Lung Cancer (Non-Small Cell)

WHAT IS LUNG CANCER - NON-SMALL CELL?

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues is what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called *metastasis*. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named (and treated) based on the place where it started. For example, breast cancer that has spread to the liver is still breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is still prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

CAUSES, RISK FACTORS, AND PREVENTION

What are the risk factors for non-small cell lung cancer?

A risk factor is anything that affects a person's chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And some people who get the disease may not have had any known risk factors. Even if a person with lung cancer has a risk factor, it is often very hard to know how much that risk factor may have contributed to the cancer.

Several risk factors can make you more likely to develop lung cancer.

Tobacco smoke

Smoking is by far the leading risk factor for lung cancer. In the early 20th century, lung cancer was much less common than some other types of cancer. But this changed once manufactured cigarettes became readily available and more people began smoking.

At least 80% of lung cancer deaths are thought to result from smoking. The risk for lung cancer among smokers is many times higher than among non-smokers. The longer you smoke and the more packs a day you smoke, the greater your risk.

Cigar smoking and pipe smoking are almost as likely to cause lung cancer as cigarette smoking. Smoking low-tar or "light" cigarettes increases lung cancer risk as much as regular cigarettes. There is concern that menthol cigarettes may increase the risk even more since the menthol allows smokers to inhale more deeply.

Secondhand smoke: If you don't smoke, breathing in the smoke of others (called secondhand smoke or environmental tobacco smoke) can increase your risk of developing lung cancer by almost 30%. Workers who have been exposed to tobacco smoke in the workplace are also more likely to get lung cancer. Secondhand smoke is thought to cause more than 7,000 deaths from lung cancer each year.

Some evidence suggests that certain people are more susceptible to the cancer-causing effect of tobacco smoke than others.

If you or someone you care about needs help in quitting, see our document called *Guide to Quitting Smoking* or call the American Cancer Society at 1-800-227-2345

Radon

Radon is a naturally occurring radioactive gas that results from the breakdown of uranium in soil and rocks. It cannot be seen, tasted, or smelled. According to the US Environmental Protection Agency (EPA), radon is the second leading cause of lung cancer in this country, and is the leading cause among non-smokers.

Outdoors, there is so little radon that it is not likely to be dangerous. But indoors, radon can be more concentrated. When it is breathed in, it enters the lungs, exposing them to small amounts of radiation. This may increase a person's risk of lung cancer.

The lung cancer risk from radon is much lower than that from tobacco smoke. However, the risk from radon is much higher in people who smoke than in those who don't.

Radon levels in the soil vary across the country, but they can be high almost anywhere. Homes in some parts of the United States built on soil with natural uranium deposits can have high indoor radon levels (especially in basements). Studies from these areas have found that the risk of lung cancer is higher in those who have lived for many years in a radon-contaminated house.

If you are concerned about radon exposure, you can use a radon detection kit to test the levels in your home. State and local offices of the EPA can also give you the names of reliable companies that can test your home (or other buildings) for radon and help you fix the problem, if needed. For more information, see our document called *Radon.*

Asbestos

Workplace exposure to asbestos fibers is an important risk factor for lung cancer. Studies have found that people who work with asbestos (in some mines, mills, textile plants, places where insulation is used, shipyards, etc.) are several times more likely to die of lung cancer. In workers exposed to asbestos who also smoke, the lung cancer risk is much greater than even adding the risks from these exposures separately. It's not clear to what extent low-level or short-term exposure to asbestos might raise lung cancer risk.

Both smokers and non-smokers exposed to asbestos also have a greater risk of developing mesothelioma, a type of cancer that starts in the pleura (the lining surrounding the lungs). Because it is not usually considered a type of lung cancer, mesothelioma is discussed in our document called *Malignant Mesothelioma*.

In recent years, government regulations have greatly reduced the use of asbestos in commercial and industrial products. It is still present in many homes and other older buildings, but it is not usually considered harmful as long as it is not released into the air by deterioration, demolition, or renovation. For more information, see our document called*Asbestos*.

