



FREQUENTLY ASKED QUESTIONS ABOUT LUNG CANCER

1. What are the causes of lung cancer?

Cigarette Smoking - The vast majority of lung cancers are related to cigarette smoking. An individual who smokes one pack of cigarettes daily has a 20-fold increased risk of developing lung cancer compared to a nonsmoker. The greater the number of cigarettes smoked on a daily basis and the greater the number of years of smoking, the greater is the risk of developing lung cancer.

Asbestos exposure is another risk factor for lung cancer. Cigarette smokers who are exposed to asbestos develop lung cancer at an extremely high rate. Exposure to asbestos also is a major risk factor for the development of mesothelioma, a cancer that originates in the pleura.

Radioactive dust and radon exposure - Uranium miners who have been exposed to radioactive dust and radon gas also have an increased incidence of lung cancer. Although there has been some controversy about the risk posed by exposure to residential radon gas, a recent study conducted in Sweden showed an increased incidence of lung cancer in individuals who were exposed to a high level of radon in their homes.

2. Is there screening or early detection of lung cancer?

Three large studies in the 1970s failed to show a survival advantage for individuals who were screened by sputum cytology and chest X-ray for lung cancer. The results led most experts to conclude that screening for lung cancer was not worthwhile. A more recent, randomized, prospective trial from Czechoslovakia showed that screening with a chest x-ray increased the diagnosis of early-stage lung cancer and reduced mortality from lung cancer. Studies are currently underway to evaluate chest CT scan for lung cancer screening. Several recent reports from Japan, Germany, and the United States have documented the ability of low-dose spiral CT scans to detect lung cancer at an early stage. Despite the renewed interest in screening for lung cancer, at present routine screening is not recommended.

3. What are the symptoms of lung cancer?

Cough is a major manifestation of lung cancer. However, it is important to remember that the majority of lung cancer patients are current or former smokers and may have a cough related to chronic irritation of the upper and/or lower airways from cigarette smoke. Therefore, a smoker should bring a change in their cough, such as an increase in frequency or severity, to the attention of a physician.

Shortness of breath (dyspnea) and **coughing up blood** (hemoptysis) may also be signs of lung cancer. Breathing problems may be caused by cancer blocking the airways or build-up of fluid around the lung (pleural effusion).



Lung cancer may present as **pneumonia**. Persistent pneumonia after appropriate antibiotic therapy should prompt investigation. Sometimes a lung cancer is masked on CXR by pneumonia.

Chest pain - Approximately 5 percent of lung tumors invade the chest wall and cause chest pain. Tumors that infiltrate surrounding structures, such as nerve roots, produce **shoulder and/or arm pain**. Sometimes lung tumors damage the nerve that supplies the voice box causing hoarseness.

Other symptoms include difficulties swallowing (dysphagia), swelling of the face and neck due to invasion of major blood vessels and wheezing/stridor secondary to compression or invasion of the trachea.

Signs and symptoms of metastatic disease: Lung cancer can metastasize to multiple sites, the most common of which are bone, liver, brain, lung and adrenal glands.

Lung cancer patients who have brain metastases may complain of headaches or specific neurologic symptoms, or family members may notice a decrease in the patient's mental acuity. Also, metastatic lung cancer may cause spinal cord compression, resulting in a characteristic sequence of symptoms: pain, followed by motor dysfunction, followed by sensory symptoms.

4. Which diagnostic studies should be considered if a diagnosis of lung cancer is suspected ?

A. Imaging studies

Chest x-rays should always be done in a high-risk patient with new respiratory symptoms. The chest x-ray should be inspected for the presence of a pleural effusion or synchronous pulmonary nodules, and the bones should be examined for evidence of osseous metastases. A widened mediastinum usually indicates metastatic disease within the mediastinal lymph nodes. Comparison with previous x-rays is frequently helpful. Chest CT A CT scan of the chest, including the liver and adrenal glands, is performed routinely to further define the primary tumor and to identify lymphatic or parenchymal metastases. Involvement of lymph nodes between both lungs (mediastinum) is of particular importance. Lymph nodes below 1 cm on chest CT are unlikely to harbor disease. Larger lymph nodes, however, are worrisome for metastatic involvement. Sometimes suspicious lymph nodes require a biopsy (mediastinoscopy) to determine the presence or absence of tumor within the mediastinal lymph nodes. Some tumors are not evident on a Chest x-ray, but readily detectable on CT scan.

