SKIN CANCER: BASAL AND SQUAMOUS CELL

What is cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person’s DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

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.

Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

What are basal and squamous cell skin cancers?

In order to understand basal and squamous cell skin cancers, it helps to know about the normal structure and function of the skin.

About normal skin

The skin is the largest organ in your body. It does several different things:

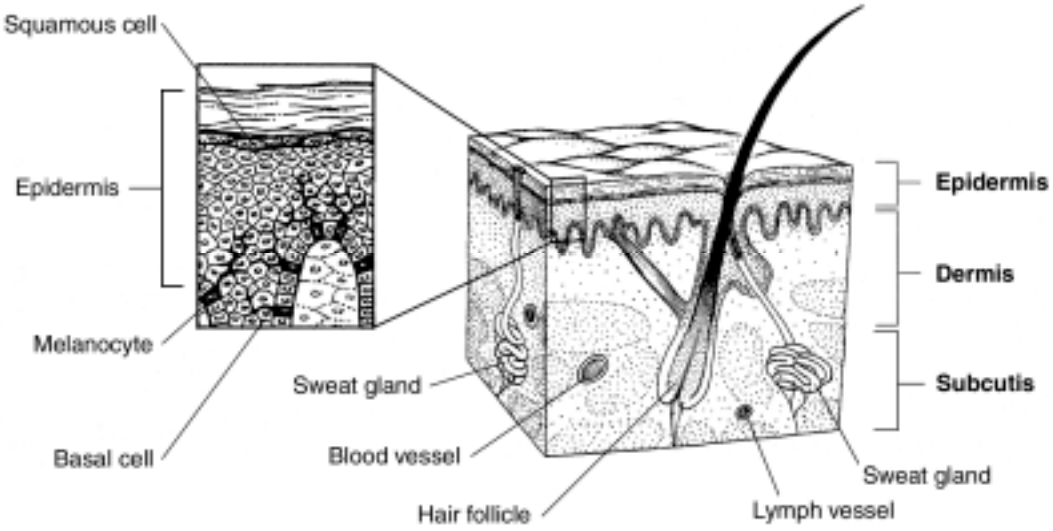
- covers the internal organs and protects them from injury
- serves as a barrier to germs such as bacteria
- prevents the loss of too much water and other fluids
- helps control body temperature

The skin has 3 layers (see picture below):

- epidermis
- dermis
- subcutis

Epidermis

The top layer of skin is the epidermis. The epidermis is thin, averaging only 0.2 millimeters (mm) thick (about 1/100 of an inch). It protects the deeper layers of skin and the organs of the body from the environment.



Keratinocytes are the main cell type of the epidermis. These cells make an important protein called keratin. Keratin contributes to the skin's ability to protect the rest of the body.

The outermost part of the epidermis is called the stratum corneum, or horny layer. It is composed of dead keratinocytes that are continually shed as new ones form. The cells in this layer are called *squamous cells* because of their flat shape.

Living squamous cells are found just below the stratum corneum. These have moved here from the lowest part of the epidermis, the basal layer. The cells of the basal layer, called *basal cells*, continually divide to form new keratinocytes. These replace the older keratinocytes that wear off the skin's surface.

Cells called *melanocytes* are also present in the epidermis. These skin cells make the protective brown pigment called melanin. Melanin is what makes the skin tan or brown. It is formed to protect the deeper layers of the skin from the harmful effects of the sun.

The epidermis is separated from the deeper layers of skin by the *basement membrane*. The basement membrane is an important structure because when a cancer becomes more advanced, it generally grows through this barrier.

Dermis

The middle layer of the skin is called the *dermis*. The dermis is much thicker than the epidermis. It contains hair follicles, sweat glands, blood vessels, and nerves that are held in

place by a protein called collagen. Collagen, made by cells called fibroblasts, gives the skin its resilience and strength.

Subcutis

The last and deepest layer of the skin is called the *subcutis*. The subcutis and the lowest part of the dermis form a network of collagen and fat cells. The subcutis conserves heat and has a shock-absorbing effect that helps protect the body's organs from injury.

Types of Skin Cancer

Melanomas

Cancers that develop from melanocytes, the pigment-making cells of the skin, are called melanomas. Melanocytes can also form benign growths called moles. Melanoma and moles are discussed in a separate American Cancer Society document, *Melanoma Skin Cancer*.

Skin cancers that are not melanoma are sometimes grouped together as *non-melanoma skin cancers* because they tend to act very differently from melanomas.

Keratinocyte Cancers

The second main type is called *keratinocyte carcinomas* or *keratinocyte cancers* because viewed under a microscope their cells share some features of keratinocytes, the most abundant cell type of normal skin. The most common types of keratinocyte cancer are basal cell carcinoma and squamous cell carcinoma.

Basal cell carcinoma: Viewed under a microscope, cells of these cancers share some features with the cells in the lowest layer of the epidermis, called the basal cell layer.

About 8 out of 10 skin cancers are basal cell carcinomas. They usually develop on sun-exposed areas, especially the head and neck. Basal cell carcinoma was once found almost exclusively in middle-aged or older people. Now it is also being seen in younger people, probably because they are spending more time in the sun with their skin exposed.

Basal cell carcinoma tends to be slow growing. It is very rare for a basal cell cancer to spread (metastasize) to nearby lymph nodes or to distant parts of the body. But if a basal cell cancer

is left untreated, it can grow into nearby areas and invade the bone or other tissues beneath the skin.

After treatment, basal cell carcinoma can recur (come back) in the same place on the skin. People who have had basal cell cancers are also more likely to get new ones elsewhere on the skin. As many as half of the people who are diagnosed with one basal cell cancer will develop a new skin cancer within 5 years.

Squamous cell carcinoma: Squamous cell carcinomas account for about 2 out of 10 skin cancers. They commonly appear on sun-exposed areas of the body such as the face, ear, neck, lip, and back of the hands. They can also develop in scars or skin ulcers elsewhere. They sometimes start in actinic keratoses (described below). Less often, they form in the skin of the genital area.

Squamous cell carcinomas tend to be more aggressive than basal cell cancers. They are more likely to invade fatty tissues just beneath the skin, and are more likely to spread to lymph nodes and/or distant parts of the body, although this is still uncommon.

Keratoacanthomas are growths that are found on sun-exposed skin. Although they may start out growing quickly, their growth usually slows down. Many keratoacanthomas shrink or even go away on their own over time without any treatment. But some continue to grow, and a few may even spread to other parts of the body. Because their growth is often hard to predict, many skin specialists think it is safest to consider them as a form of squamous cell skin cancer.

Less common types of skin cancer

Along with melanoma and keratinocyte cancers, there are some other types of skin cancer that are much less common. While these cancers are also "non-melanoma skin cancers," they are quite different from keratinocyte cancers and are treated differently, so it is useful to consider them separately.

Other non-melanoma skin cancers include:

- Merkel cell carcinoma
- Kaposi sarcoma
- cutaneous (skin) lymphoma
- skin adnexal tumors
- various types of sarcomas

Together, these types account for less than 1% of non-melanoma skin cancers.

Merkel cell carcinoma: This rare type of skin cancer develops from neuroendocrine cells (hormone-making cells that resemble nerve cells in some ways) in the skin. These cancers are thought to be caused in part by sun exposure. They are most often found on the head, neck, and arms but can start anywhere.

Treatment of Merkel cell carcinoma is described in the section "How are basal and squamous cell skin cancers treated?" Unlike basal cell and squamous cell carcinomas, Merkel cell carcinomas often come back after treatment and spread to nearby lymph nodes. They can also spread to internal organs, something that is quite uncommon for squamous cell carcinomas and even less common for basal cell carcinomas.

Kaposi sarcoma: This cancer usually starts within the dermis but can also form in internal organs. Before the mid-1980s, this cancer was rare and found mostly in elderly people of Mediterranean descent. Kaposi sarcoma has become more common because it is more likely to develop in people with human immunodeficiency virus (HIV) infection and the acquired immunodeficiency syndrome (AIDS). It is discussed in the separate American Cancer Society document, *Kaposi Sarcoma*.

Skin lymphomas: Lymphomas are cancers that start in *lymphocytes*, a type of immune system cell found in the bone marrow (the soft inner part of some bones), lymph nodes (bean-sized collections of immune system cells), the bloodstream, and some internal organs. The skin also contains a significant number of lymphocytes.

