Lung cancer is the second most common cancer and the number one cause of cancer death in both men and women in the United States. Although there has always been a higher incidence in men, the incidence in women has risen rapidly in recent years. In fact, lung cancer has now surpassed breast cancer as the number one cancer killer of women, killing twice as many women as breast cancer. It has long been the leading cancer killer of men.

An estimated 213,380 people will develop lung cancer in the United States in 2007, and about 160,390 people will die of it. This is especially unfortunate because it is one of the most preventable cancers. The cause is well known. Before tobacco use became popular, lung cancer was a rare disease. Furthermore, it has been estimated that if all tobacco were removed from the earth, the number of all cancers would fall by 17 percent.

There are two general types of lung cancer—small cell and nonsmall cell. The nonsmall cell variety is much more common, accounting for 80 percent of all lung cancer cases. There has been slow but definite improvement in the survival rate over the past two decades. The slow rate of improvement is due to the fact that we lack a satisfactory, widely applicable screening test that could increase our ability to detect lung cancer at an early stage, when it has the best chance of being cured, and also to the fact that lung cancer is a biologically aggressive cancer. In addition, while there has been some progress in our ability to control lung cancer and extend the survival of some patients with advanced lung cancer, there is a continued need for more effective therapy.

**Types** There are at least four distinct types of nonsmall cell lung cancer—squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and bronchoalveolar carcinoma—the treatment of all four subtypes is generally similar. Squamous cell carcinoma used to be the most common, but, for reasons that are poorly understood,
adenocarcinoma has steadily increased in frequency and is now the most common type of nonsmall cell lung cancer, especially in women.

Squamous cell (also known as epithelioid) carcinoma of the lung is the microscopic type formerly most frequently related to smoking. Surgical removal of the tumor along with the nearby lymph nodes can produce a cure more often than with other types. Squamous cell tumors can cavitate (break up from the inside out) on their own and lead to coughing up blood. They account for only 30 percent of nonsmall cell lung cancer in the United States, but account for a higher percentage in western Europe and Asia.

Adenocarcinoma of the lung accounts for over 50 percent of all lung cancer cases in the United States. It is more common in women and is still the most frequent type seen in nonsmokers. However, it occurs frequently in smokers as well. It is more likely than other types to be in the peripheral portions of the lung (near the edge), and therefore may invade the lining of the chest and produce fluid in the chest cavity more commonly than in other types. It also has a tendency to spread early to other sites (metastasize) away from the primary, so that it is often diagnosed at a more advanced stage.

Large cell carcinoma, especially those tumors with neuroendocrine features, is commonly associated with spread of the tumor to the brain. It is arguably the most aggressive nonsmall cell subtype.

Bronchoalveolar carcinoma accounts for a minority of nonsmall cell lung cancers. It often presents with advanced stage, yet patients are likely to have very few symptoms because the rate at which the cancer grows may be slower than that of other subtypes. It is more difficult to diagnose microscopically, so its true incidence is probably higher than the 3 percent generally quoted in various lung cancer papers. It may develop more in women and in nonsmokers. It may also be more common in Asian patients, especially Asian women.

How It Spreads Nonsmall cell cancer can spread through the lymphatic system and through the blood. It can directly invade the center of the chest (mediastinum), the lining of the chest, the ribs, or, if it is in the top part of the lung, the nerves and blood vessels leading into the arm. If it invades the lymphatic system, it often spreads to the lymph nodes, either in the lung itself or in the mediastinum. When nonsmall cell lung cancer enters the bloodstream, it can spread to distant sites such as the liver, bone, brain, adrenal glands, and other places in the lung.

What Causes It Cigarette smoking has been a major factor in the development of both small cell and nonsmall cell lung cancers. The increase in cigarette smoking by men in the 1920s, apparently related to increased cigarette production, advertising, and marketing at that time, was followed in the 1940s by a dramatic increase in the incidence of lung cancer in men. The marked increase in cigarette smoking by women in the 1940s was unfortunately followed two decades later by a similar increase in the incidence of lung cancer among women, so that now, lung cancer has overtaken breast cancer as the leading cause of cancer-related death in women. It should be noted, however, that there has also been an increase in the rate of lung cancer among people who have never smoked, especially women. The reasons for this increase are not well understood, but may have something to do with secondhand smoke exposure or other as yet unidentified factors. Finally, while quitting smoking does reduce the risk of developing lung cancer, it does not remove it completely. The majority of patients diagnosed with lung cancer have effectively quit for quite some time prior to their diagnosis.
Lung tissue scarred by a connective tissue disease such as scleroderma may be associated with the development of bronchoalveolar carcinoma. Lung cancer may predispose a person to a higher incidence of developing another lung cancer later. Lung cancer may also occur at sites of old scars in the lung resulting from an infection (tuberculosis, for example) or an injury (scar carcinoma) or prior radiation.