Other cancer-causing agents in the workplace

Other carcinogens (cancer-causing agents) found in some workplaces that can increase lung cancer risk include:

- Radioactive ores such as uranium
- Inhaled chemicals or minerals such as arsenic, beryllium, cadmium, silica, vinyl chloride, nickel compounds, chromium compounds, coal products, mustard gas, and chloromethyl ethers
- Diesel exhaust

The government and industry have taken steps in recent years to help protect workers from many of these exposures. But the dangers are still present, so if you work around these agents, you should be careful to limit your exposure whenever possible.

Air pollution

In cities, air pollution (especially near heavily trafficked roads) appears to raise the risk of lung cancer slightly. This risk is far less than the risk caused by smoking, but some researchers estimate that worldwide about 5% of all deaths from lung cancer may be due to outdoor air pollution.

Radiation therapy to the lungs

People who have had radiation therapy to the chest for other cancers are at higher risk for lung cancer, particularly if they smoke; for example, people who have been treated for Hodgkin disease or women who get radiation after a mastectomy for breast cancer. Women who receive radiation therapy to the breast after a lumpectomy do not appear to have a higher than expected risk of lung cancer.

Arsenic in drinking water

Studies of people in parts of Southeast Asia and South America with high levels of arsenic in their drinking water have found a higher risk of lung cancer. In most of these studies, the levels of arsenic in the water were many times higher than those typically seen in the United States, even in areas where arsenic levels are above normal. For most Americans who are on public water systems, drinking water is not a major source of arsenic.

Personal or family history of lung cancer

If you have had lung cancer, you have a higher risk of developing another lung cancer.

Brothers, sisters, and children of those who have had lung cancer may have a slightly higher risk of lung cancer themselves, especially if the relative was diagnosed at a younger age. It is not clear how much of this risk might be due to genetics and how much might be from shared household exposures (such as tobacco smoke or radon).

Researchers have found that genetics does seem to play a role in some families with a strong history of lung cancer. For example, people who inherit certain DNA changes in a particular chromosome (chromosome 6) are more likely to develop lung cancer, even if they don't smoke or only smoke a little. At this time these DNA changes cannot be routinely tested for. Research is ongoing in this area.

Certain dietary supplements

Studies looking at the possible role of vitamin supplements in reducing lung cancer risk have not been promising so far. In fact, 2 large studies found that smokers who took beta carotene supplements actually had an increased risk of lung cancer. The results of these studies suggest that smokers should avoid taking beta carotene supplements.

Factors with uncertain or unproven effects on lung cancer risk

Marijuana smoking

There are some reasons to think that marijuana smoking might increase lung cancer risk. Marijuana smoke contains tar and many of same cancer-causing substances that are in tobacco smoke. (Tar is the sticky, solid material that remains after burning, and is thought to contain most of the harmful substances in smoke.) Marijuana cigarettes (joints) are typically smoked all the way to the end, where tar content is the highest. Marijuana is also inhaled very deeply and the smoke is held in the lungs for a long time, which gives any cancer causing substances more opportunity to deposit in the lungs. And because marijuana is often an illegal substance, it may not be possible to control what other substances it might contain.

But those who use marijuana tend to smoke fewer marijuana cigarettes in a day or week than the amount of tobacco consumed by cigarette smokers. For example, a light smoker may smoke half of a pack (10 cigarettes) a day, but 10 marijuana cigarettes in a day would be very heavy use of marijuana. In one study, most people who smoked marijuana did so 2 to 3 times per month. The lesser amount smoked would make it harder to see an impact on lung cancer risk.

It has been hard to study whether there is a link between marijuana and lung cancer because marijuana was illegal in many countries for so long, and it is not easy to gather information about the use of illegal drugs. Also, in the studies that looked at past marijuana use in people who had lung cancer, most of the marijuana smokers also smoked cigarettes. This can make it hard to know how much of the risk is from tobacco and how much might be from marijuana. More research is needed to know the cancer risks from smoking marijuana.

