The Mediastinum

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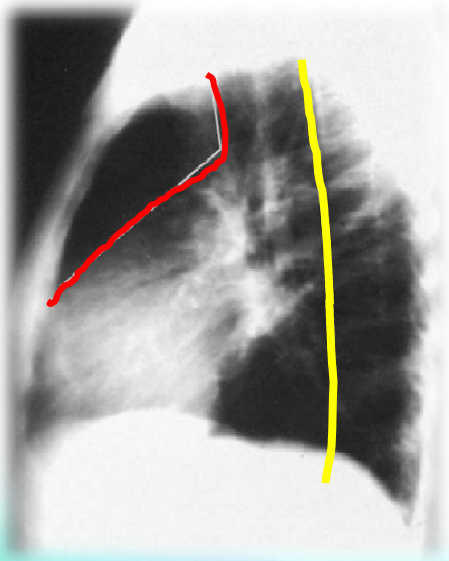
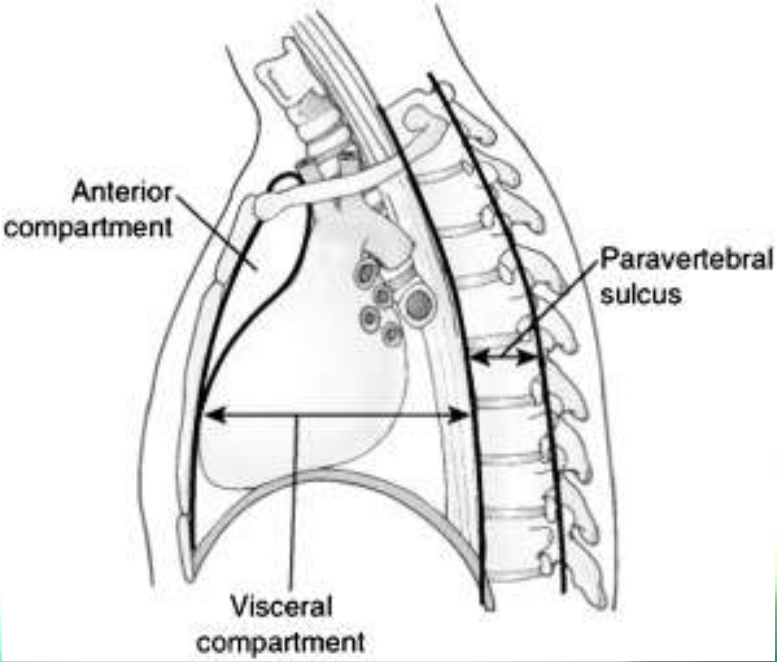
Contents

- Anatomy
- Non invasive and invasive Investigations
- Mediastinal infection
- Primary mediastinal tumors and syndromes associated with mediastinal lesions
- Mediastinal cysts

Anatomy

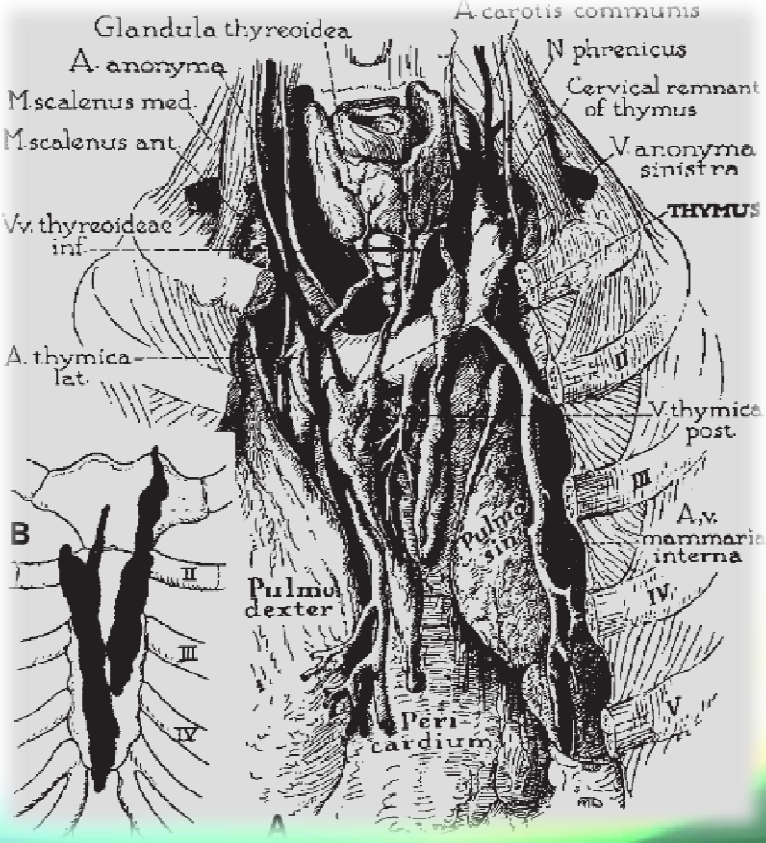
- Subdivision
  - Ant compartment
  - Middle or visceral compartment
  - Post compartment or paravertebral sulcus





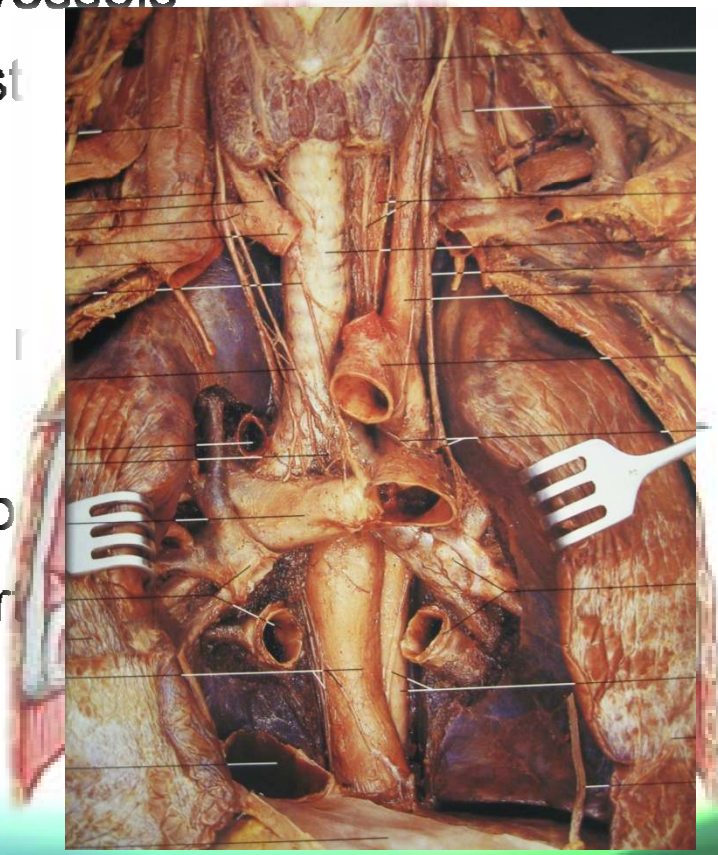
Anatomy

- Ant compartment
  - **Thymus**
  - Internal mammary vessels
  - Lymph nodes
  - Connective tissue with fat



