Epidemiology

- #1 cause of cancer death in M/F (decreasing for men but increasing for women)
- #2 cause of cancer in M/F (prostate/breast)
- 170k new cases per year with equal number of deaths per year
- In general lung cancer would be exceedingly rare if it not for smoking

RFs

- Cigarette Smoking
  - Active Primary Smoking (20x)
  - Passive Second Hand Smoke (1.5x)
  - Cigar Smoking (3x)
  - Represents 85% of cases
  - Linear relationship b/t pack-years and risk of cancer
  - b/c "closest to cigarette" small cell and squamous, which are located centrally, are most closely linked with smoking
- Environmental Exposure
  - Asbestos (3x but when combined with smoking there is a synergistic effect increasing risk to 250x)
  - Radon (10x)
    - Product from the decay of natural uranium in soil beneath basements
  - Silicosis (?x)
  - Others w/ Definite Risk: Arsenic, Beryllium, Cadmium, Chromium, Nickel, Polyaromatic Hydrocarbons
  - Others w/ Probable Risk: formaldehyde, diesel exhaust, welding fumes, et al
- Lung Disease
  - COPD (2x and is independent of the risk from smoking)
  - Pulmonary Fibrosis
- Poor Diet
  - Diet poor in vit E, beta-carotene, and retinoids was associated with increased r/o cancer but when these vitamins were supplemented instead of decreasing risk they were actually associated with increased risk esp with beta-carotene and retinoids (CARET and ATBC trial)

Types

- SCLC and NSCLC (90%) cancer of bronchial epithelium
- Other (10%): Carcinoid, Sarcomas, Mucoepidermoid Carcinomas, Undifferentiated Tumors, et al
- Metastasis
  - Nodular (93%)
  - Lymphangitic Carcinomatosis (7%): diffuse infiltration and obstruction of pulmonary parenchymal lymphatic channels by tumor, most are adenocarcinomas esp breast, lung, colon, stomach, etc, occurs as a result of the initial hematogenous spread of tumor to the lungs, with subsequent malignant invasion through the vessel wall into the pulmonary interstitium and lymphatics, tumor then proliferates and easily spreads through these low-resistance channels
- Mediastinal Masses
  - Anterior: thyroid, teratoma, thymoma, T-cell lymphoma ("T's")
  - Middle: lung cancer, lymphoma, aortic aneurysm, cysts (pericardial/bronchogenic), Morgagni's hernia
  - Posterior: neurogenic tumor, esophageal masses, enteric cysts, aneurysms, Bochdalek's hernia, pheo

Types	Subtype	Incidence	Smokers		Metastasis	Special Features
SCLC (25%)	Small Cell aka "Oat Cell" Carcinoma • Considered a systemic disease b/c even in pts with seemingly localized dz they almost always have micrometastasis	25%	100%	Central	95%	**S**IADH (ADH) **C**arcinoid (Serotonin) **L**ambert Eaton Syndrome (Voltage Gated Ca Channel Ab) **C**ushing (ACTH)
NSCLC (75%)	Squamous Cell Carcinoma • Squamous pearls of keratin on Bx • Intercellular bridge formation • cavitates	30% (and ↓)	95%		50%	Hypercalcemia (PTHrP)
	Adenocarcinom Bronchiol Derived 28% • Develops at a site w/ prior inflammation and scarring	35% (and ↑) Why the above two trends? The	50%	Peripheral	80%	(Hypertrophic Pulmonary Osteoarthropathy – HPO) new bone formation and periosteal proliferation at end of long bones resulting in

		Bronchiol Alveolar 7% • <45yo • Women • Non-smokers • Often bilateral • Multifocal • Very Sensitive to EGFR- • Slow growth w/ late mets • Mimics pneumonia w/ lots of sputum	content of cigarettes has changed and along with the use of filters smoke is able to get deeper into lungs hence more peripheral tumors				symmetric bone pain and arthritis esp at ankles/knees, can be seen on Bone Scan Thrombophilia/Thrombophlebitis Nonbacterial Verrucous Endocarditis Acanthosis Nigricans
	Large Cell Carcinoma • It was probably SCC or AC that has become so undifferentiated that it doesn't look the same		10%	80%		80%	Gynecomastia