Talc and talcum powder

Talc is a mineral that in its natural form may contain asbestos. Some studies have suggested that talc miners and millers might have a higher risk of lung cancer and other respiratory diseases because of their exposure to industrial grade talc. But other studies have not found an increase in lung cancer rate.

Talcum powder is made from talc. By law since 1973, all home-use talcum products (baby, body, and facial powders) in the United States have been asbestos-free. The use of cosmetic talcum powder has not been found to increase the risk of lung cancer.

EARLY DETECTION, DIAGNOSIS, AND STAGING

Can non-small cell lung cancer be found early?

Usually symptoms of lung cancer do not appear until the disease is already in an advanced, non-curable stage. Even when symptoms of lung cancer do appear, many people may mistake them for other problems, such as an infection or long-term effects from smoking. This may delay the diagnosis.

Some lung cancers are diagnosed early because they are found by accident as a result of tests for other medical conditions. For example, lung cancer may be found by imaging tests (such as a chest x-ray or chest CT scan), bronchoscopy (viewing the inside of lung airways through a flexible lighted tube), or sputum exam (microscopic examination of cells in coughed up phlegm) done for other reasons in patients with heart disease, pneumonia, or other lung conditions. A small portion of these patients do very well and may be cured of lung cancer.

Screening is the use of tests or exams to detect a disease in people without symptoms of that disease. Doctors have looked for many years for a test to find lung cancer early and help people live longer, but only in recent years has a study shown that a lung cancer screening test can help lower the risk of dying from this disease.

The National Lung Screening Trial

The National Lung Screening Trial (NLST) was a large clinical trial that looked at using a type of CT scan known as low-dose CT (sometimes called low-dose spiral or helical CT) to screen for lung cancer. CT scans of the chest provide more detailed pictures than chest x-rays and are better at finding small abnormalities in the lungs (discussed in more detail in the next section). Low-dose CT (LDCT) of the chest uses lower amounts of radiation than a standard chest CT and does not require the use of intravenous (IV) contrast dye.

The NLST compared LDCT of the chest to chest x-rays in people at high risk of lung cancer to see if these scans could help lower the risk of dying from lung cancer. The study included more than 50,000 people aged 55 to 74 who were current or former smokers and were in fairly good health. To be on the study, they had to have at least a 30 pack-year history of smoking. A pack-year is the number of cigarette packs smoked each day multiplied by the number of years a person has smoked. Someone who smoked a pack of cigarettes per day for 30 years has a 30 pack-year smoking history, as does someone who smoked 2 packs a day for 10 years and then a pack a day for another 10 years. Former smokers could enter the study if they had quit within the past 15 years. The study did not include people if they had a prior history of lung cancer or lung cancer symptoms, if they had part of a lung removed, if they needed to be on oxygen at home to help them breathe, or if they had other serious medical problems.

People in the study got either 3 LDCT scans or 3 chest x-rays, each a year apart, to look for abnormal areas in the lungs that might be cancer. After several years, the study found that people who got LDCT had a 16% lower chance of dying from lung cancer than those who got chest x-rays. They were also 7% less likely to die overall (from any cause) than those who got chest x-rays.

Screening with LDCT was also shown to have some downsides that need to be considered. One drawback of this test is that it also finds a lot of abnormalities that have to be checked out with more tests, but turn out not to be cancer. (About 1 out of 4 people in the NLST had such a finding.)

This may lead to additional tests such as other CT scans or more invasive tests such as needle biopsies or even surgery to remove a portion of lung in some people. These tests can sometimes lead to complications (like a collapsed lung) or rarely, death, even in people who do not have cancer (or who have very early stage cancer).

