APPROACH TO A CASE OF LUNG NEOPLASM AND MEDIASTINAL TUMOURS

CASE SCENARIO

- A 55 YEAR OLD MALE PRESENTS IN OPD WITH NON RESOLVING RIGHT SIDE CHEST PAIN WITH ASSOCIATED BREATHLESSNESS ON EXERTION. HE HAS THE ABOVE SYMPTOMS SINCE LAST 6 MONTHS

- HE ALSO COMPLAINS OF FEVER MODERATE GRADE WITH CHILLS SINCE PAST 7 DAYS

- ON FURTHER QUERY HE REVEALS HAVING ONE EPISODE OF BOUTS OF BLOOD STREAKED SPUTUM AROUND 1 YEAR BACK, WHICH RESOLVED ON SOME LOCAL MEDICATIONS AND PATIENT DID NOT CONSULT FOR THAT ANY FURTHER

FURTHER . . . .

- OCCUPATION: FARMER
- HE HAS NO OTHER COMORBIDITIES, DENIES HAVING TAKEN ATT IN THE PAST AND CONTACT HISTORY
- FAMILY HISTORY IS NON CONTRIBUTORY
- SMOKING: 10 CIGARETTE/ DAY SINCE 30 YEARS
- PACK YEARS: ?
- SMOKING INDEX: ?

SMOKING INDEX-A MEASURE TO QUANTIFY CUMULATIVE SMOKING EXPOSURE

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ABSTRACT

'Smoking Index' is a parameter used to express cumulative smoking exposure quantitatively. This is especially useful in defining risk ratio of a smoking related disease. The parameter is smiliar to 'Pack Year' but more suitable to Indian subjects.

Introduction

Most of the smoking related diseases (e.g. chronic obstructive lung disease and lung carcinoma) are dose-dependant. It is therefore, important to measure smoking exposure quantitatively. This is important in estimating risk ratios in a population and for the estimation of relative risk of a smoking related disease in an individual. It is often the cumulative dose of smoking which determines risk. Parameters like pack-year have been used to express this exposure in the West.

Pack Year

S.I is defined as the product of average number of cigarettes (or bidis) smoked per day and the total duration of smoking in years.

S. I = No. per day X total duration (yrs). Both degree (number per day) and duration of smoking are given equal weightage. For example, a subject smoking 10 cigarettes (or bidis) per day for one year, and another smoking 1 cigarette (or bidi) per day for ten years will have S.I of 10. Both these subjects would have smoked a total of 3650 cigarettes (or bidis). Since we are largely concerned with cumulative expsoure, both these individuals are considered to be at equal risk.

EXAMINATION

GENERAL

- PALLOR: PRESENT
- ICTERUS: ABSENT
- CYNOSIS: ABSENT
- LYMPHADENOPATHY: LEFT SUPRACLAVICULAR 1cm
- CLUBBING: PRESENT
- PEDAL EDEMA: ABSENT

SYSTEMIC

RESPIRATORY

DIMINISHED RIGHT SIDE BREATH SOUNDS ON AUSCULTATION WITH STONY DULLNESS ON PERCUSSION

CVS

NORMAL

ABDOMEN

TENDERNESS IN RIGHT HYPOCHONDRIAC REGION

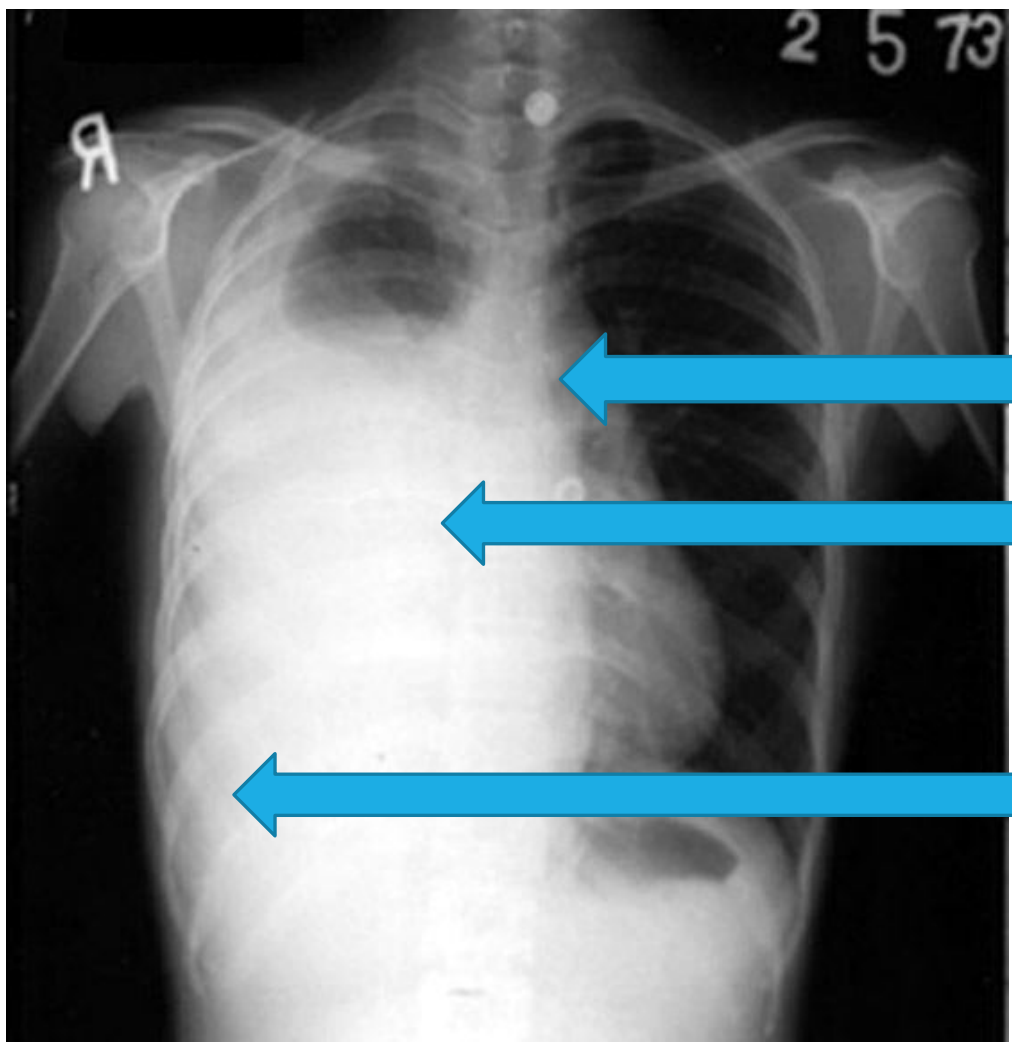
CNS

NORMAL

INVESTIGATIONS

- ROUTINE BLOOD TESTS: CBC, LFT, KFT
- CHEST RADIOGRAPH [PA]
- ECG
- USG ABDOMEN

CXR (PA)



WHAT DO WE SEE ?

MEDIASTINAL SHIFT ??