Risk Factors

**At Significantly Higher Risk**

- Cigarette smokers.
- The male to female ratio remains 4 to 1. Peak incidence occurs between ages fifty and sixty, with less than a 1 percent incidence under the age of thirty and about a 10 percent incidence in people over seventy.
- Workers exposed to industrial substances such as asbestos, nickel, chromium, cadmium, uranium, radon compounds, and chloromethyl ether, especially those who smoke.
- Prior early-stage lung cancer or head and neck cancer.

**At Slightly Higher Risk**

- Patients with previous or preexisting lung disease, especially a type of lung disease leading to heavy scarring, such as interstitial lung disease.
- Former smokers.
- People exposed to secondhand smoke over many years.
- People exposed to radon.

Screening

Lung cancer is very difficult to detect at an early stage. Tests such as the examination of sputum (phlegm) for malignant cells and regular chest X-rays have not proven to be beneficial. Chest X-rays can detect lung cancer in smokers, but these findings may not always be early enough to improve the survival of patients. Other techniques such as fluorescence bronchoscopy and spiral-computed tomography are also in the process of being perfected with a goal to detect the cancer as early as possible. Recently, the use of spiral CT scanning in patients at high risk for developing lung cancer has shown promising preliminary results in detecting nonsmall cell lung cancer at a very early stage, when it may still be curable. Efforts are currently under way to confirm these promising results through a large national randomized clinical trial. Additionally, efforts are under way to develop tests that can detect very early molecular changes associated with nonsmall cell lung cancer in the bloodstream or the sputum. The goal of these efforts is to develop effective screening tests in order to increase the number of early-stage cancers that we can detect and treat.

Common Signs and Symptoms

A new or changing cough, the sputum sometimes containing blood, is a common symptom, along with hoarseness and shortness of breath or increased shortness of breath during exertion. There may also be an increase in the amount of sputum, recurrent episodes of lung infection (sometimes in the same lobe of the lung as the cancer), weight loss, and swelling of the face or arms. By far the most common symptom is fatigue.

If the tumor has spread, or metastasized, the symptoms can include severe headaches, double vision, and pain in the bones, chest, abdomen, and neck and down the arms.

Diagnosis

**Physical Examination**

- Lymph node enlargement in the neck or in the region above the collarbone.
- Enlarged liver or another mass in the abdomen.
• Signs of a mass in one lung, such as decreased breath sounds, noises in the lung that are not usually present, and areas of dullness when the chest is tapped with the fingers, indicating the presence of fluid in the lung.

Blood and Other Tests Sputum examination for malignant cells.

Imaging

• A chest X-ray that shows an abnormality does not establish a diagnosis until some tissue is obtained and examined under the microscope.
• CT scans of the chest and abdomen, to include the entire liver and the adrenal glands.
• PET scans can be helpful in staging the mediastinum (the area between both lungs where a lot of the lymph nodes that drain the lungs are located). A positive PET scan strongly suggests that cancer might be present. Lately, the use of simultaneous CT and PET scans, so-called CT-PET fusion scans, is increasing the accuracy and usefulness of preoperative scanning to stage patients prior to initiating treatment. CT-PET fusion scans generally include the brain, neck, chest, abdomen, and pelvis, all the way through the thighs.
• Sometimes PET, CT, or MRI scans of the brain can provide useful information.

