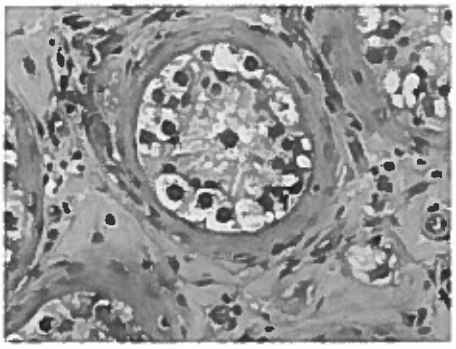
Risk Factors for MGCTs

Condition	Increased Risk
Prior MGCT	10x
Cryptorchid testis	5x
Family history	6x
Gonadal dysgenesis	50x
Androgen insensitivity syndrome	15x

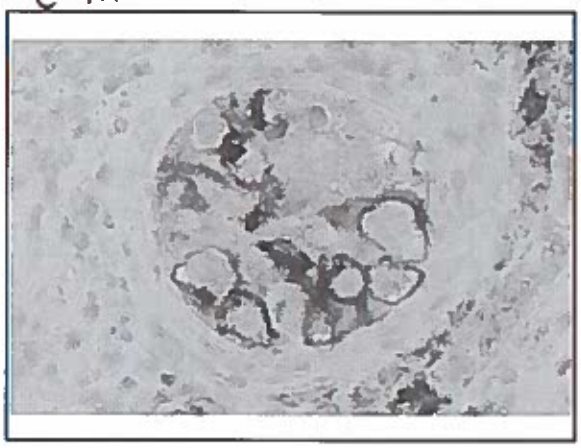
Case #1

A 34-year-old male presents to the infertility clinic and is found to have azoospermia, and a testicular biopsy is performed.





c-kit



Diagnosis

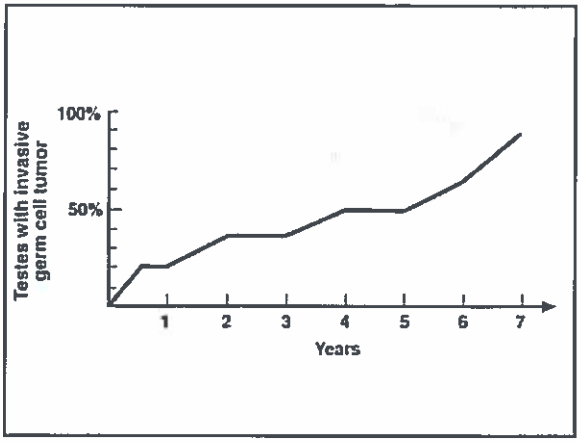
- Intratubular Germ Cell Neoplasia, Unclassified Type

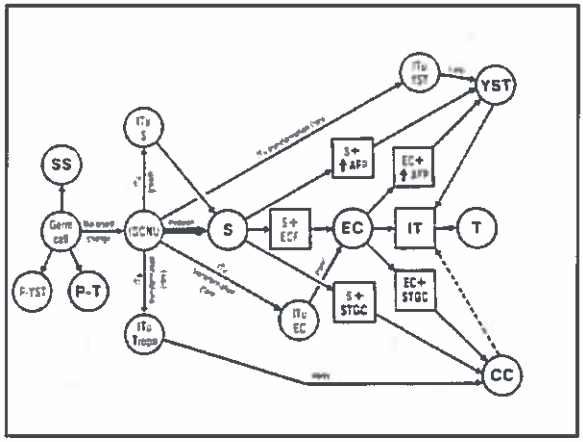
ITGCN

- Testicular biopsy is sensitive for ITGCN
- Treatment
  - Observation
  - Radiation
  - Orchiectomy
- Role in testicular biopsy
  - Cryptorchidism
  - Contralateral invasive GCT
  - Extragonadal GCT

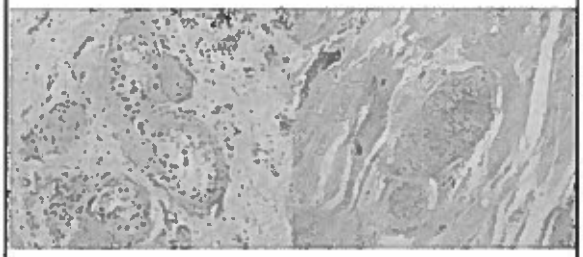
ITGCN

- 50% of patients with ITGCN will develop invasive GCT in 5 years
- 98% of GCT have ITGCN in adjacent tubules (except SS, and pediatric YST or teratoma)
- Patients with retroperitoneal GCT have ITGCN in up to 50% of cases
- i(12p) related to invasive disease