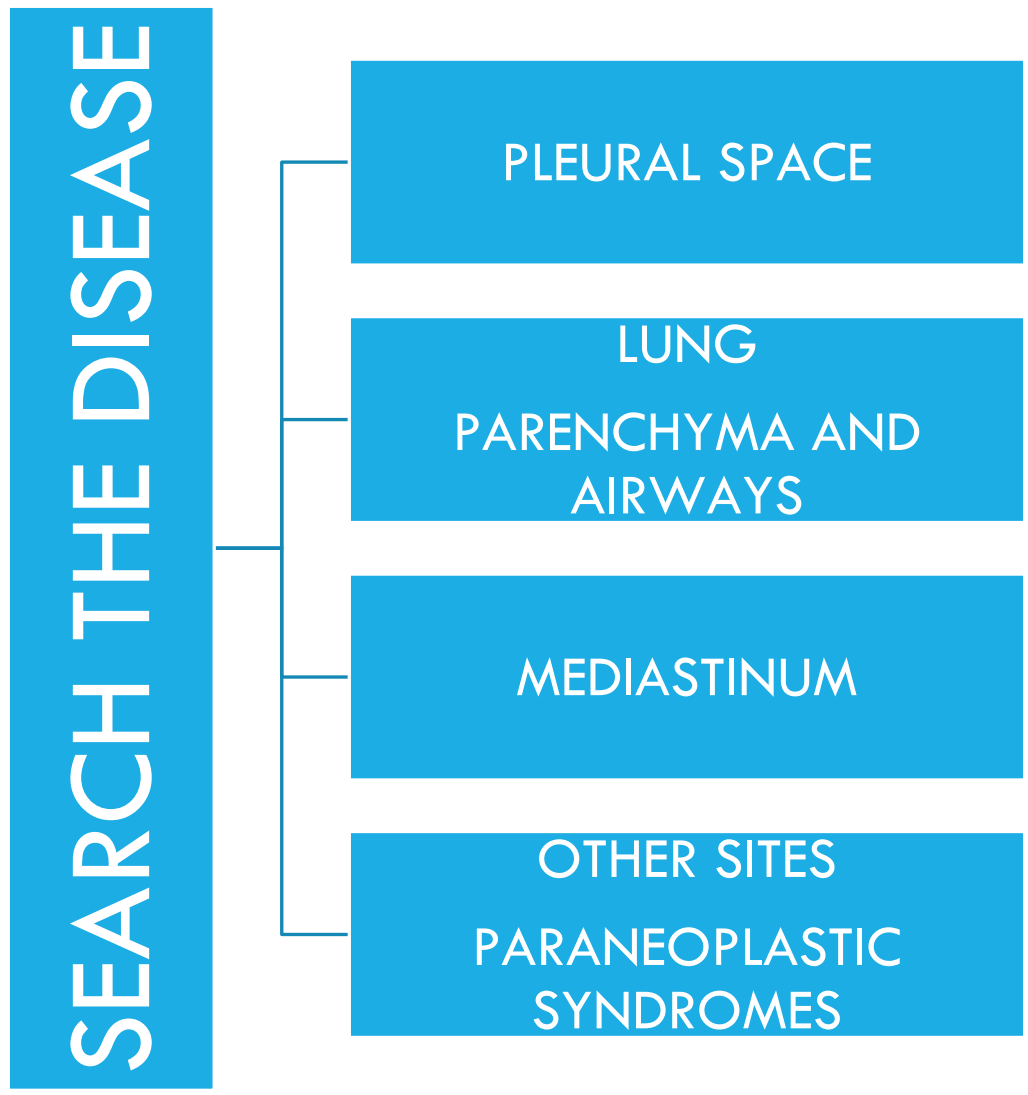
RIGHT HILUM ??

RIGHT PLEURAL SPACE ??

DIFFERENTIAL DIAGNOSIS??

1. RIGHT SIDED PLEURAL EFFUSION
2. RIGHT LUNG COLLAPSE

WHAT NEXT??



INVESTIGATIONS??

- **USG THORAX**
- **THORACOCENTESIS**

  DIAGNOSTIC/ THERAEUTIC

  → FLUID FOR CYTOLOGY AND CELL BLOCK
- **CT THORAX**
- **BRONCHOSCOPY**

  → TISSUE FOR HPE AND IHC/ MUTATION ANALYSIS

  CONVENTIONAL/ EBUS GUIDED TBNA/ RADIAL PROBE TBNA

USG THORAX

THORACOCENTESIS

PLEURAL FLUID:

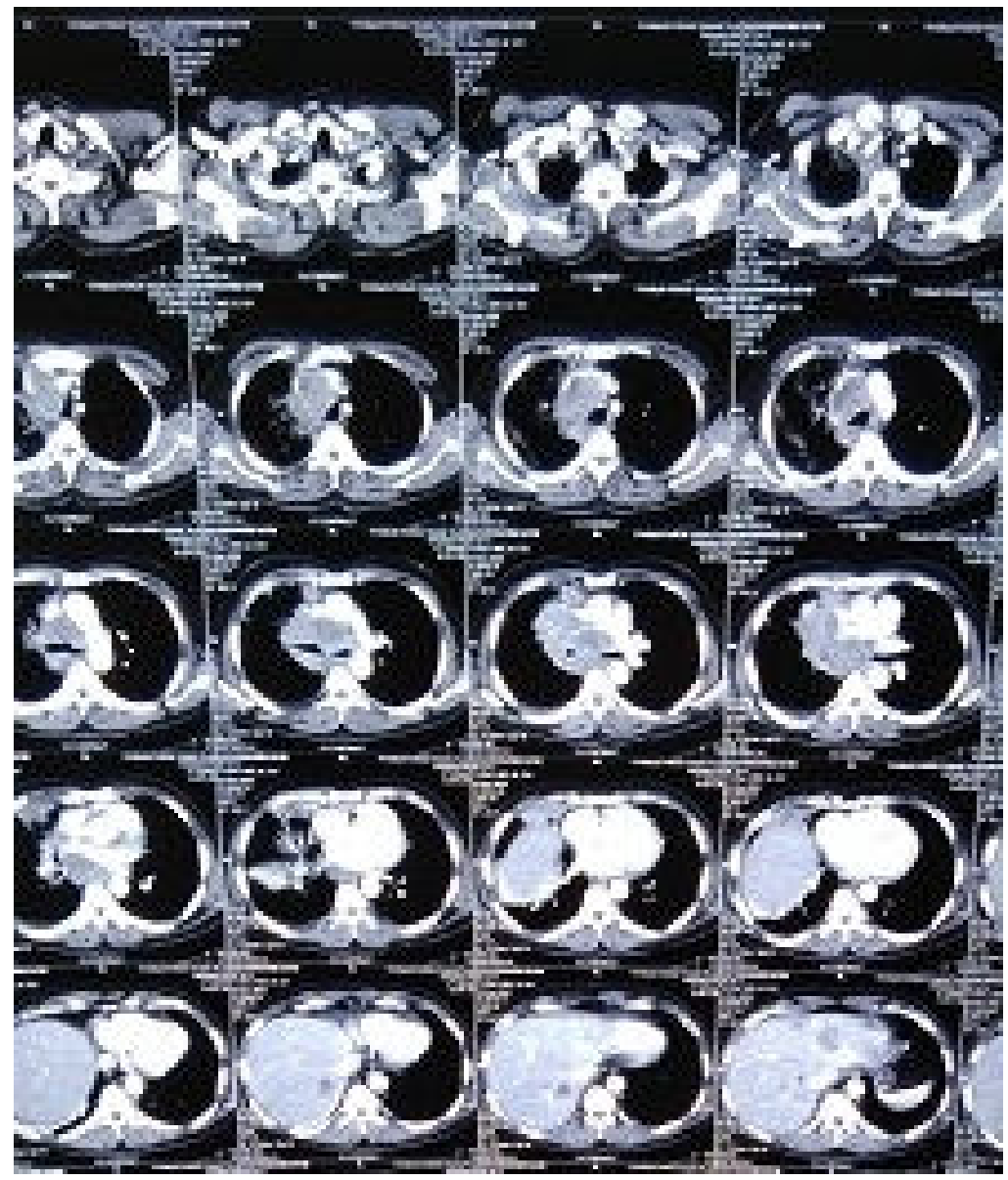
LOOK AT:

1. COLOR
2. TURBIDITY
3. REFILLING

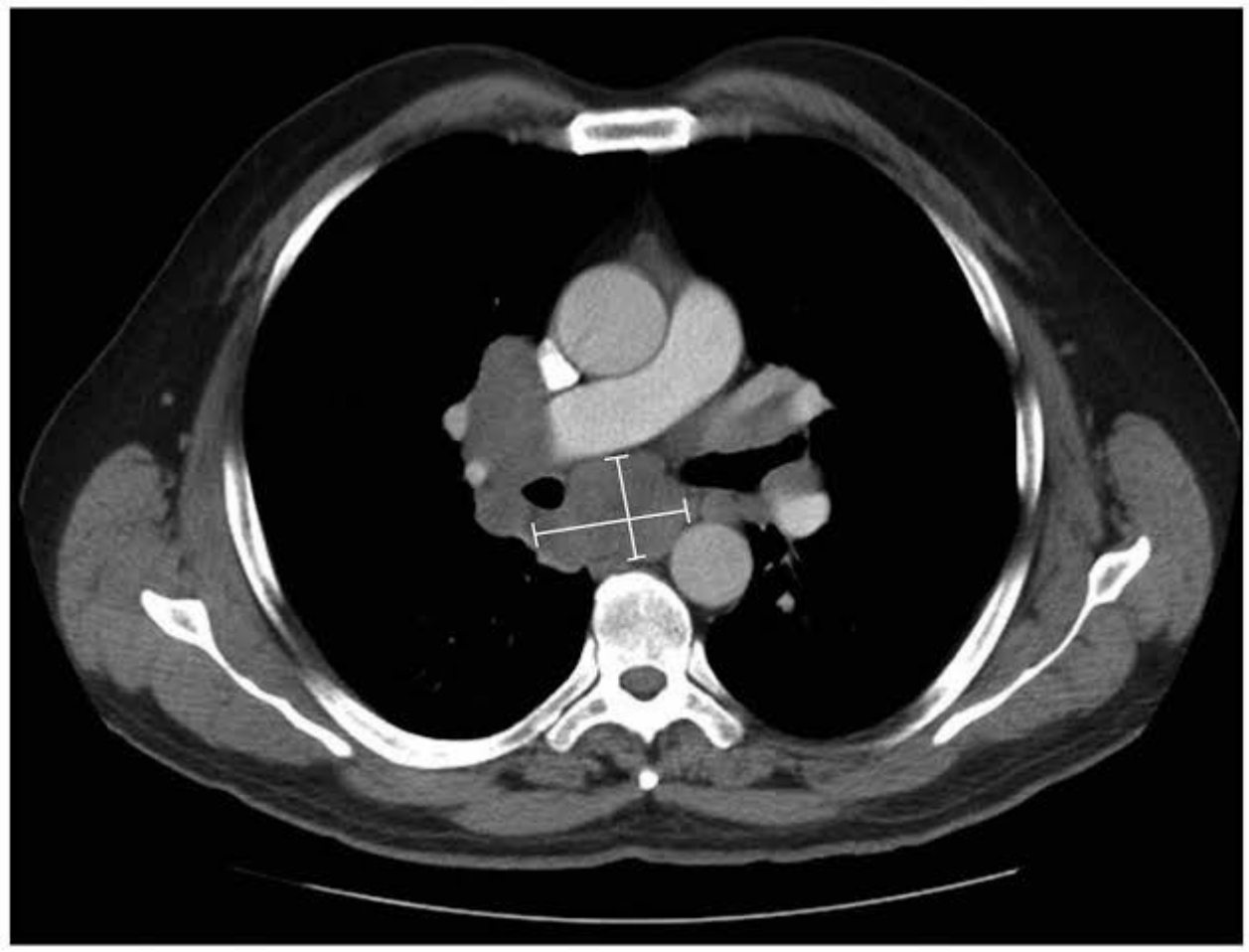
SEND FOR:

1. CYTOLOGY MALIGNANT CELLS
2. CELL COUNT AND DIFFERENTIALS
3. LDH
4. ADA/ ZN SMEAR
5. BIOCHEMISTRY: PROTEINS AND SUGAR

CT THORAX



CT THORAX CONTD.

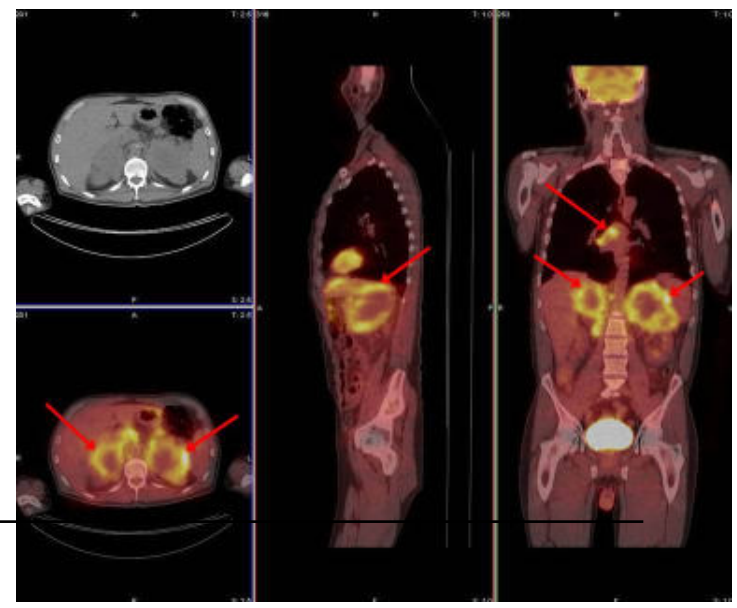


BRONCHOSCOPY

- BRONCHOSCOPY
  - CONVENTIONAL [ENDOBRONCHIAL/ TBLB/ CRYOBIOPSY]
  - EBUS GUIDED TBNA [CENTRAL AND MEDIASTINAL]
  - RADIAL EBUS [PERIPHERAL]

WORKUP

- METASTASIS SEARCH
  - ABDOMEN
    - FEMALES GENITAL ORGANS
      - MALES PROSTATE
  - CNS
  - THYROID
  - BONE



TNM GRADING

TNM 8th - Primary tumor characteristics	
T_x	Tumor in sputum/bronchial washings but not be assessed in imaging or bronchoscopy
T_0	No evidence of tumor
T_{is}	Carcinoma in situ
T_1	≤ 3 cm surrounded by lung/visceral pleura, not involving main bronchus
$T_{1a(mi)}$	Minimally invasive carcinoma
T_{1a}	≤ 1 cm
T_{1b}	> 1 to ≤ 2 cm
T_{1c}	> 2 to ≤ 3 cm
T_2	> 3 to ≤ 5 cm *or* involvement of main bronchus without carina, regardless of distance from carina or invasion visceral pleural *or* atelectasis or post obstructive pneumonitis extending to hilum
T_{2a}	>3 to ≤4cm
T_{2b}	>4 to ≤5cm
T_3	>5 to ≤7cm in greatest dimension *or* tumor of any size that involves chest wall, pericardium, phrenic nerve *or* satellite nodules in the same lobe
T_4	> 7cm in greatest dimension *or* any tumor with invasion of mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, oesophagus, spine *or* separate tumor in different lobe of ipsilateral lung
N_1	Ipsilateral peribronchial and/or hilar nodes and intrapulmonary nodes
2	Ipsilateral mediastinal and/or subcarinal nodes
3	Contralateral mediastinal or hilar; ipsilateral/contralateral scalene/ supraclavicular
M_1	Distant metastasis
M_{1a}	Tumor in contralateral lung or pleural/pericardial nodule/malignant effusion
M_{1b}	Single extrathoracic metastasis, including single non-regional lymphnode
M_{1c}	Multiple extrathoracic metastases in one or more organs

	TNM 7th EDITION	TNM 8th EDITION
T	-	Tis
	-	Tmi
	-	Tss
	T1a (≤2 cm) →	T1a (≤1 cm)
	T1b (>2 -3 cm)	T1b (>1-2cm)
		T1c (>2-3cm)
	T2a (>3-5 cm) →	T2a (>3cm but ≤4cm)
	T2b (>5-7 cm)	T2b (>4cm but ≤5cm)
	T3 (>7 cm) →	T4
	T3 - atelectasis/pneumonitis involving whole lung)	T2 atelectasis/pneumonitis irrespective of involving lobe or whole lung
	T3 tumor involving the main bronchus <2cm distance to carina →	T2 -tumor involving the main bronchus irrespective of distance to carina
	T3 -invasion of the diaphragm →	T4 (invasion of the diaphragm)
N	No changes	
M	M1b - distant metastasis →	M1b - single extrathoracic metastasis M1c - multiple extrathoracic metastases

STAGING

	N0	N1	N2	N3
T1	IA	IIB	IIIA	IIIB
T2a	IB	IIB	IIIA	IIIB
T2b	IIA	IIB	IIIA	IIIB
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC
M1a	IVA	IVA	IVA	IVA
M1b	IVA	IVA	IVA	IVA
M1c	IVB	IVB	IVB	IVB

WHAT NEXT??