Endoscopy and Biopsy

• Fiber-optic bronchoscopy with brushing, lavage, and/or biopsy.
• Mediastinoscopy with biopsies. In this procedure, a small incision is made at the base of the neck and a long, thin tube called a mediastinoscope is inserted down to the lymph nodes in the middle of the chest. Tissue can be obtained through this instrument. The procedure is usually safe and easy but does require general anesthesia and a short hospital stay.
• Needle aspiration through the chest wall (see the section on FNA biopsy in chapter 2, “How Cancer Is Diagnosed”) with a local anesthetic and often under CT guidance.
• Removal and analysis of fluid in the chest to detect tumor cells.
• Pleural (chest lining) biopsy.
• Lymph node biopsy.
• Bone biopsy.
• Liver biopsy.
• Biopsy of a nodule during surgery.
• DNA analysis. With the advent of genetic probe studies, certain genes appear to be more frequent in patients who develop lung cancer. Patients, women especially, with amplification of the k-ras oncogene, for example, may have a much worse prognosis. We are rapidly approaching the time when we can have our genes analyzed and we can be made aware of our risks, not only for lung cancer, but for other cancers as well. These types of genetic analyses will soon be carried out on a simple blood sample, thereby avoiding the need to obtain lung tissue and making it easy and safe to obtain these important answers.

Staging

Once a diagnosis of a malignant tumor is made, further staging studies are carried out to establish the stage of disease. More than any other factor, the stage helps determine the prognosis and helps guide the selection of treatment.

Stage is based on a combination of clinical findings (physical examination, chest X-ray, and lab studies) and pathologic findings (biopsy). The stages are now commonly defined according to the TNM classification.

Treatment Overview

Surgery Surgical treatment—removal of the tumor—remains the mainstay of curative treatment in early-stage (I, II) nonsmall cell lung cancer.
This will involve removing a lobe of the lung when a tumor is very central in the lung. When a tumor is small and located in the periphery of the lung, it can be removed by a smaller surgery, called a wedge resection. Whenever possible, though, the fuller lobectomy procedure should be employed, as it is usually more effective in improving the chance of survival. It should be stressed that surgery for lung cancer has evolved significantly over the past twenty years. Now patients can undergo resection with smaller, muscle-sparing incisions, which, with the use of epidural catheters, greatly improve the control of postoperative pain. When pain is better controlled, patients are more likely to be up and about faster, thus reducing the risk of major complications. Typically, the risk of serious complications for a routine lobectomy should be less than 1 to 2 percent.

In the last few years, the use of video-assisted surgery using special instruments called thorascopes have allowed a greater number of patients, who might otherwise not have been candidates for normal open surgery, to undergo removal of their primary lung cancer. It remains to be seen if the use of video-assisted surgery is as effective in controlling lung cancer as the more involved open procedures.

Radiation Radiation is used in different scenarios. It is used as an addition to surgery if it appears that there might be some disease left after surgery. In cases where the lymph nodes in the mediastinum are involved and surgery might not be possible, radiation is used at the same time as chemotherapy to control and cure nonsmall cell lung cancer. Finally, in patients with lung cancer that has spread to organs like the bones or the brain, radiation is used to improve the symptoms caused by the involvement of these organs. In these cases, radiation is not felt to be curative, but instead felt to be palliative.

Chemotherapy The role of chemotherapy has evolved over the past number of years. Several recent analyses of multiple studies have led to the following conclusions:

1. While not a cure for advanced nonsmall cell lung cancer, chemotherapy can provide a significant survival benefit in selected patients.
2. Chemotherapy appears to be more effective than simple palliative care for patients with advanced nonsmall cell lung cancer.
3. Chemotherapy combined with surgery improves outcomes for patients with Stages II–IIIA nonsmall cell lung cancer that has been fully resected. At this time, it is not clear if the addition of chemotherapy to surgery for patients with Stage I disease yields a survival benefit.

When a platinum drug is combined with drugs such as paclitaxel (Taxol), docetaxel (Taxotre), gemcitabine (Gemzar), and vinorelbine (Navelbine), response rates of 30 to 40 percent can be observed in Stage IV cancer. All of these compounds have excellent activity in combination with the platinum compounds cisplatin (Platinol) and carboplatin (Paraplatin). Forty percent or more of patients receiving chemotherapy for advanced nonsmall cell lung cancer can expect to live at least one year. There is now consistent evidence of survival improvement through the use of these agents in Stage IV nonsmall cell lung cancer. In addition, these agents may give palliative benefit by reducing the size of the tumors and relieving symptoms. A large, randomized clinical trial comparing four different platinum and modern chemotherapy drug combinations confirmed the efficacy of the drugs, while demonstrating that the various combinations were essentially equivalent in terms of effectiveness and overall benefit.
The addition of the new drug bevacizumab (Avastin) to a platinum-based combination can yield further improvements in survival of patients with metastatic nonsmall cell lung cancer. Bevacizumab can, however, increase the risk of serious, life-threatening complications, so its use is limited to patients who do not have tumors located in the middle of their chest or in close proximity to large blood vessels. In addition, patients should not present with hemoptysis (coughing up blood) and should not have brain metastases, as the risk of life-threatening complications may be higher in these patients.