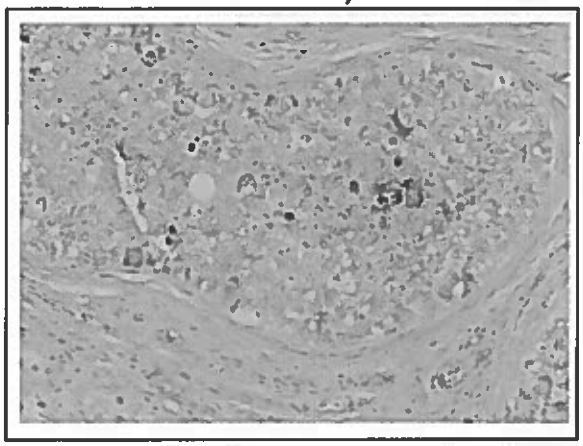


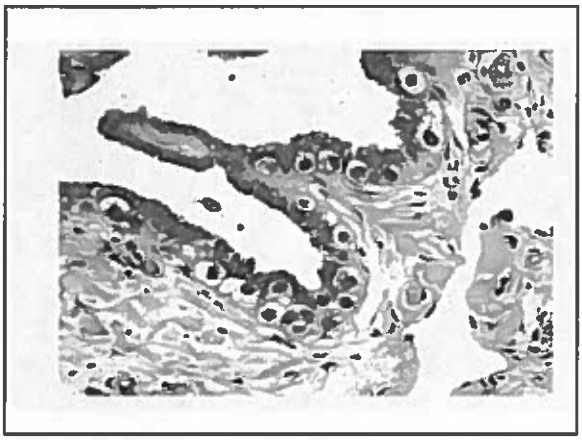


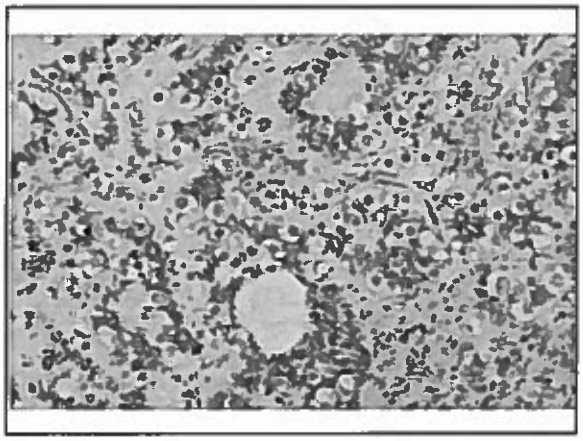
IGCNU vs Intratubular GCT



Intratubular Embryonal Carcinoma

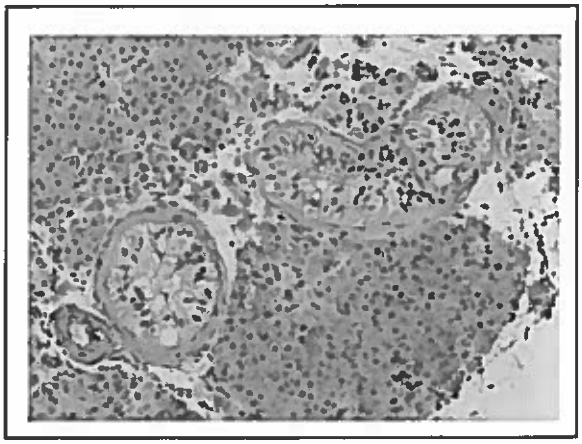




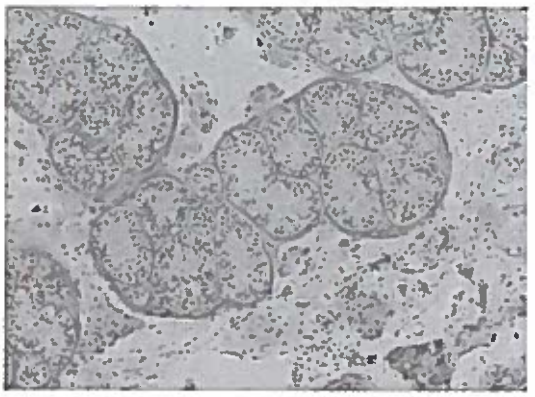


Cryptorchidism

- 3.5 to 14.5 of patients with GCT have or had cryptorchidism
- 2.5 to 35 times risk
- Risk increased for both the cryptorchid and contralateral testis



Pick's Adenoma

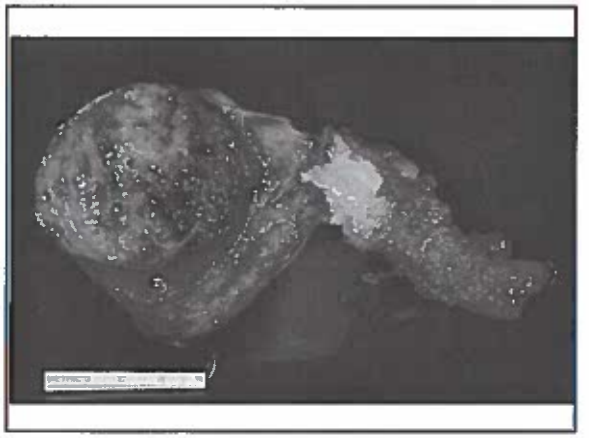


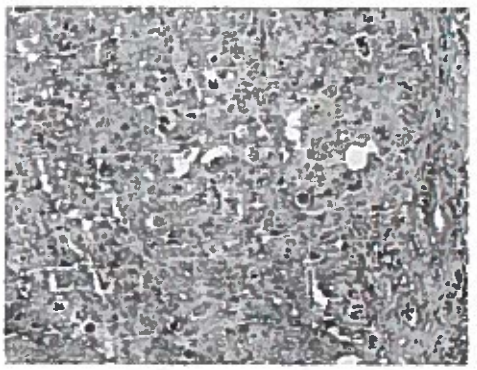
Case #2

A 40-year-old male presents with a large testicular mass and undergoes orchiectomy.