HISTOPATHOLOGY AND ROLE OF IMUNOHISTOCHEMISTRY

ADENOCARCINOMA: TTF 1, NAPSIN A {SENSITIVITY=80%}

SQUAMOUS: p40 {MOST SENSITIVE AND SPECIFIC}

OTHERS= p 63 AND ck 5/6

BEST COMBO= TTF1 AND p40/ p63

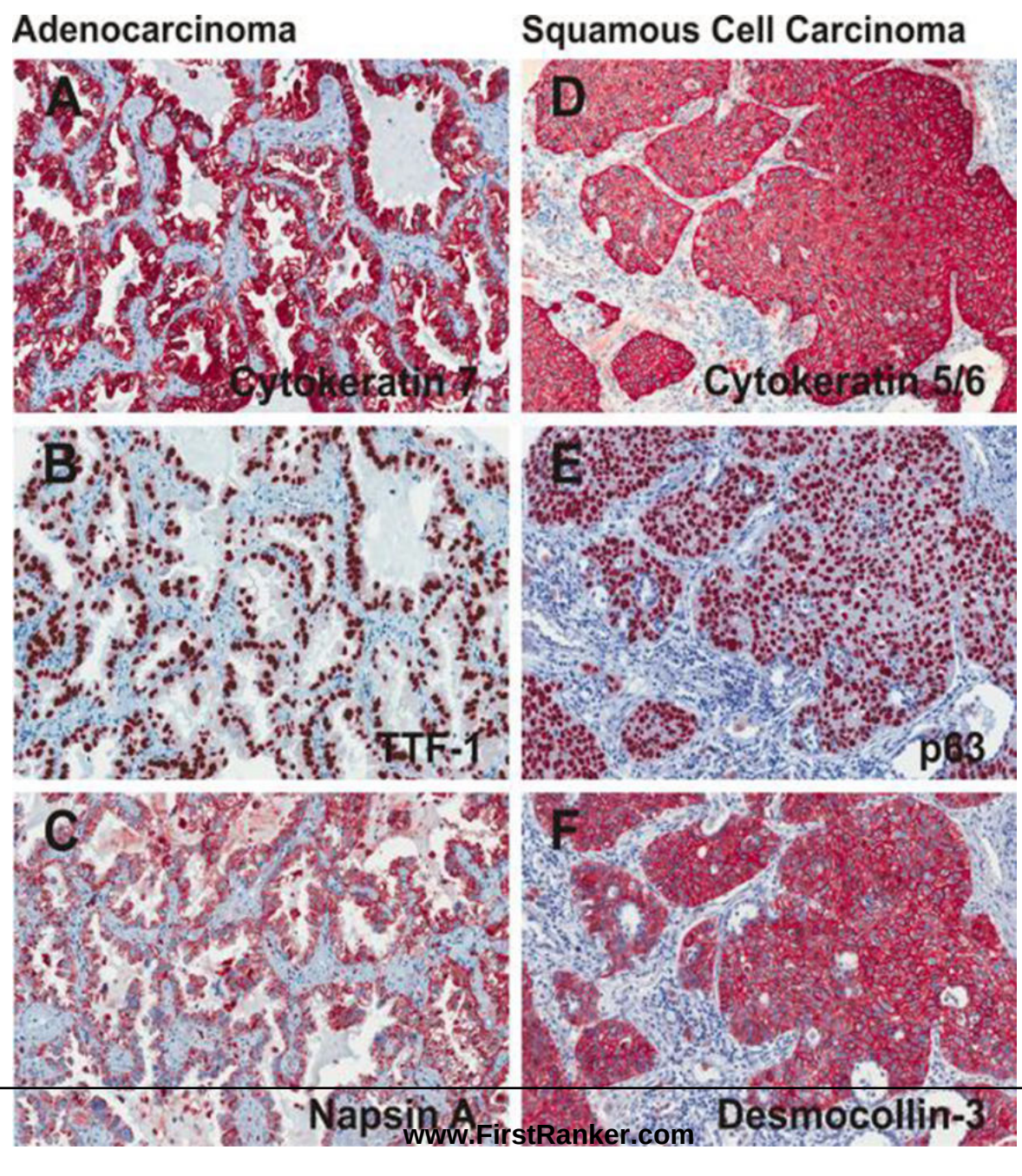
MUTATION ANALYSIS

EGFR, ALK1, ROS 1, KRAS, PDL 1 ANTIBODY

WHY??

CERTAIN THERAPEUTIC IMPLICATIONS, LIKE

- PEMETREXED IS EFFECTIVE FOR ADVANCED ADENOCARCINOMA
- BEVAIZUMAB IS CONTRAINDICATED IN SQUAMOUS CELL CARCINOMA
- NIVOLUMAB EFFECTIVE FOR ADVANCED SQUAMOUS CELL CARCINOMA



MANAGEMENT: GENERAL CONDITION

ECOG	Description
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on selfcare. Totally confined to bed or chair

Performance Status Scales

Zubrod Scale		Karnofsky Scale	
0	Normal activity	100	Normal; no evidence of disease
		90	Able to perform normal activities with only minor symptoms
1	Symptomatic and ambulatory; cares for self	80	Normal activity with effort; some symptoms
		70	Able to care for self but unable to do normal activities
2	Ambulatory >50% of time; occasional assistance	60	Requires occasional assistance; cares for most needs
3	Ambulatory ≤50% of time; nursing care needed	50	Requires considerable assistance
		40	Disabled; requires special assistance
		30	Severely disabled
4	Bedridden	20	Very sick; requires active supportive treatment
		10	Moribund

STAGES AND TREATMENT OF NSCLC

STAGE	DESCRIPTION	TREATMENT OPTIONS
STAGE 1	Tumor of any size is found only in the lung	Surgery
STAGE 2	Tumor has spread to lymph nodes associated with the lung	surgery
STAGE 3A	Tumor ha spread to the lymph nodes in the tracheal area, including chest wall and diaphragm	surgery or chemotherapy
STAGE 3B	Tumor has spread into lymph nodes on the pop lung or in the neck	Combination of chemotherapy and radiation
STAGE 4	Tumor has spared beyond the chest	Chemotherapy only

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2018
Non-Small Cell Lung Cancer