PET Current data suggest that PET may be very helpful for the evaluation of lung masses, lymph nodes, and distant metastases. When a lung mass "lights up" on a PET scan, there is a 90%-95% chance that it is cancerous. PET is approximately 90% reliable in detecting lymph node metastases.



B. Obtaining a tissue diagnosis

The next step is to try to obtain a histologic or cytologic diagnosis of the radiologic lesion. Even though some lung cancers can be diagnosed by analyzing the sputum, in most instances the patient will undergo bronchoscopy in order to obtain a tissue sample. If the lung lesion is close to the chest wall, a CT-guided biopsy through the chest may be the preferred procedure. A CT-guided needle biopsy may diagnose up to 90 percent of peripheral lung cancers.

Mediastinoscopy provides not only a histologic diagnosis but also yields important staging information. If multiple lymph node levels contain tumor, most thoracic surgeons would not proceed directly to operation, but rather, would offer these patients chemotherapy alone or followed by surgery.

Thoracentesis and thoracoscopy - Individuals who have pleural effusions should undergo thoracentesis.

Adrenal gland biopsy - The adrenal gland may be the sole site of metastatic disease in as many as 10 percent of patients with NSCLC. Therefore, an enlarged or deformed adrenal gland should be biopsied. Patients should not be assumed to have metastatic disease and denied a potentially curative operation on the basis of a scan; histologic confirmation must be obtained.

5. What are the different types of lung cancer?

Lung cancers are characterized based on the appearance of the cancer cells under the microscope. We distinguish 2 different groups:

Small cell lung cancer [link to following page]

Non-small cell lung cancer

There is only one type of small cell lung cancer, but there are several different types of non-small cell lung cancer: adenocarcinoma, bronchoalveolar carcinoma, squamous cell carcinoma, large cell carcinoma and carcinoids.

Adenocarcinoma is currently the most common type of NSCLC, accounting for approximately 40 percent of cases. Of all the types of lung cancer, adenocarcinoma is most likely to occur in nonsmokers or former smokers. In addition, it is the most common tumor in women. Typically, adenocarcinoma presents as a small peripheral lesion that has a high propensity to metastasize to both regional lymph nodes and distant sites. Because of the tendency of the primary tumor to occur in peripheral locations, it frequently produces no symptoms.

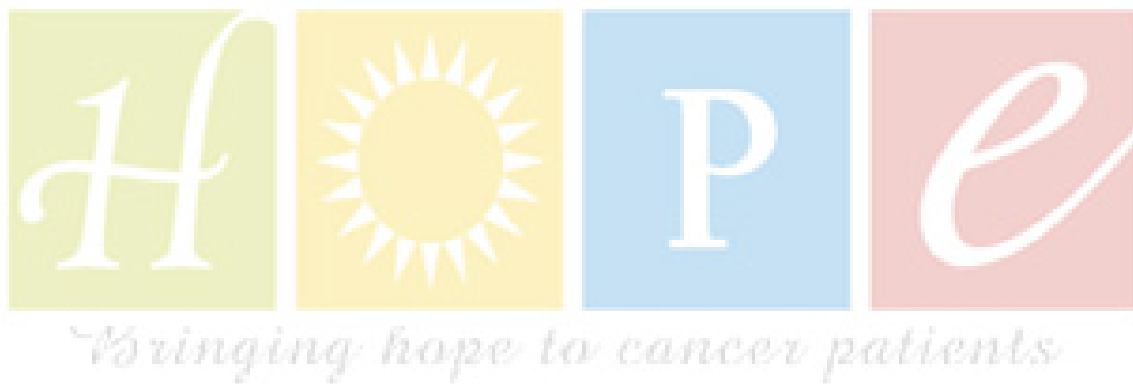
Bronchoalveolar adenocarcinoma: During the last decade, it has become apparent that the incidence of the bronchoalveolar type of adenocarcinoma is increasing. This tumor may present as a pneumonic infiltrate, as multiple nodules scattered throughout the lung, and, occasionally, as a single nodule.