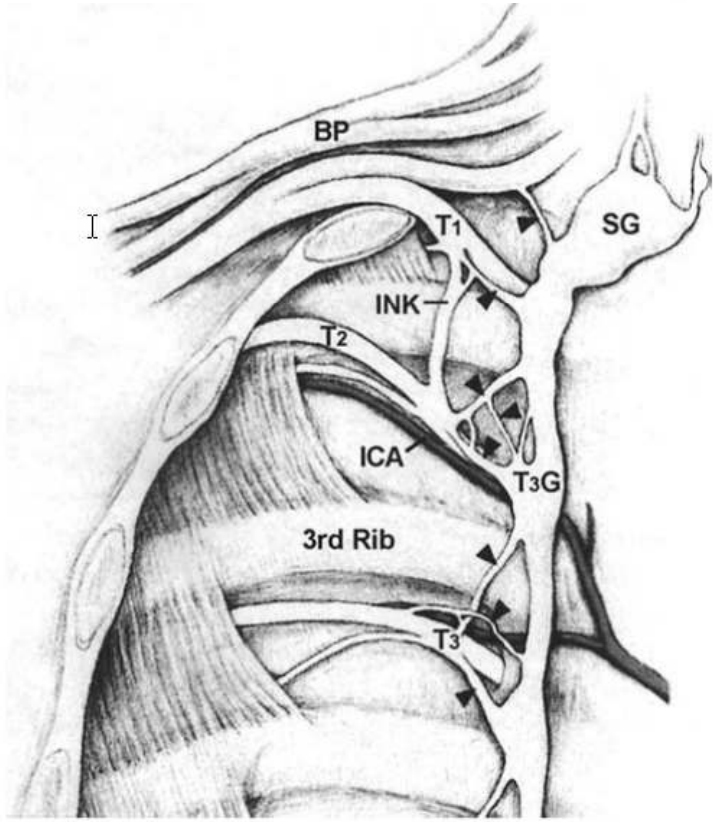
Anatomy

- Middle compartment
  - Pericardium, heart, and great vessels
  - Trachea, proximal portions of st
    esophagus
  - Extensive lymphatic tissues
  - Vagus and phrenic nerves and
    and fibers
  - Supra-aortic and para-aortic bo
  - Thoracic duct, the proximal por
  - Connective tissue and fat



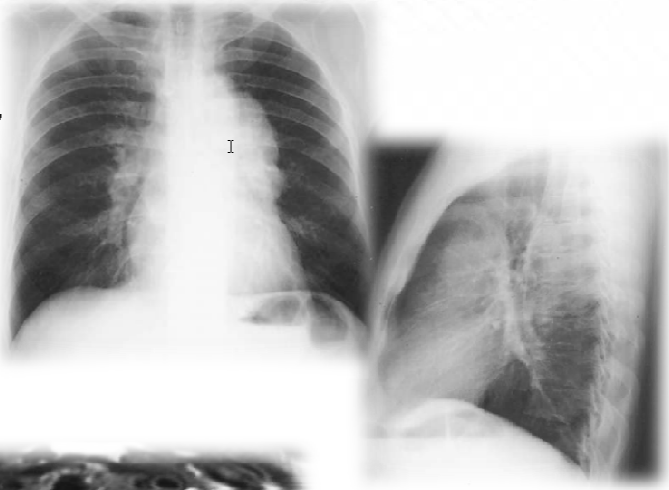
Anatomy

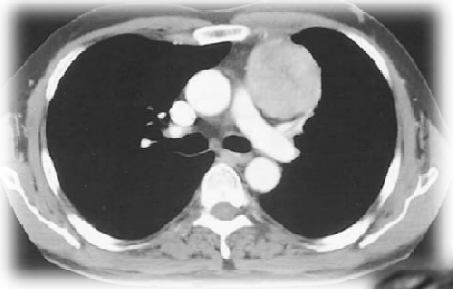
- Post compartment
  - Proximal portions of the interc
  - Thoracic spinal ganglions, sym branches
  - Connective and lymphatic tissu

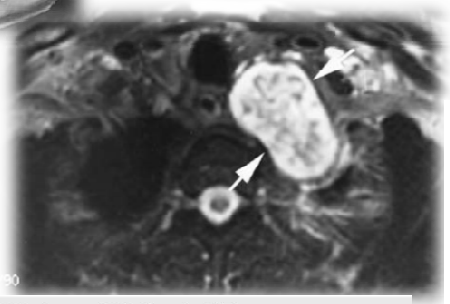


Non invasive Investigations

- Chest plain film including lateral view
- Chest CT
- Chest MRI
- Radionuclide studies
- Mediastinal tumor markers







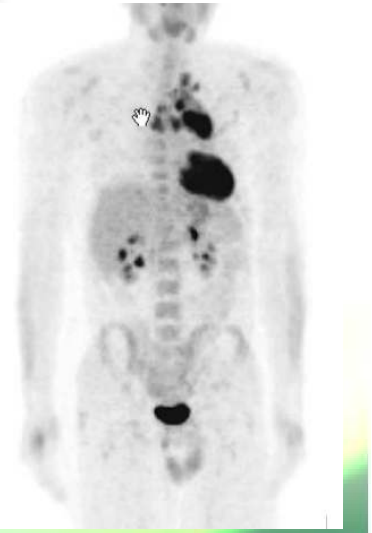


TABLE 168-2 Serum or Urine Markers of Mediastinal Tumors

Mediastinal location	*Tumor*	*Serum marker*
Anterior compartment	Yolk sac tumor[a]	AFP, LDH
	Embryonal carcinoma	LDH, TRA-1–60, CD30, β-HCG[b]
	Choriocarcinoma	β-HCG, LDH
	Seminoma	PLAP, LDH, NSE, β-HCG[b]
	Thymoma	None
	Thymic carcinoma	None
	Thymic carcinoid	ACTH, chromogranin, NSE
	Thymic small cell carcinoma	Bombesin, NCAM, NSE
	Parathyroid adenoma	PTH, chromogranin
Visceral and posterior compartments	Pheochromocytoma, neuroblastoma, and ganglioneuroblastoma	Urine[c] and plasma[d] catecholamines, and chromogranin, NSE

Invasive Investigations and surgical approaches

- Transcervical mediastinal LN sampling and Lymphadenectomy
  - Mediastinoscopy: extended, video-assisted
- Video-assisted thoracic surgery
- Sternotomy and Thoracotomy
- Posterior Mediastinotomy

Mediastinal infections

- **Acute and chronic mediastinitis**
  - **Perforation of the aero-digestive tract**
  - **Postoperative sternal infection and mediastinitis**
  - **Descending necrotizing mediastinitis**
  - **Sub-acute mediastinitis**
  - **Fibrosing mediastinitis**

Perforation of the aero-digestive tract

- Four principles of treatment
  1. Eliminate source of soilage by primary repair or diversion away from the esophageal perforation
  2. Provide thorough and wide mediastinal drainage to control on going mediastinal suppuration occurring after primary repair or diversion. Inaddition, gastrostomy tube decompression should be performed to decrease gastric reflux and mediastinal soilage.
  3. Appropriate antibiotics should be administered to augment host defenses, which must be effective against both gram positive and gram negative bacteria and against both aerobic and anaerobic bacteria.
  4. Maintain adequate nutrition.