NCCN Guidelines Index
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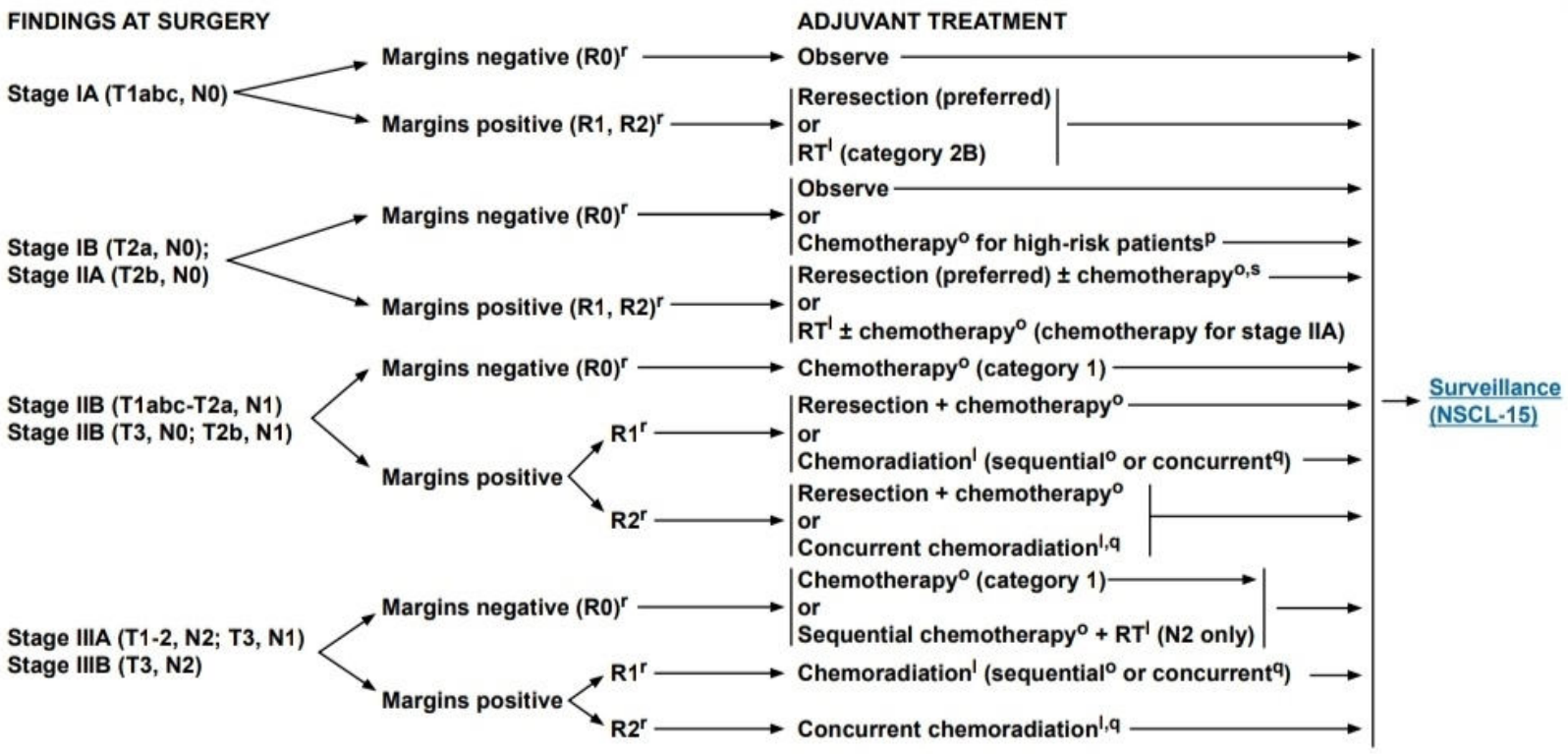
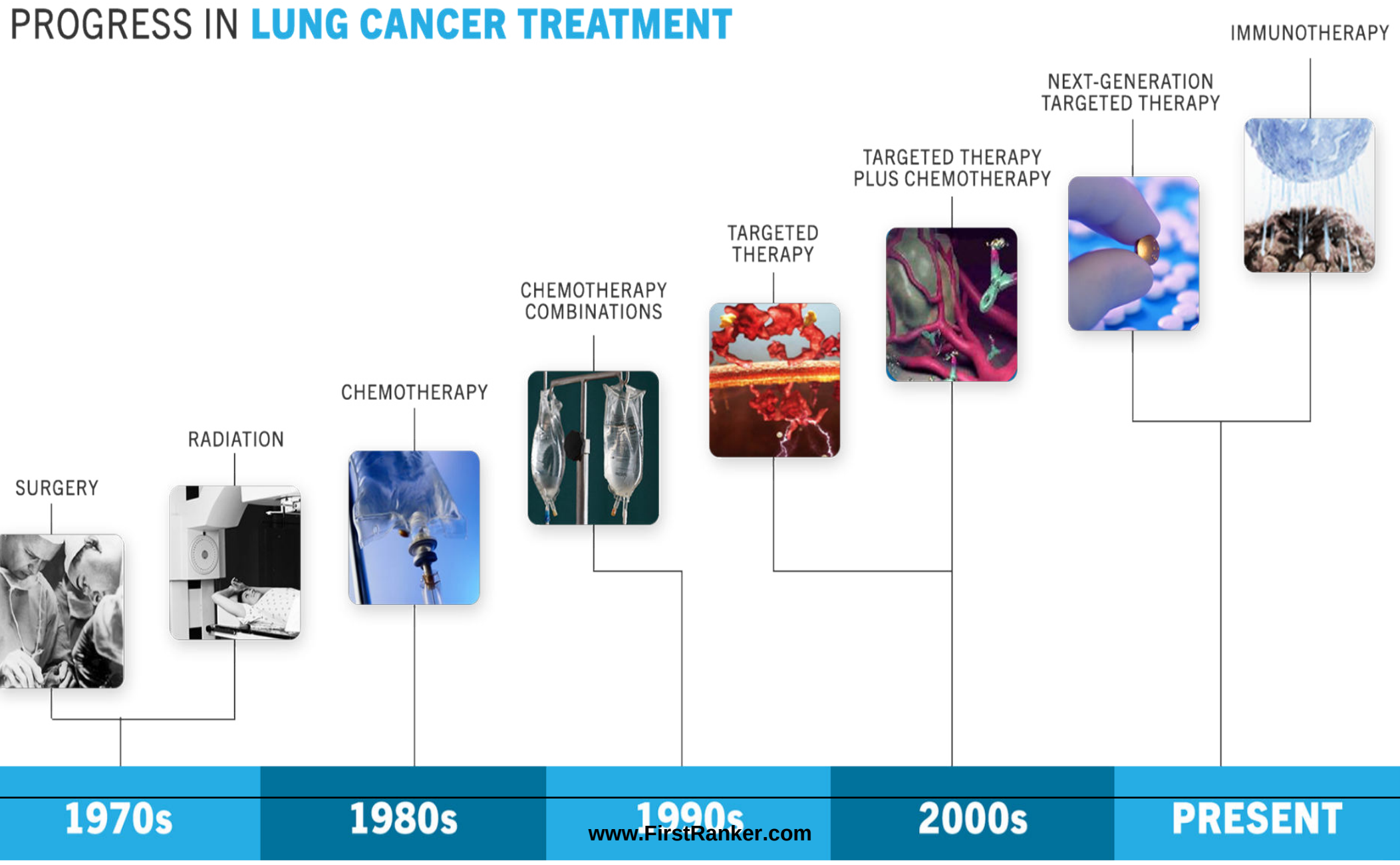
Discussion



[l] See Principles of Radiation Therapy (NSCL-C).
[o] See Chemotherapy Regimens for Neoadjuvant and Adjuvant Therapy (NSCL-D).
[p] Examples of high-risk factors may include poorly differentiated tumors (including lung neuroendocrine tumors [excluding well-differentiated neuroendocrine tumors]), vascular invasion, wedge resection, tumors >4 cm, visceral pleural involvement, and unknown lymph node status (Nx). These factors independently may not be an indication and may be considered when determining treatment with adjuvant chemotherapy.
[q] See Chemotherapy Regimens Used with Radiation Therapy (NSCL-E).
[r] R0 = no residual tumor, R1 = microscopic residual tumor, R2 = macroscopic residual tumor.
[s] Increasing size is an important variable when evaluating the need for adjuvant chemotherapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.



