

Lung Cancer

Incidence

According to statistics presented by Edelman & Gandara, 2004, Lung cancer is the most common malignancy in men 35 years of age and older and women 55-74 years of age. It accounts for approximately 1/3 of all cancer deaths, and is therefore the most common cause of cancer-related death in men and women. Recently there has been an increased incidence of non-small cell lung cancer in relatively young nonsmoking women.

According to Breathnack, 2001, death from lung cancer was relatively rare until this century. In 1912 there were only 374 cases of lung cancer described in the literature but by 1935 there were 4300. To date there are approximately 172, 000 new cases of lung cancer diagnosed in the United States. In 1954 the first relationship was made between smoking and cancer. It was noted that lung cancer mortality rates in people who smoked two packs per day for 10 years (20-pack years) are 15-25 times higher than nonsmokers. The period between initiation of smoking and the development of cancer is about 15-20 years.

Etiological Facts of Lung Cancer (Breathnack, 2001; Edelman & Gandara, 2004; Glisson, Movsas, & Scott, 2007; Srinivasan & Kaye, 2001, NCCN Practice Guidelines, 2007).

- 85-90% of lung cancers are due to cigarette smoking
- The risk for lung cancer in smokers is 30 times greater than in nonsmokers
- Smoking cigars or pipes doubles the risk compared to nonsmokers
- Passive smoking probably increases the risk by about two times that of a nonsmoker
- Risk for lung cancer as a result of smoking is related to a cumulative dose which is quantified by “pack years”
- Incidence of death from lung cancer begins to diverge from the nonsmoking population at 10 pack years
- After cessation of smoking the risk steadily declines, approaching but not quite reaching that of non-smokers, after 15 years of abstinence for those who smoked less than 20 years
- Large percentage of new diagnosis of lung cancer occur in former smokers
- Some adenocarcinomas (especially in women) are unrelated to smoking
- Asbestos is related to mesothelioma

- Asbestos exposure also increases the risk for lung cancers especially in smokers
- Radon exposure in both smokers and nonsmokers occurs as small cell lung cancer in 6% of cases
- Lung cancer itself is associated with an increased risk for a *second* cancer (head and neck, esophageal)
- Other substances: arsenic, nickel, chromium compounds, chloromethyl ether, and air pollutants are associated with lung cancer
- Other diseases: lung scars and COPD are associated with an increased risk for lung cancer

To review the NCCN Clinical Practice Guidelines in Oncology click on the following link and select lung cancer overview.

http://www.nccn.org/professionals/physician_gls/default.asp

Pathology and Natural History:

Small Cell Lung Cancer (SCLC):

According to Glisson, Movsas & Scott, 2007; Murren, Turrisi, & Pass, 2005, SCLC accounts for approximately 15% of all lung cancers. SCLC comprises several subtypes. They tend to be more central or hilar in location (95%) than peripheral (5%). They are often present as widespread disease at the time of diagnosis. Metastases involve the brain, bone marrow or liver. Pleural effusions are common. Associated paraneoplastic syndromes occur and include syndrome of inappropriate antidiuretic hormone (SIADH) (common), hypercoagulable state (common), ectopic adrenocorticotrophic hormone (ACTH) syndrome (uncommon).

Non-small cell lung cancer (NSCLC):

According to Movsas, Khuri & Kerstine, 2007, NSCLC occurs in 85% of all lung cancers. Other histological variants (squamous, adenocarcinoma, large cell) of lung cancer are all clumped together as NSCLC because of the similarities in clinical presentation, treatment and natural history.

Squamous Cell Carcinoma: (Movsas, Khuri & Kerstine, 2007).

- Accounts for 20-25% of all NSCLC
- Tend to occur centrally
- Most likely to remain localized early in the disease and recur locally

Paraneoplastic syndromes:

1. hypercalcemia
2. hypertrophic osteoarthropathy
3. paraneoplastic neutrophilia
4. prominent joint syndromes
5. hypercoagulability

Adenocarcinoma: ((Movsas, Khuri & Kerstine, 2007)

- accounts for 50-60% of NSCLC
- It is the most common cell type occurring in nonsmokers, especially young women
- often present as peripheral nodules
- More than half of patients with adenocarcinoma present with regional lymph node metastasis
- These tumors tend to spread widely outside the thorax most commonly to the bone, liver, and brain.

Paraneoplastic syndromes for **adenocarcinoma** are: (Movsas, Khuri & Kerstine, 2007)

1. hypertrophic osteoarthropathy (digital clubbing)
(<http://www.nlm.nih.gov/medlineplus/ency/imagepages/1598.htm>)
2. Hypercoagulable state
3. hypercalcemia
4. gynecomastia (enlarged breasts)

Bronchoalveolar Carcinoma:

Bronchoalveolar carcinoma is a subtype of adenocarcinoma. Pure bronchoalveolar carcinoma is characterized by a spreading "lepidic" pattern within the bronchioles without evidence of invasion. The disease is characterized radiologically by an infiltrative pattern and is frequently multicentric (Movsas, Khuri & Kerstine, 2007).