Improvements in the effectiveness and tolerability of chemotherapy have made it possible to go beyond first-line chemotherapy. Patients whose disease is stabilized by the first line of treatment are often candidates for further therapy with different treatment options. In the last few years, docetaxel, first, followed by pemetrexed (Alimta), has been approved by the FDA specifically as a treatment option for nonsmall cell lung cancer patients whose disease has progressed after first-line therapy.

A new class of drugs labeled targeted chemotherapy has emerged as an important option for patients with nonsmall cell lung cancer. The first drug to be approved in this class was gefitinib (Iressa). However, in the United States and Europe, gefitinib did not confirm its initial encouraging results. Gefitinib remains in use in Asia, where it appears to have excellent activity. The leading drug in nonsmall cell lung cancer to come from this class is erlotinib (Tarceva). The drugs from this class target a precise molecular event in the cancer cell. These drugs are inhibitors of the actions that occur when the epidermal growth factor receptor (EGFR) is stimulated by the epidermal growth factor (EGF). EGFR stimulation leads to a number of molecular signals that allow the cancer cell to survive and thrive. The EGFR is present in normal cells, like skin cells, but its actions are not crucial for normal cells. As a result, the side-effect profile of these drugs tends to be gentler for most patients than that seen with conventional chemotherapy. Patients taking erlotinib can expect a characteristic skin rash and occasionally diarrhea. Less often, the drug can cause fatigue and nausea. It can also cause the skin to crack, which can be quite uncomfortable. Very rarely and mostly in Asian patients or in patients who have received a great deal of radiation to their chest, erlotinib can cause a life-threatening inflammation of the lungs. The vast majority of patients treated with erlotinib have the gentler forms of the side effects mentioned above.

Erlotinib has been shown in clinical trials to be useful in patients whose disease is resistant to at least one prior chemotherapy treatment. It can reverse the disease dramatically in a few patients and less so in other patients. The majority of patients who respond to treatment with erlotinib experience stabilization of their disease with improvement in their symptoms. Certain groups of patients appear to have a higher chance of response to erlotinib—nonsmokers, women, and Asian patients have the best chance of response to treatment with erlotinib. These groups of patients are more likely to have a mutation on the EGFR, which is the target for erlotinib and which makes their cancer cells more vulnerable to treatment with this drug.

Advances in our understanding of the molecular biology of lung cancer have allowed us to identify targets for drugs like erlotinib. Many more possible targets and drugs are in development and we should have a whole new generation of safe and effective options in a few short years.

Neoadjuvant Chemotherapy and Radiation New protocols to explore curative
strategies in lung cancer include using chemotherapy or radiation therapy, or both, before surgery, to try to convert some patients from an inoperable stage to one where the tumor can be removed. An example is the use of chemotherapy initially in Stages IB–IIIA lung cancer patients. Small studies have indicated that this approach may be beneficial, although it is too early to make any definite claims about this technique. Several larger studies in Europe and North America have been completed, and their results should be available in a few years, but for now the technique is best reserved for use in the setting of a clinical trial.

When one adds radiation to chemotherapy followed by surgery for Stage IIIA nonsmall cell lung cancer, there may be a benefit, but the risk of severe postoperative complications does exist. The decision to use these techniques prior to surgery must be carefully weighed against the chance of life-threatening complications.

**Laser Therapy** Laser bronchoscopy with light sensitzers has been an interesting experimental technique to try to open the airways when they are blocked by a tumor (see chapter 10, “Laser Therapy”).

**Gene Therapy** We are now beginning to understand precisely the molecular defects that lead to the transformation of a normal cell into a cancerous cell. The damage to some of the more crucial controlling steps can be repaired in cells in the lab. In those experiments, copies of the damaged gene are replaced with new copies, usually delivered by a virus. When a specially engineered virus carrying a copy of the desired gene infects an abnormal cell, it can restore the cell to a more normal state. The difficulty lies in being able to deliver the normal gene to all of the cancer cells or to as many as possible.

