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| Title | Basics of Cancer Treatments |
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| Course No | CT4020708 |
| Contact Hours | 3 |

Purpose

The goal of this course is to help health care professionals learn about several different kinds of cancer treatments, and answers to frequently asked questions.

Objectives

1. Discuss how cancer grows.
 2. Identify the three most common types of cancer treatment.
 3. Differentiate between some common problems that might be faced immediately after surgery and longer-term complications that may occur.
 4. List four goals of radiation therapy.
 5. List three different types of radiation therapy.
 6. State the median age at diagnosis for cancer of all sites.
 7. List three goals of chemotherapy.
 8. List four possible side effects of chemotherapy.
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Cancer Treatments

All living things are made up of cells. Cells are microscopic packages of living material that come in many different types. Our cells grow and divide slowly and under very tight control so that each tissue in our body stays the same. Cancer begins when one cell changes and starts growing and dividing rapidly and out of control. The one cell divides to give two cells, then four, eight and so on until they form a growing mass of cancer cells called a tumor. Some tumors stay in the same place and stop growing before they get very large, often because it simply runs out of space to grow. These are called benign tumors and they are not normally dangerous. We all have benign tumors, such as moles and warts. But tumors that are able to grow and invade the surrounding tissue and spread into nearby organs are called malignant tumors. They can cause serious damage and are often even fatal.

In many malignant tumors, as the cells spread, they get into blood vessels and are carried around the body. They can begin to divide and grow again in another area, forming a new tumor, which is called metastasis.

Every cell carries a set of coded instructions for every activity or function that it performs. Different genes are active in different cells, which is why a brain cell carries out many different activities from a muscle cell. Genes also carry the coded instructions for basic functions of the cell such as the way cells grow and divide. The growth and division of normal cells is tightly controlled by the activity of certain genes. When these genes are faulty or when the mechanisms controlling the activity of the genes is damaged, it can cause the growth and division of the cells to go out of control, or to become cancerous. Genes themselves do not cause cancer. When they function normally, genes prevent cancer. But when genes become

damaged they can malfunction and cause cancer.

Cancer itself cannot be inherited, but some people do inherit a higher risk of getting cancer. This is because they inherit a slightly damaged version of one of the genes involved in controlling cell division. On its own, this damaged gene is not enough to make cells cancerous. Normally, two or three different genes have to be damaged before a cell will become cancerous. That is why so very few of the billions of cells in our body ever become cancerous. However, if someone starts out with every cell in their body carrying damage in one of these genes, the chance of a cell getting the other types of gene damage and becoming cancerous is much higher. Some of these inherited damaged genes have been identified, such as BRCA1 and BRCA2, which increase the risk of getting breast cancer by 5-7 times.

A tumor usually starts with a single cancerous cell that begins growing and dividing. The resulting mass of cancer cells soon gets large enough to need a new blood supply to provide oxygen and nutrients and to remove waste products. Without a blood supply, the cells in the middle of the tumor will die off. Tumors without a blood supply are unable to grow more than about one millimeter across. As soon as they start growing, tumors release small, hormone-like molecules that cause nearby blood vessels to start growing towards the tumor until they actually form a new branch supplying the tumor with blood.

Doctors use a system called 'staging' to describe the size of a tumor and whether it has spread. Some cancers are more likely to spread than others. Doctors know where cancers are likely to spread. Different cancer types are more likely to spread to particular parts of the body. Cancers tend to occur by chance. This means that the main reason one person gets cancer and another does not, is bad luck. But some things make it more likely that some may be unlucky enough to get cancer. If we inherit certain genes it would make it more likely that we will get cancer. Things around us can also damage our genes and make a cell cancerous. This includes poisons in cigarette smoke and radiation. Age is also a factor. The older a person gets, the more likely it is that they will get cancer.