Large Cell and "not otherwise specified" Lung Cancers:

The remainder of NSCLC consists of large cell and other histologies.

Diagnostic and Further Evaluation:

It is important to establish a histological (tissue) diagnosis since this will determine the need for additional tests. A tissue diagnosis will also guide the selection of specific therapies. If NSCLC is diagnosed, staging procedures are undertaken to determine which modalities of therapy should be employed. Historically, surgery has been the mainstay of therapy for NSCLC and remains the primary mode in early stage I and II disease (Movsas, Khuri & Kerstine, 2007; NCCN Practice Guidelines, 2007, Breathnack, 2001). The initial evaluation determines whether the tumor is potentially resectable and operable.

If SCLC is detected the evaluation is directed towards determining whether the patient has limited or extensive stage disease. Generally the management of SCLC involves chemotherapy with or without radiotherapy. Only occasionally does surgery play a role in this disease (Glisson, Mavvas & Scott, 2007, Srinivasan & Kaye, 2001).

To Review lung cancer images, scans, procedures and staging click on the following link

<http://www.fccc.edu/pdq/English/Patients/NonSmallCellLungCancerTreatmentPDQ.html>

Review Classic Signs and Symptoms: (Glisson, Mavvas & Scott, 2007; Srinivasan & Kaye, 2001; Movsas, Khuri & Kerstine, 2007; Murren, Turrisi, & Pass, 2005; Edelman & Gandara, 2004).

- history of smoking
- new or changing cough
- hoarseness
- hemoptysis
- anorexia
- weight loss
- dyspnea
- unresolving pneumonias
- chest wall pain
- **SVCS** (superior vena cava syndrome)
- symptoms of paraneoplastic syndromes
- note: symptoms often inspire a smoker to quit smoking just before the diagnosis of lung cancer
- **Pancoast's tumor** = located in the lung apices or superior sulcus, may have paresthesias and weakness of the arm and hand as well as **Horner's syndrome** (ptosis, miosis, and anhidrosis) caused by involvement of the cervical sympathetic nerves

- Metastatic disease: bone pain, neurological changes, jaundice, bowel, and abdominal symptoms, rapidly enlarging liver, subcutaneous masses, regional lymphadenopathy
- **Hypertrophic pulmonary osteoarthropathy** (HPO)

To learn about the S&S of SVC syndrome click on the following link;

<http://www.meddean.luc.edu/lumen/MedEd/medicine/pulmonar/apd/svcf.htm>

To see a picture of SVC syndrome click on the following link;

<http://www.meddean.luc.edu/lumen/MedEd/medicine/pulmonar/images/phyabn/image15a.jpg>

To participate in an online case study with imaging, history and physical exam information click the following link;

http://rad.usuhs.mil/medpix/tf_case.html?mode=pt&pt_id=8768

To learn more about Horner's syndrome with imaging click on the following link;

<http://www.ghorayeb.com/HornersSyndrome.html>

Remember that **pathologic evidence** of lung cancer must be established. This is done by the least invasive procedure. See examples below.

After histological diagnosis of lung cancer an evaluation should be done to determine whether the disease is confined to the chest and therefore be treated with curative intent (limited stage SCLC and stages I-III NSCLC) (Glisson, Mavsas & Scott, 2007; Srinivasan & Kaye, 2001; NCCN Practice Guidelines, 2007).

Examples of common tests are as follows;

- Bone scan
- Bone radiograph
- Spinal MRI
- Brain CT or MRI
- Mediastinoscopy
- Percutaneous and transbronchial needle biopsy
- PET scan or PET-CT
- Bone marrow aspiration and biopsy

Test yourself on radiology interpretation or learn how to review radiology images click on the following on-line course "Introduction to Chest Imaging"
<http://www.med-ed.virginia.edu/courses/rad/cxr/index.html>

Fiberoptic Bronchoscopy	Radiology	Transthoracic Biopsy
Bronchial tree secretions	Plain PA and lateral view	Fine needle aspiration
Bacteriology and cytology	Computed tomography (CT)	Cutting needle biopsy
Bronchial biopsy	Magnetic Resonance Imaging (MRI)	Video assisted thoracoscopic
Transbronchial needle aspiration	Gallium citrate Ga 67 scanning	biopsy/resection
Selective bronchial brushing	Angiography	
Bronchioalveolar lavage		

* when the biopsy studies given here are negative, mediastinoscopy or mediastinotomy may be indicated in selected patients (Edelman & Gandara, 2004; Glisson, Mavzas & Scott, 2007; Practice Guidelines, 2007).