Preliminary studies have been carried out to prove the concept that replacing a damaged gene leads to improvement. To date, these initial efforts show that when the virus can be delivered to the cancer cells, the cancer cells can be controlled more easily. In order to achieve more significant improvements, the next step will be to successfully replace copies of the damaged gene in all of the cancer cells. Therein lies the great difficulty in establishing this option as a viable solution.

**Vaccine Therapy** Harnessing a patient’s own immune system to fight cancer cells has been a strategy that can work for some cancers. To date, there have been attempts at making a vaccine by taking a patient’s own cells and altering them to allow them to stimulate the patient’s immune system more effectively. The approach has a great deal of scientific merit and has on occasion yielded provocative results. Unfortunately, it requires surgery to remove enough cancer cells to make the vaccine. Clinical trials performed with this approach have not shown strong enough results to make it a reasonable choice at this time. Other vaccine approaches try to stimulate the immune system to recognize a specific molecule associated with the cancer. Clinical trials are ongoing to see if this latest vaccine strategy is reasonable.

**Treatment by Stage**

**Stage I**

TNM T1–2, N0, M0

The tumor can be removed surgically and has not spread to involve the lymph nodes.

**Standard Treatment** If possible, the lobe of the involved lung with the tumor in place is removed along with the nearby lymph nodes. Sometimes the entire lung on one side needs to
be removed to ensure that the entire tumor is resected.

In patients with a small (T1) tumor, or in patients with impaired lung function, only a wedge segmental resection, which removes the tumor with a small amount of normal surrounding tissue, is done. The limited wedge resection is reserved for patients who are otherwise felt not to be able to tolerate the removal of standard amounts of lung tissue as necessitated by the removal of a lobe. Whenever possible, a lobectomy or a segmentectomy should be performed, as it has better success in preventing a local recurrence than a wedge resection. Almost all patients can tolerate an upper lobectomy unless they have severely reduced pulmonary function.

In those patients with severe lung or heart disease who cannot tolerate surgery, limited radiation therapy is sometimes used, with much smaller survival benefits. In recent years, the use of advanced radiation techniques, including stereotactic radiosurgery (CyberKnife or Gamma Knife) have yielded promising results. Further clinical trials are needed to determine the true value of these newer techniques.
Chemotherapy after surgery has yet to be proven useful in patients with Stage IA disease and remains controversial for patients with Stage IB disease.

**Five-Year Survival** 50 to 80 percent

- **Stage II**
  
  TNM T1–2, N1, M0 or T3, N0, M0
  
  The tumor has spread to the hilar (N1) nodes or the tumor invades the chest wall, mediastinum, or diaphragm (T3).

  **Standard Treatment** This stage is likewise treated with surgery. Recently, several large-scale international clinical trials have shown that patients with Stage II nonsmall cell lung cancer may derive a survival benefit from the addition of platinum-based chemotherapy (cisplatin [Plantinol] or carboplatin [Paraplatin]) after they recover from their surgery. Patients who do not experience serious complications from their surgery can be considered for postoperative chemotherapy. The benefit from postoperative chemotherapy is on the order of a 5 to 15 percent improvement in overall survival.

  Patients unable to withstand surgery may be candidates for radiation therapy with intent to cure, although the chance of cure is generally less than what is expected with surgery.

  A special situation under Stage II is a superior sulcus tumor, which involves cancers in the top of the lung that invade local nerves and cause pain in the arm (they are often classified as T3, N0, M0). These tumors seem to have a reduced potential for distant metastases, so local radiation therapy is possible for cure. Surgery is frequently used after radiation. The results of a recently completed national clinical trial strongly supported adding chemotherapy to radiation, followed by surgery, to significantly increase the cure rate of these upper-lung tumors.

  **Five-Year Survival** 30 to 50 percent

- **Investigational Trials** are exploring whether the use of chemotherapy before surgery can improve the cure rate. Preliminary trial data suggest that preoperative chemotherapy is safe and well tolerated. Whether or not preoperative chemotherapy leads to improved survival remains to be determined.

- **Stage IIIA**
  
  TNM T1–2, N2, M0 or T3, N1–2, M0
  
  Stage III is divided into IIIA and IIIB. Both show involvement of nodes in the center of the chest, but Stage IIIA tumors may be removed surgically under certain circumstances.

  **Standard Treatment** These tumors are treated mainly with radiation therapy and chemotherapy, surgery, or all three, depending on the clinical circumstances.