The right treatment depends on the type of cancer a person has and the stage (size and spread). It may be possible to have surgery to remove it. But cancers can come back. Radiotherapy means treatment with radiation, which kills cancer cells. Chemotherapy is treatment with drugs that kill cancer cells. Some types of cancer need hormones to grow. Hormone therapy treats the cancer by cutting off the hormone supply. These different types of treatment can be given on their own or together. For some types of cancer, you may have all of them. Research into cancer treatment is going on all the time. There are some newer forms of treatment available for some types of cancer. Biological therapies use natural body substances (or drugs developed to block them) to fight cancer. This includes research into vaccines and monoclonal antibody therapy (or targeted cancer treatment) as well as immunotherapies such as interferon or interleukins. Another new area of cancer treatment is gene therapy. One important area of research is examining how to cut off the cancer's blood supply so that the cancer will not be able to grow as fast. This paper will focus on different types of cancer treatments.(1)

Statistics

The American Cancer Society estimated that 1,399,790 men and women would be diagnosed with cancer of all sites in 2006. From 2000-2003, the median age at diagnosis for cancer of all sites was 67 years of age. Approximately 1.1% were diagnosed under age 20; 2.7% between 20-34; 6% between 35-44; 13.5% between 45-54; 20.8% between 55-64; 26% between 65-74; 22.6% between 75-84; and 7.3% 85+ years of age. The age-adjusted incidence rate was 471.3 per 100,000 men and women per year. These rates are based on cases diagnosed in 2000-2003. Incidence rates by race and sex were:

| <u>Race-Ethnicity</u> | <u>Men</u> | <u>Women</u> |
|----------------------------------|-----------------------|-------------------------|
| All Races | 558.1 per 100,000 men | 412.0 per 100,000 women |
| White | 558.3 per 100,000 men | 424.6 per 100,000 women |
| Black | 666.4 per 100,000 men | 395.4 per 100,000 women |
| Asian/Pacific Islander | 361.8 per 100,000 men | 285.4 per 100,000 women |
| American Indian/Alaska Native | 359.9 per 100,000 men | 305.0 per 100,000 women |
| Hispanic | 419.1 per 100,000 men | 310.9 per 100,000 women |

U.S. Mortality

From 2000-2003, the median age at death for cancer of all sites was 73 years of age. Approximately 0.4% died under age 20; 0.9% between 20-34; 2.9% between 35-44; 8.9% between 45-54; 16.6% between 55-64; 26.3% between 65-74; 30% between 75-84; and 14.1% 85+ years of age. The age-adjusted death rate was 194.5 per 100,000 men and women per year. These rates are based on patients who died in 2000-2003 in the U.S. Death rates by race and sex were:

| <u>Race/Ethnicity</u> | <u>Men</u> | <u>Women</u> |
|----------------------------------|-----------------------|-------------------------|
| All Races | 241.5 per 100,000 men | 163.5 per 100,000 women |
| White | 237.3 per 100,000 men | 162.8 per 100,000 women |
| Black | 326.8 per 100,000 men | 191.1 per 100,000 women |
| Asian/Pacific Islander | 143.3 per 100,000 men | 98.0 per 100,000 women |
| American Indian/Alaska Native | 150.0 per 100,000 men | 111.1 per 100,000 women |
| Hispanic | 165.1 per 100,000 men | 108.1 per 100,000 women |

Survival

Survival rates can be calculated by different methods for different purposes. The survival rates presented here are based on the relative survival rate, which measures the survival of the cancer patients in comparison to the general population to estimate the effect of cancer. The overall 5-year relative survival rate for 1996-2002 was 65%. Five-year relative survival rates by race and sex were: 66.8% for white men; 65.9% for white women; 59.7% for black men; 53.4% for black women.

Prevalence

On January 1, 2003, in the United States there were approximately 10,496,000 men and women alive who had a history of cancer of all sites – 4,692,397 men and 5,803,603 women. This includes any person alive on January 1, 2003 that had been diagnosed with cancer of all sites at any point prior to January 1, 2003 and includes persons with active disease and those who are cured of their disease. Prevalence can also be expressed as a percentage and it can also be calculated for a specific amount of time prior to January 1, 2003 such as diagnosed within 5 years of January 1, 2003.

Statistics cannot tell you what will happen to you. They are general pieces of information that apply to a 'population' of people from which the statistics were calculated. This could be tens, hundreds, or thousands of people. Statistics may be able to tell you what the chances of something happening to you are. If 65% of people with the same type of cancer as you responded to a treatment, then there is a two out of three chance that you will too. But no one can say definitely one way or the other.