Staging (two types)

- SCLC (Limited vs Extensive) staging is non-invasive using just imaging unlike in NSCLC

Stage	**Description**	**Survival after Tx**	**Tx (NO SURGERY, very few can undergo surgery and when they do they are actually found to have atypical carcinoid or well differentiated neuroendocrine tumors which are easily mistaken for small cell)**
Limited 35%	Hemithorax and/or Regional LNs (Ipsilateral Supraclavicular/Mediastinal/Hilar)	1-2yr (and ½ of those 10% who are so called dz free at 2yrs end up having recurrence in 10yrs)	Chemo + XRT +PCI (Prophylactic Cranial Irradiation) • Chemo is usually etoposide + cisplatin x4-6 cycles • disease can be confined w/in single radiotherapy port • PCI (even in limited SCLC that has responded very well the chemo there is a 60% chance of brain mets in 2yrs hence PCI which decreases the risk to 30%)
Extensive 65%	Bithorax and/or Distant LNs (Ipsi Axillary/Cervical or Any Contralateral/Distant LNs) and/or Other Organs	<1yr	Chemo + PCI • Tumor cannot be encompassed by a tolerable radiation field

- NSCLC (TNM)

Stage		**T**	**N**	**M**	**5yr Survival after Tx**	**Tx** You can also do XRT, endobronchial laser/cryo, stents etc for symptomatic local invasion like compression of trachea or esophagus Pts are living long enough that 25% are getting brain mets so PCI is now being entertained
X		X (tumor cells in bronchopulmonary secretions but not seen on imaging)	0	0		
0		IS	CIS			
I 10%	A	1 (<3cm)	0		70%	Surgery • w/in a lobe = lobectomy w/ 3% post-op mortality (never do a wedge resection) • across fissures = whole pneumonectomy w/ 6% mortality • ½ will have recurrence (1/3 locally and 2/3 distant) • f/u surveillance Q6mo for 5yrs Adjuvant Chemo • Double Regiment w/ One Platinum Based (Paclitaxel + Carboplatin or Cisplatin + Vinorelbine or Cisplatin + Docetaxel or Cisplatin + Gemcitabine) Typically NO Radiation
	B	2 (>3cm)	0		50%	
II 20%	A	1	1 (LNs **w/in the lung**: peribronchial, hilar,		40%	Surgery

			etc)			• If T3 then marginally operable requiring removal of not just lung but also chest wall, diaphragm, etc (very difficult) Adjuvant Chemo Adjuvant Radiation
	B	2	1		30%	
		3 (any size but involves **structures that are amenable to surgery** like chest wall, diaphragm, parietal pleura, pericardium)	0			
III 30%	A	3	1-2		15%	Surgery • **The dividing line b/t surgery and no surgery is the presence of N3 and/or T4** (REMEMBER THIS) therefore must stage mediastinal LNs not only radiographically but surgically b/c CT is 60% sens and 80% spec and PET is 90% sens and 85% spec • Neoadjuvant Chemo/Radiation is used to bring pts from N3 to N2 Adjuvant Chemo Adjuvant Radiation
		1-2	2 (LNs **slightly outside of the lung**: ipsilateral mediastinal, subcarinal, peritracheal, etc)			
	B	#	3 (LNs **further away from lung**: any contralateral LNs, distant ipsilateral LNs like supraclavicular LNs, etc)		10%	Chemo Radiation Biologics (increase survival by 2mo, only for IIIb and IV) • EGFR Inhibitors (cetuximab (Erbitux)) and Tyrosine Kinase Inhibitors (erlotinib (Tarceva) and gefitinib (Iressa)) esp effective in non-smoking Asian female pts w/ broncho-alveolar adenocarcinoma • VEGF Inhibitors (bevacizimab (Avastin)) • Alimta
		4 (any size but involves **structures that are NOT amenable to surgery** like heart, great vessels, trachea, esophagus, vertebral bodies, effusion, mediastinum)	#			
IV 40%		#	#	1	0% (6-8mo w/ 25% reaching 1yr)	