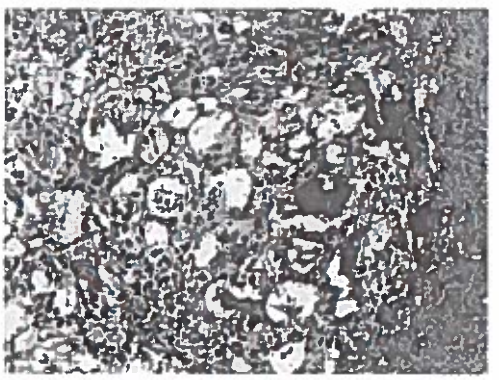
Three biological profiles

Age	Histology	Incidence (per 100,000 hab)	Genetic Abnormality	Ploidy
Prepub	Teratoma YST	0.12	-1p, -6q	T: diploid YST: aneuploid
Postpub	Seminoma Mixed GCT	6.0	i(12p)	S: hypertriploid NS: hypotriploid
>45	Spermatocytic Seminoma	0.2	+9	Tetraploid/diploid

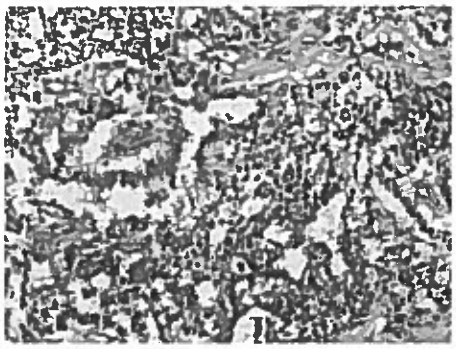




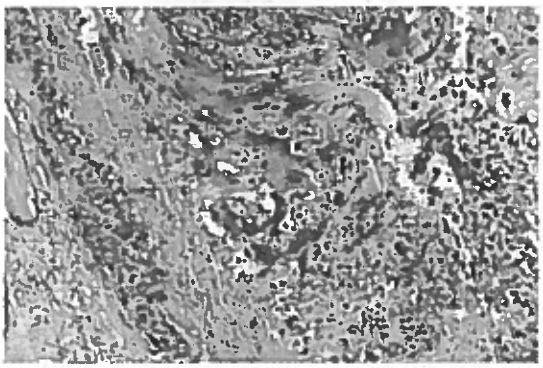
Embryonal Carcinoma



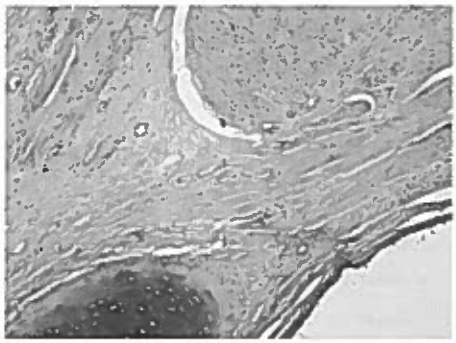
Yolk Sac Tumor



Choriocarcinoma



Teratoma



Diagnosis

- Malignant Mixed Germ Cell Tumor Composed of Embryonal Carcinoma, Yolk Sac Tumor, Choriocarcinoma and Teratoma

Mixed GCT

Tumor type	Percentage of cases
EC + T	28
EC + S	16
EC + YST + T	11
EC + T + CC	7
EC + T + S	6
T + S	6
EC + YST	4
EC + YST + T + CC	4
EC + CC	4
EC + YST + S	3
Other combinations	10

Jacobsen GK et al. 1984

Reporting

- Seminoma versus non-seminomatous GCT
- Amount of each component in mixed GCT
- Angiolymphatic invasion
- Stage

pT Classification

pT0	No evidence of tumor (scar)
pTis	IGCN
pT1	Tumor limited to testis and epididymis without angiolymphatic invasion. Can invade tunica albuginea but not vaginalis
pT2	Tumor limited to testis with angiolymphatic invasion Invasion of the tunica vaginalis
pT3	Tumor invades spermatic cord w/ or w/o angiolymphatic invasion
pT4	Tumor invades scrotum

Stage Groupings

0	Tis, N0, M0
IA	T1, N0, M0
IB	T2-4, N0, M0
IIA-C	Any T, N1-3, M0
III	Any T, any N, M1a, 1b (IIIB-any T, N1-3, M0, S2; IIIC-any T, N1-3, M0, S3)

	LDH	hCG (mIU/ml)	AFP (ng/ml)
S1	< 1.5 x N	and < 5000	and < 1,000
S2	1.5 – 10 x N	and 5000-50000	or 1,000- 10,000
S3	> 10 x N	or > 50 000	or > 10,000

Management of Stage I disease

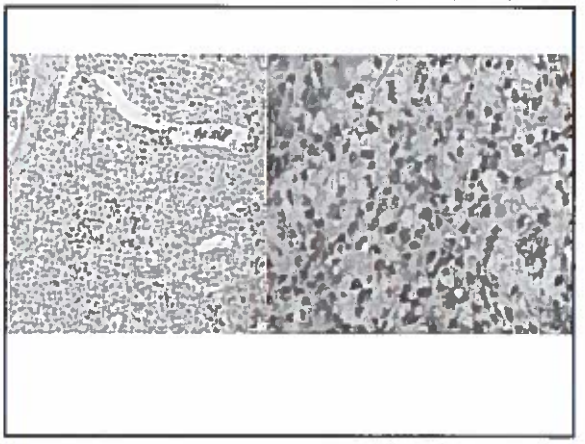
- Seminoma→ radiation therapy (even stage II non-bulky disease)
- Non-seminomatous (mixed)
  - Observation
    - Up to 60% require no further treatment
  - RPLND