Survival statistics for cancer are usually written as '5 year survival' or '10 year survival'. These statistics probably cause more confusion than any others do. What 5 year survival means is that X% of patients were alive 5 years after they were diagnosed. It does not mean that these people lived for exactly five years and then died. It does not mean they were all cured either. Some of them will be cured. Some will have already had a recurrence of their cancer, but still be alive. Some will get a recurrence after the five-year period. 5 year and 10 year time periods are used largely for convenience. Research studies often follow people up to 5 or 10 years. So figures for 5 and 10 years are often available to be quoted. For some types of cancer the chances of the cancer coming back after 5 years is quite small and 5 year survival is sometimes used to mean 'cure' when actually it does not. For almost all types of cancer, the chances of recurrence after 5 years are much lower than they are after two years. So the more time passes, the less likely it is that your cancer will come back. Sometimes 'disease free' survival figures are used. This does mean everyone with that type of cancer who is alive and well (without a recurrence of their cancer) 5 years after diagnosis. (2)

Treatments

The three most common types of cancer treatment are surgery, radiotherapy and chemotherapy. Treatment is aimed at removing the cancer cells or destroying them in the body with medicines or other agents.

Surgery

Surgery is one of the main treatments for cancer. It is a local treatment. This means it only treats one particular part of the body, which is where the surgeon operates. So if you have a cancer that is completely contained in one area and has not spread, surgery may cure it. But because it is a local treatment, surgery may not be a good choice of treatment for people whose cancer has spread to another part of their body. They may be offered a systemic treatment such as chemotherapy, biological therapy, or hormone therapy instead. If a person has cancer of the lymphatic system (lymphoma) or blood system (leukemia) surgery won't help because the cancer cells could be anywhere in the body. If surgery is possible, it may well cure a cancer. This will depend on

- Whether the cancer can be completely removed
- Whether a border of healthy tissue, free of cancer cells, is removed with the cancer
- Whether the cancer has already spread before the surgery

Sometimes, although all the scans look clear, cancer cells have already broken away from the primary cancer and traveled to another part of the body. These secondary cancers may just be too small to see and are called micrometastases. Or despite clear scans, the surgeon finds that the cancer has spread further than first thought. This may mean the operation takes longer, or in some cases cannot go ahead. Usually, the surgeon will remove the main lymphatic vessels and lymph nodes that are nearest to the cancer, or the organ where the cancer is. This is because the main draining lymph nodes and vessels are the most likely place for cancer cells to have spread. Because there may be cancer cells that have broken away from the primary cancer, the doctor may recommend that the patient have radiotherapy or chemotherapy after surgery. This is called 'adjuvant' treatment. Sometimes radiotherapy or chemotherapy is given before surgery to help shrink the cancer and make it easier to remove. This is called 'neo-adjuvant' treatment.

There are some common problems after any surgery. These are:

- Pain
- Local infection
- Chest infection
- Blood clots
- Fluid collection around the wound

There can be longer-term complications after an operation. Some of these will depend on the type of operation you have and where in the body it is done. These problems do not happen to everyone. Two of the problems that can occur are:

- Nerve pain
- Lymphedema

Nerve pain is a burning sensation. It can sometimes come on a couple months after an operation. This is due to nerve endings that were damaged during the operation growing back. It can last for a few months or longer. Usually it goes away, but very occasionally, it can be permanent. Nerve pain sometimes happens after operations where the rib cage has to be opened up (thoracotomy), for example, lung surgery.

Lymphedema is fluid build up. It usually occurs in an arm or leg, but can happen elsewhere in the body. It will only affect an area where lymph nodes have been removed. Most people will not get lymphedema. Once lymphedema has happened, it cannot be cured. But if caught early it can be treated and controlled very effectively.