Although most lymphomas start in lymph nodes or internal organs, there are certain types of lymphoma that appear to begin mostly or entirely in the skin. *Primary cutaneous lymphoma* is the medical term meaning "a lymphoma that starts in the skin." The most common type of primary cutaneous lymphoma is *cutaneous T-cell lymphoma* (most of these are called *mycosis fungoides*). Cutaneous lymphomas are discussed in a separate American Cancer Society document, *Lymphoma of the Skin.*

Adnexal tumors: These tumors start in the hair follicles or glands (such as sweat glands) of the skin. Malignant (cancerous) adnexal tumors are extremely rare, but benign (non-cancerous) ones are common.

Sarcomas: These cancers develop from connective tissue cells, usually in tissues deep beneath the skin. Much less often they may develop in the skin's dermis and subcutis. There are several types of sarcoma that can develop in the skin, including *dermatofibrosarcoma protuberans* (DFSP) and *angiosarcoma* (a blood vessel cancer).

Benign skin tumors

Most tumors of the skin are not cancerous and rarely if ever turn into cancers. These tumors include the following:

- most types of moles (see the American Cancer Society document, *Melanoma Skin Cancer* for information on moles)
- seborrheic keratoses: tan, brown, or black raised spots with a "waxy" texture or rough surface
- hemangiomas: benign blood vessel growths often called strawberry spots or port wine stains
- lipomas: soft growths of benign fat cells
- warts: rough-surfaced growths caused by a virus

Pre-cancerous and pre-invasive skin conditions

These conditions may develop into skin cancer or may be very early stages in the development of skin cancer.

Actinic keratosis (solar keratosis)

Actinic keratosis, also known as solar keratosis, is a pre-cancerous skin condition caused by overexposure to the sun. Actinic keratoses are small (usually less than one-fourth inch across), rough spots that may be pink-red or flesh-colored. Usually they develop on the face, ears, back of the hands, and arms of middle-aged or older people with fair skin, although they can arise on other sun-exposed areas. People with one actinic keratosis usually develop many more.

Actinic keratoses are slow growing. They usually do not cause any symptoms. It is possible, but not common, for actinic keratoses to turn into squamous cell cancer. They often go away on their own, but they may come back.

Even though most actinic keratoses do not become cancers, they are a warning that your skin has suffered sun damage. Some actinic keratoses and other skin conditions that could become cancers may have to be removed. Your doctor should regularly check any that are not removed for changes that could indicate cancer.

Squamous cell carcinoma in situ (Bowen disease)

Squamous cell carcinoma in situ, also called Bowen disease, is the earliest form of squamous cell skin cancer. "In situ" means that the cells of these cancers are still entirely within the epidermis and have not invaded the dermis.

Bowen disease appears as reddish patches. Compared with actinic keratoses, Bowen disease patches tend to be larger (sometimes over one-half inch across), redder, scalier, and sometimes crusted.

Like invasive squamous cell skin cancers, the major risk factor is overexposure to the sun. Bowen disease of the anal and genital skin is often related to sexually transmitted infection with human papilloma viruses (HPVs), the viruses that can also cause genital warts.

What are the key statistics about basal and squamous cell skin cancers?

Cancer of the skin (including melanoma and basal and squamous cell skin cancers) is the most common of all types of cancer. It is thought to account for at least half of all cancers.

The number of people who develop basal and squamous cell skin cancers each year is not known for certain. Statistics of most other cancers are known because they are reported to cancer registries, but basal and squamous cell skin cancers are not reported. This means that all the numbers presented here are estimates.

There are more than 1 million basal and squamous cell skin cancers diagnosed each year. Most of these (about 800,000 to 900,000) are basal cell cancers. Squamous cell cancers occur less often -- perhaps about 200,000 to 300,000 per year.

The number of these cancers has been increasing for many years. This is probably due to a combination of increased detection, more sun exposure, and aging of the population.

Death from these cancers is uncommon. It is thought that about 2,000 people die each year from non-melanoma skin cancers. The death rate has dropped about 30% in the past 30 years. Most people who die are elderly. Other people more likely to die of skin cancer are those whose immune system is suppressed, such as those who have received organ transplants.

What are the risk factors for basal and squamous cell skin cancers?

A *risk factor* is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, unprotected exposure to strong sunlight is a risk factor for skin cancer, and smoking is a risk factor for cancers of the lung, mouth, throat, kidneys, bladder, and several other organs.

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 many people who get the disease may not have had any known risk factors. Even if a person with basal or squamous cell skin cancer has a risk factor, it is often very hard to know how much that risk factor may have contributed to the cancer.

The following are known risk factors for basal cell and squamous cell carcinomas (but do not apply to other forms of non-melanoma skin cancer such as Kaposi sarcoma and cutaneous lymphoma).

Ultraviolet (UV) light exposure

Ultraviolet (UV) radiation is thought to be the major risk factor for most skin cancers. Sunlight is the main source of UV radiation, which can damage the genes in your skin cells. Tanning lamps and booths are another source of UV radiation. People with excessive exposure to light from these sources are at greater risk for skin cancer.

The amount of UV exposure depends on the intensity of the radiation, length of time the skin was exposed, and whether the skin was protected with clothing and sunscreen. Many studies also point to exposure at a young age as an added risk factor.

Ultraviolet radiation is divided into 3 wavelength ranges:

- *UVA rays* are involved in the aging of cells and cause some damage to cells' DNA. They are mainly linked to long-term skin damage such as wrinkles, but are also thought to play a role in some skin cancers.

- *UVB rays* are mainly responsible for direct damage to the DNA, and are the rays that primarily cause sunburns. They are also thought to cause most skin cancers.

- *UVC rays* don't penetrate our atmosphere and therefore are not present in sunlight. They are not normally a risk factor for skin cancer.

While UVA and UVB rays make up only a very small portion of the sun's wavelengths, they are mainly responsible for the damaging effects of the sun on the skin. UVB radiation damages the DNA of skin cells. Skin cancers begin when this damage affects the DNA of genes that control skin cell growth. Recent research has found that UVA also contributes to skin cancer formation. Scientists now believe that both UVA and UVB rays damage skin and cause skin cancer. UVB rays are a more potent cause of at least some skin cancers, but there are *no* safe UV rays.

People who live in areas with year-round, bright sunlight have a higher risk. For example, the risk of skin cancer is twice as high in Arizona compared to Minnesota. The highest rate of

skin cancer in the world is in Australia. Spending a lot of time outdoors for work or recreation without protective clothing and sunscreen increases your risk.

Having fair skin

The risk of skin cancer is much higher for whites than for African Americans or Hispanics. This is due to the protective effect of melanin (skin pigment). Whites with fair (light-colored) skin that freckles or burns easily are at especially high risk. This is another reason for the high skin cancer rate in Australia, as the major settlers were fair-skinned immigrants from the British Isles.

Albinism is a congenital (present at birth) absence of skin pigment. People with this condition may have pink-white skin and white hair. They have a high risk of getting skin cancer unless they are careful to protect their skin.

Older age

The risk of basal and squamous cell skin cancers grows as people get older. This is likely due to the accumulation of sun exposure over time. Still, these cancers are now being seen in younger people as well, probably because they are spending more time in the sun with their skin exposed.

Male gender

Men are about 2 times as likely as women to have basal cell cancers and about 3 times as likely to have squamous cell cancers of the skin. This is thought to be due mainly to higher levels of sun exposure.

Exposure to certain chemicals

Exposure to large amounts of arsenic increases the risk of developing skin cancer. Arsenic is a heavy metal found naturally in well water in some areas. It is also used in making some pesticides and certain medicines. Workers exposed to industrial tar, coal, paraffin, and certain types of oil may also have an increased risk for non-melanoma skin cancer.

Radiation exposure

People who have had radiation treatment have a higher risk of developing skin cancer in the area that received the treatment. This is particularly a problem in children who have had cancer treatment. Almost all of these cancers are basal cell carcinomas.

Previous skin cancer

Anyone who has had a skin cancer has a much higher chance of developing another one.

Long-term or severe skin inflammation or injury

Scars from severe burns, areas of skin over severe bone infections, and skin damaged by some severe inflammatory skin diseases are more likely to develop keratinocyte skin cancers, although this risk is generally small.

Psoriasis treatment

Psoralen and ultraviolet light treatments (PUVA) given to some patients with psoriasis (a long-lasting inflammatory skin disease) can increase the risk of developing squamous cell skin cancer and probably other skin cancers also.

Xeroderma pigmentosum (XP)

This very rare inherited condition reduces the skin's ability to repair damage to DNA caused by sun exposure. People with this disorder often develop many skin cancers, sometimes starting in childhood.