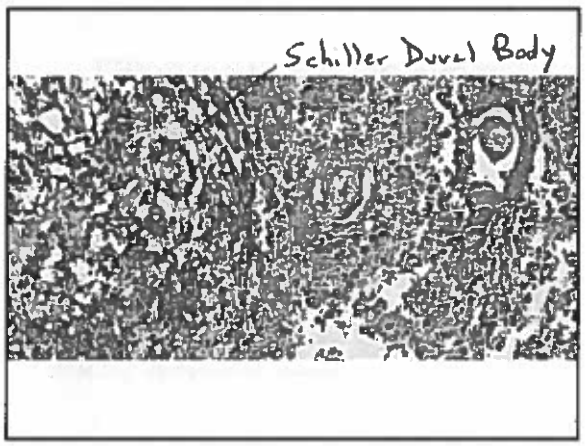
Factors that would discourage observation approach

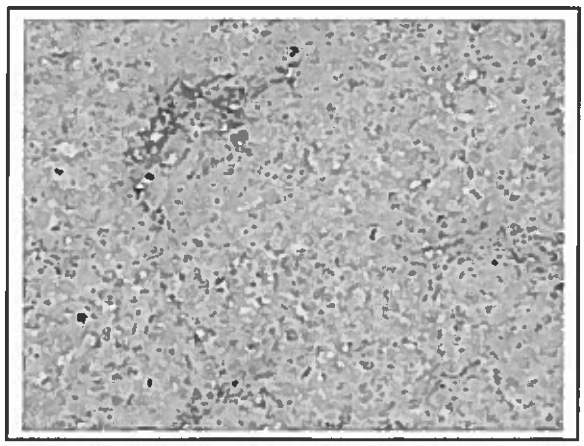
- Angiolymphatic invasion
- More than 50% embryonal carcinoma
- Presence of choriocarcinoma
- Other
  - Absence of yolk sac tumor
  - Absence of mature teratoma
  - Unreliable patient

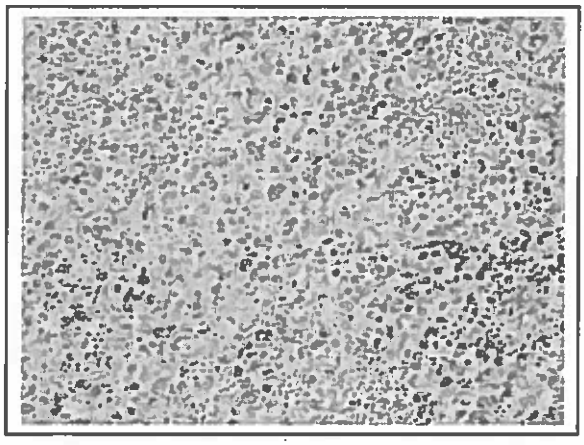
Problem Areas

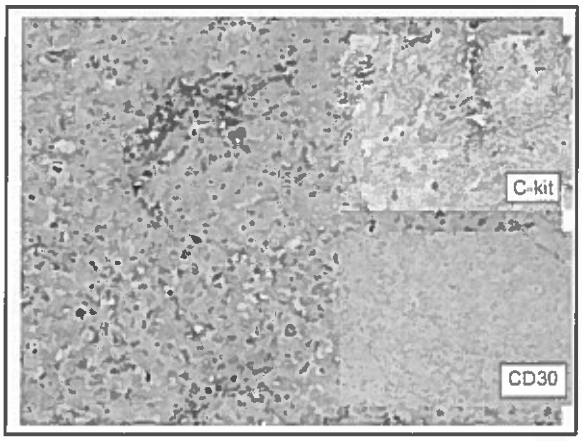
- Separation of YST, seminoma and embryonal carcinoma
- Identification of angiolymphatic invasion and separation from artifact and intratubular GCT
- Separating synctiotrophoblastic cells in GCT from choriocarcinoma

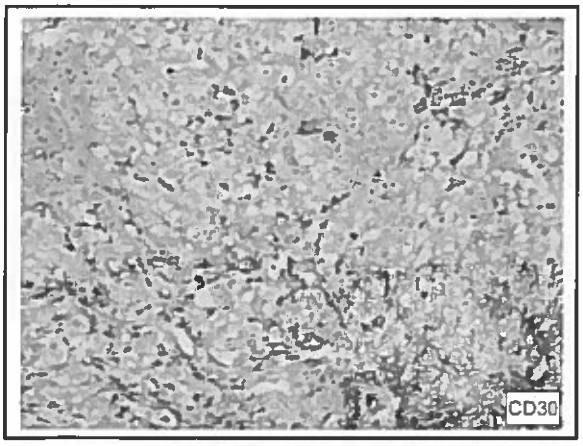








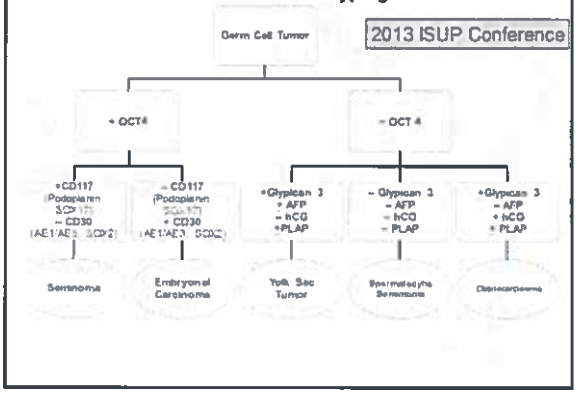




Immunohistochemical Profile

Tumor type	PLAP	OCT3/4	CK	C-kit (CD117)	CD30	AFP
Seminoma	■	■		■		
Embryonal Carcinoma	■	■	■		■	
Yolk Sac Tumor			■			■