Squamous cell tumors comprise approximately 30 percent of all cases of lung cancer. This tumor tends to occur in a central location and tends to spread to regional lymph nodes; it is the most likely of all the lung cancers to remain localized.

Large-cell carcinoma accounts for approximately 10-15 percent of all lung cancers. It tends to be a relatively large peripheral lesion, and like adenocarcinoma, it has a high propensity to metastasize to regional lymph nodes and distant sites.

Carcinoids: These neoplasms, which contain neurosecretory granules and neural filaments, are relatively rare. The classic carcinoid tumor presents as an endobronchial lesion, tends to be quite indolent, and rarely metastasizes. Some carcinoid tumors spread to regional lymph nodes and distant sites. These tumors are classified as atypical carcinoids or anaplastic carcinoids.





Frequently Asked Questions about Small Lung Cancer

1. What determines the prognosis of patients diagnosed with Small Cell Lung Cancer (SCLC)?

The stage is important. Unlike most cancers in which there are four stages, in SCLC we distinguish only two stages: "limited stage disease" and "extensive stage disease".

The second prognostic factor is the performance status of the patient. Someone who has had significant weight loss, decreased activity level and need for assistance with daily activities of living (bathing, dressing, preparing meals, etc.) is considered "poor performance status" and tends to do less well.

2. How is the stage of the disease determined?

Patients routinely undergo CT scans of the chest, abdomen and pelvis to define which organs (liver, lymph nodes, etc.) are involved. These tests also include a CT or MRI of the brain and a bone scan. If the disease is limited to the chest and if no fluid accumulation around the lung is present (malignant pleural effusion), the disease is considered "limited stage." If the tumor has spread to organs outside the chest (liver, bones, brain, etc.), it is considered "extensive stage disease."

3. What is the recommended treatment for limited stage disease?

If the tumor is limited to one single area in the lung, then the lung lobe containing the tumor should be removed. Surgery should only be done if no mediastinal or supraclavicular lymph nodes are involved with cancer. Almost all patients with limited stage disease require chemotherapy and radiation therapy.

4. Why is chemotherapy and radiation therapy needed if the disease is limited to the chest?

In early studies in which either radiation therapy or surgery alone was used to treat such patients, median survival was only 3-4 months and the 5-year survival rate was in the range of 1-2 percent. The reason for the failure of these therapies was rapid appearance of distant metastases in liver, bones or brain shortly after surgery or radiation therapy. Only chemotherapy will reach these areas that are harbingers of cancer disease.

5. What is the goal of treatment in "limited stage disease?"

In spite of the fact that small cell lung cancer is very sensitive to chemotherapy and radiation therapy, the cancer cells eventually develop a resistance to the treatment and the cancer grows back. Only 10-15 percent of patients will accomplish a cure. Nevertheless, chemotherapy and radiation therapy controls cancer-related symptoms such as fatigue, weight loss, shortness of breath, etc. for some time, thereby improving the quality of life of the patient.

6. What is the treatment for "extensive stage disease?"



Once the tumor has spread to areas outside the chest, local treatment such as radiation therapy and surgery are of limited value. Without treatment, median survival in this group of patients is 6-8 weeks. Treatment with combination chemotherapy increases median survival duration to approximately 8-10 months. Systemic chemotherapy is likely to improve the quality of life and the survival. The treatment is usually able to combat cancer-related symptoms such as fatigue, shortness of breath and weight loss.

7. What do the chemotherapy and radiation treatments entail?

The present standard is to deliver thoracic radiation, simultaneously with chemotherapy. Two chemotherapy drugs are commonly used: Platinol, on the first day only, and Etoposide daily for the first 3 days. These drugs are administered intravenously (through the vein). This regimen is repeated every 21 days for a total of 4-6 courses.

8. What are some of the newer chemotherapeutic agents that can be used once standard treatment with Platinol and Etoposide fails?

A variety of novel agents have been investigated in SCLC. Of these, Taxol and topotecan (Hycamtin), have demonstrated the greatest efficacy.

Taxanes - Because of their novel mechanism of action and clinical activity in other solid tumors, including NSCLC, the taxanes -- paclitaxel (Taxol) and docetaxel (Taxotere) -- are particularly attractive agents for evaluation in the treatment of SCLC.