Basal cell nevus syndrome

This rare congenital (present at birth) condition causes multiple basal cell cancers. Most, but not all, cases are inherited. Affected people may also have abnormalities of the jaw and other bones, eyes, and nervous tissue. One clue to having this syndrome in your family is if the affected person began developing basal cell cancers when he or she was young (for example, under age 20).

Reduced immunity

The immune system helps the body fight cancers of the skin and other organs. People with weakened immune systems (due to certain diseases or medical treatments) are more likely to develop non-melanoma skin cancer, particularly squamous cell cancer.

For example, organ transplant patients are usually given medicines that weaken their immune system to prevent their body from rejecting the new organ. This increases their risk of developing skin cancer. The rate of skin cancer in people who have had transplants can be as high as 80% within 20 years after the transplant. Skin cancers in people with weakened immune systems grow faster and are more likely to be fatal.

Treatment with corticosteroid drugs can also depress the immune system. This may also increase a person's risk of skin cancer.

Human papilloma virus (HPV) infection

Human papilloma viruses (HPVs) are a group of more than 100 viruses that can cause papillomas, or warts. The types of warts that people commonly get on their hands and feet appear to be unrelated to any form of cancer. But some of the HPV types that people get in their genital and anal area appear to be related to skin cancers in these areas.

Smoking

People who smoke are more likely to develop squamous cell skin cancer, especially on the lips. Smoking is not a risk factor for basal cell cancer.

Genetic susceptibility

Scientists have found that certain people are more likely to develop (susceptibility) skin cancer than others after sun exposure. In these people, the chromosomes are more sensitive to being damaged by sunlight.

Do we know what causes basal and squamous cell skin cancers?

Most basal cell and squamous cell skin cancers are caused by unprotected ultraviolet (UV) radiation exposure to the area of skin that develops the cancer. Most of this radiation comes from sunlight, but some may come from manmade sources such as tanning booths.

Some of this exposure may have occurred within the few years of the development of the cancer, particularly for squamous cell carcinoma. But many of the cases may be caused by exposures that happened many years earlier. Children and young adults often receive a lot of intense sun exposure that may not result in an actual cancer until many years or decades later. Repeated and unprotected sun exposure over many years increases the person's risk of skin cancer.

DNA is the genetic material in each of our cells. It passes along genetic information to the next generation that makes children resemble their parents. Along with information about how we look, DNA also contains information that tells the cells of our body how to grow and how to perform all the activities needed for life.

UV radiation (from sunlight or tanning lamps) damages DNA. Sometimes this damage affects certain genes (segments of DNA with a specific function) that control how and when cells grow and divide. Usually the body can repair the DNA damage. But if there is too much, in some situations, this results in the start of a cancer.

Researchers don't yet know all of the DNA changes that result in skin cancer, but they have found that many skin cancers contain changes in *tumor suppressor genes*. These genes normally function to help keep cells from growing out of control.

The gene most often found to be altered in squamous cell cancers is called *p53.* This gene normally causes damaged cells to die. When this gene is altered, these abnormal cells may live longer and perhaps go on to become cancerous.

A gene commonly found to be mutated in basal cell cancers is the "patched" (PTCH) gene. This tumor suppressor gene normally helps keep cell growth in check, so changes in this gene can allow cells to grow out of control.

These are not the only gene changes that may play a role in the development of skin cancer. There are likely to be many others as well.

People with xeroderma pigmentosum (XP) have a high risk for skin cancer. XP is a rare, inherited condition resulting from a defect in an enzyme that repairs damage to DNA. Because people with XP are less able to repair DNA damage caused by sunlight, they develop huge numbers of cancers on sun-exposed areas of their skin.

The link between squamous cell skin cancer and human papilloma virus (HPV) infection also involves DNA and genes. These viruses contain genes that instruct infected cells to make certain proteins that affect the growth-regulating proteins of normal skin cells. This can cause skin cells to grow too much and to not die when they're supposed to.

Scientists are studying other links between DNA changes and skin cancer. In the future, better understanding of how damaged DNA leads to skin cancer might be used to design treatments to overcome or repair that damage.

Can basal and squamous cell skin cancers be prevented?

While not all basal and squamous cell skin cancers can be prevented, there are ways to reduce your risk of getting skin cancer.

Limit ultraviolet (UV) exposure

The most important way to lower the risk of basal and squamous cell skin cancers is to limit your exposure to ultraviolet (UV) radiation. Practice sun safety when you are outdoors. "Slip! Slop! Slap! … and Wrap" is a catch phrase that reminds people of the 4 key methods they can use to protect themselves from UV radiation. Slip on a shirt, slop on sunscreen, slap on a hat, and wrap on sunglasses to protect the eyes and sensitive skin around them from ultraviolet light.

Protect your skin with clothing

Clothes provide different levels of protection, depending on many factors. Long-sleeved shirts, long pants, or long skirts are the most protective. Dark colors generally provide more protection than light colors. A tightly woven fabric protects better than loosely woven clothing. Dry fabric is generally more protective than wet fabric.

Be aware that covering up doesn't block out all UV rays. A typical light T-shirt worn in the summer usually provides less protection than a sunscreen with a sun protection factor (SPF) of 15 or higher.

A few companies in the United States now make clothing that is lightweight, comfortable, and protects against UV exposure even when wet. Some sun-protective clothes have a label listing the ultraviolet protection factor (UPF) value -- the level of protection the garment provides from the sun's UV rays (on a scale from 15 to 50+). The higher the UPF, the higher the protection from UV rays.

Newer products are also available to increase the UPF value of clothes you already own. Used like laundry detergents, they add a layer of UV protection to your clothes without changing the color or texture.

Wear a hat

A hat with at least a 2- to 3-inch brim all around is ideal because it protects areas often exposed to the sun, such as the neck, ears, eyes, forehead, nose, and scalp. A shade cap (which looks like a baseball cap with about 7 inches of fabric draping down the sides and back) also is good. These are often sold in sports and outdoor supply stores.

A baseball cap can protect the front and top of the head but not the neck or the ears, where skin cancers commonly develop. Straw hats are not recommended unless they are tightly woven.

Use sunscreen

The American Cancer Society recommends using sunscreen as part of a sun protection program.

Use sunscreens and lip balms with an SPF factor of 15 or more on areas of skin exposed to the sun, especially when the sunlight is strong (for example, in hot or high-altitude locations or between the hours of 10 am and 4 pm). Use sunscreen even on hazy days or days with light or broken cloud cover because the UV light still comes through.

Always follow directions when applying sunscreen. For it to work best, sunscreen should be applied about 20 to 30 minutes before you go outside. A 1-ounce application (a palmful of sunscreen) is recommended to cover the arms, legs, neck, and face of the average adult. Protection is greatest when sunscreen is used thickly on all sun-exposed skin. To ensure continued protection, many sunscreens should be reapplied at least every 2 hours. Many sunscreens wash off when you sweat or swim and must be reapplied for maximum effectiveness. And don't forget your lips; lip balm with sunscreen is also available.

Some people use sunscreens in order to stay out in the sun longer without getting sunburned. Sunscreen should not be used to gain extra time in the sun, as you will still end up with damage to your skin.

Sunscreen may reduce your chance of skin cancer, particularly actinic keratoses and squamous cell cancer. But there is no guarantee, and if you stay in the sun a long time, you

are at risk of developing skin cancer even if you have applied sunscreen. It is not clear whether sunscreen can help prevent basal cell cancers.

If you want a tan, try using a "sunless" tanning lotion. These can provide the look, without the danger. Sunless tanning lotions contain a substance called dihydroxyacetone (DHA). DHA works by interacting with proteins on the surface of the skin to produce color. You do not have to go out in the sun for these to work. The color tends to wear off after a few days.

Wear sunglasses

Wrap-around sunglasses with at least 99% UV absorption provide the best protection for the eyes and the skin area around the eyes. Look for sunglasses labeled as blocking UVA and UVB light. Labels that say "UV absorption up to 400 nm" or "Meets ANSI UV Requirements" mean the glasses block at least 99% of UV rays. It there is no label, don't assume the sunglasses provide any protection.

Seek shade

Another way to limit exposure to UV light is to avoid being outdoors in sunlight too long. This is particularly important in the middle of the day between the hours of 10 am and 4 pm, when UV light is strongest. If you are unsure about the sun's intensity, take the shadow test: If your shadow is shorter than you, the sun's rays are the strongest. Plan activities out of the sun during these times. If you must be outdoors, protect your skin. Keep in mind that sunlight (and UV rays) can come through clouds, can reflect off water, sand, concrete, and snow, and can reach below the water's surface.