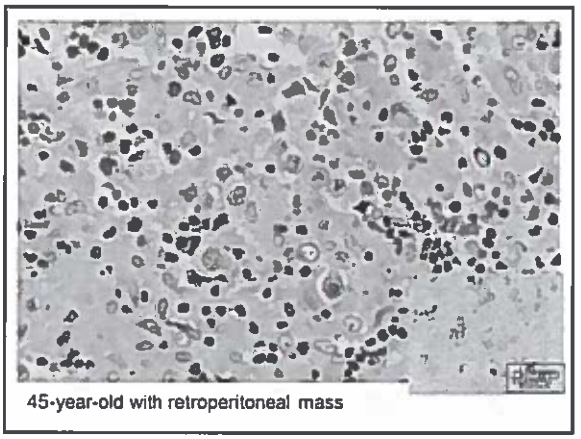
Germ Cell Subtyping



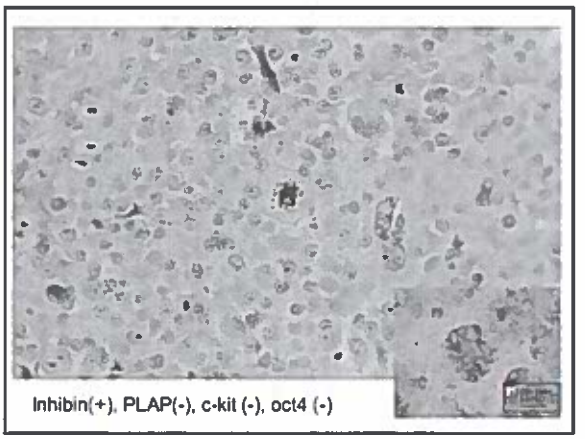
Immunoprofile in solid YST

IHC	No. Cases	% Cases Positive
AE1/AE3	30	100
Glypican 3	**36**	**97**
AFP	29	62
Podoplanin (D2-40)	33	3
CD117	32	59
OCT 3/4	36	0

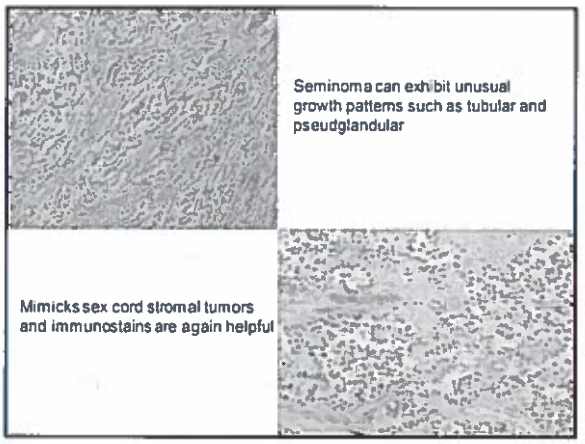
Kao et al. Am J Surg Pathol 2012;36:360

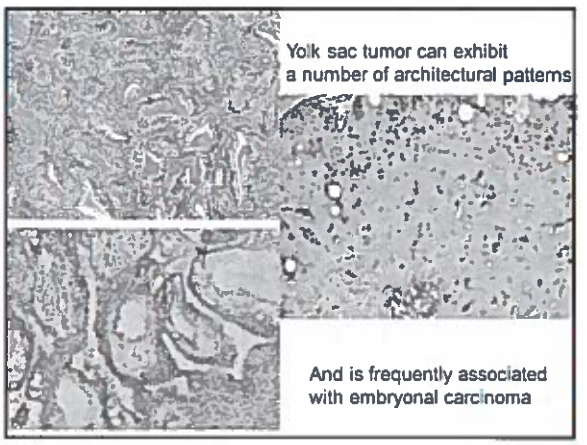


45-year-old with retroperitoneal mass



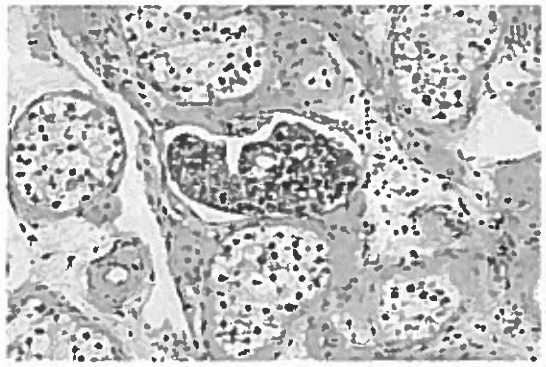
Inhibin(+), PLAP(-), c-kit (-), oct4 (-)