Paclitaxel (Taxol): This taxane is currently being evaluated in combination with a variety of different agents, including etoposide and Platinol (or carboplatin [Paraplatin]), in SCLC patients.

Docetaxel (Taxotere): Compared with paclitaxel, docetaxel appears to have a slightly lower response rate of 26 percent.

CPT-11 [Camptosar], Topotecan) are clearly active in SCLC, with single-agent response rates of 40-60 percent.

Other agents, such as gemcitabine (Gemzar) and vinorelbine (Navelbine), have shown activity in SCLC, but this has been less impressive than that reported for the taxanes and topoisomerase I inhibitors.

Experimental Approaches

A variety of experimental approaches have been tested in SCLC. These include high doses of chemotherapy and autologous bone marrow transplantation (BMT), alternating regimens of chemotherapy, and weekly administration of chemotherapy.

High-dose chemotherapy plus BMT - Most phase II trials using high doses of chemotherapy plus BMT appear to show no advantage of the high-dose approach over standard doses of chemotherapy.



Non-Small Cell Lung Cancer (NSCLC)

Frequently Asked Questions

1. Once a diagnosis of non-small cell lung cancer has been made on biopsy, what determines the prognosis and treatment?

The stage of the disease correlates well with the expected outcome and also determines which kind of treatment is most appropriate (surgery, radiation therapy, chemotherapy or a combination thereof).

2. How is the stage determined?

CT-scans provide information on tumor size, tumor location, involvement of lymph nodes with tumor and the presence or absence of metastases which determines the clinical stage.

Stage I: Tumor is limited to one lung and no lymph nodes are involved.

Stage II: In addition to a tumor mass in the lung, lymph nodes within the lung are involved.

Stage III: The cancer has spread to lymph nodes in the space between the lungs (mediastinum)

Stage IV: Metastases are present (lung, bones brain etc)

In some instances, the CT scans alone are not sufficient to be relied on as far as staging is concerned. Whether the patient is a candidate for surgery often depends on the question whether mediastinal lymph nodes contain cancer. Mediastinoscopy can be used to sample lymph nodes that are questionable on CT scan and provide pathologic staging.

3. Which lung cancer patients should undergo surgery?

Patients with stage I, stage II and selected patients with stage III are candidates for surgery. Surgery usually involves removal of a lung lobe (lobectomy) or of a lung (pneumonectomy). The risk of dying immediately following lobectomy and pneumonectomy approximates 3 percent and 7 percent, respectively.

4. How can one be sure that the patient will tolerate removal of a substantial part of the lung?

In order to determine the volume of lung that can be removed without rendering the patient a pulmonary cripple and to identify those individuals at risk for postoperative complications, each patient must undergo pulmonary function testing.

5. What is the prognosis with appropriate treatment?

Patients with pathologic stage I disease have a 60-80 percent five-year survival rate after resection, whereas the five-year survival rate drops to 40-50 percent in those with stage II disease. Patients found to have limited mediastinal lymph node involvement



(stage IIIA) have a 25-30 percent five-year survival rate. Patients with stage IV disease rarely survive for more than 1 year.

6. What is the role of chemotherapy and radiation therapy in the treatment of lung cancer?

Radiation therapy alone has not been shown to improve survival in patients that have undergone resection of their lung cancer. Occasionally, however, radiation to the site of the original tumor is used if there is concern that the tumor could not be removed completely (positive surgical margins).

Stage I-IIIa disease: Adjuvant chemotherapy has been shown to play a role even in early-stage disease. Survival was significantly longer in the patients randomized to receive adjuvant chemotherapy than in those treated with surgery alone.

7. Are all patients with respectable lung cancer candidates for surgery?

Some patients with resectable stage I, II or III NSCLC are high-risk operative candidates because of poor lung function, heart disease, other medical problems, or advanced age. Other patients refuse to undergo surgery despite the recommendation of their treating physicians. In such patients, an attempt should be made to optimize pulmonary function by encouraging smoking cessation and initiating vigorous treatment with bronchodilators, corticosteroids, and antibiotics. Several institutions have reported their experience with definitive radiation therapy for such patients. Although the results are not as good as those reported in patients selected for surgery, medically inoperable patients with early-stage NSCLC clearly should be offered radiation therapy, with reasonable expectation of cure.