  Patients who undergo surgery should be considered for treatment with chemotherapy upon their recovery from surgery. Recently, several large-scale international clinical trials have shown that patients with Stage IIIA nonsmall cell lung cancer may derive a survival benefit from the addition of platinum-based chemotherapy after they recover from their surgery. This benefit is on the order of a 5 percent improvement in overall survival.

  Radiation therapy is frequently given after surgery. Although there is no evidence that this improves survival, there can be a decrease in recurrences at the original tumor site.

  For patients who are not felt to be surgical candidates, the use of chemotherapy concurrently with radiation is more effective than either treatment followed by the other.

  Although most patients do not completely respond to radiation therapy alone, 15 to 20 percent do experience long-term survival benefit.

  Patients whose tumors invade the chest wall or the upper portions of the lung or chest can often be treated with
surgery, which may involve the removal of some of the chest wall, including ribs, and chest wall reconstruction. Radiation therapy is often used along with surgery.

Some patients with extensive metastatic disease in the center of the chest may develop what is called the superior vena cava syndrome, in which the great vessels in the chest are compressed by the tumor. When this involves the large vein that returns blood to the heart, the blood gets backed up into the tissues of the neck, head, and arms. This is an urgent situation and patients should be given prompt radiation therapy.

**Five-Year Survival** 10 to 30 percent

**Investigational** Treatment with radiation or chemotherapy or both before surgery (neoadjuvant) has been used on an investigational basis. Preliminary results suggest that there may be benefit by combining all three treatments in selected cases. Newer trials are giving cisplatin (Platinol) and docetaxel (Taxotere) by themselves or together with radiation, followed by surgery. T4 lesions can oftentimes be completely resected in centers with experienced general thoracic surgeons using induction chemotherapy and radiation followed by surgery; three-year survival of greater than 30 to 40 percent can be achieved using reduction chemotherapy and radiation.

- **Stage III B**
  - **TNM** Any T, N3, M0 or T4 (noneffusion lesions), any N, M0
  - The tumor cannot be removed because of technical reasons or because there would be no benefit to the patient.

**Standard Treatment** These tumors are best managed with radiation therapy and chemotherapy. Recently completed clinical trials both in the United States and Japan and Europe strongly support the use of chemotherapy administered concurrently with radiation therapy as a more effective approach than chemotherapy followed by radiation, or radiation without the use of chemotherapy. T4 (effusion) or N3 treatment predominately includes definitive chemoradiation or investigational treatment.

**Five-Year Survival** 5 to 20 percent

**Investigational** Trials are examining the effectiveness of chemotherapy and/or radiation therapy before surgery. These treatments have occasionally converted some patients to an operable stage, but it is too soon to know if using this aggressive approach will increase the rate of cure. Other trials are examining using newer chemotherapy agents at the same time as radiation.

- **Stage IV**
  - **TNM** Any T, any N, M1
  - The cancer has spread to distant sites.

**Standard Treatment** Metastatic disease cannot be cured by surgery, so treatment for this stage is directed toward relieving symptoms with either radiation therapy or chemotherapy.

Radiation may relieve local symptoms such as tracheal, esophageal, or bronchial compression; bone or brain metastases; pain; vocal cord paralysis; coughing up blood (hemoptysis); and superior vena cava syndrome. Patients without symptoms should be kept under close observation. Sometimes treatment may appropriately be deferred until symptoms or signs of a progressive tumor develop.

Chemotherapy with a platinum compound combined with drugs such as paclitaxel (Taxol), docetaxel (Taxotere), irinotecan (Camptoza r, CPT-11), gemcitabine (Gemzar), and vinorelbine (Navelbine) has response rates of 30 to 50 percent in Stage IV cases. Chemotherapy will give modest but consistent and
significant improvements in survival. The new combinations are usually well tolerated; the more severe side effects deal mostly with suppression of the bone marrow. Nausea and vomiting are usually well controlled through the use of medications such as dexamethasone (Decadron), ondansetron (Zofran), granisetron (Kytril), dolasetron (Anzemet), and palonosetron (Aloxi). Newer antinausea drugs like aprepitant (Emend) have been very effective for patients who develop nausea and vomiting with drugs like cisplatin (Platinol). Loss of hair is mostly seen with the use of either paclitaxel, docetaxel, or irinotecan.