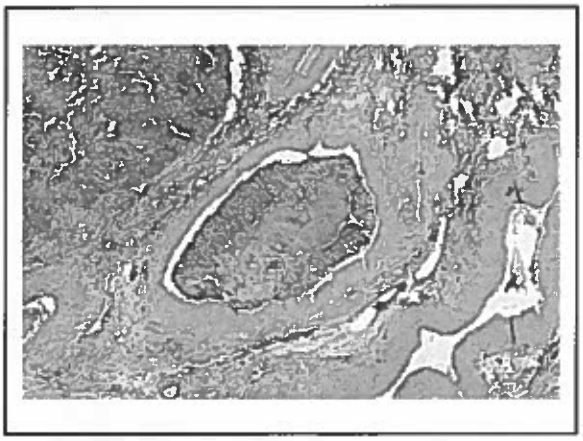


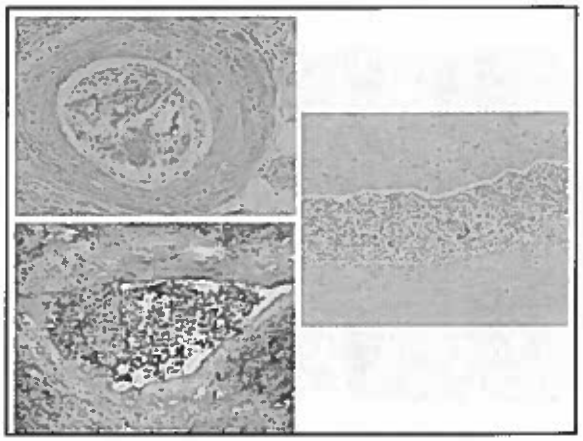


Angiolymphatic Invasion

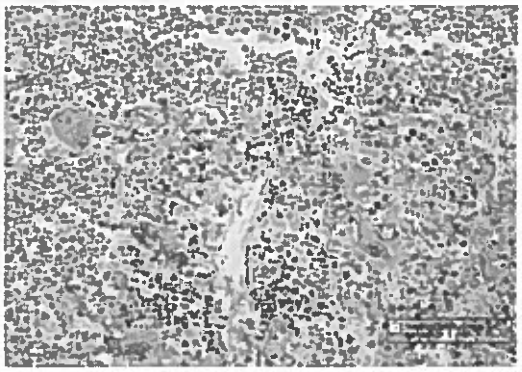
- Upstages T1 to T2
- Important in non-seminomatous GCT; role in seminoma is uncertain
- Separation of true invasion from artifact is important

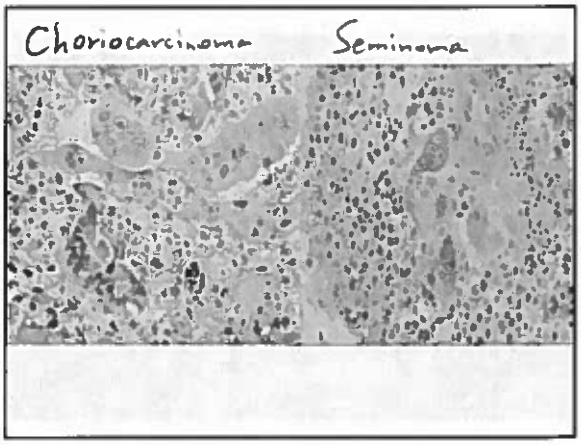






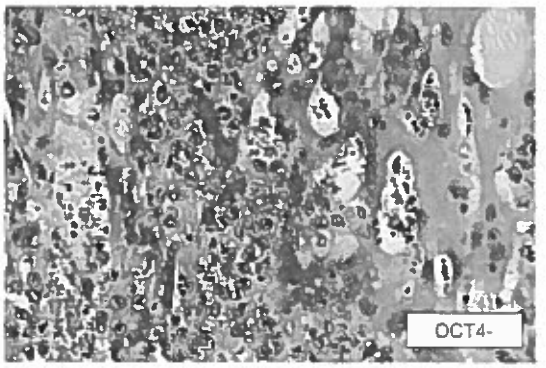
Synctiotrophoblast vs Choriocarcinoma

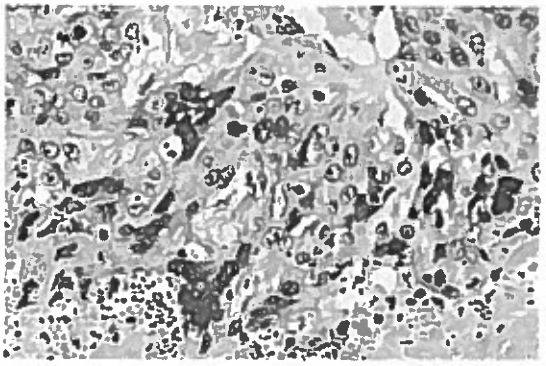




Choriocarcinoma

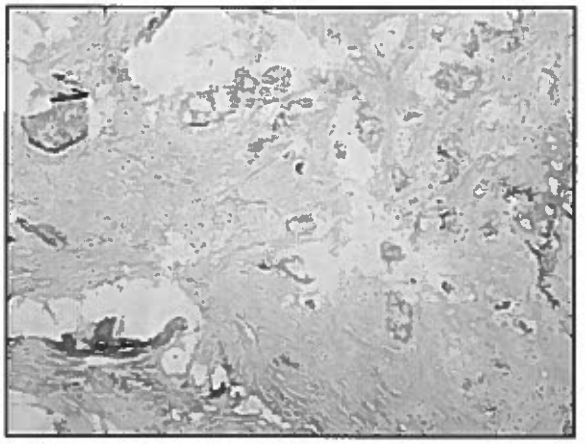
- Present in 8% of testicular GCT
- Pure 0.3%
- Increased levels of hCG
- When pure- symptoms of metastatic disease
- In mixed GCT is associated with worse prognosis