LDCTs also expose people to a small amount of radiation with each test. It is less than the dose from a standard CT, but it is more than the dose from a chest x-ray. Some people who are screened may end up needing further CT scans, which means more radiation exposure. When done in tens of thousands of people, this radiation may cause a few people to develop breast, lung, or thyroid cancers later on.

The NLST was a large study, but it left some questions that still need to be answered. For example, it's not clear if screening with LDCT scans would have the same effect on people different than those allowed in the study, such as those who smoke less (or not at all), or people younger than age 55 or older than 74. Also, in the NLST, patients got a total of 3 scans over 2 years. It's not yet clear what the effect would be if people were screened for longer than 2 years.

These factors, and others, need to be taken into account by people and their doctors who are considering whether or not screening with LDCT scans is right for them.

American Cancer Society's guidelines for lung cancer screening

The American Cancer Society has thoroughly reviewed the subject of lung cancer screening and issued guidelines that are aimed at doctors and other health care providers:

Patients should be asked about their smoking history. Patients who meet ALL of the following criteria may be candidates for lung cancer screening:

- 55 to 74 years old
- In fairly good health (discussed further down)
- Have at least a 30 pack-year smoking history (this was discussed above)
- Are either still smoking or have quit smoking within the last 15 years

These criteria were based on what was used in the NLST.

Doctors should talk to these patients about the benefits, limitations, and potential harms of lung cancer screening. Screening should only be done at facilities that have the right type of CT scan and that have a great deal of experience in LDCT scans for lung cancer screening. The facility should also have a team of specialists that can provide the appropriate care and follow-up of patients with abnormal results on the scans.

For patients

If you fit all of the criteria for lung cancer screening listed above, you and your doctor (or other health care provider) should talk about starting screening. He or she will talk to you about what you can expect from screening, including possible benefits and harms, as well as the limitations of screening.

The main benefit is a lower chance of dying of lung cancer, which accounts for many deaths in current and former smokers. Still, it is important to be aware that, like with any type of screening, not everyone who gets screened will benefit. Screening with LDCT will not find all lung cancers, and not all of the cancers that are found will be found early. Even if a cancer is found by screening, you may still die from lung cancer. Also, LDCT often finds things that turn out not to be cancer, but have to be checked out with more tests to know what they are. This can mean more CT scans, or even invasive tests such as a lung biopsy, in which a piece of lung tissue is removed with a needle or in surgery. These tests have risks of their own (see above).

At this time, government and private insurance programs are not likely to provide coverage for a LDCT done for lung cancer screening.

Screening should only be done at facilities that have the right type of CT scanner and that have experience in LDCT scans for lung cancer screening. The facility should also have a team of specialists that can provide the appropriate care and follow-up of patients with abnormal results on the scans. You might not have the right kind of facility nearby, so you may need to travel some distance to be screened.

If you and your doctor decide that you should be screened, you should get a LDCT every year until you reach the age of 74, as long as you remain in good health.

If you are a current smoker, you should receive counseling about stopping. You should be told about your risk of lung cancer and referred to a smoking cessation program. Screening is not a good alternative to stopping smoking. For help quitting smoking, see our document *Guide to Quitting Smoking* or call the American Cancer Society at 1-800-227-2345.

What does "in fairly good health" mean?

Screening is meant to find cancer in people who do not have symptoms of the disease. People who already have symptoms that might be caused by lung cancer may need tests such as CT scans to find the underlying cause, which in some cases may be cancer. But this kind of testing is for diagnosis and is not the same as screening. Some of the possible symptoms of lung cancer that kept people out of the NLST were coughing up blood and weight loss without trying.

To get the most potential benefit from screening, patients need to be in good health. For example, they need to be able to have surgery and other treatments to try to cure lung cancer if it is found. Patients who require home oxygen therapy most likely could not withstand having part of a lung removed, and so are not candidates for screening. Patients with other serious medical problems that would shorten their lives or keep them from having surgery may also not be able to benefit enough from screening for it to be worth the risks, and so should also not be screened.