Recent trials using a cisplatin-based regimen of chemotherapy showed some survival benefit and give hope for more benefit in the future. Combinations currently in use include carboplatin (Paraplatin) or cisplatin + paclitaxel, cisplatin or carboplatin + vinorelbine, cisplatin or carboplatin + gemcitabine, cisplatin + docetaxel, and cisplatin + irinotecan. Recent studies with newer combinations such as docetaxel + gemcitabine suggest that cisplatin-containing regimens are probably more effective, even if the noncisplatin regimen may be better tolerated. The use of three conventional chemotherapy drugs has been abandoned as too toxic while not more effective.

For patients who progress after first-line chemotherapy, the use of second-line chemotherapy with either pemetrexed (Alimta), docetaxel, or erlotinib (Tarceva) is an excellent option.

Other potentially useful adjuncts to the treatment of advanced lung cancer include feeding gastrostomies when the esophagus is obstructed by the cancer, and the use of lasers to open up an airway obstructed by a tumor mass.

Occasionally, persons with excellent performance status and a limited metastatic disease (isolated from advanced metastases) can benefit (at 20 to 25 percent three- to five-year survival) with aggressive combined treatment, including chemotherapy, radiation, and resection or stereotactic radiotherapy of metastases and the primary tumor.

**Five-Year Survival** Less than 5 percent

**Investigational** New drugs that target the growth of blood vessels (angiogenesis inhibitors) are in accelerated development. Drugs that target the internal communication system of the cancer cell (signal transduction inhibitors) are also receiving a great deal of attention. Combinations of these drugs, or drugs that affect multiple internal pathways, are being developed.

**Supportive Therapy**

The importance of supportive therapy in the treatment of lung cancer cannot be overemphasized.

- Psychosocial support to help maintain a positive attitude and the will to live and to aid in coping with cancer can help a patient survive the rigors of surgery, chemotherapy, and radiation therapy (see chapter 19, “Living with Cancer,” and chapter 32, “The Will to Live”).
- Quite clearly, malnutrition results in a bad outcome in patients with lung cancer. Patients must be served palatable meals and attempts must be made to work with patients to determine food preferences (see chapter 23, “Maintaining Good Nutrition”).
- Pain control is of critical importance, and the tools to achieve control are available even for the most advanced cases. These include the use of pain-relieving (analgesic) drugs such as nonsteroidal anti-inflammatory agents, mild narcotics, strong narcotics, and narcotics delivered into the spinal canal (epidural). Pain control can generally be achieved without interfering
with mental competence (see chapter 24, “Controlling Pain”).

- Nausea can be controlled with a variety of drugs (see chapter 20, “Coping with the Side Effects of Chemotherapy”).
- Physical therapy will help maintain muscle strength to keep life as normal as possible (see chapter 29 “Staying Physically Fit”).

Maintaining Quality of Life  In the management of lung cancer (as well as all other malignancies), it is critical that patients maintain as high a quality of life as possible. Patients must feel that they are contributing members of society. Certainly, this keeps them in a happier mental frame.

Being with family and friends, going out to meals and movies, and participating in enjoyable recreational events are all important parts of maintaining lifestyle. With the services now available and the help of family members and physicians, it is usually possible to maintain these goals.

However, when the time comes that patients are no longer able to participate in such activities, we must all be sensible enough to ensure comfort by whatever methods we can. Even if mental ability has been compromised in order to relieve the pain, pain control should come first and remain all-important. Comfort care is the key phrase at this stage of life.

Treatment Follow-Up

People who have lung cancer have to be followed carefully by their physician, generally being examined every one to three months during the first two years, for that is when the risk of relapse is greatest.

- Chest CT scans every three to four months in the absence of symptoms
- Chest CT scans more often if symptoms occur
- Blood chemistry tests every three to four months
- Physical examination of the chest, lymph nodes, and abdomen
- Neurologic examination
- After two years, follow-up every six months with CT scans and blood surveillance

Patients should, of course, see their physician if any unusual symptoms occur.

Recurrent Cancer

See treatment for Stage IV disease.

The Most Important Questions You Can Ask

- What is the stage of my disease and what is my prognosis?
- What is the role of surgery and what is the chance of it curing me?
- What is the role of radiation therapy?
- How sick will I be on chemotherapy and can we control the sickness?
- If chemotherapy cannot cure my cancer, why should I expose myself to its side effects and toxicities?
- What is the chance that I will die from this tumor? How much time am I likely to have?