Postoperative sternal infection and mediastinitis

- Risk factor
  - Sternotomy: incomplete closure
  - Tracheostomy
  - CPB duration
  - Postoperative bleeding
  - Infection
  - Low cardiac output
  - Poor general condition
  - Steroid

Descending necrotizing mediastinitis

- Acute purulent mediastinitis due to oropharyngeal infection
- uncommon but still lethal form of mediastinitis
- 60 ~ 70%, secondary to odontogenic infections
- Peritonsillar abscess, Retropharyngeal and parapharyngeal abscess, Epiglottitis
- Other less common causes
  - trauma to the neck, including neck or mediastinal surgery
  - cervical lymphadenitis, endotracheal intubation

Sub-acute mediastinitis

- The definition of subacute mediastinitis is unclear, but this term should embrace those inflammatory processes involving the mediastinum that produce minimal to mild and evanescent symptomatology (substernal pain, fever, night sweats) and an identifiable anterior or visceral mediastinal mass by radiographic or CT examination.
- These infections most often are the result of fungal, mycobacterial, or, rarely, actinomycotic organisms.
- Such subacute infections are observed only infrequently in previously normal, healthy persons but are becoming more common inimmunocompromised patients, particularly those with AIDS.

Fibrosing mediastinitis

- Fibrosing mediastinitis is an uncommon benign process resulting in the deposition and proliferation of dense fibrous tissue through out the visceral compartment of the mediastinum.
- This chronic inflammatory process can lead to entrapment and compression of vital mediastinal structures.

Primary mediastinal tumors and syndromes

- Myasthenia Gravis
- Thymic tumors
- Benign LN disease
- Germ cell tumor
- Neurogenic tumors

Myasthenia Gravis

- Neuromuscular junction disorder
- caused by the autoimmune destruction of the acetylcholine receptors of voluntary muscle
- Sx: diplopia, ptosis, dysphagia, weakness, fatigue
- 30 - 50 % of patients with thymomas have myasthenia gravis
- rare in thymic carcinoma

Thymic tumors

Classification of Thymic Tumors
Epithelial cell tumors
Thymoma
Type A (Spindle cell, medullary)
Type AB (Mixed)
Type B1 (Predominate cortical, lymphocyte-rich, organoid)
Type B2 (Cortical)
Type B3 (Epithelial)
Other types
Micronodular thymoma with lymphoid stroma
Metaplastic thymoma
Microscopic thymoma
Sclerosing thymoma
Combined thymoma and thymic carcinoma
Thymic carcinoma
Neuroendocrine cell tumors
Thymic carcinoid, well differentiated
Atypical thymic carcinoid, moderately differentiated
Small cell carcinoma, poorly differentiated
Tumors of adipose tissue
Thymolipoma
Thymoliposarcoma
Miscellaneous tumors
Thymic hemangioma
Neuroblastoma and ganglioneuroblastoma
Primary malignant melanoma
Myoid tumor
Lymphoid tumors

Thymoma

- Neoplasm of the thymus that originates in the gland's epithelial tissue.
- Incidence: 0.15 /100,000 person years (United States)
- Typically slow-growing tumors
- Spread by local extension
- Metastases are usually confined to the pleura, pericardium, or diaphragm, whereas extrathoracic metastases are uncommon.

The New World Health Organization Histologic Classification of Thymic Epithelial Tumors

Type A thymoma (medullary)
Type AB thymoma (mixed)
Type B thymoma[a]
  Type B1 (organoid)
  Type B2 (cortical)
  Type B3 (epithelial)
Type C (thymic carcinoma)

[a]May include combinations of B2 and B3 as well as Bl and B2.

TABLE 188-7 Staging Schemes of Thymoma

Stage	*Bergh, et al.*[21]	*Masaoka, et al.*[179]
I	Intact capsule or growth within the capsule	Macroscopically, completely encapsulated; microscopically, no capsular invasion
II	Pericapsular growth into mediastinal fat tissue	
IIA		Macroscopic invasion into surrounding fatty tissue or mediastinal pleura
IIB		Microscopic invasion into capsule
III	Invasive growth into the surrounding organs, intrathoracic metastases, or both	Macroscopic invasion into a neighboring organ (e.g., pericardium, great vessels, or lung)
IVA		Pleural or pericardial dissemination
IVB		Hematogenous or lymphogenous metastases

5 year survival rate

Stage I — 94 - 100 %
Stage II — 86 - 95 %
Stage III — 56 - 69 %
Stage IV — 11 - 50 %

Clinical presentation

- Thoracic symptoms
  - Related to the size of the tumor and its effects on adjacent organs

    : chest pain, shortness of breath, cough, phrenic nerve palsy, superior vena cava obstruction
  - Systemic ("B") symptoms

    : fever, weight loss, and/or night sweats

Paraneoplastic disorders

- Myasthenia gravis
- Pure red cell aplasia
- Immunodeficiency
- Thymoma-associated multiorgan autoimmunity