Metal implants in the chest (like pacemakers) or back (like rods in the spine) can interfere with x-rays and lead to poor quality CT images of the lungs. People with these types of implants were also kept out of the NLST, and so should not be screened with CT scans for lung cancer according to the ACS guidelines.

People who have been treated for lung cancer often have follow-up tests, including CT scans to see if the cancer has come back or spread. This is called surveillance and is not the same as screening. (People with a prior history of lung cancer were not eligible for the NLST.)

TREATING LUNG CANCER - NON-SMALL CELL

How is non-small cell lung cancer treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Making treatment decisions for non-small cell lung cancer

After the cancer is found and staged, your cancer care team will discuss your treatment options with you. Depending on the stage of the disease and other factors, the main treatment options for people with non-small cell lung cancer (NSCLC) can include:

- Surgery
- Radiofrequency ablation (RFA)
- Radiation therapy
- Chemotherapy
- Targeted therapies
- Immunotherapy

Palliative procedures can also be used to help with symptoms.

In many cases, more than one of type of treatment is used.

You may have different types of doctors on your treatment team, depending on the stage of your cancer and your treatment options. These doctors may include:

- A thoracic surgeon: a doctor who treats diseases of the lungs and chest with surgery.
- A radiation oncologist: a doctor who treats cancer with radiation therapy.
- A medical oncologist: a doctor who treats cancer with medicines such as chemotherapy.
- A pulmonologist: a doctor who specializes in medical treatment of diseases of the lungs.

Many other specialists may be involved in your care as well, including physician assistants, nurse practitioners, nurses, respiratory therapists, social workers, and other health professionals.

It is important to discuss all of your treatment options as well as their possible side effects with your doctors to help make the decision that best fits your needs. (See the section "What should you ask your doctor about non-small cell lung cancer?") One of the most important factors in choosing a

treatment plan is the stage of the cancer, so be sure your doctor has ordered all the tests needed to determine the cancer's stage.

Other factors to consider include your overall health, the likely side effects of the treatment, and the probability of curing the disease, extending life, or relieving symptoms. Age alone is not a barrier to treatment. Older people can benefit from treatment as much as younger people, as long as they are in good health overall. Be sure that you understand the risks and side effects of the various treatments before making a decision.

If time permits, it is often a good idea to get a second opinion. This can provide you with more information and help you feel more confident about the treatment plan that you choose. Your doctor should be willing to help you find another cancer doctor who can give you a second opinion. If you have already had tests done, the results can be sent to the second doctor so that you will not have to have them done again.

The next few sections describe the various types of treatments used for non-small cell lung cancer. This is followed by a description of the most common approaches used for these cancers based on the stage of the cancer.

TALKING WITH YOUR DOCTOR

What should you ask your doctor about non-small cell lung cancer?

It is important for you to have honest, open discussions with your cancer care team. You should feel free to ask any question, no matter how small it might seem. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions. Here are some questions you might want to ask:

- What kind of lung cancer do I have?
- Where exactly is the cancer? Has it spread beyond where it started?
- What is the stage of my cancer, and what does that mean in my case?
- Are there other tests that need to be done before we can decide on treatment? Have the cancer cells been checked for gene changes that could affect my treatment options?
- Are there other doctors I need to see?
- How much experience do you have treating this type of cancer?
- What treatment choices do I have?
- What do you recommend and why?
- What is the goal of the treatment?
- What are the chances my cancer can be cured with these options?
- What risks or side effects are there to the treatments you suggest? How long are they likely to last?
- How quickly do we need to decide on treatment?

- What should I do to be ready for treatment?
- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect my daily activities?
- What would we do if the treatment doesn't work or if the cancer comes back?
- What type of follow-up will I need after treatment?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so you can plan your work or activity schedule. Or you may want to ask about getting a second opinion or about clinical trials for which you may qualify. You can find more information about communicating with your health care team in our document *Talking With Your Doctor*.