The UV Index: The amount of UV light reaching the ground in any given place depends on a number of factors, including the time of day, time of year, elevation, and cloud cover. To help people better understand the intensity of UV light in their area on a given day, the National Weather Service and the US Environmental Protection Agency have developed the UV Index. It gives people an idea of how strong the UV light is in their area, on a scale from 1 to 11+. A higher number means a higher chance of sunburn, skin damage and ultimately skin cancers of all kinds. Your local UV Index should be available daily in your local newspaper, on TV weather reports, and online (www.epa.gov/sunwise/uvindex.html).

Protect children from the sun

Children require special attention, since they tend to spend more time outdoors and can burn more easily. Parents and other caregivers should protect children from excess sun exposure

by using the measures described above. Older children need to be cautioned about sun exposure as they become more independent. It is important, particularly in parts of the world where it is sunnier, to cover your children as fully as is reasonable. You should develop the habit of using sunscreen on exposed skin for yourself and your children whenever you go outdoors and may be exposed to large amounts of sunlight.

A word about sun exposure and vitamin D

Doctors are learning that vitamin D has many health benefits. It may even help to lower the risk for some cancers. Vitamin D is made naturally by your skin when you are in the sun. How much vitamin D is made depends on many things, including how old you are, how dark your skin is, and how intensely the sun shines where you live. At this time, doctors aren't sure what the optimal level of vitamin D is, or how best to balance the possible benefits of getting vitamin D from sunlight versus the possible risks of skin cancer. This is an area of very active research. If you have darker skin or live in an area with little daily sunlight, many experts at this time recommend taking vitamin D by mouth, such as in supplements or certain foods. For example, most milk has vitamin D added.

For more information on how to protect yourself and your family from UV exposure, see the American Cancer Society Document, *Skin Cancer Prevention and Early Detection.*

Avoid harmful chemicals

Exposure to certain chemicals, such as arsenic, can increase a person's risk of skin cancer. People can be exposed to arsenic from well water in some areas, pesticides and herbicides, some medicines (such as arsenic trioxide) and herbal remedies (arsenic has been found in some traditional herbal remedies imported from China), and in certain occupations (such as mining and smelting). High exposure to arsenic should be avoided.

Learn more about skin cancer prevention

Many organizations conduct skin cancer prevention activities in schools and recreational areas. Others develop brochures and public service announcements. For more information, refer to the "Additional resources" section of this document.

Can basal and squamous cell skin cancers be found early?

Basal cell and squamous cell skin cancers can be found early. As part of a routine cancer-related checkup, your health care professional should check your skin carefully. He or she should be willing to discuss any doubts or concerns you might have about this exam.

You can also play an important role in finding skin cancer early. It's important to check your own skin, preferably once a month. Learn the pattern of moles, blemishes, freckles, and other marks on your skin so that you'll notice any changes. Self-examination is best done in a well-lit room in front of a full-length mirror. A hand-held mirror can be used for areas that are hard to see.

All areas should be examined, including your palms and soles, scalp, ears, nails, and your back. (For a more thorough description of a skin self-exam, see the American Cancer Society documents, *Skin Cancer Prevention and Early Detection* and *Why You Should Know About Melanoma*.) Friends and family members can also help you with these exams, especially for those hard-to-see areas, such as the lower back or the back of your thighs. Be sure to show your doctor any area that concerns you.

Basal cell and squamous cell skin cancers can look like a variety of marks on the skin. The key warning signs are a new growth, a spot or bump that's getting larger (over a few months or 1 to 2 years), or a sore that doesn't heal within 3 months. (See the next section, "How are basal and squamous cell skin cancers diagnosed?" for a more detailed description of what to look for.)

How are basal and squamous cell skin cancers diagnosed?

If an abnormal area of skin raises the possibility of skin cancer, certain medical exams and tests such as a biopsy may be used to find out if it is cancer or some other skin condition. If there is a chance the skin cancer may have spread to other areas of the body, other tests may be done as well.

Signs and symptoms of basal and squamous cell skin cancers

Skin cancers rarely cause bothersome symptoms until they become quite large. Then they may bleed or even hurt.

Basal cell carcinomas often appear as flat, firm, pale areas or small, raised, pink or red, translucent, shiny, waxy areas that may bleed after a minor injury. They may have one or more visible abnormal blood vessels, a depressed area in their center, and/or blue, brown, or black areas. Large basal cell carcinomas may have oozing or crusted areas.

Squamous cell carcinomas may appear as growing lumps, often with a rough surface, or as flat reddish patches in the skin that grow slowly.

Both of these types of non-melanoma skin cancer may develop as a flat area showing only slight changes from normal skin.

There are skin cancers other than melanoma, basal cell carcinoma, and squamous cell carcinoma. Although they are much less common, they include the following:

- *Kaposi sarcoma* generally starts as small bruise-like areas that develop into tumors.
- *Mycosis fungoides* (a type of lymphoma that starts in the skin) usually begins as a rash, often on the buttocks, hips, or lower abdomen. It can look similar to skin allergies and other types of skin irritations.
- *Adnexal tumors* appear as bumps within the skin.
- *Skin sarcomas* appear as large masses under the skin surface.
- *Merkel cell tumors* are usually firm, pink, red, or purple nodules or ulcers (sores) found on the face or, less often, the arms or legs.

If your doctor suspects you might have skin cancer, he or she will use one or more of the following methods to find out if the disease is really present.

History and physical exam

Usually the first step is to take your medical history (asking questions about symptoms and risk factors). The doctor probably will ask your age, when the mark on the skin first appeared, and whether it has changed in size or appearance. You may also be asked about past exposures to known causes of skin cancer and whether you or anyone in your family has had skin cancer.

During the physical exam, the doctor will note the size, shape, color, and texture of the area(s) in question, and whether there is bleeding or scaling. The rest of your body may be checked for spots and moles that may be related to skin cancer.

The doctor may also check nearby lymph nodes, which are bean-sized collections of immune system cells that fight infections that can be felt under the skin in certain areas. Some skin cancers may spread to lymph nodes. When such spread occurs, the lymph nodes may become larger and firmer than usual.

If you are being seen by your primary doctor and skin cancer is suspected, you may be referred to a dermatologist (a doctor who specializes in diagnosing and treating skin diseases), who will look at the area more closely.

Along with a standard physical exam, some dermatologists use a technique called *dermatoscopy* (also called epiluminescence microscopy [ELM] or surface microscopy) to see spots on the skin more clearly. This involves the use of a dermatoscope, which is a special magnifying lens and light source held near the skin. Sometimes a thin layer of oil is used with this instrument. A photographic image of the spot may be taken.

When used by an experienced dermatologist, this test can improve the accuracy of finding skin cancers early. It can also often reassure you that a lesion is benign (non-cancerous) without the need for a biopsy.

Skin biopsy

If the doctor thinks that an area might be skin cancer, he or she will take a sample of skin from the suspicious area to look at under a microscope. This is called a *skin biopsy*. Different methods can be used for a skin biopsy. The choice depends on the suspected type of skin cancer, where it is on the body, and the size of the affected area. Any biopsy is likely to leave a scar. Since different methods produce different scars, you should ask the doctor about biopsies and scarring before the biopsy is done.

Shave biopsy

A shave biopsy is one way to take a skin biopsy. After numbing the area with a local anesthetic, the doctor "shaves" off the top layers of the skin (the epidermis and the most superficial part of the dermis) with a surgical blade.

Punch biopsy

A punch biopsy removes a deeper sample of skin. The doctor uses a punch biopsy tool that looks like a tiny round cookie cutter. Once the skin is numbed with a local anesthetic, the doctor rotates the punch biopsy tool on the surface of the skin until it cuts through all the layers of the skin, including the dermis, epidermis, and the upper parts of the subcutis.

Incisional and excisional biopsies

If the doctor has to examine a tumor that may have grown into deeper layers of the skin, he or she will use an incisional or excisional biopsy technique. Incisional biopsy involves removing only a portion of the tumor. Removal of the entire tumor is called an excisional

biopsy. A surgical knife is used to cut through the full thickness of skin. A wedge or ellipse of skin is removed for further examination, and the edges of the wound are sewn together. Both of these types of biopsies can be done using local anesthesia.

Examining the biopsy samples

All skin biopsy samples are looked at under a microscope. The skin sample is sent to a *pathologist*, a doctor who has been specially trained in the microscopic examination and diagnosis of tissue samples. Often, the sample is sent to a *dermatopathologist*, a doctor who has special training in making diagnoses from skin samples.