Treatment

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013

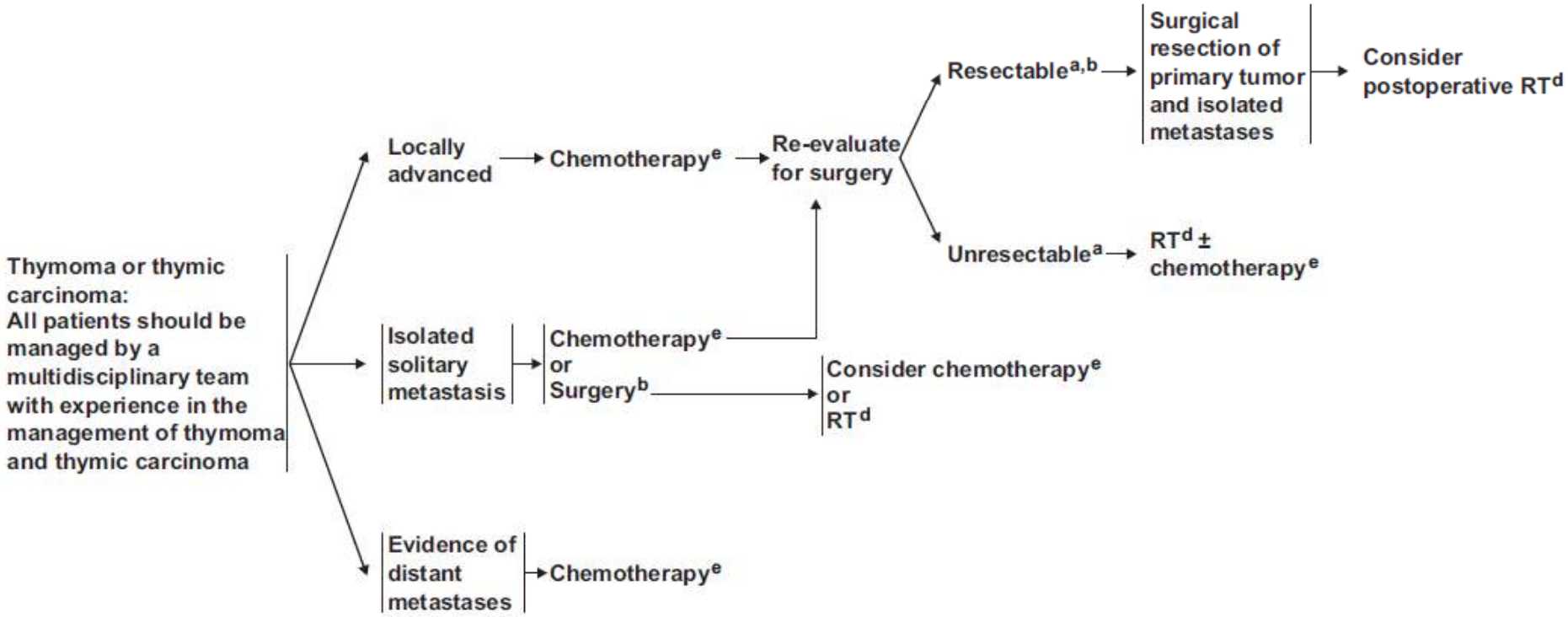
NCCN Guidelines Index

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013
Thymomas and Thymic Carcinomas

NCCN Guidelines Index
Thymic Table of Contents
Discussion

LOCALLY ADVANCED, ADVANCED, OR RECURRENT DISEASE — **TREATMENT**



Prognosis

- Thymomas
  - usually slow-growing tumors
  - presence of invasion is an important adverse prognostic marker
- The overall five-year survival : 70 %
  - 50 % with local invasion
  - 75 % without invasion
- 10-year survival : 50 %
  - 30 % with invasion
  - 60 % without invasion

Benign LN disease

Benign Mediastinal Lymphadenopathies

I. Mediastinal granulomatous disease
   - Tuberculosis
   - Fungal infection
   - Sarcoidosis
   - Silicosis
   - Wegener's granulomatosis

II. Castleman's disease

III. Others
   - Systemic lupus erythematosus
   - Infectious mononucleosis
   - Reactive lymph node hyperplasia
   - Amyloidosis
   - HIV–associated *Pneumocystis carinii*

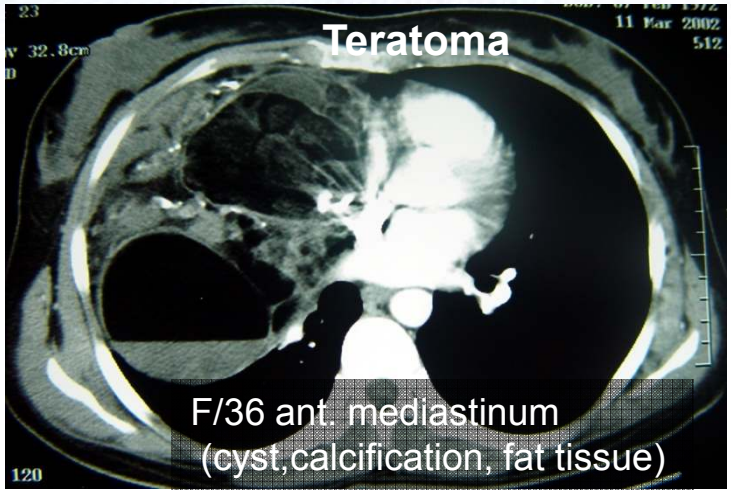
Source: Machevsky MA, Kaneko M. *Surgical Pathology of the Mediastinum*. New York: Raven Press, 1984:174. With permission.

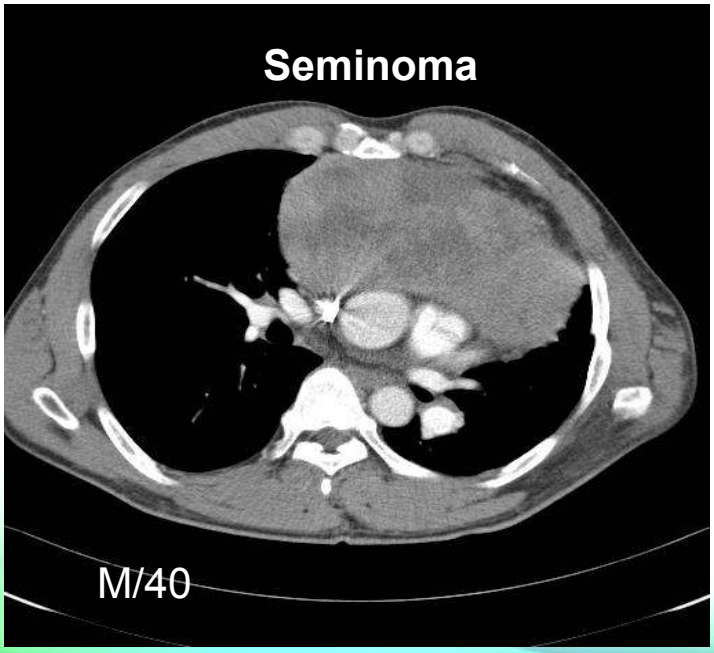
Germ cell tumor

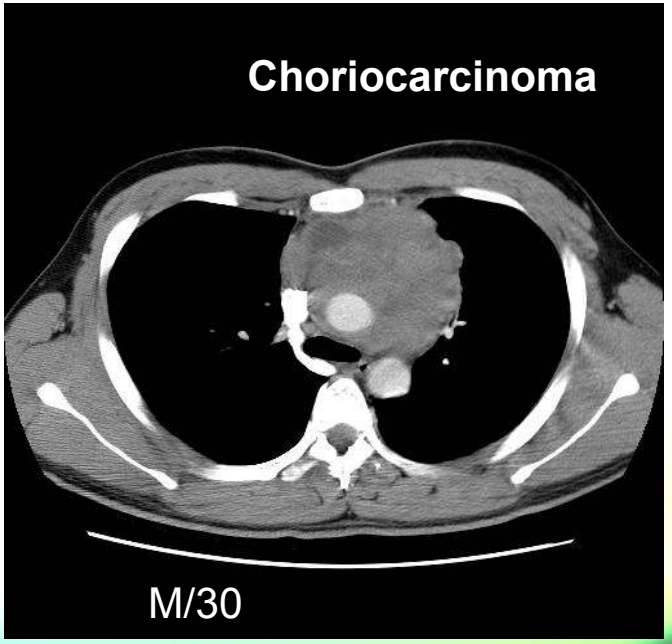
1. Benign germ cell tumors
2. Primary seminomas
3. Non-seminomatous malignant germ cell tumors