AFTER TREATMENT

What happens after treatment for non-small cell lung cancer?

For some people with lung cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer growing or coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are living full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this.

For some other people, the lung cancer may never go away completely. These people may get regular treatments with chemotherapy, radiation therapy, or other therapies to help keep the cancer in check. Learning to live with cancer as a more of a chronic disease can be difficult and very stressful. It has its own type of uncertainty. Our document called *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

If you have completed treatment, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask about any problems you may have and may do exams and lab tests or imaging tests (such as x-rays or CT scans).

In people with no signs of cancer remaining, many doctors recommend follow-up visits and CT scans about every 6 to 12 months for the first 2 years after treatment, and yearly visits and CT scans after this, although doctor visits might be more frequent at first.

Follow-up is needed to look for signs of cancer recurrence or spread, as well as possible side effects of certain treatments. This is a good time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can last the rest of your life. Be sure to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

It is important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

If cancer does recur, treatment will depend on where the cancer is and what treatments you've had before. Surgery,radiation therapy, chemotherapy, targeted therapy, or some combination of these might be options. Other types of treatment might also be used to help relieve any symptoms from the cancer. For more on how recurrent cancer is treated, see the section "Treatment choices by stage for non-small cell lung cancer." For more general information on dealing with a recurrence, you may also want to see our document *When Your Cancer Comes Back: Cancer Recurrence*.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you stayed in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had radiation therapy, a copy of the treatment summary
- If you had chemotherapy or targeted therapies, a list of the drugs, drug doses, and when you took them
- Copies of your x-rays, CT scans, and other imaging tests (these can often be stored digitally on a DVD, etc.)

WHAT`S NEW IN LUNG CANCER - NON-SMALL CELL RESEARCH?

What's new in non-small cell lung cancer research and treatment?

Research into the prevention, early detection, and treatment of lung cancer is being done in many medical centers throughout the world.

Prevention

Tobacco

Prevention offers the greatest opportunity to fight lung cancer. Although decades have passed since the link between smoking and lung cancers became clear, smoking is still responsible for at least 80% of lung cancer deaths. Research is continuing on:

- Ways to help people quit smoking and stay quit through counseling, nicotine replacement, and other medicines
- Ways to convince young people to never start smoking
- Inherited differences in genes that may make some people much more likely to get lung cancer if they smoke or are exposed to someone else's smoke

Environmental causes

Researchers also continue to look into some of the other causes of lung cancer, such as exposure to radon and diesel exhaust. Finding new ways to limit these exposures could potentially save many more lives.

Diet, nutrition, and medicines

Researchers are looking for ways to use vitamins or medicines to prevent lung cancer in people at high risk, but so far none have been shown to conclusively reduce risk.

Some studies have suggested that a diet high in fruits and vegetables may offer some protection, but more research is needed to confirm this. While any protective effect of fruits and vegetables on lung cancer risk is likely to be much less than the increased risk from smoking, following the American Cancer Society dietary recommendations (such as maintaining a healthy weight and eating a diet high in fruits and vegetables, and whole grains) may still be helpful.

Early detection

As mentioned in the section "Can non-small cell lung cancer be found early?", a large clinical trial called the National Lung Screening Trial (NLST) recently found that spiral CT scans in people at high risk of lung cancer (due to smoking history) lowers the risk of death from lung cancer, when compared to chest x-rays. This finding has led to the development of screening guidelines for lung cancer.

Another approach now being studied uses newer, more sensitive tests to look for cancer cells in sputum samples. Researchers have found several changes often seen in the DNA of lung cancer cells. Current studies are looking at new tests that can spot these DNA changes to see if this approach is useful in finding lung cancers at an earlier stage.

Diagnosis

Fluorescence bronchoscopy

Also known as *autofluorescence bronchoscopy*, this technique may help doctors find some lung cancers earlier, when they may be easier to treat. For this test, the doctor inserts a bronchoscope through the mouth or nose and into the lungs. The end of the bronchoscope has a special fluorescent light on it, instead of a normal (white) light.