Lymph node biopsy

If your doctor feels lymph nodes that are too large and/or too firm, a lymph node biopsy may be done to determine whether cancer has spread from the skin to the lymph nodes.

Fine needle aspiration biopsy

A fine needle aspiration (FNA) biopsy uses a syringe with a thin needle to remove very small tissue fragments from a tumor. The needle is smaller than the needle used for a blood test. A local anesthetic is sometimes used to numb the area. This test rarely causes much discomfort and does not leave a scar. An FNA biopsy is not used to diagnose a suspicious skin tumor, but it may be used to biopsy large lymph nodes near a skin cancer to find out if the cancer has spread to them.

Surgical (excisional) lymph node biopsy

If the doctor suspects spread of cancer to a lymph node but the FNA result is negative or is not clear, the lymph node should be removed by surgery and examined. This can often be done using local anesthesia in a doctor's office or outpatient surgical center and will leave a small scar.

How are basal and squamous cell skin cancers staged?

Staging is a process of finding out how widespread a cancer is. Because basal cell cancer so rarely spreads to other organs, it is seldom staged unless the cancer is very large. Squamous cell cancers have a somewhat greater (although still quite small) risk of spreading, so staging may sometimes be done, particularly in people who have a high risk of spread. This includes people with suppressed immune systems, such as those who have had organ transplants and people infected with HIV, the virus that causes AIDS.

The tests and exams described in the section, "How are basal and squamous cell skin cancers diagnosed?" are the ones used to help determine the stage of the cancer.

A staging system is a way to summarize how far a cancer has spread. This helps members of the cancer care team to plan appropriate treatment and determine a patient's prognosis (outlook).

The American Joint Committee on Cancer (AJCC) TNM System

The system most often used to stage keratinocyte cancers (especially squamous cell skin cancer) is the American Joint Commission on Cancer (AJCC) TNM system. Physical exams and other tests may be used to assign T, N, and M categories and a grouped stage. The TNM system for staging contains 3 key pieces of information:

- T stands for **t**umor (its size and how far it has spread within the skin and to nearby tissues).
- N stands for spread to nearby lymph **n**odes (small bean-shaped collections of immune system cells that help the body fight infections and cancers).
- M is for **m**etastasis (spread to distant organs).

The possible values for T are:

TX: Primary tumor cannot be assessed
T0: No evidence of primary tumor
Tis: Carcinoma in situ (tumor is still confined to the epidermis)
T1: The tumor is 2 centimeters (cm) across (about 4/5 inch) or smaller
T2: Tumor is larger than 2 cm across but smaller than 5 cm (about 2 inches)
T3: Tumor is larger than 5 cm across
T4: Tumor of any size that invades deeply into muscle, cartilage, or bone

The possible values for N are:

NX: Nearby lymph nodes cannot be assessed
N0: No spread to nearby lymph nodes
N1: Spread to nearby lymph nodes

The M values are:

MX: Presence of distant metastasis cannot be assessed
M0: No distant metastasis
M1: Distant metastasis is present

To assign a stage, information about the tumor and whether it has spread to lymph nodes and other organs in the body is combined in a process called *stage grouping*. The stages are described using the number 0 and Roman numerals from I to IV. In general, patients with lower stage cancers tend to have a better prognosis for a cure or long-term survival.

Stage 0
Tis, N0, M0: Squamous cell carcinoma in situ, also called Bowen disease, is the earliest stage of squamous cell skin carcinoma. The cancer involves only the epidermis and has not spread to the dermis. In contrast, higher stage cancers involve both the epidermis and dermis.

Stage I
T1, N0, M0: The cancer is no larger than 2 centimeters across (about 4/5 inch). It does not invade deeply into muscle, cartilage, or bone and has not spread to nearby lymph nodes or other organs.

Stage II
T2 or 3, N0, M0: The cancer is larger than 2 cm across. It does not invade deeply into muscle, cartilage, or bone and has not spread to nearby lymph nodes or other organs.

Stage III
T4, N0, M0 or Any T, N1, M0: The cancer has grown into tissues beneath the skin (such as muscle, bone, or cartilage) and/or it has spread to nearby lymph nodes. The cancer has not spread to other organs such as the lungs or brain.

Stage IV
Any T, Any N, M1: The cancer can be any size and may or may not have spread to local lymph nodes. It has spread to other organs such as the lungs or brain.

How are basal and squamous cell skin cancers 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.

The treatments described in this section apply to actinic keratosis, squamous cell carcinoma, basal cell carcinoma, and Merkel cell carcinoma. Lymphoma of the skin, Kaposi sarcoma, and other sarcomas are treated differently and are discussed in separate American Cancer Society documents.

This section starts with general comments about the types of treatments used for non-melanoma skin cancers. This is followed by a discussion of the typical treatment options based on the type of skin cancer.

Surgery

Fortunately, most basal cell and squamous cell carcinomas can often be completely cured by fairly minor surgery and sometimes by applying medicines to the skin surface. There are many different kinds of surgery for these cancers. The type of treatment chosen depends on how large the cancer is, where it is found on the body, and the specific type of skin cancer. For certain squamous cell cancers with a high risk of spreading, surgery may sometimes be followed by radiation or chemotherapy.

Simple excision

This is similar to an excisional biopsy, although in this case the diagnosis is already known. For this procedure, the skin is first numbed with a local anesthetic. The tumor is then cut out with a surgical knife, along with some surrounding normal skin. The remaining skin is carefully stitched back together, leaving a small scar.

Curettage and electrodesiccation

This treatment removes the cancer by scraping it with a curette (a long, thin instrument with a scraping edge on one end), then treating the area where the tumor was located with an electric needle (electrode) to destroy any remaining cancer cells. This process is often repeated. Curettage and electrodesiccation is a good treatment for small basal cell and squamous cell cancers. It will leave a scar.

Mohs surgery (microscopically-controlled surgery)

Using the Mohs technique, the surgeon removes a thin layer of the skin that the tumor may have invaded and then checks the sample under a microscope. If cancer cells are seen, deeper layers are removed and examined until the skin samples are found to be free of cancer cells. This process is slow, but it means that more normal skin near the tumor can be saved. This creates a better appearance after surgery. This is a highly specialized technique that should be used only by doctors who have been trained in this specific type of surgery.

Lymph node surgery

If lymph nodes near a non-melanoma skin cancer (especially a squamous cell or Merkel cell carcinoma) are growing larger, doctors will be concerned that the cancer may have spread to these lymph nodes. The nodes may be biopsied (see the section, "How are basal and squamous cell skin cancers diagnosed?") or removed by an operation called a *lymph node dissection* and looked at under a microscope for signs of cancer. This operation is more involved than surgery on the skin, and usually requires general anesthesia (where you are asleep).

Lymphedema, a complication where excess fluid collects in the legs or arms, is a possible long-term side effect of a lymph node dissection. Lymph nodes in the groin or under the arm normally help drain fluid from the legs and arms. If the lymph nodes are removed, fluid may build up, leading to swelling in these limbs. Elastic stockings or compression sleeves can help some people with this condition. For more information, see the separate American Cancer Society document, *Understanding Lymphedema (For Cancers Other Than Breast Cancer)*.

Skin grafting and reconstructive surgery

After removing large non-melanoma skin cancers, it may not be possible to stretch the nearby skin enough to sew the edges of the wound together. In these cases, skin grafts or

other reconstructive surgical procedures can help the wound heal and replace tissue, restoring the appearance of the affected area.

Other forms of local therapy

Several other techniques can be used to treat basal and squamous cell skin cancers that have not spread to lymph nodes or other parts of the body. Some of these treatments are described as types of "surgery" since they destroy a targeted area of body tissue. But these techniques don't involve using scalpels or cutting into the skin.

Cryosurgery (cryotherapy)

This treatment involves applying liquid nitrogen to the tumor to freeze and kill abnormal cells. After the dead tissue thaws, blistering and crusting may occur. The wound may take a month or 2 to heal and will leave a scar. The treated area may have less color after treatment. Cryosurgery is often used for pre-cancerous conditions such as actinic keratosis and for small basal cell and squamous cell carcinomas.

Photodynamic therapy (PDT)

This treatment involves giving patients a chemical (either by applying it to the skin or injecting it into the blood) that collects in the tumor cells over the course of several hours or days and makes the cells sensitive to certain types/colors of light. A light source is then focused on the tumor(s), which causes the cells to die. A possible side effect of PDT is that it can make a person's skin very sensitive to sunlight for a period of time, so precautions may need to be taken to avoid severe burns.