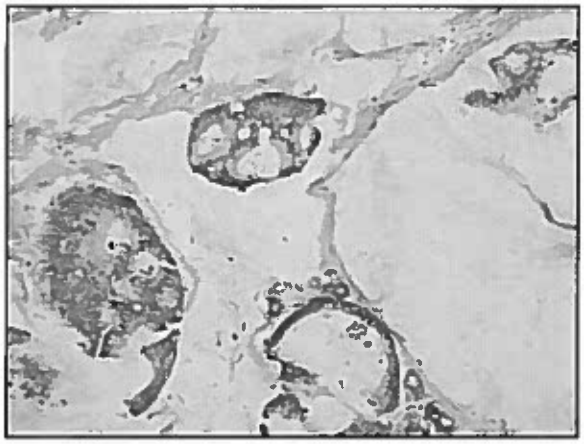


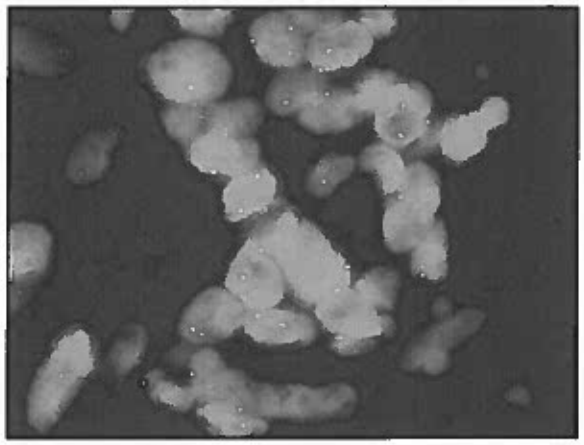


Case #3

- A 44-year-old male presents with a retroperitoneal mass. The patient has a mixed GCT 20 years earlier. The retroperitoneal mass is resected.



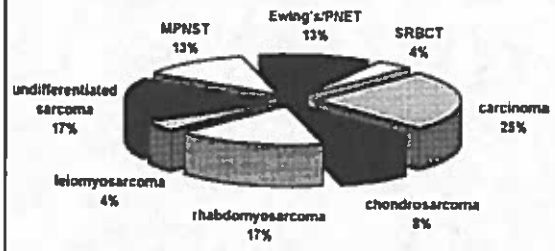




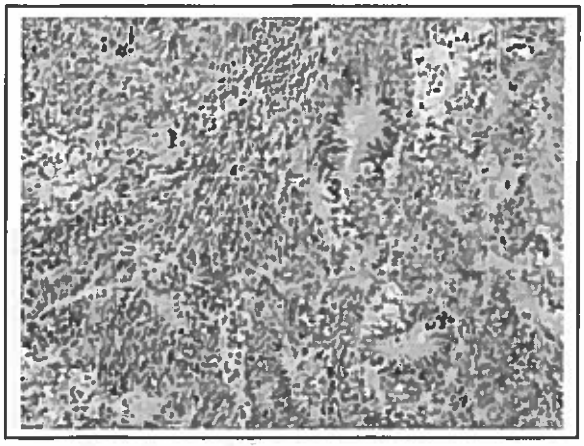
Germ Cell Tumor with Somatic-Type Malignancy

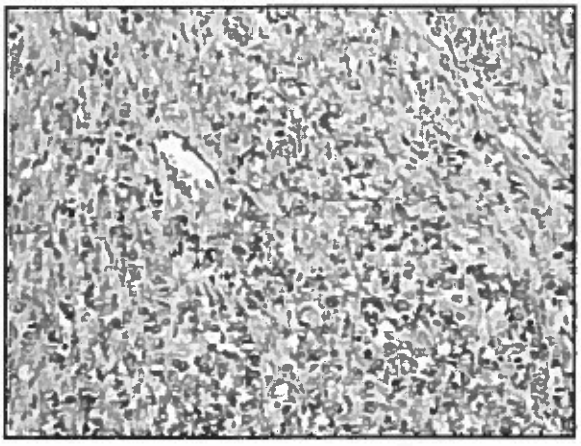
- Nearly 40% occur in primary GCT; remainder in metastases or relapse
- Epithelial malignancies
  - Tumefactive with desmoplastic reaction
- Mesenchymal neoplasms:
  - Quantitative criteria to establish malignancy
    - Usually one lpf (40x)