8. What are the options in patients that cannot have surgery?

A combination of chemotherapy and radiation therapy has been shown to result in an improvement in survival in the majority of studies when compared to radiation therapy alone. In general, radiation and low-dose daily seems superior to radiation alone with 4-year survival rates of 22 percent vs. 9 percent. It may be that the use of chemotherapy combats systemic disease (spread of disease to distant organs), whereas the simultaneous delivery of low-dose chemotherapy with radiation may be necessary to improve local tumor control (prevent the tumor from coming back where it originally started). At present, it is reasonable to consider sequential chemoradiation as standard treatment in stage III lung cancer patients who are ambulatory and who have not lost more than 5 percent of their usual body weight.

New chemotherapeutic agents plus radiation -- Several recent phase I-II trials evaluated relatively low doses of carboplatin and paclitaxel (Taxol), given concurrently with thoracic radiation. These studies showed acceptable toxicity and relatively high response rates, and in one of the studies the three-year survival rate was quite high (39 percent).



In addition to paclitaxel and carboplatin, many other chemotherapeutic agents with activity in NSCLC have emerged in the 1990s, including docetaxel (Taxotere), vinorelbine (Navelbine), gemcitabine (Gemzar), and irinotecan (CPT-11 [Camptosar]).

Radiation alone is appropriate for patients with stage III NSCLC who are otherwise not good candidates for chemoradiation, eg, those with 5 percent weight loss.

9. Is there any benefit from treatment in patients with metastases to distant organs (stage IV disease)?

Until recently, there was considerable controversy over the value of treating stage IV NSCLC patients with chemotherapy. Treatment with older regimens showed only a modest effect on survival, improving median survival by approximately 6 weeks, according to a meta-analysis, and yielding a 1-year survival rate of approximately 20 percent (as compared with a rate of approximately 10 percent for supportive care).

However, several new chemotherapeutic agents have produced response rates in the range of 15 percent in NSCLC. The potentially useful new agents include the taxanes (paclitaxel and docetaxel), vinorelbine, gemcitabine, and irinotecan. Several of these new drugs have unique mechanisms of action compared to the mechanisms of agents that have previously shown some effectiveness against NSCLC.

A completely new class of drugs has appeared on the horizon for colorectal cancer therapy: Medications that affect the hormonal growth pathways of tumors or the formation of blood vessels supplying the tumor.

Taxol plus Carboplatin

The combination of paclitaxel and a platinum agent, either cisplatin or carboplatin, appears to be particularly promising. Although results with paclitaxel plus cisplatin have varied somewhat, multiple studies have reported response rates of 31 percent-56 percent. Survival with Taxol plus Carboplatin therapy appeared to be markedly superior, compared with the older combinations. In addition, patients responding to chemotherapy enjoyed an improvement in their quality of life. This includes a recent study comparing doxetaxol (Taxotere) with best supportive care. Significant improvements favoring the Taxotere arm were seen with respect to quality of life; a reduction in both narcotic and nonnarcotic analgesic usage was noted as well.

10. If patients that are not candidates for chemotherapy become symptomatic from their metastatic disease – for example with pain from a bone metastasis – is there anything that can be done other than pain medication?

Many patients with lung cancer experience distressing local symptoms at some time. These may arise from airway obstruction by the primary tumor, compression of mediastinal structures by nodal metastases, or metastatic involvement of distant organs. Radiation therapy is quite effective in palliating most local symptoms, as well as symptoms at common metastatic sites, such as bone and brain. For selected patients



with a solitary brain metastasis and controlled disease in other sites, resection followed by radiation appears to be superior to radiation therapy alone in improving both survival and quality of life.

11. What kind of follow-up is recommended after treatment for lung cancer is completed?

Currently there is no general agreement how often patients with cured NSCLC or SCLC should be evaluated. However, serial physical examinations should be performed every one-two months initially, and then less frequently until the patient has reached the five-year mark. There is no proven benefit to routine CT scanning or even chest x-rays for the long-term follow-up of lung cancer patients.