S/S

- Constitutional Sx of cancer (weight loss, anorexia, fatigue, etc)
- Pulmonary Symptoms (presenting Sx of 5/10 pts)
  - Central Located Tumors (**S**CC, **S**CLC)
    - Recurrent Post-Obstructive Pneumonias
    - Airway Obstruction w/ Wheezing, Dyspnea, Cough, Hemoptysis
  - Peripherally Located Tumors (Adeno, Large Cell)
    - Pleuritic Chest Pain
    - Malignant Pleural Effusion
- Symptoms from Local Invasion, LAD, Metastasis (presenting Sx of 3/10 pts)
  - **SVC Syndrome**: SVC compression resulting in ipsilateral facial/arm fullness/edema, dilated collateral veins over anterior chest/arms/face, JVD, cough, hoarseness, headaches from increased ICP, etc (seen in central tumors) considered a medical emergency, NB can also be seen in lymphoma, mediastinal tumors, etc, Tx: XRT and steroids
  - **Horner's Syndrome**: sympathetic nerve compression resulting in ipsilateral facial anhidrosis, ptosis, miosis
  - **Pancoast Tumor**: rib/vertebral destruction and impingement on C8, T1, T2 nerve roots of Brachial plexus causing shoulder pain radiating down arm and upper extremity weakness w/ muscle atrophy (seen in superior sulcus apical peripheral tumors)
  - **Esophageal Compression**: dysphagia
  - Palsies
    - **Phrenic Nerve Palsy**: hemidiaphragmatic paralysis
    - **Recurrent Laryngeal Nerve Palsy**: hoarseness
  - Metastasis
    - **1st Adrenal, 2nd Liver, 3rd Brain/Bone/Skin**: with symptoms from their dysfunction
- Paraneoplastic Syndrome (presenting Sx of 1/10 pts) refer above
- No Symptoms just an incidental mass on imaging (1/10 pts)

Dx

- Average age of diagnosis: 65yo
- For Screening
    - b/c high risk populations can be identified and b/c lung cancer presents at such an advanced stage it is thought that early detection would improve M/M
    - It was once though that screening via sputum cytology or CXR in smokers would help but there was no reduction in mortality despite showing improvement in stage distribution and resectability
    - Currently, studies (National Lung Screening Trial – NSLT) are looking into low-radiation spiral CT but controversial in who to screen, how often, and what to do if a nodule is actually found
    - Many times an incidental Solitary Pulmonary Nodule (SPN) is found on imaging… what do you do?

	Benign	**Malignant**
Age	<50	>50
Smoker or Prior Cancer	No	Yes
TB, Fungal, etc Exposure	Yes	No
Growth Rate	<30d or >2yrs	30d-2yrs
Size	<2cm	>3cm
Double Time (always get an old CXR)	>1yr	<1yr
Shape	Smooth/Circular	Irregular/Speculated
Calcification or CT Density	Lots and Centric/Lamination = means old lesion	No/Little but Eccentric/Stippled
LAD	No	Yes
Types	Hamartoma (”popcorn”) most common Granuloma (“bull’s eye”) infectious/noninfectious Lipoma/Fibroma Bronchogenic Cysts AVM Resolving Infarct	Primary Mets (lung, colon, breast, melanoma, renal)
	If benign gestalt then follow w/ spiral CT in 3mo, in 6mo, then Qyr	If malignant gestalt then check PET/Bx or just go straight to Surgery

- For Diagnosis (Bx is necessary… you cannot make a diagnosis based on imaging alone)
    - Imaging
        - CXR
        - CT Chest make sure it includes liver and adrenal glands if at all possible
    - Biopsy
        - Thoracentesis for peripheral tumors
        - Sputum Cytology for central tumors (highly variable)
        - Fiberoptic Bronchocoscopy w/ Bx for central nodules
        - Fluoroscopy/CT Guided Transthoracic Needle Bx for peripheral nodules
        - Mediastinoscopy: incision thru manubrium allowing for direct visualization of sup/ant mediastinum and LN Bx
        - VATS w/ Pleural Bx
        - Biopsy of mass/LN in distant tissue when you suspect lung cancer b/c of nodules on lung imaging is actually enough to make the diagnosis
- For Staging
    - Whole Body CT/PET Scan (all mets)
    - CT Ab w/ Contrast (Adrenal/Liver)
    - MRI Brain w/ Gandolinium (Brain) not CT
    - Bone Scan (Bone)