Mediastinal Tumor

- Anterior mediastinum
- Thymoma? Lymphoma? Teratoma? or other
- Biopsy?
- Operation?
    - When?
    - (VATS or sternotomy? thoracotomy?)
- Postop. ?







Classification

양성 생식세포종 **(Benign GCT)**	***Epidermoid cyst***	***Teratomatous tumor***
	Dermoids (dermoid cyst)	***Mature teratoma***
	Teratoma (mature teratoma)	***Immature teratoma***
		Teratoma with additional malignant component
정상피종 **(Seminoma)**		***Non-teratomatous Tumors***
비정상피종성 생식세포종 **(NSGCT)**	*Malignant teratoma*	
	Choriocarcinoma	
	Yolk sac carcinoma *(endodermal sinus tumor)*	
	Embryonal carcinoma	
	Teratocarcinoma	

GCT; Germ cell tumor NSGCT; non-seminomatous germ cell tumor

Mullen & Richadson (1986)
WHO (Mostofi and Sobin, 1977) - Mediastinal Germ Cell tumors(1977a)
Testicular GCT (British testicular Tumor Panel; 1953, 1973, 1976)

Incidence

5-10% (extra-gonadal, mediastinum)	of Germ cell tumor
15% (85% benign) 25% (children, 대부분 benign)	of Anterior mediastinal tumors *Mullen & Richardson (1986)*
42 (10%) (50% benign)	400 mediastinal mass *Duke Univ. medical center (1930-1982)*

Benign GCT (Teratoma) *Shirodkar (1997)*

97-98% anterior mediastinum

3-8% posterior mediastinum)

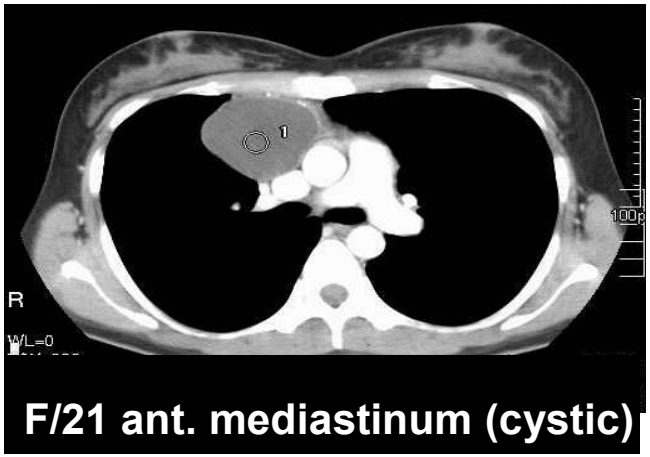
Malignant GCT

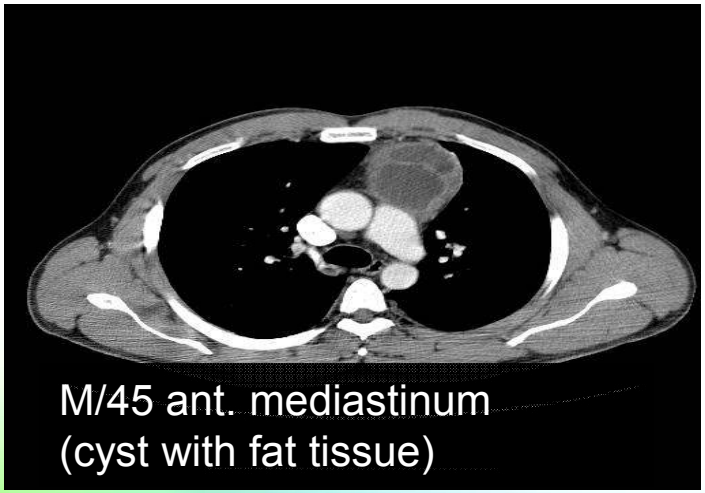
1-5% of all germ cell neoplasm

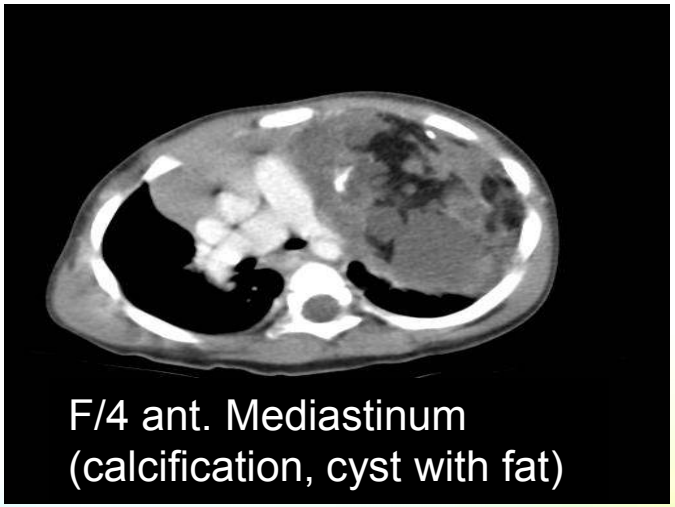
3-5% of mediastinal tumors

Seminoma 50% / Non-seminomatous GCT 50%

Benign Germ Cell Tumors







- **Three primodial layers**
  - Ectoderm; skin, hair
  - Mesoderm; bone, fat, muscle
  - Endoderm; respiratory epithelium, GIT

- Mature cells or tissues – **Mature teratoma**
- Less well-differentiated tissues – **Immature**
  - Infant; behave similarly to mature teratoma
  - Older patient; more aggressive (malignant teratoma)

Ruptured mediastinal Teratoma

- Incidence of spontaneous rupture

  up to 36% into lung & bronchial tree,
  pleural space,pericardial space, great vessels