TYPES OF LUNG CANCER WHO 2015 CLASSIFICATION

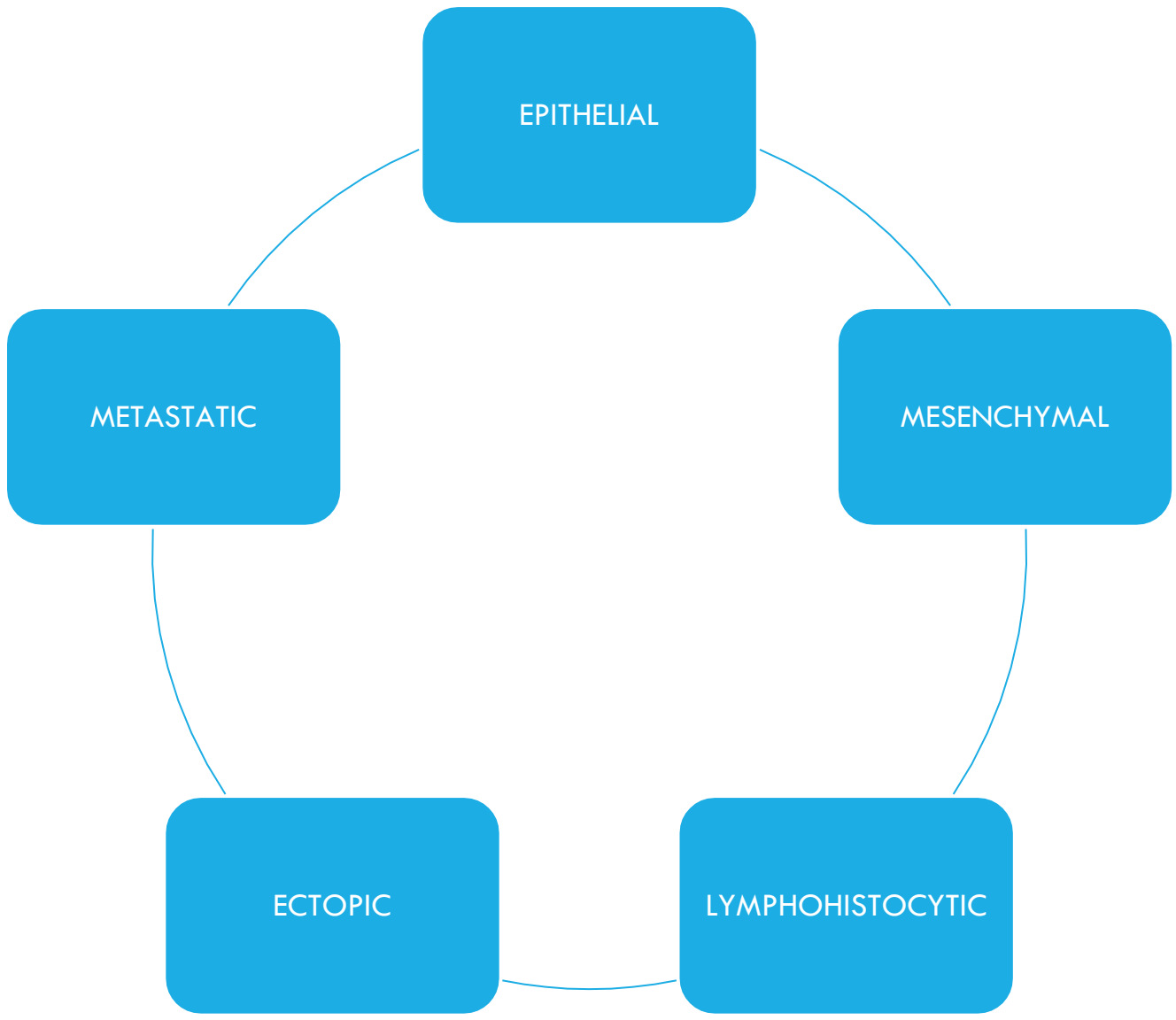


TABLE 1. 2015 WHO Classification of Lung Tumors[a,b,c]

Histologic Type and Subtypes	ICDO Code
Epithelial tumors	
Adenocarcinoma	8140/3
Lepidic adenocarcinoma[e]	8250/3[d]
Acinar adenocarcinoma	8551/3[d]
Papillary adenocarcinoma	8260/3
Micropapillary adenocarcinoma[e]	8265/3
Solid adenocarcinoma	8230/3
Invasive mucinous adenocarcinoma[e]	8253/3[d]
Mixed invasive mucinous and nonmucinous adenocarcinoma	8254/3[d]
Colloid adenocarcinoma	8480/3
Fetal adenocarcinoma	8333/3
Enteric adenocarcinoma[e]	8144/3
Minimally invasive adenocarcinoma[e]	
Nonmucinous	8256/3[d]
Mucinous	8257/3[d]
Preinvasive lesions	
Atypical adenomatous hyperplasia	8250/0[d]
Adenocarcinoma in situ[e]	
Nonmucinous	8250/2[d]
Mucinous	8253/2[d]
Squamous cell carcinoma	8070/3
Keratinizing squamous cell carcinoma[e]	8071/3
Nonkeratinizing squamous cell carcinoma[e]	8072/3
Basaloid squamous cell carcinoma[e]	8083/3
Preinvasive lesion	
Squamous cell carcinoma in situ	8070/2
Neuroendocrine tumors	
Small cell carcinoma	8041/3
Combined small cell carcinoma	8045/3
Large cell neuroendocrine carcinoma	8013/3
Combined large cell neuroendocrine carcinoma	8013/3
Carcinoid tumors	
Typical carcinoid tumor	8240/3
Atypical carcinoid tumor	8249/3
Preinvasive lesion	
Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia	8040/0[d]
Large cell carcinoma	8012/3
Adenosquamous carcinoma	8560/3
Sarcomatoid carcinomas	
Pleomorphic carcinoma	8022/3
Spindle cell carcinoma	8032/3
Giant cell carcinoma	8031/3
Carcinosarcoma	8980/3
Pulmonary blastoma	8972/3
Other and Unclassified carcinomas	
Lymphoepithelioma-like carcinoma	8082/3
NUT carcinoma[e]	8023/3[d]
Salivary gland-type tumors	
Mucoepidermoid carcinoma	8430/3
Adenoid cystic carcinoma	8200/3
Epithelial-myoepithelial carcinoma	8562/3
Pleomorphic adenoma	8940/0

(*Continued*)

TABLE 1. (*Continued*)

Histologic Type and Subtypes	ICDO Code
Papillomas	
Squamous cell papilloma	8052/0
Exophytic	8052/0
Inverted	8053/0
Glandular papilloma	8260/0
Mixed squamous and glandular papilloma	8560/0
Adenomas	
Sclerosing pneumocytoma[e]	8832/0
Alveolar adenoma	8251/0
Papillary adenoma	8260/0
Mucinous cystadenoma	8470/0
Mucous gland adenoma	8480/0
Mesenchymal tumors	
Pulmonary hamartoma	8992/0[d]
Chondroma	9220/0
PEComatous tumors[e]	
Lymphangioleiomyomatosis	9174/1
PEComa, benign[e]	8714/0
Clear cell tumor	8005/0
PEComa, malignant[e]	8714/3
Congenital peribronchial myofibroblastic tumor	8827/1
Diffuse pulmonary lymphangiomatosis	
Inflammatory myofibroblastic tumor	8825/1
Epithelioid hemangioendothelioma	9133/3
Pleuropulmonary blastoma	8973/3
Synovial sarcoma	9040/3
Pulmonary artery intimal sarcoma	9137/3
Pulmonary myxoid sarcoma with *EWSR1–CREB1* translocation[e]	8842/3[d]
Myoepithelial tumors[e]	
Myoepithelioma	8982/0
[illegible]	8982/3
Lymphohistiocytic tumors	
Extranodal marginal zone lymphomas of mucosa-associated Lymphoid tissue (MALT lymphoma)	9699/3
Diffuse large cell lymphoma	9680/3
Lymphomatoid granulomatosis	9766/1
Intravascular large B cell lymphoma[e]	9712/3
Pulmonary Langerhans cell histiocytosis	9751/1
Erdheim–Chester disease	9750/1
Tumors of ectopic origin	
Germ cell tumors	
Teratoma, mature	9080/0
Teratoma, immature	9080/1
Intrapulmonary thymoma	8580/3
Melanoma	8270/3
Meningioma, NOS	9530/0
Metastatic tumors	

[a]The morphology codes are from the ICDO.[2] Behavior is coded /0 for benign tumors, /1 for unspecified, borderline or uncertain behavior, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumors.
[b]The classification is modified from the previous WHO classification[3] taking into account changes in our understanding of these lesions.
[c]This table is reproduced from the 2015 WHO Classification by Travis et al.[1]
[d]These new codes were approved by the International Agency on Cancer Research WHO Committee for ICDO.
[e]New terms changed or entities added since 2004 WHO Classification.[3]
LCNEC, large cell neuroendocrine carcinoma, WHO, World Health Organization; ICDO International Classification of Diseases for Oncology.