PDT can be used to treat actinic keratoses. But its exact role in treating non-melanoma skin cancers, if any, remains to be established.

Topical chemotherapy

Chemotherapy uses drugs that kill cancer cells. Topical chemotherapy means that an anti-cancer medicine is placed directly on the skin (usually in a cream or ointment) rather than being given by mouth or injected into a vein. The drug most often used in topical treatment of basal and squamous cell skin cancers is 5-fluorouracil (5-FU).

When applied directly on the skin in the form of a cream, 5-FU reaches cancer cells near the skin surface, but it does not reach cancer cells that have invaded deeply into the skin or spread to other organs. For this reason, treatment with 5-FU generally is used only for pre-cancerous conditions such as actinic keratosis and for some very superficial skin cancers.

Because it is only applied to the skin, the drug does not spread throughout the body, so it doesn't cause the same side effects that can occur with systemic chemotherapy (treatment that affects the whole body). But it can cause the treated skin to be red and sensitive for a few weeks, which can be quite bothersome for some people. Other topical medicines can be used to help relieve these side effects. Fluorouracil also increases the skin's sensitivity to sunlight, so treated areas must be protected from the sun to prevent sunburn for a few weeks after use of this cream.

A gel containing the drug diclofenac is sometimes used to treat actinic keratoses. This drug belongs to the non-steroidal anti-inflammatory drugs (NSAIDs), a group that includes pain relievers such as aspirin and ibuprofen.

Immune response modifiers

Certain drugs can cause an immune response to the cancer, causing it to regress, or get smaller and go away.

Imiquimod is a cream that can be applied to actinic keratoses and some basal cell cancers. It is not a chemotherapy drug. Instead, it causes the body's immune system to react to the skin lesion and cause its destruction.

Interferon is a manmade version of an immune system protein. It can be injected directly into the tumor to boost the body's immune response against it. It may be used when surgery is not possible, but it may not be as effective as other treatments.

Laser surgery

This relatively new approach uses a beam of laser light to vaporize cancer cells. It is sometimes used for squamous cell carcinoma in situ (involving only the epidermis) and for very superficial basal cell carcinomas (those located near the surface of the skin). It is not yet known if this type of treatment is as effective as standard methods of treatment, and it is not widely used.

Radiation therapy

Radiation therapy uses high-energy rays (such as x-rays) and particles (such as photons, electrons, or protons) to kill cancer cells. External beam radiation therapy focuses radiation from outside the body on the skin tumor.

If a tumor is very large or is located on an area of the skin that makes surgery difficult, radiation may be used as the primary (main) treatment instead of surgery. Primary radiation therapy is often useful for some elderly patients who, because of poor general health, cannot tolerate surgery. Radiation therapy can cure small non-melanoma skin cancers and can delay the growth of more advanced cancers. Radiation is also useful in combination with other therapies. It is particularly useful for Merkel cell carcinoma.

In some cases, radiation can be used after surgery as adjuvant (additional) therapy to kill any small deposits of remaining cancer cells that may not have been visible during surgery. This lowers the risk of cancer coming back after surgery. Radiation may also be used to help treat non-melanoma skin cancer that has spread to lymph nodes or other organs.

Side effects of radiation include skin irritation, redness, and drying. With longer treatments, these side effects may get worse. After many years, new skin cancers sometimes arise in areas previously treated by radiation. For this reason, radiation usually is not used to treat skin cancer in young people. Radiation is also not recommended for people with certain inherited conditions (such as basal cell nevus syndrome) because they may be more at risk to the cancer-causing effect of radiation.

Systemic chemotherapy

Systemic chemotherapy uses anti-cancer drugs that are injected into a vein or given by mouth. These drugs travel through the bloodstream to all parts of the body. In contrast to topical chemotherapy, systemic chemotherapy can attack cancer cells that have spread to lymph nodes and other organs.

One or more chemotherapy drugs may be used to treat squamous cell carcinoma or Merkel cell carcinoma that has spread to other organs. Chemotherapy drugs such as cisplatin, doxorubicin, fluorouracil (5-FU), and mitomycin are given intravenously, usually once every few weeks. They can often delay the spread of these cancers and relieve some symptoms. In some cases, they may shrink tumors enough so that other treatments such as surgery or radiation therapy may be used.

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are taken. These side effects may include:

- hair loss
- mouth sores
- loss of appetite
- nausea and vomiting
- lowered resistance to infection (due to low white blood cell counts)
- easy bruising or bleeding (due to low blood platelets)
- fatigue (due to low red blood cells)

These side effects are usually short-term and go away once treatment is finished.

Be sure to talk with your cancer care team about any side effects you have because there are often ways to lessen them. For example, drugs can be given to help prevent or reduce nausea and vomiting.

Clinical trials

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is deciding which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you. Clinical trials are one way to get state-of-the art cancer care. Still, they are not right for everyone.

Here we will give you a brief review of clinical trials. Talking to your health care team, your family, and your friends can help you make the best treatment choice for you.

What are clinical trials?

Clinical trials are carefully controlled research studies that are done with patients. These studies test whether a new treatment is safe and how well it works in patients, or they may test new ways to diagnose or prevent a disease. Clinical trials have led to many advances in cancer prevention, diagnosis, and treatment.

The purpose of clinical trials

Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only done when there is good reason to believe that the treatment,

test, or procedure being studied may be better than the one used now. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment.

Clinical trials can focus on many things, such as:

- new uses of drugs that are already approved by the US Food and Drug Administration (FDA)
- new drugs that have not yet been approved by the FDA
- non-drug treatments (such as radiation therapy)
- medical procedures (such as types of surgery)
- herbs and vitamins
- tools to improve the ways medicines or diagnostic tests are used
- medicines or procedures to relieve symptoms or improve comfort
- combinations of treatments and procedures

Researchers conduct studies of new treatments to try to answer the following questions:

- Is the treatment helpful?
- What's the best way to give it?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are there more or fewer side effects than the standard treatment used now?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Phases of clinical trials

There are 4 phases of clinical trials, which are numbered I, II, III, and IV. We will use the example of testing a new cancer treatment drug to look at what each phase is like.

Phase I clinical trials: The purpose of a phase I study is to find the best way to give a new treatment safely to patients. The cancer care team closely watches patients for any harmful side effects.

For phase I studies, the drug has already been tested in lab and animal studies, but the side effects in patients are not fully known. Doctors start by giving very low doses of the drug to the first patients and increase the doses for later groups of patients until side effects appear or the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase I clinical trials are often done in small groups of people with different cancers that have not responded to standard treatment, or that keep coming back (recurring) after treatment. If a drug is found to be reasonably safe in phase I studies, it can be tested in a phase II clinical trial.

Phase II clinical trials: These studies are designed to see if the drug works. Patients are given the best dose as determined from phase I studies. They are closely watched for an effect on the cancer. The cancer care team also looks for side effects.

Phase II trials are often done in larger groups of patients with a specific cancer type that has not responded to standard treatment. If a drug is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

Phase III clinical trials: Phase III studies involve large numbers of patients -- most often those who have just been diagnosed with a specific type of cancer. Phase III clinical trials may enroll thousands of patients.

Often, these studies are randomized. This means that patients are randomly put in one of two (or more) groups. One group (called the control group) gets the standard, most accepted treatment. Another group (or more than one group) gets the new treatment being studied. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others.

Phase III clinical trials are usually needed before the FDA will approve a treatment for use by the general public.

Phase IV clinical trials: Once a drug has been approved by the FDA and is available for all patients, it is still studied in other clinical trials (sometimes referred to as phase IV studies). This way more can be learned about short-term and long-term side effects and safety as the drug is used in larger numbers of patients with many types of diseases. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways (such as in combination with other treatments).

What it will be like to be in a clinical trial

If you are in a clinical trial, you will have a team of experts taking care of you and watching your progress very carefully. Depending on the phase of the clinical trial, you may receive more attention (such as having more doctor visits and lab tests) than you would if you were treated outside of a clinical trial. Clinical trials are specially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects go away in time, some may be long-lasting or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enter (enroll in) a clinical trial.

Deciding to enter a clinical trial

If you would like to take part in a clinical trial, you should begin by asking your doctor if your clinic or hospital conducts clinical trials. There are requirements you must meet to take part in any clinical trial. But whether or not you enter (enroll in) a clinical trial is completely up to you.