Radiography:

CXR: mass or persistent infiltrates, particularly in the anterior segments of the upper lobes

CT Scan of the Chest and Abdomen: needs to extend through the adrenal glands. CT scans are superior to CXR. Mediastinal lymph nodes are generally considered abnormal when larger than 1.5 cm in diameter and normal when considered less than 1 cm. Nodes in between are considered indeterminate. CT scans will provide information about the extent or invasion of the primary tumor, the presence of pleural effusion, and lymph node status. Note that MRI rarely adds additional information (Edelman & Gandara, 2004; Glisson, Mavzas & Scott, 2007; Practice Guidelines, 2007; Movsas, Khuri & Kerstine, 2007).

Key: Adrenal metastases are common in NSCLC and alter management if the patient appears to have an early stage disease. The problem is that non-malignant adrenal masses are also common (adrenal adenomas). The density of the adrenal mass may distinguish between metastatic or benign adenoma. When in doubt, a biopsy is indicated if the adrenal appears to be the only site of metastatic disease (Edelman & Gandara, 2004; Glisson, Mavzas & Scott, 2007; Practice Guidelines, 2007; Movsas, Khuri & Kerstine, 2007).

Evaluation of Solitary Pulmonary Nodules:

Characteristics that define a solitary pulmonary nodule are as follows (Glisson, Mavzas & Scott, 2007; Practice Guidelines, 2007; Movsas, Khuri & Kerstine, 2007).

- A peripheral lung mass (less than 6 cm in diameter)
- Asymptomatic nodule
- Normal physical exam
- CBC and liver function tests are normal
- Calcifications (calcified nodules are more likely to be malignant unless the pattern is circular, crescentic, or completely and densely calcified)

Risk that a solitary pulmonary nodule is malignant

- Younger than 35 years of age: less than 2%
- 35-45 years of age: 15%
- older than 45 years of age: 30-50%

Management of Stage I and II NSCLC: (Movsas, Khuri & Kerstine, 2007; Edelman & Gandara, 2004; Schrupp, Altorki, Henschke, Carter, Turrisi, & Gutierrez, 2005, NCCN Practice Guidelines, 2007).

Surgical resection of the primary tumor is the treatment of choice for patients who are considered good candidates. Types of surgical procedures are as follows;

- incomplete resection (rare)
- lobectomy
- bilobectomy, sleeve lobectomy, or pneumonectomy
- video-assisted thoracoscopic surgery (VATS)

Pancoast's tumors usually require XRT first and then surgery but newer data indicates that the use of preoperative chemoradiotherapy can now be considered the standard of care.

Management of Stages IIIa and IIIb NSCLC: (Movsas, Khuri & Kerstine, 2007; Edelman & Gandara, 2004; Schrump, Altorki, Henschke, Carter, Turrisi, & Gutierrez, 2005, NCCN Practice Guidelines, 2007).

If tumors are deemed respectable but inoperable then XRT should be the primary treatment. Chemoradiation may also be recommended for selected patients who are thought to have a poorer outcome with XRT alone.

Common first Line chemotherapy Regimens for advanced NSCLC:

- Cisplatin/ vinorelbine
- Carboplatin/ Paclitaxol
- Carboplatin/ Gemcitabine
- Cisplatin/ Docetaxol

Management of Stage IV NSCLC: (Movsas, Khuri & Kerstine, 2007; Edelman & Gandara, 2004; Schrump, Altorki, Henschke, Carter, Turrisi, & Gutierrez, 2005, NCCN Practice Guidelines, 2007).

Management is often individualized based on the performance status of the patient. A variety of therapies may be prescribed in this setting. Additional drug therapies used in this setting are Pemetrexed (Alimta) and Gefitinib (Iressa), Elotinib (Tarceva).

Management of SCLC:

According to Glisson, Movsas, & Scott, 2007, limited stage (I, II, III) is confined to one hemithorax including the contralateral (opposite side) supraclavicular adenopathy. Less than 5% of patients will present with stage I or II disease. About 1/3 will have disease that is clinically confined to the hemithorax and draining regional nodes at presentation (stages IIIa and IIIb). These patients should receive concurrent chemotherapy and thoracic XRT. Prophylactic cranial irradiation (PCI) decreases the rate of brain metastases. The use of PCI however, is controversial because of the occurrence of synchronous metastases has made it difficult to demonstrate a survival advantage. PCI results in about a 5% improvement in survival.

Examples of Common Regimens for SCLC:

Regimen	Dose (mg/m ²)	Days Given	Cycle Length (days)
Cisplatin	60	1	21
Etoposide	120	1,2,3	21
Chest XRT	1.5 Gy (45 Gy total)	twice daily	5 weeks
PCI	2.5 Gy (25 Gy total)	daily	3 weeks
Cisplatin	100	1	21
Etoposide	100	1,2,3	
Cisplatin	60	1	28
Irinotecan	60	1,8,15	
Topotecan	1.5	1,2,3,4,5	21

(Edelman & Gandara, 2004, NCCN Practice Guidelines, 2007).