Radiation Therapy

Radiation therapy uses ionizing radiation to kill cancer cells and shrink tumors. About half of all people with cancer are treated with radiation therapy, either alone or in combination with other types of cancer treatment. You may have radiotherapy:

- To shrink a cancer before surgery
- To reduce the risk of a cancer coming back after surgery
- Along with chemotherapy
- By itself to cure a cancer
- To control symptoms and improve quality of life when a cancer is too advanced to cure

Radiotherapy can be external or internal. External radiation is the type most often used. This is given on an outpatient basis. External radiotherapy is a bit like having a x-ray, although you will usually have a course of treatments. In some situations the doctor may suggest just one

treatment, for example to treat lung cancer, or cancer that has spread to the bones. The high-energy rays are produced by a large machine and are directed at the part of the body being treated.

Internal radiotherapy is radiotherapy from inside the body. This can be targeted radiotherapy in the form of a drink or injection. Or it may be radioactive wires or pellets implanted into the area where there is a tumor. Internal radiation may require a hospital stay. Different types of radiation are used to treat different types of cancer. A team of health care providers helps to plan and deliver radiation treatment to the patient. Treatment planning and simulation are critical first steps in the radiation therapy process. The goal of planning and simulation is to make the treatment more precise, more effective, and less damaging to healthy tissues.

Radiation therapy injures or destroys cells in the area being treated (the "target tissue") by damaging their genetic material, making it impossible for these cells to continue to grow and divide. Although radiation damages both cancer cells and normal cells, most normal cells can recover from the effects of radiation and function properly. The goal of radiation therapy is to damage as many cancer cells as possible, while limiting harm to nearby healthy tissue.

There are different types of radiation and different ways to deliver the radiation. For example, certain types of radiation can penetrate more deeply into the body than can others. In addition, some types of radiation can be very finely controlled to treat only a small area (an inch of tissue, for example) without damaging nearby tissues and organs. Other types of radiation are better for treating larger areas. In some cases, the goal of radiation treatment is the complete destruction of an entire tumor. In other cases, the aim is to shrink a tumor and relieve symptoms. In either case, doctors plan treatment to spare as much health tissue as possible. In some cases, a patient may receive more than one type of radiation treatment.

Radiation therapy may be used to treat almost every type of solid tumor, including cancers of the brain, breast, cervix, larynx, lung, pancreas, prostate, skin, spine, stomach, uterus, or soft tissue sarcomas. Radiation can also be used to treat leukemia and lymphoma. Radiation dose to each site depends on a number of factors, including the type of cancer and whether there are tissues and organs nearby that may be damaged by radiation. For some types of cancer, radiation may be given to areas that do not have evidence of cancer. This is done to prevent cancer cells from growing in the area receiving the radiation. This technique is called prophylactic radiation therapy. Radiation therapy also can be given to help reduce symptoms such as pain from cancer that has spread to the bones or other parts of the body. This is called palliative radiation therapy.

Radiation may be external, internal or may use unsealed radioactive materials that go throughout the body, which is called systemic radiation therapy. The type of radiation to be given depends on the type of cancer, its location, how far into the body the radiation will need to go, the patient's general health and medical history, whether the patient will have other types of cancer treatment, and other factors. Most people who receive radiation therapy for cancer have external radiation. Some patients have both external and internal or systemic radiation therapy, either one after the other or at the same time.

Intraoperative radiation therapy (IORT) is a form of external radiation that is given during surgery. IORT is used to treat localized cancers that cannot be completely removed or that have a high risk of recurring in nearby tissues. After all or most of the cancer is removed, one large, high-energy dose of radiation is aimed directly at the tumor site during surgery – nearby healthy tissue is protected with special shields. The patient stays in the hospital to recover from the surgery. IORT may be used in the treatment of thyroid and colorectal cancers, gynecological cancers, cancer of the small intestine, and cancer of the pancreas. It is also being studied in clinical trials to treat some types of brain tumors and pelvic sarcomas in adults.

Prophylactic cranial irradiation (PCI) is external radiation given to the brain when the primary cancer (for example, small cell lung cancer) has a high risk of spreading to the brain.

Internal radiation therapy (also called brachytherapy) uses radiation that is placed very close to or inside the tumor. The radiation source is usually sealed in a small holder called an implant. Implants may be in the form of thin wires, plastic tubes called catheters, ribbons, capsules, or seeds. The implant is put directly into the body. Internal radiation therapy may require a hospital stay.