The fluorescent light causes abnormal areas in the airways to show up in a different color than healthy parts of the airway. Some of these areas might not be visible under white light, so the color difference may help doctors find these areas sooner. Some cancer centers now use this technique to look for early lung cancers, especially if there are no obvious tumors seen with normal bronchoscopy.

Virtual bronchoscopy

This imaging test uses CT scans to create detailed 3-dimensional pictures of the airways in the lungs. The images can be viewed as if the doctor were actually using a bronchoscope.

Virtual bronchoscopy has some possible advantages over standard bronchoscopy. First, it is non-invasive and doesn't require anesthesia. It also helps doctors view some airways that might not be seen with standard bronchoscopy, such as those being blocked by a tumor. But it has some drawbacks as well. For example, it doesn't show color changes in the airways that might indicate a problem. It also doesn't let a doctor take samples of suspicious areas like bronchoscopy does. Still, it can be a useful tool in some situations, such as in people who might be too sick to get a standard bronchoscopy.

This test will likely become more available as the technology improves.

Electromagnetic navigation bronchoscopy

Lung tumors near the center of the chest can be biopsied during bronchoscopy, but bronchoscopes have trouble reaching the outer parts of the lungs, so tumors in that part of the lung often need to have a needle biopsy. This test can be a way to use a bronchoscope to biopsy a tumor in the outer part of the lung.

First, CT scans are used to create a virtual bronchoscopy. The abnormal area is identified, and a computer helps guide a bronchoscope to the area so that it can be biopsied. The bronchoscope used has some special attachments that allow it to reach further than a regular bronchoscope.

This takes extra equipment and training for the doctor, and is not widely available.

Treatment

Surgery

Doctors now use video-assisted thoracic surgery (VATS) to treat some small lung tumors. It lets doctors remove parts of the lung through smaller incisions, which can result in shorter hospital stays and less pain for patients. Doctors are now studying whether it can be used for larger lung tumors.

In a newer approach to this type of operation, the doctor sits at a specially designed control panel inside the operating room to maneuver long surgical instruments using robotic arms. This approach, known as *robotic-assisted surgery*, is now being tested in some larger cancer centers.

Real-time tumor imaging

Researchers are looking to use new imaging techniques, such as four-dimensional computed tomography (4DCT), to help improve treatment. In this technique, the CT machine scans the chest continuously for about 30 seconds. It shows where the tumor is in relation to other structures as a person breathes, as opposed to just giving a 'snapshot' of a point in time, like a standard CT does.

4DCT can be used to determine exactly where the tumor is during each part of the breathing cycle, which can help doctors deliver radiation to a tumor more precisely. This technique might also be used to help show if a tumor is attached to or invading important structures in the chest, which could help doctors determine if a patient might be eligible for surgery.

Chemotherapy

New combinations: Many clinical trials are looking at newer combinations of chemotherapy drugs to determine which are the safest and most effective. This is especially important in patients who are older and have other health problems. Doctors are also studying better ways to combine chemotherapy with radiation therapy and other treatments.

Lab tests to help predict if chemo will be helpful: Doctors know that adjuvant chemotherapy after surgery may be more helpful for some people with early (stage I or II) cancers than for others, but figuring out which patients to give it to is not easy. In early studies, newer lab tests that look at patterns of certain genes in the cancer cells have shown promise in telling which people might benefit most. Larger studies of these tests are now trying to confirm their usefulness.

Other lab tests may help predict whether a lung cancer will respond to particular chemo drugs. For example, studies have found that tumors with high levels of the ERCC1 protein are less likely to respond to chemo that includes cisplatin or carboplatin, while tumors with high levels of the RRM1 protein seem less likely to respond to chemo with gemcitabine. Doctors are now looking to see if tests for these markers can help guide the choice of treatment, so these are not a part of standard treatment.