- Hypothesis of rupture

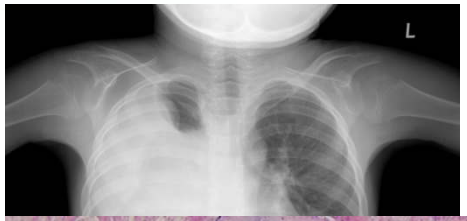
  - **Autolysis** : most compelling cause, digestive enzymes
    (pancreatic tissue, salivary gland tissue)
  - **Chemical inflammation** : sebaceous gland secretions
  - **Ischemia** : rapid enlargement
  - **Pressure necrosis** : thinning of the cyst wall d/t secretions
  - **Infection** : tumor wall fragile(pulmonary or hematologic)

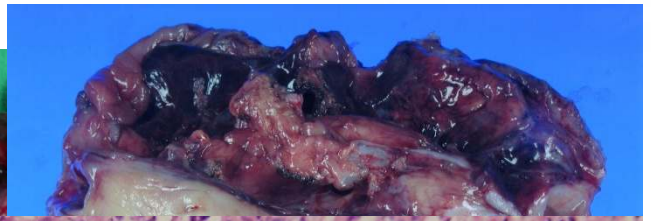
Spontaneous rupture of benign mature teratomas of the mediastinum
Am J Roentgenol. 1998 Feb:170(2):323-328
Teratoma with malignant transformation in the ant. Mediastinum
Korean J Radiol. 2000 Jul-Sep:1(3):162-4