Your doctors and nurses will explain the study to you in detail. They will go over the possible risks and benefits and give you a form to read and sign. The form says that you understand the clinical trial and want to take part in it. This process is known as giving your informed consent. Even after reading and signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason. Taking part in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Here are some questions you might ask:

- Is there a clinical trial that I could take part in?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their pros and cons?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

How can I find out more about clinical trials that might be right for me?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at http://clinicaltrials.cancer.org.

Based on the information you give about your cancer type, stage, and previous treatments, this service can put together a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center that you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

For even more information on clinical trials, the American Cancer Society has a document called *Clinical Trials: What You Need to Know.* You can read this on the Web site, www.cancer.org, or have it sent to you by calling 1-800-ACS-2345.

Complementary and alternative therapies

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that are different from mainstream (standard) medical treatment. These methods can include vitamins, herbs, and special diets, or methods such as acupuncture or massage -- among many others. You may have a lot of questions about these treatments. Here are some you may have thought of already:

- How do I know if a non-standard treatment is safe?
- How do I know if it works?
- Should I try one or more of these treatments?
- What does my doctor know/think about these methods? Should I tell the doctor that I'm thinking about trying them?
- Will these treatments cause a problem with my standard medical treatment?
- What is the difference between "complementary" and "alternative" methods?
- Where can I find out more about these treatments?

The terms can be confusing

Not everyone uses these terms the same way, so it can be confusing. The American Cancer Society uses *complementary* to refer to medicines or methods that are used *along with* your regular medical care. *Alternative* medicine is a treatment used *instead of* standard medical treatment.

Complementary methods: Complementary treatment methods, for the most part, are not presented as cures for cancer. Most often they are used to help you feel better. Some methods that can be used in a complementary way are meditation to reduce stress, acupuncture to relieve pain or peppermint tea to relieve nausea. There are many others. Some of these methods are known to help, while others have not been tested. Some have been proven not be helpful. A few have even been found harmful. However, some of these methods may add to your comfort and well-being.

There are many complementary methods that you can safely use right along with your medical treatment to help relieve symptoms or side effects, to ease pain, and to help you enjoy life more. For example, some people find methods such as aromatherapy, massage therapy, meditation, or yoga to be useful.

Alternative treatments: Alternative treatments are those that are used instead of standard medical care. These treatments have not been proven safe and effective in clinical trials. Some of these methods may even be dangerous and some have life-threatening side effects. The biggest danger in most cases is that you may lose the chance to benefit from standard treatment. Delays or interruptions in your standard medical treatment may give the cancer more time to grow.

Deciding what to do

It is easy to see why people with cancer may consider alternative methods. You want to do all you can to fight the cancer. Sometimes mainstream treatments such as chemotherapy can be hard to take, or they may no longer be working.

Sometimes people suggest that their method can cure your cancer without having serious side effects, and it's normal to want to believe them. But the truth is that most non-standard methods of treatment have not been tested and proven to be effective for treating cancer.

As you consider your options, here are 3 important steps you can take:

- Talk to your doctor or nurse about any method you are thinking about using.
- Check the list of "red flags" below.
- Contact the American Cancer Society at 1-800-ACS-2345 to learn more about complementary and alternative methods in general and to learn more about the specific methods you are thinking about.

Red flags

You can use the questions below to spot treatments or methods to avoid. A "yes" answer to any one of these questions should raise a "red flag."

- Does the treatment promise a cure for all or most cancers?
- Are you told not to use standard medical treatment?
- Is the treatment or drug a "secret" that only certain people can give?
- Does the treatment require you to travel to another country?
- Do the promoters attack the medical or scientific community?

The decision is yours

Decisions about how to treat or manage your cancer are always yours to make. If you are thinking about using a complementary or alternative method, be sure to learn about the method and talk to your doctor about it. With reliable information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treating basal cell carcinoma

Basal cell carcinoma very rarely spreads to other parts of the body, although it can invade nearby tissues if not treated. There are several methods that can be used to remove or destroy these cancers. The choice may depend on factors such as tumor size and location, as well as on the patient's age, general health, and preferences.

All of the treatment methods below can be effective. The recurrence rates range from around 1% for Mohs surgery to up to 10% for the others, but this depends on the size of the tumor. Small tumors are less likely to recur than larger ones.

Electrodesiccation and curettage

Electrodesiccation and curettage is a commonly used treatment for basal cell carcinomas smaller than 1 centimeter (slightly less than a half inch) across.

Simple excision

Simple excision (cutting the tumor out) is often used to remove basal cell carcinomas, along with a margin of normal skin.

Mohs surgery

Mohs surgery has the best cure rate for basal cell carcinoma. It is especially useful in treating large tumors, tumors where the edges are not well-defined, tumors in certain critical locations (such as on or near the nose, eyes, ears, forehead, scalp, fingers, and genital area), and those that have come back after other treatments. However, it is also more complex and expensive than other methods.

Radiation therapy

Radiation therapy is a good option for treating older patients and for tumors involving the eyelids, nose or ears -- areas that are hard to treat surgically.

Immune response modifiers, photodynamic therapy, or topical chemotherapy

These treatments are sometimes considered as options for treating very superficial tumors (tumors that have not extended too deeply under the skin surface). Close follow-up is needed because these treatments do not destroy any cancer cells that are deep under the skin surface.

Cryosurgery

Cryosurgery can be used for some small basal cell carcinomas but is not recommended for larger tumors or those in certain parts of the nose, ears, eyelids, scalp, or legs.

Treating squamous cell carcinoma

Most squamous cell cancers are found and treated at an early stage, when they can be removed or destroyed with local treatment methods. In rare cases, they may spread to lymph nodes or distant sites, which require more intensive treatment.

For very small squamous cell cancers, the recurrence rate is similar to that for basal cell cancers. Larger squamous cell cancers are harder to treat, and the recurrence rates for aggressive cases of this cancer can be as high as 50% for large, deep tumors.

Simple excision

Simple excision is often used to treat squamous cell carcinomas.

Electrodesiccation and curettage

Electrodesiccation and curettage is sometimes useful in treating small squamous cell carcinomas, but it is not recommended for larger tumors.

Cryosurgery

Cryosurgery is used for some cases of squamous cell carcinoma but is not recommended for larger invasive tumors or those on certain parts of the nose, ears, eyelids, scalp, or legs.

Mohs Surgery

Mohs surgery has the highest cure rate. It is especially useful for squamous cell carcinomas larger than 2 cm (about 4/5 inch) across or with poorly defined edges, for tumors that have come back after other treatments, for cancers that are spreading along nerves under the skin, and for cancers on certain areas of the face or genital area.

Radiation therapy

Radiation therapy is a good option for treating older patients with large cancers, especially in areas where surgery is difficult (eyelids, ears, or nose).

Radiation is sometimes used after surgery (simple excision or lymph node dissection) if all of the cancer was not removed (if the surgical margins were positive), or if there is a chance that some cancer may remain. It can also be used to treat cancers that have come back after surgery and have become too large or deep to be removed surgically.

Lymph node dissection

Removing regional (nearby) lymph nodes is recommended for some squamous cell carcinomas that are very large or deeply invasive and in cases where the lymph nodes feel enlarged and/or hard. After the lymph nodes are removed, they are looked at under a microscope to see if they contain cancerous cells.

Systemic chemotherapy

Systemic chemotherapy is an option for patients with squamous cell skin carcinoma that has spread to lymph nodes or distant organs. In some cases it may be combined with surgery or radiation therapy.

Treating actinic keratosis

Actinic keratosis is often treated because of its potential to turn into squamous cell cancer. But because this risk is low, treatments are generally aimed at avoiding scars or other disfiguring marks as much as possible.

Actinic keratosis is commonly treated with either cryosurgery or topical fluorouracil (5-FU). These treatments destroy the affected area of the epidermis, the outermost layer of the skin. Blood vessels and lymphatic vessels, which can serve as transports for cancer cells throughout the body, are not present in this layer, so simply destroying the affected parts of the epidermis usually cures actinic keratosis.

Other topical creams such as imiquimod or diclofenac, or other localized treatments (shave excision, electrodesiccation and curettage, photodynamic therapy) are also sometimes used.

Treating Bowen disease

Bowen disease (squamous cell carcinoma in situ) is usually treated by simple excision. Electrodesiccation and curettage, radiation therapy, topical 5-FU, and cryosurgery are other options. Laser surgery or topical therapy may be considered in special situations.

Treating Merkel cell carcinoma

Merkel cell carcinomas are first treated with wide local excision (removal of the cancer and a wide margin of normal skin) or Mohs surgery.