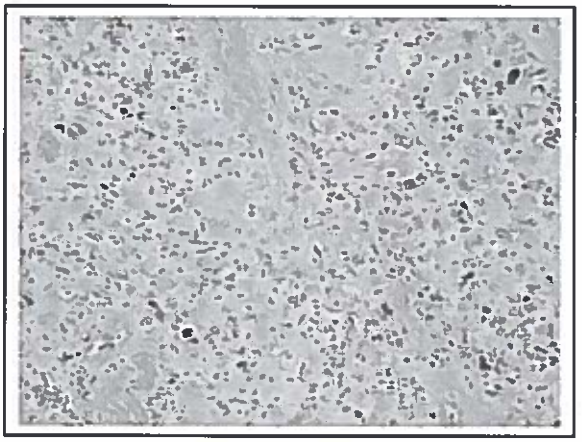
Somatic malignancies in teratoma

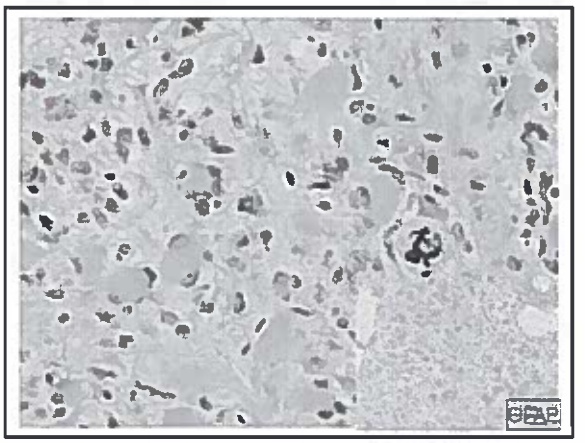


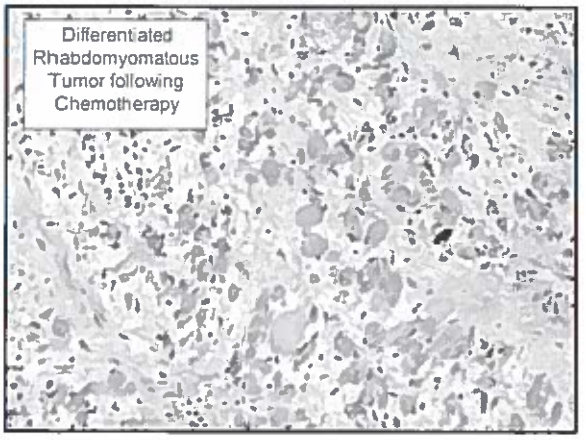
Comiter et al. J Urol 1998; 159: 859-63









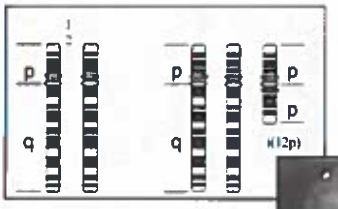


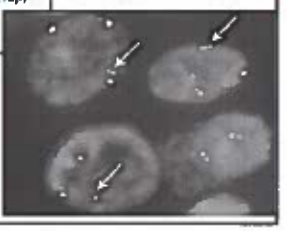
Prognosis

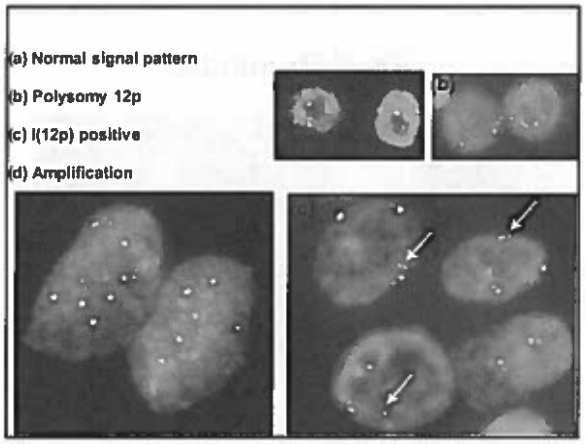
- Development in primary GCT has better outcome than in recurrence
- Secondary malignancy conveys poor prognosis in recurrent GCT
  - 90% OS in pure teratoma recurrences
  - 58-65% OS in cases with secondary malignancy
- Worse prognosis
  - Rhabdomyosarcoma (25% survival in some series)
  - PNET
  - Mediastinal primary

i(12p)	Gain of 12p
■ Identified in all GCT types and all locations ■ High frequency in testicular GCT (70-90%) ■ Lower frequency in other locations ■ Ovary: 40-60% ■ CNS: 20-50% ■ Mediastinum: 60%	■ Duplication of 12p arm ■ Less frequent event ■ 10-20% of testicular GCT without i(12p) ■ Higher frequency in GCT from other sites

12p Probe Strategy

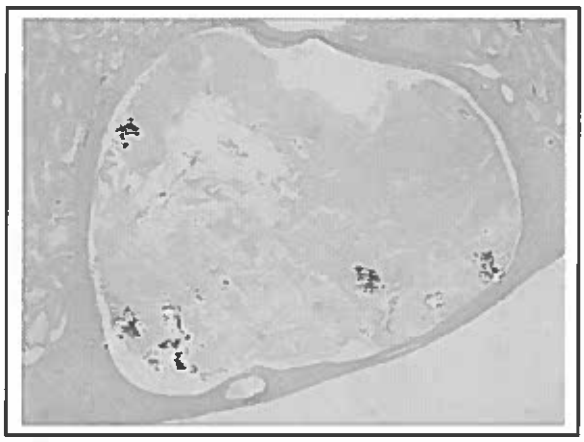


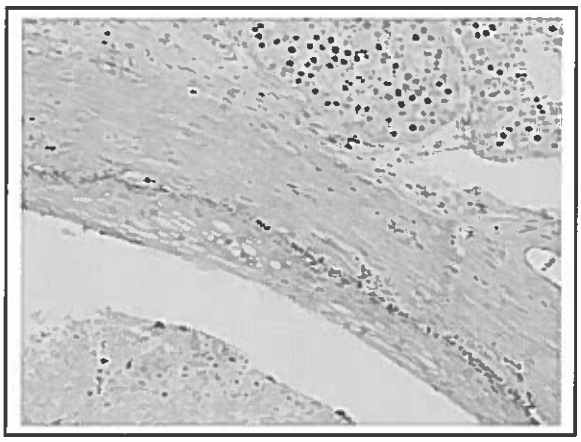


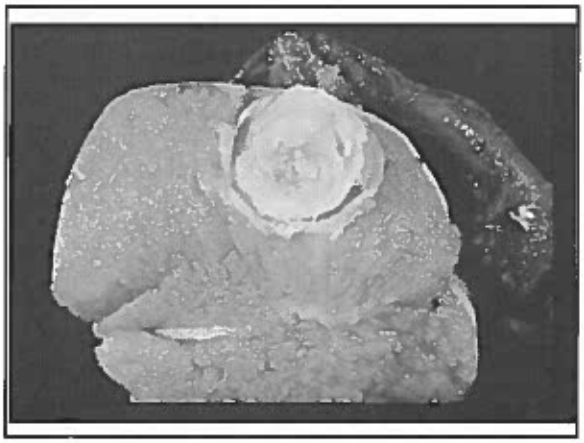


Case #4

- A 28-year-old presents with a peripheral small testicular tumor. The tumor is excised in a wedge biopsy, and a frozen section is requested with the query- should I remove the testis?







Diagnosis

- Epidermoid cyst

Epidermoid and Dermoid Cyst and "Benign Teratoma"

- Benign
- For diagnosis should lack the following
  - IGCNU
  - Cytologic atypia
  - Scarred areas
  - Microlithiasis
  - Lack of significant atrophy
  - Lack of i(12p)

Final Reminder