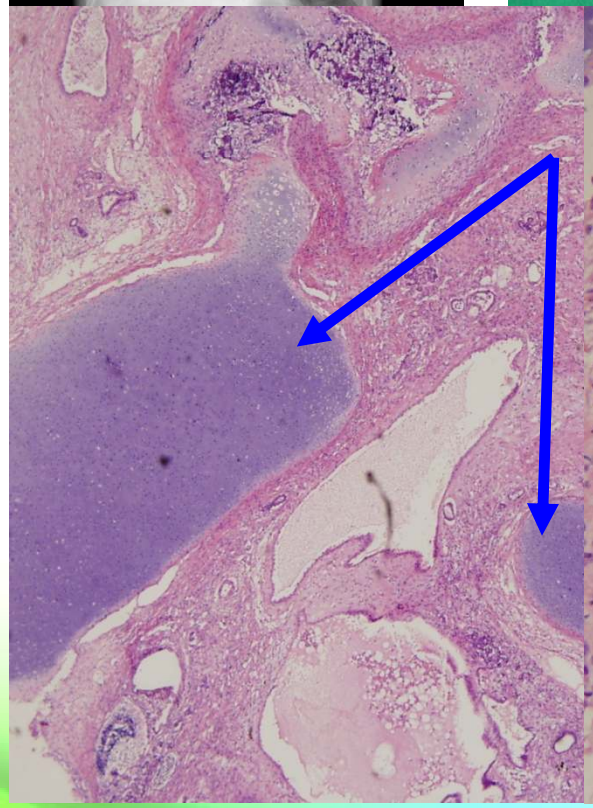
Immature Teratoma

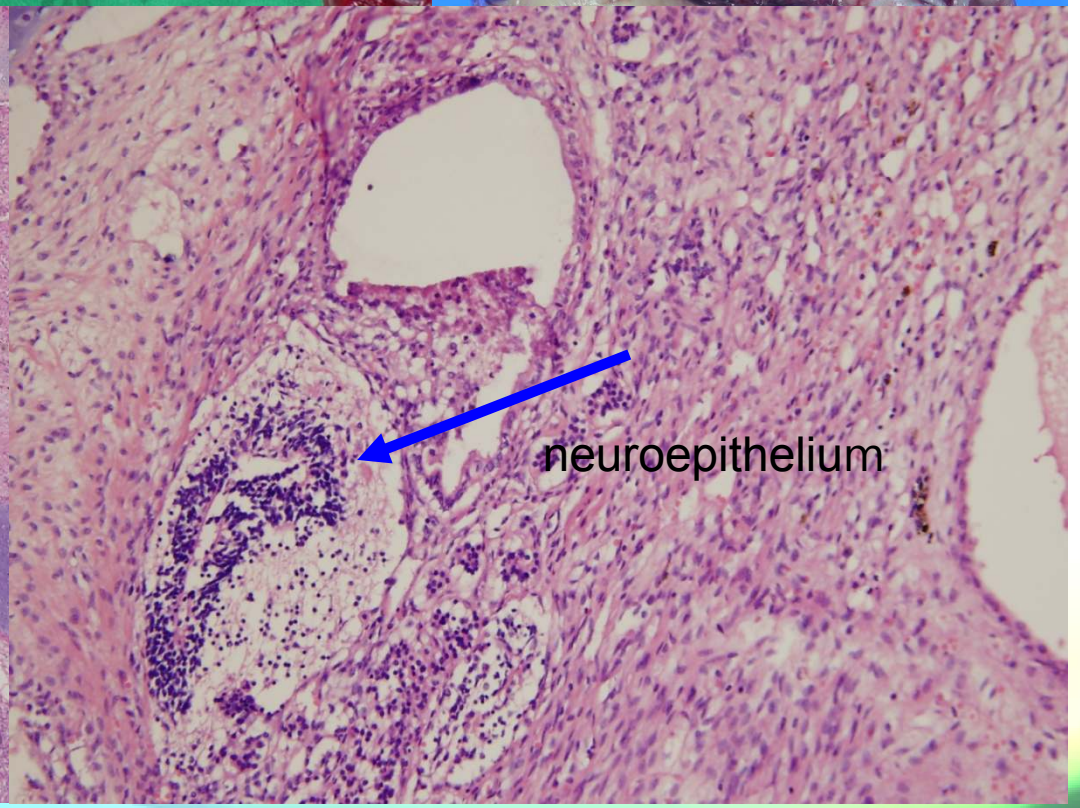
10 months old male

Huge mediastinal mass with pleural effusion



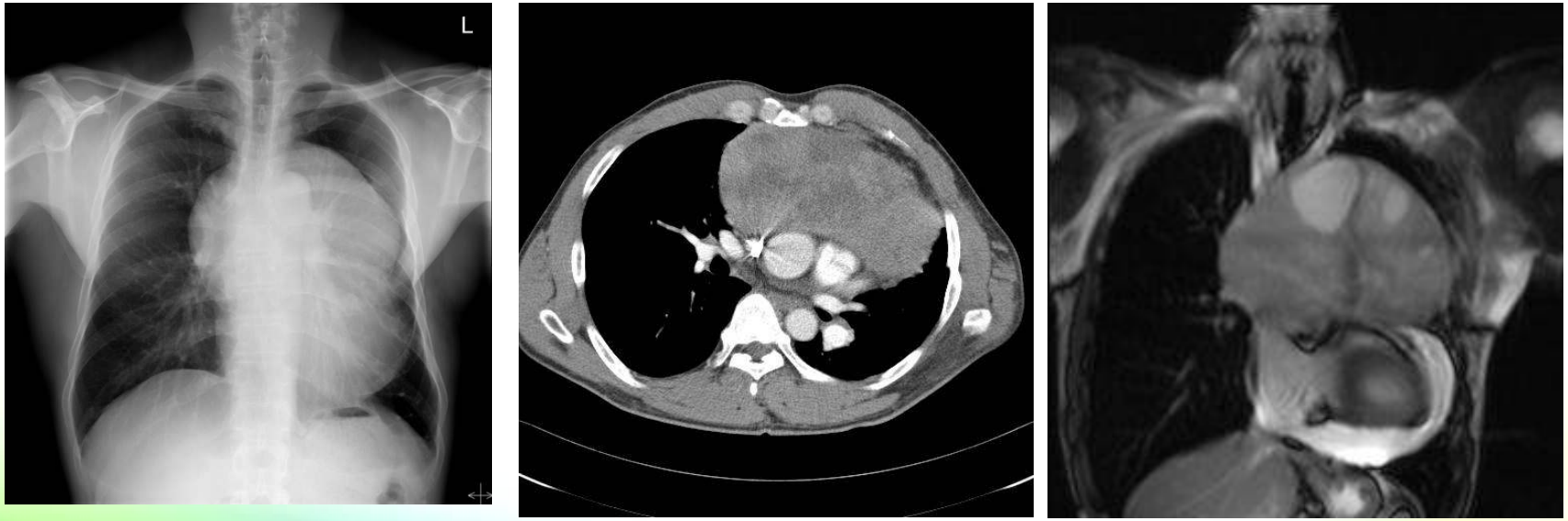






Seminoma

- Second common mediastinal GCT / TMC malignant mediastinal GCT
- 3 rd ~ 5 th decade men, white men predominant
- Slow-growing tumors with lobular appearance including necrosis, hemorrhage
  - encapsulation – half of time, calcification – infrequently



40/M Seminoma

Seminoma

Young man with anterior mediastinal tumor

Serum Tumor markers
hCG AFP LDH

(+) hCG * (-) AFP

Seminoma (pure)

(++) hCG (+) AFP

Mixed tumor or NSGCT → *NSGCT*

Testicular exam. : bimanual exam. & U/S
Abdominal CT/ Bone scan/ Brain CT or MR

Biopsy Mediastinoscpy or Sternotomy
VATS

Seminoma

Radiotherapy or adjuvant radiotherapy

Surgery

Chemotherapy

Poor Prognostic factor

Heitmiller & Marasco(1995)

Age greater than 35 years
Bulky mediastinal disease
SVC obstruction
Lymphadenopathy

Platinum-based
complete remission 88 ~ 100 %
5 YSR 70 ~ 85 %

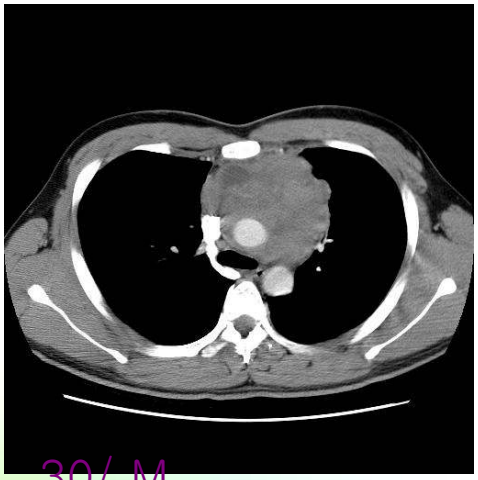
International Germ Cell Cancer Collaboration Group
J Clin Oncol 1977

Good Prognosis		
	Any Primary site	**90% of seminomas**
	No NPVM	**5 year PFS 82 %**
	Normal AFP, hCG, LDH	**5 YSR 86 %**
Intermediate Prognosis		
	Any Primary site	**10% of seminomas**
	NPVM (liver, bone, brain)	**5 year PFS 67 %**
	Normal AFP, hCG, LDH	**5 YSR 72 %**

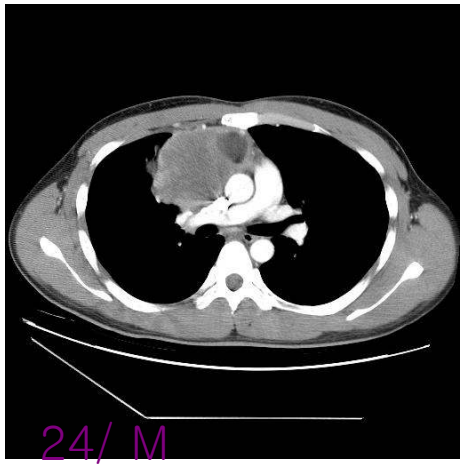
NPVM non-pulmonary visceral metastasis
PFS progression free survival

Non-seminomatous GCT

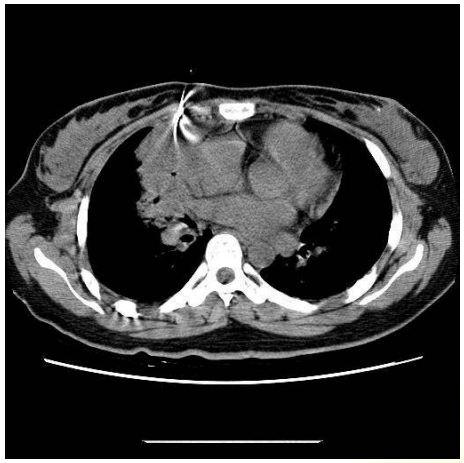
- Potentially curable with surgery
- Exclusively in young adult, men (fewer than 30 cases reported in women)
- Rapid local growing tumors with early metastasis (85-90% at diagnosis)
- In-homogenous mass with multiple areas of necrosis & hemorrhage



30/ M
Choriocarcinoma



24/ M
Endodermal sinus tumor



Incidence

	Moran & Suster (1997) *229 cases*	*강창현 (2008)* *29cases*
Teratocarcinoma	41 %	9.5 %
58% non-germ cell component (sarcoma, epithelial carcinoma)		
Endodermal sinus (Yolk sac) tumor	35 %	42.9 %
Choriocarcinama	7 %	4.8 %
Embryonal carcinoma	6 %	9.5 %
Mixed	11 %	9.5 %
Unknown		23.8 %

Differ from testis origin

Pure endodermal sinus tumor, extremely rare in testis
Embryonal carcinoma, much higher in testis
Non-germ call histologies is more common in mediastinum