Internal radiation is usually delivered in one of two ways. Both methods use sealed implants. Interstitial radiation therapy is inserted into tissue at or near the tumor site. It is used to treat tumors of the head and neck, prostate, cervix, ovary, breast, and perianal and pelvic regions. Some women treated with external radiation for breast cancer receive a "booster dose" of radiation that may use interstitial radiation or external radiation. Intracavitary or intraluminal radiation therapy is inserted into the body with an applicator. It is commonly used in the treatment of uterine cancer. Researchers are also studying these types of internal radiation therapy for other cancers, including breast, bronchial, cervical, gallbladder, oral, rectal, tracheal, uterine, and vaginal.

Systemic radiation therapy uses radioactive materials such as iodine 131 and strontium 89. The materials may be taken by mouth or injected into the body. Systemic radiation therapy is sometimes used to treat cancer of the thyroid and adult non-Hodgkin's lymphoma. Researchers are investigating agents to treat other types of cancer.

Cancer patients receiving radiation therapy are often concerned that the treatment will make them radioactive. The answer to this depends on the type of radiation therapy being given. External radiation therapy will not make the patient radioactive. Patients do not need to avoid being around other people because of the treatment. Internal radiation therapy (interstitial, intracavitary, or intraluminal) that involves sealed implants emits radioactivity, so a stay in the hospital may be needed. Certain precautions are taken to protect hospital staff and visitors. The sealed sources deliver most of their radiation mainly around the area of the implant, so while the area around the implant is radioactive, the patient's whole body is not radioactive. Systemic radiation therapy uses unsealed radioactive materials that travel throughout the body. Some of this radioactive material will leave the body through saliva, sweat, and urine before the radioactivity decays, making these fluids radioactive. Therefore, certain precautions are sometimes used for people who come in close contact with the patient. The patient's doctor or nurse provides information if these special precautions are needed.

The amount of radiation absorbed by the tissues is called the radiation dose. Before 1985, dose was measured in a unit called a "rad" (radiation absorbed dose). Now the unit is called a gray (abbreviated as Gy). One Gy is equal to 100 rads. One centigray (abbreviated as cGy) is the same as one rad. Different tissues can tolerate various amounts of radiation (measured in centigrays). For example, the liver can receive a total dose of 3,000 cGy, while the kidneys can tolerate only 1,800 cGy. The total dose of radiation is usually divided into smaller doses (called fractions) that are given daily over a specific time period. This maximizes the destruction of cancer cells while minimizing the damage to healthy tissue. The doctor works with a figure called the therapeutic ratio. This ratio compares the damage to the cancer cells with the damage to healthy cells. Techniques are available to increase the damage to cancer cells without doing greater harm to healthy tissues.

The energy (source of radiation) used in external radiation therapy may come from x-rays or gamma rays. These are both forms of electromagnetic radiation. Although they are produced in different ways, both use photons (packets of energy). Machines called linear accelerators create X-rays. Depending on the amount of energy the x-rays have, they can be used to destroy

cancer cells on the surface of the body (lower energy) or deeper into tissues and organs (higher energy). Compared with other types of radiation, x-rays can deliver radiation to a relatively large area. Gamma rays are produced when isotopes of certain elements (such as iridium and cobalt 60) release radiation energy as they break down. Each element breaks down at a specific rate and each gives off a different amount of energy, which affects how deeply it can penetrate into the body. Gamma rays produced by the breakdown of cobalt 60 are used in the treatment called the "gamma knife".

Particle beams use fast-moving subatomic particles instead of photons. This type of radiation may be called particle beam radiation therapy or particulate radiation. Particle beams are created by linear accelerators, synchrotrons, and cyclotrons, which produce and accelerate the particles required for this type of radiation therapy. Particle beam therapy uses electrons, which are produced by an x-ray tube (this may be called electron-beam radiation); neutrons, which are produced by radioactive elements and special equipment; heavy ions (such as protons and helium); and pi-mesons (also called pions), which are small, negatively charged particles produced by an accelerator and a system of magnets. Unlike x-rays and gamma rays, some particle beams can penetrate only a short distance into tissue. Therefore, they are often used to treat cancers located on the surface of or just below the skin.