Maintenance chemotherapy: For people with advanced lung cancers who can tolerate chemotherapy, combinations of 2 chemo drugs (sometimes along with a targeted drug) are typically given for about 4 to 6 cycles. Some recent studies have found that with cancers that have not progressed, continuing treatment beyond the 4 to 6 cycles with a single chemo drug such as pemetrexed or a targeted drug such as erlotinib may help some people live longer. This is known as *maintenance therapy*. A possible downside to this continued treatment is that people may not get a break from having side effects from chemotherapy. Some doctors now recommend maintenance therapy, while others await further research on this topic.

Targeted therapies

Researchers are learning more about the inner workings of lung cancer cells that control their growth and spread. This is being used to develop new targeted therapies. Some of these treatments, such as bevacizumab (Avastin), erlotinib (Tarceva), cetuximab (Erbitux), and crizotinib (Xalkori) are already being used to treat non-small cell lung cancer. Others are now being tested in clinical trials to see if they can help people with advanced lung cancer live longer or relieve their symptoms.

Other targeted drugs being studied include ganetespib, custirsen, and dacomitinib. Some targeted drugs already approved for use against other types of cancer, such as sorafenib (Nexavar) and sunitinib (Sutent), are also being tested for use against NSCLC.

Researchers are also working on lab tests to help predict which patients might be helped by which drugs. Studies have found that some patients do not benefit from certain targeted therapies, whereas others are more likely to have their tumors shrink. For example, a test can find changes in the *EGFR* gene that make it much more likely that a person's lung cancer will respond to treatment with erlotinib (Tarceva), an EGFR inhibitor. Similar gene tests for other treatments are now being studied. Predicting who might benefit could save some people from trying treatments that are unlikely to work for them and would probably cause unneeded side effects.

Immune treatments

Researchers are hoping to develop drugs that can help the body's immune system fight the cancer.

Drugs that block PD-1 and PD-L1: Cancer cells may use natural pathways in the body to help avoid detection and destruction by the immune system. For example, they often have a protein called PD-L1 on their surface that helps them evade the immune system. New drugs that block the PD-L1 protein, or the corresponding PD-1 protein on immune cells called T cells, can help the immune system recognize the cancer cells and attack them.

Nivolumab (Opdivo) is an anti-PD-1 drug that has been shown to shrink or slow the growth of some tumors. It is now approved for use in advanced squamous cell NSCLC.

Other, similar drugs such as pembrolizumab, MPDL3280A, and MEDI4736 can also to shrink tumors in patients with lung cancer. Larger studies of these new drugs are now being done.

Vaccines: Several types of vaccines for boosting the body's immune response against lung cancer cells are being tested in clinical trials. Unlike vaccines against infections like measles or mumps, these vaccines are designed to help treat, not prevent, lung cancer. These types of treatments seem to have very limited side effects, so they might be useful in people who can't tolerate other treatments.

Some vaccines are made up of lung cancer cells that have been grown in the lab, or even of cell components, such as parts of proteins commonly found on cancer cells. For example, the MUC1 protein is found on some lung cancer cells. A vaccine called TG4010 causes the immune system to react against that protein. A recent study compared combining the vaccine with chemotherapy to treatment with the same chemotherapy alone in patients with advanced lung cancer. The cancers in the group that got the vaccine were more likely to shrink or stop growing than the cancers in the group that just got chemo. More studies are planned to see if the vaccine will actually help patients live longer.

L-BLP25 (tecemotide) is another vaccine that targets the MUC1 protein. It is made up of the protein (MUC1) encased in a fat droplet (liposome) to try to make it more effective. A small study of patients with advanced NSCLC suggested it might improve survival time, although recent results from a larger study did not find it helped people live longer. This vaccine is now being studied for patients with stage III disease after treatment with chemotherapy and radiation, in efforts to improve the cure rate.

At this time, vaccines are only available in clinical trials.

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