Tumor markers

hCG or AFP	90%
AFP with/without hCG	80%
hCG	30-35%
LDH	80-90%

APF 이 증가된 경우는 조직검사상 pure seminoma로 보인다고 해도 NSGCT와 같이 치료

hCG가 100 ng/ml 이상은 pure seminoma에서 uncommon

Differ from testis origin

Testicular NSGCT AFP & hCG equal frequency

Associated syndromes

Hematologic malignancies

Acute non-lymphocytic leukemia	**Acute lymphocytic leukemia**
Erythroleukemia	**Acute megakaryocytic leukemia**
Myelodysplastic syndrome	**Malignant histiocytosis**
Hartmann(2000) 2% ***(287 mediastinal NSGCT)***	***Median survival 5 months*** ***No patient more than 2 years***

Idiopathic thrombocytopenia

Hemophagocytic syndrome — ***single case of endodermal sinus tumor***

Klinefelter's syndrome — ***not associated with testicular GCT***
 common underlying germ cell defect

NSGCT

Young man with anterior mediastinal tumor

Serum Tumor markers
hCG AFP LDH

(+) hCG * (-) AFP

Seminoma (pure)

(++) hCG (+) AFP

Mixed tumor or NSGCT

Biopsy, least invasive approach
Excess 500 ng/ml of hCG or AFP not delay chemotherapy due to biopsy

Chemotherapy

Platinum-based
Long-term survival 41 %

Surgery ? or not

Poor Prognostic factor *강창현 (2008)*
Bulky mediastinal disease – incomplete surgical resection
Histology – pure endodermal sinus tumor
Pre-chemotherapy hCG concentration

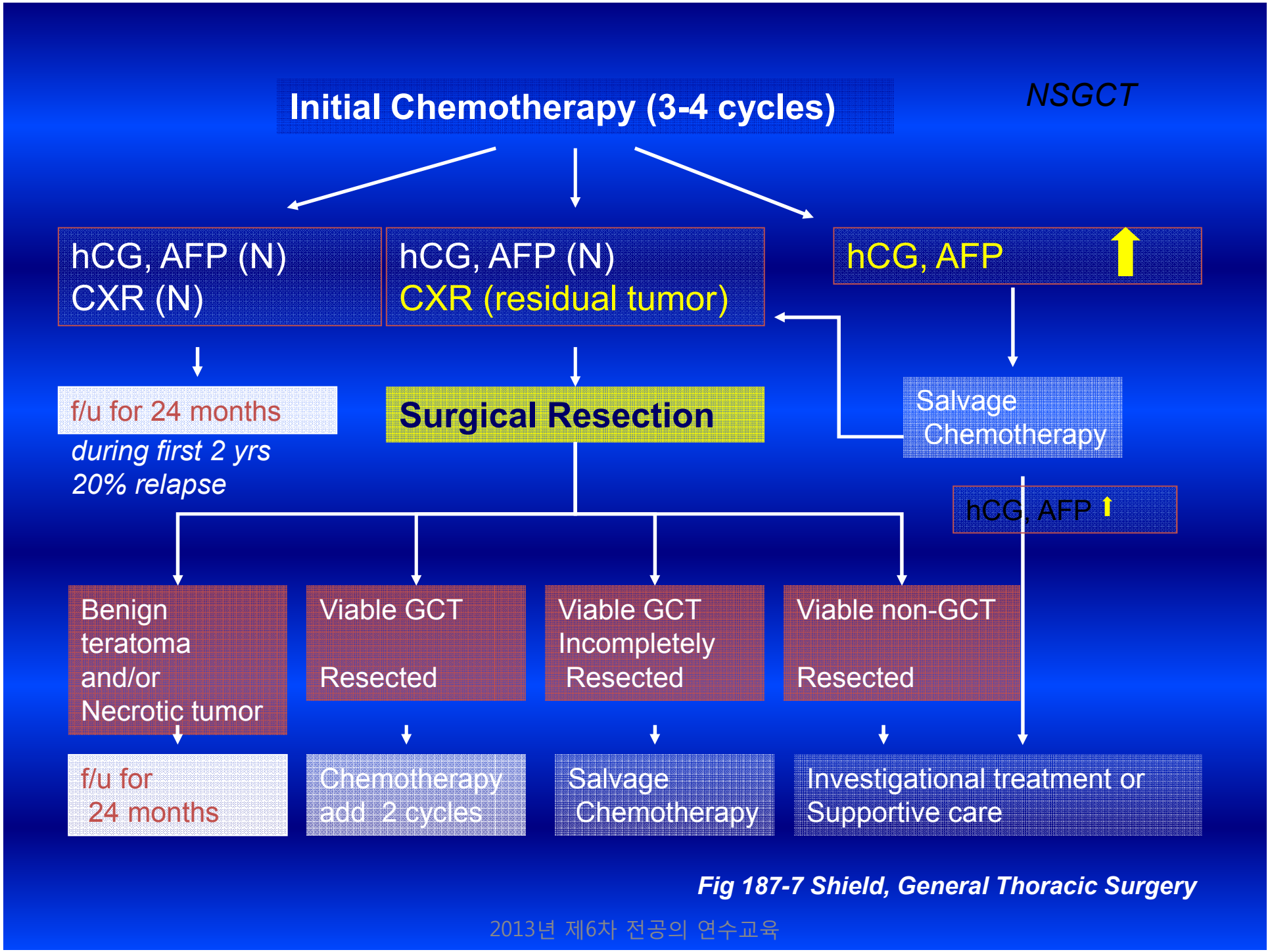


Fig 187-7 Shield, General Thoracic Surgery

International Germ Cell Cancer Collaboration Group *J Clin Oncol 1977*

	AFP	*hCG*	*LDH*	non-semonomas	
Good Prognosis					
Testis/retroperitoneal				56%	
No NPVM				5 year PFS	82 %
Good markers	< 1000	< 1000	< 1.5 x N	5 YSR	86 %
Intermediate Prognosis					
Testis/retroperitoneal				28%	
No NPVM				5 year PFS	75 %
Intermediate markers	1,000~ 10,000	1,000~ 10,000	1.5 x~ 10 x N	5 YSR	80 %
Poor Prognosis					
Mediastinal primary				16%	
NPVM (liver bone, brain)				5 year PFS	41 %
Poor markers	> 10,000	> 10,000	> 10 x N	5 YSR	48 %

NPVM non-pulmonary visceral metastasis
PFS progression free survival

Neurogenic tumors

TABLE 196-1 Mediastinal Neurogenic Tumors in Infants and Children

Tumors of autonomic ganglia	*Neuroblastoma*	*Ganglioneuroblastoma*	*Ganglioneuroma*
Tumors of nerve sheath origin	Schwannoma	Neurofibroma	Neurogenic sarcoma
Tumors of neuroectodermal origin	Melanotic progonoma	Askin's tumor	
Tumors of paraganglia	Paraganglioma		

Mediastinal cyst

- Foregut cyst
- Gastroenteric and Neurenteric cyst