After primary therapy for NSCLC, or SCLC there is little evidence that frequent laboratory or radiological studies detect disease before the development of symptoms or that early detection improves outcomes In a non-protocol setting, a standard follow-up plan would be history and physical every 2-3 months and a CXR twice yearly for the first few years after resection. (NCCN Practice Guidleines, 2007; Movsas, Khuri & Kerstine, 2007; Edelman & Gandara, 2004; Schrump, Altorki, Henschke, Carter, Turrisi, & Gutierrez, 2005) . Note that patients who undergo chemoradiotherapy frequently demonstrate scarring and infiltrates on x-ray. These abnormalities are often misinterpreted as progressive disease. Patients who are undergoing therapy for metastatic disease should have periodic reassessments of the known site of disease. Progressive disease (> 25% increase or the appearance of new disease) or deteriorating performance status is a reason to stop therapy (NCCN Practice Guidelines, 2007; Movsas, Khuri & Kerstine, 2007; Edelman & Gandara, 2004; Schrump, Altorki, Henschke, Carter, Turrisi, & Gutierrez, 2005).

For a Current 2008 overview of the pharmacologic management of both NSCLC and SCLC click on the following link to review

http://www.nccn.org/professionals/physician_gls/default.asp

Nursing Management (Henke Yarbo, Hansen Frogge, & Goodman, 2005).

Surgery:

- The patient should relate knowledge of reason for surgery
- Describe the type procedure to be done
- Discuss the need for possible ventilation
- Explain the need for leg and arm exercises (prevention of DVT)
- Discuss different methods of pain relief and evaluate pain pre medication and post medication (document both)
- Explain postoperative routine and the fact that the patient will most likely have a chest tube in place.
- Reinforce the need for early ambulation
- Assist in performing deep breathing and coughing exercises
- Reinforce all preoperative teaching
- Review surgical results and proper follow-up

Chemotherapy:

- Review patient knowledge of chemotherapy and explain the anticipated therapeutic effects
- Provide written material about chemotherapeutic agents
- Explain immediate and late(7-14 days) side effects of specific agents
- Provide information about self-management of stomatitis, nausea/vomiting, diarrhea, constipation, alopecia, myelosuppression, fatigue, and sexuality
- Discuss what side-effects must be reported to the physician/nurse
- Explain what side-effects are reversible
- Explain what medication/foods should be avoided
- Review how the patient makes contact with the health care team
- Review community resources
- Encourage the patient/family to verbalize their feelings related to chemotherapy and its potential side-effects
- Consider complications of chemotherapy for lung cancer
 1. myelosuppression (sepsis, bleeding, weakness, fatigue)(
 2. nephrotoxicity (compromised renal function, magnesium wasting)
 3. hemorrhagic cystitis
 4. neurotoxicity (peripheral neuropathies, parasthesias, jaw pain, sensory loss, motor weakness, constipation, ileus, tinnitus, permanent hearing loss
 5. central nervous system toxicity (confusion, hallucinations, somnolence, coma)
 6. Cardiac (myopathy, dysrhythmia, congestive heart failure, myocardial infarction)

7. Pneumonitis or pulmonary fibrosis
8. nausea & vomiting (dehydration & weight loss)
9. taste changes (anorexia, weight loss)
10. mucositis (pain, difficulty swallowing, weight loss, diarrhea)
11. anaphylaxis or hypotension
12. alopecia
13. tissue damage and pain if vesicant extravasation
14. syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and hyponatremia
15. Rash management (Tarceva)

To review management of Tarceva rash click on the following link;

http://www.tarceva.com/docs/Tarceva_HCP_RashManagementGuide.pdf

Radiation Therapy:

- review general side effects
- teach energy conservation
- discuss measures to maintain adequate nutritional intake
- explain the control of radiodermatitis
- describe signs and symptoms of pneumonitis, esophagitis, and cough
- discuss measures to maintain adequate oxygenation
- administer antiemetics
- avoid tobacco & alcohol
- educate about radiation procedures
- explain that side effects may last 2-4 weeks after treatment is complete
- monitor for and discuss skin complications related to radiotherapy (erythema to wet desquamation)
- complications: esophagitis, dysphagia, strictures, weight loss, acute pneumonitis or pulmonary fibrosis, pericarditis, pleural effusion, myelosuppression and fatigue
- special complications should be considered for those receiving cranial irradiation: temporary loss of hair, skin erythema, nausea, cerebral edema, memory loss, problems in judgment, parkinsonian symptoms, weakness, confusion, depression, dizziness, abnormal gait, intention tremor, inability to concentrate, cerebral atrophy