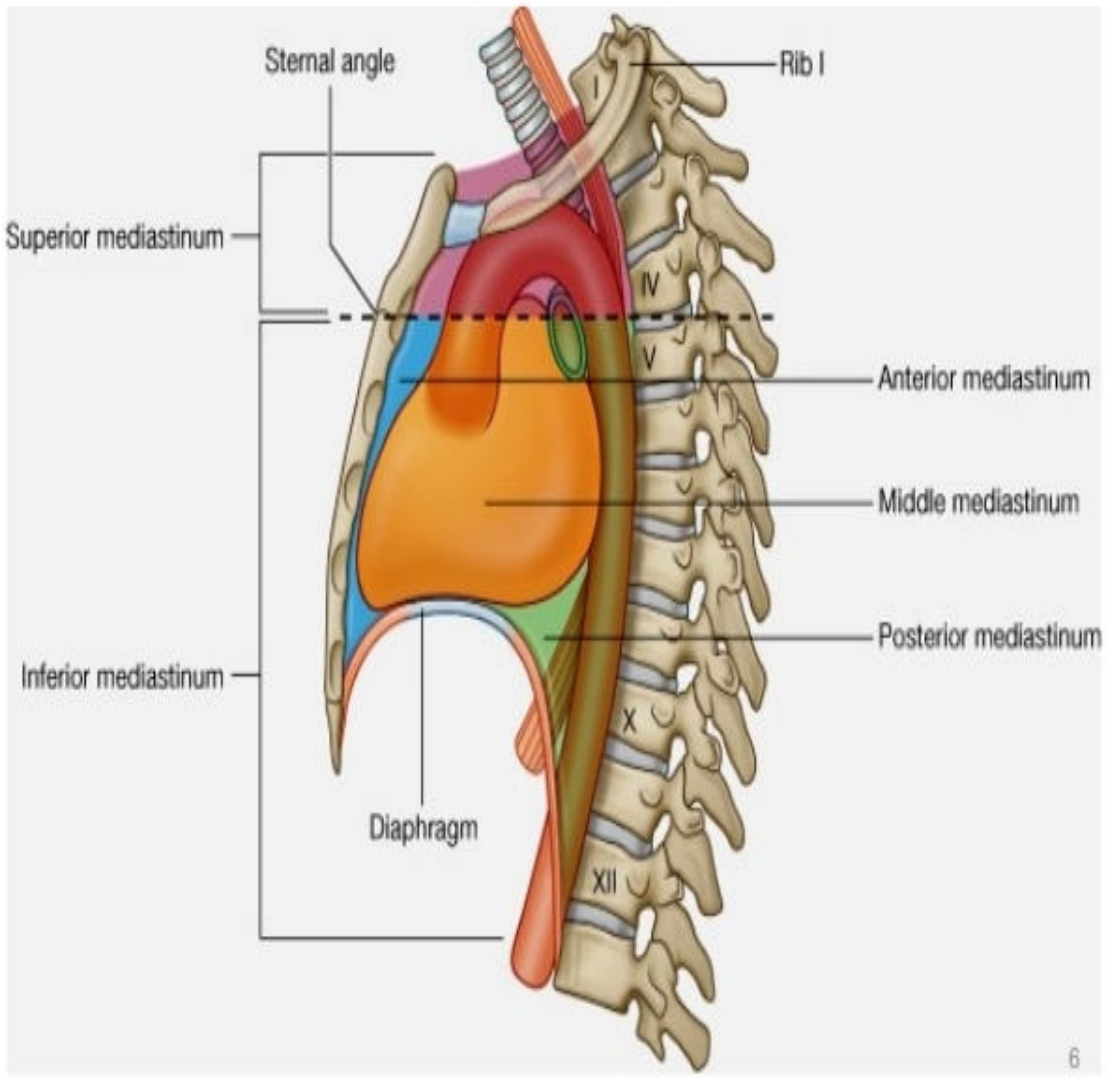
STATE OF THE ART: CONCISE REVIEW

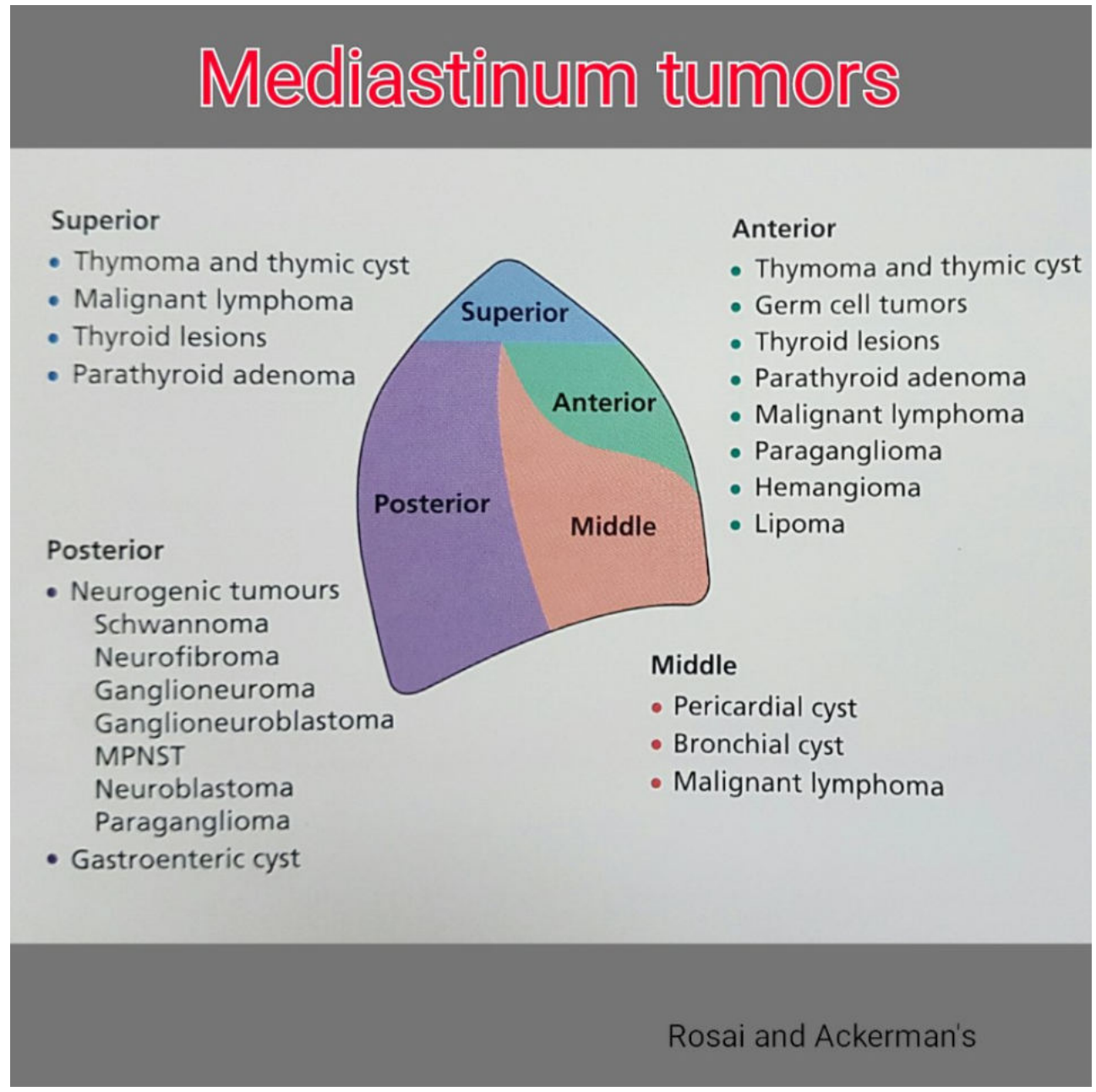
The 2015 World Health Organization Classification of Lung Tumors

Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification

William D. Travis, MD, Elisabeth Brambilla, MD,† Andrew G. Nicholson, MD,‡ Yasushi Yatabe, MD,§ John H. M. Austin, MD,‖ Mary Beth Beasley, MD,¶ Lucian. R. Chirieac, MD,# Sanja Dacic, MD,** Edwina Duhig, MD,†† Douglas B. Flieder, MD,‡‡ Kim Geisinger, MD,§§ Fred R. Hirsch, MD,‖‖ Yuichi Ishikawa, MD,¶¶ Keith M. Kerr, MD,## Masayuki Noguchi, MD,*** Giuseppe Pelosi, MD,††† Charles A. Powell, MD,‡‡‡ Ming Sound Tsao, MD,§§§ and Ignacio Wistuba, MD,‖‖‖ On Behalf of the WHO Panel*

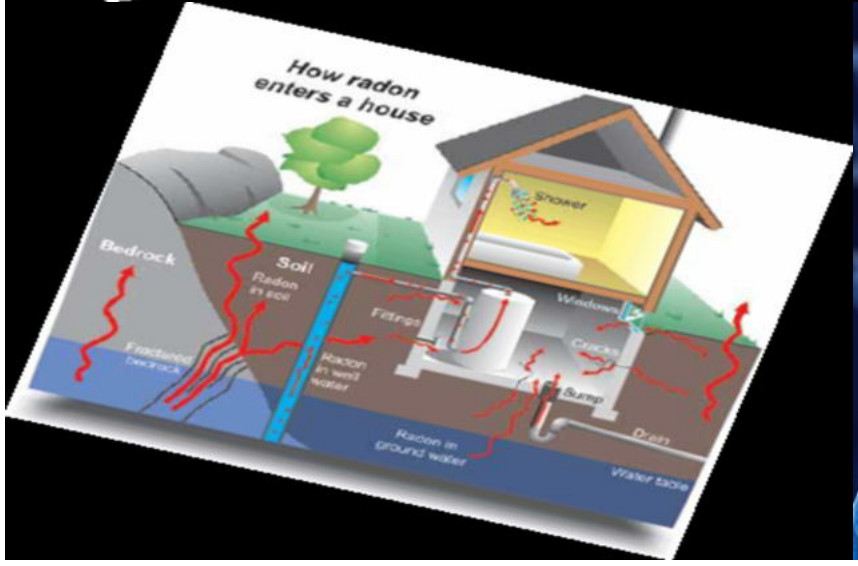
MEDIASTINAL TUMOURS





	Lesions	Fluid	Fat	Vascular
Anterior	Thymic Lymphoma Germ Cell Goiter	Thymic C Thymoma Pericardial C Germ Cell Lymphoma	Germ cell-b Thymolipoma Fat Pad	Thyroid Cardiac Coronary
Middle	Lymph nodes Duplication C Arch anomaly	Duplication C Necrotic nodes Pericard recess Retroperitoneal	Lipoma Esophageal FV polyp	Arch anomaly Azygous Vein Vascular nodes
Posterior	Neurogenic Bone and marrow	Neuroenteric C Schwannoma Meningocoele	Extramedullary Hematopoiesis	Desc Aorta
>1 comp	Infection Hemorrhage Lung Cancer	Lymphangioma Mediastinitis	Liposarcoma	Hemangioma

ETIOLOGY AND RISK FACTORS



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Risk factors for lung cancer worldwide

Jyoti Malhotra, Matteo Malvezzi, Eva Negri, Carlo La Vecchia, Paolo Boffetta
European Respiratory Journal 2016 48: 889-902; DOI: 10.1183/13993003.00359-2016

Article Figures & Data Info & Metrics PDF

Abstract

Lung cancer is the most frequent malignant neoplasm in most countries, and the main cancer-related cause of mortality worldwide in both sexes combined.

The geographic and temporal patterns of lung cancer incidence, as well as lung cancer mortality, on a population level are chiefly determined by tobacco consumption, the main aetiological factor in lung carcinogenesis.

Other factors such as genetic susceptibility, poor diet, occupational exposures and air pollution may act independently or in concert with tobacco smoking in shaping the descriptive epidemiology of lung cancer. Moreover, novel approaches in the classification of lung cancer based on molecular techniques have started to bring new insights to its aetiology, in particular among nonsmokers. Despite the success in delineation of tobacco smoking as the major risk factor for lung cancer, this highly preventable disease remains among the most common and most lethal cancers globally.

Future preventive efforts and research need to focus on non-cigarette tobacco smoking products, as well as better understanding of risk factors underlying lung carcinogenesis in never-smokers.

Intrinsic risk factors	Non-intrinsic risk factors	
	Endogenous risk factors	Exogenous risk factors
❖ Random errors in DNA replication	❖ Biologic aging ❖ Genetic susceptibility ❖ DNA repair machinery ❖ Hormones ❖ Growth factors ❖ Inflammation ❖ etc.	❖ Radiation ❖ Chemical carcinogens ❖ Tumour causing viruses ❖ Bad lifestyles such as smoking, lack of exercise, nutrient imbalance ❖ etc.
[Unmodifiable]	[Partially modifiable]	[Modifiable]

SIGNS AND SYMPTOMS

- OCCASIONALLY INCIDENTAL FINDING
- SYMPTOMS DEPEND UPON LOCATION OF TUMOR IN LUNG
- SIGN AND SYMPTOMS ALSO DEPEND UPON SIZE, DEGREE OF OBSTRUCTION AND METASTASIS

SIGNS AND SYMPTOMS (CONTD.)

THERE ARE 4 TYPES OF SIGNS AND SYMPTOMS OF LUNG CANCER:

1) LOCALIZED – INVOLVING THE LUNG.

2) GENERALIZED – INVOLVES OTHER AREAS THROUGHOUT THE BODY IF THE CANCER HAS SPREAD.

3) PARANEOPLASTIC SYNDROMES

4) THORACIC ONCOLOGY MEDICAL EMERGENCIES

LOCALIZED SIGNS AND SYMPTOMS

1. COUGH
2. BREATHING PROBLEMS, SOB, STRIDOR
3. CHANGE IN PHLEGM
4. LUNG INFECTION, HEMOPTYSIS
5. HOARSENESS, HICCUPS
6. WEIGHT LOSS
7. CHEST PAIN AND TIGHTNESS
8. PANCOAST'S SYNDROME
9. HORNER'S SYNDROME
10. PLEURAL EFFUSION
11. SUPERIOR VENA CAVA SYNDROME
12. FATIGUE

GENERALIZED SIGNS AND SYMPTOMS

1. BONE PAIN
2. HEADACHES, MENTAL STATUS CHANGES OR NEUROLOGIC FINDINGS
3. ABDOMINAL PAIN, ELEVATED LIVER FUNCTION TESTS, ENLARGED LIVER, GASTROINTESTINAL DISTURBANCES (ANOREXIA, CACHEXIA), JAUNDICE, HEPATOMEGALY
4. WEIGHT LOSS
5. ENDOCRINAL , METABOLIC AND VASCULAR CHANGES

THORACIC ONCOLOGY MEDICAL EMERGENCIES

1. SUPERIOR VENA CAVA OBSTRUCTION
2. TUMOR AND PULMONARY EMBOLISM
3. TUMOR LYSIS SYNDROME
4. HYPERCALCEMIA
5. PERICARDIAL TAMPONADE
6. MASSIVE PLEURAL EFFUSION

THANK YOU