These cancers have a tendency to spread to the lymph nodes or distant sites. Because of this, even if the lymph nodes do not seem enlarged, many doctors recommend a sentinel lymph node biopsy to look for possible spread of cancer to the lymph nodes. When possible, this should be done before surgery to the skin. If the sentinel node contains cancer, a full lymph node dissection is usually done. In either case, radiation therapy to the affected area after surgery is often used to reduce the risk of cancer coming back. If many lymph nodes were found to have cancer, adjuvant (additional) chemotherapy may be recommended as well.

If nearby lymph nodes are enlarged at the time the cancer is diagnosed, a fine needle aspiration (FNA) biopsy may be done to determine if they contain cancer. If cancer is found, treatment options include a lymph node dissection, radiation therapy to the area, or a combination of the two. Adjuvant treatment with chemotherapy may also be considered.

For cancers that have spread to or recur in distant sites, surgery, radiation therapy, chemotherapy, or some combination of these treatments may be used. These treatments may relieve symptoms or shrink these cancers for a time, but they rarely cure Merkel cell carcinoma that has spread beyond the skin.

Overall, the 5-year survival rate (the percentage of patients who live at least 5 years after diagnosis) for Merkel cell carcinoma is about 50%.

More treatment information

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about basal and squamous cell skin cancers?

As you cope with cancer and cancer treatment, you need to have honest, open discussions with your doctor. You should feel free to ask any question that's on your mind, 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 type of skin cancer do I have?
- Can you explain the different types of skin cancer?
- Has my cancer spread beneath the skin? Has it spread to lymph nodes or other organs?
- What are my treatment options? What do you recommend? Why?
- Will I be okay if the cancer is just removed with no follow-up treatment?
- What are the risks or side effects that I should expect?
- Will a scar remain after treatment?
- What are the chances of my cancer coming back with the treatment options we have discussed? What would we do if that happens?
- What should I do to be ready for treatment?
- What is my expected prognosis, based on my cancer as you view it?
- What are my chances of developing another skin cancer?
- Should I take special precautions to avoid sun exposure? What are the most important steps I can take to protect myself from the sun?
- Are any of my family members at risk for skin cancer? What should I tell them to do? Should I tell my children's doctor that I have been diagnosed with a skin cancer?

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 schedule. Or you may want to ask about second opinions or about clinical trials for which you may qualify.

What will happen after treatment for basal and squamous cell skin cancers?

Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called recurrence.) This is a very common concern among those who have had cancer.

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. Even with no recurrences, people who have had cancer learn to live with uncertainty.

Follow-up care

After your treatment is over, your doctor will likely recommend that you examine your skin once a month and protect yourself from the sun. Family members and friends can also be asked to watch for new lesions in areas that are hard to see.

If skin cancer does recur, it is most likely to happen in the first 5 years after treatment. In addition, a person who has had skin cancer is at higher risk for developing another one in a different location.

You should have follow-up exams as advised by your doctor. Your schedule for follow-up visits will depend on the type of cancer you had and on other factors. Different doctors may recommend different schedules. For basal cell cancers, visits are often recommended about every 6 months for the first 5 years, followed by yearly visits thereafter. Visits are usually more frequent after squamous cell cancers -- often every 3 to 6 months for the first several years, then followed by longer times between visits.

During your follow-up visits, your doctor will ask about symptoms and do physical exams to look for signs of recurrence or new skin cancers. For higher risk cancers, such as those that had reached the lymph nodes, he or she may also order imaging tests such as CT scans or x-rays.

Follow-up is also needed to check for possible side effects of certain treatments. This is the time for you to ask your health care team any questions and to discuss any concerns you might have. Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsies or surgeries
- if you had surgery, a copy of your operative report
- if you were hospitalized, a copy of the discharge summary that doctors must prepare when patients are sent home
- if you had radiation therapy, a summary of the type and dose of radiation and when and where it was given

- if you had chemotherapy, a list of your drugs, drug doses, and when you took them

It is also important to keep medical insurance. Even though no one wants to think of their cancer coming back, it is always a possibility. If it happens, the last thing you want is to have to worry about paying for treatment.

Lifestyle changes to consider during and after treatment

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even begin this process during cancer treatment.

Make healthier choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn't exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes today that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society's Quitline® tobacco cessation program at 1-800-ACS-2345.

What's new in research and treatment of basal and squamous cell skin cancers?

Research into the causes, prevention, and treatment of non-melanoma skin cancer is under way in many medical centers throughout the world.

Basic skin cancer research

Scientists have made a great deal of progress during the past few years in understanding how ultraviolet light damages DNA and how changes in DNA cause normal skin cells to become cancerous. Researchers are continually working to apply this new information to new strategies for treating skin cancers.

Public education

Most skin cancer is preventable. The greatest reduction in the number of skin cancer cases, as well as in the pain and loss of life from this disease, will come from preventive strategies. This means educating the public about skin cancer risk factors, prevention, and detection. It is important for health care professionals and skin cancer survivors to remind others about the dangers of excessive unprotected sun exposure and about how easily you can protect your skin from UV radiation.

The American Academy of Dermatology (AAD) sponsors annual free skin cancer screenings throughout the country. Many local American Cancer Society offices work closely with AAD to provide volunteers for registration, coordination, and education efforts related to these free screenings. Look for information locally about these screenings or call the American Academy of Dermatology for more information. Their phone number and Web address are listed in the "Additional resources" section of this document.

Preventing genital skin cancers

Squamous cell cancers that start in the genital region account for almost half of the deaths from keratinocyte cancers. At least some of these cancers may be related to infection with certain types of human papilloma virus (HPV), which can be spread through sexual contact.

In recent years, vaccines have been developed to help protect against infection from some types of HPV. The main intent of the vaccines has been to reduce the risk of cervical cancer, but they may also lower a person's risk of other cancers that might be related to HPV. The vaccines have only been around for a short time, so this will not be known for sure for many years.

Chemoprevention

An area of active research is the field of chemoprevention -- using drugs to prevent cancers from forming. Chemoprevention is likely to be more useful for people at high risk of skin cancers (especially squamous cell cancers), such as those with a prior history of skin cancer or those who have received organ transplants, rather than for people at average risk of skin cancer.

The most widely studied drugs so far are the retinoids, which are drugs related to vitamin A. But while they have shown some promise, these drugs can have side effects, including the potential to cause birth defects. For this reason they are not widely used at this time, except in some people at very high risk. Further studies of retinoids are under way. Other compounds being looked at to reduce the risk of skin cancer include eflornithine and certain antioxidants, including green tea extracts.

Treatment

Local treatments

Current local treatments are successful for the vast majority of non-melanoma skin cancers. Still, even some small cancers can be hard to treat if they're in certain areas. Newer forms of non-surgical treatment such as imiquimod cream, photodynamic therapy, immune response modulators, and laser surgery may help reduce scarring and other possible side effects of treatment. Studies are now under way to determine the best way to use these treatments, and to try to improve on their effectiveness.

Treating advanced disease

While most skin cancers are found and treated at a fairly early stage, some may spread to other parts of the body. These cancers can often be hard to treat with current therapies such as radiation and chemotherapy.

Several studies are testing newer targeted drugs for advanced squamous cell cancers. Cells from these cancers often have too much of a protein called EGFR on their surfaces, which may help them grow. Drugs that target this protein, such as cetuximab (Erbitux) and gefitinib (Iressa), are now being tested in clinical trials. A drug that targets different cell proteins, known as dasatinib (Sprycel), is also being studied for advanced skin cancers.

Additional resources

More information from your American Cancer Society

The following related information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-ACS-2345.

A Parent's Guide to Skin Protection

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Photodynamic Therapy

Skin Cancer Prevention and Early Detection

Sun Basics: Skin Protection Made Simple (information for children)

Understanding Radiation: A Guide for Patients and Their Families (also available in Spanish)

National organizations and Web sites*

In addition to the American Cancer Society, other sources of patient information and support include:

American Academy of Dermatology
Toll-free number: 1-888-462-3376(1-888-462-DERM)
Web site: www.aad.org

National Cancer Institute
Toll-free number: 1-800-422-6237 (1-800-4-CANCER); TYY: 1-800-332-8615
Web site: www.cancer.gov

Skin Cancer Foundation
Toll-free number: 1-800-754-6490 (1-800-SKIN-490)
Web site: www.skincancer.org

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-ACS-2345** or visit www.cancer.org.

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For additional assistance please contact your American Cancer Society
1 · 800 · ACS-2345 or www.cancer.org