Proton beam therapy is a type of particle beam radiation therapy. Protons deposit their energy over a very small area, which is called the Bragg peak. The Bragg peak can be used to target high doses of proton beam therapy to a tumor while doing less damage to normal tissues in front of and behind the tumor. Proton beam therapy is available at only a few facilities in the United States. Its use is generally reserved for cancers that are difficult or dangerous to treat with surgery (such as a chondrosarcoma at the base of the skull), or it is combined with other types of radiation. Proton beam therapy is also being used in clinical trials for intraocular melanoma (melanoma that begins in the eye), retinoblastoma (an eye cancer that most often occurs in children under age 5), rhabdomyosarcoma (a tumor of the muscle tissue), some cancers of the head and neck, and cancers of the prostate, brain, and lung.

The energy (source of radiation) used in internal radiation comes from the radioactive isotope in radioactive iodine (iodine 125 or iodine 131), and from strontium 89, phosphorous, palladium, cesium, iridium, phosphate, or cobalt. Other sources are being investigated. Stereotactic (or stereotaxic) radiosurgery uses a large dose of radiation to destroy tumor tissue in the brain. The procedure does not involve actual surgery. The patient's head is placed in a special frame, which is attached to the patient's skull. The frame is used to aim high-dose radiation beams directly at the tumor inside the patient's head. The dose and area receiving the radiation are coordinated very precisely. Most nearby tissues are not damaged by this procedure. Stereotactic radiosurgery can be done in one of three ways. The most common technique uses a linear accelerator to administer high-energy photon radiation to the tumor (called "linac-based stereotactic radiosurgery"). The gamma knife, the second most common technique, uses cobalt 60 to deliver radiation. The third technique uses heavy charged particle beams (such as protons and helium ions) to deliver stereotactic radiation to the tumor.

Stereotactic radiosurgery is mostly used in the treatment of small benign and malignant brain tumors (including meningiomas, acoustic neuromas, and pituitary cancer). It can also be used to treat other conditions (for example, Parkinson's disease and epilepsy). In addition, stereotactic radiosurgery can be used to treat metastatic brain tumors (cancer that has spread to the brain from another part of the body) either alone or along with whole-brain radiation therapy. (Whole brain radiation therapy is a form of external radiation therapy that treats the entire brain with radiation.

Stereotactic radiotherapy uses essentially the same approach as stereotactic radiosurgery to deliver radiation to the target tissue. However, stereotactic radiotherapy uses multiple small fractions of radiation as opposed to one large dose. Giving multiple smaller doses may improve

outcomes and minimize side effects. Stereotactic radiotherapy is used to treat tumors in the brain as well as other parts of the body. Clinical trials are under way to study the effectiveness of stereotactic radiosurgery and stereotactic radiotherapy alone and in combination with other types of radiation therapy.

Because there are so many types of radiation and many ways to deliver it, treatment planning is a very important first step for every patient who will have radiation therapy. Before radiation therapy is given, the patient's radiation therapy team determines the amount and type of radiation the patient will receive. If the patient will have external radiation, the radiation oncologist uses a process called simulation to define where to aim the radiation. During simulation, the patient lies very still on an examining table while the radiation therapist uses a special x-ray machine to define the treatment port or field, the exact place on the body where the radiation will be aimed. Most patients have more than one treatment port. Simulation may also involve CT scans or other imaging studies to help the radiation therapist plan how to direct the radiation. The simulation may result in some changes to the treatment plan so that the greatest possible amount of healthy tissue can be spared from receiving radiation.

The areas to receive radiation are marked with a temporary or permanent marker, tiny dots or a "tattoo" showing where the radiation should be aimed. These marks are also used to determine the exact site of the initial treatments if the patient should need radiation treatment later. Depending on the type of radiation treatment, the radiation therapist may make body molds or other devices that keep the patient from moving during treatment. These are usually made from foam, plastic, or plaster. In some cases, the therapist will also make shields that cannot be penetrated by radiation to protect organs and tissues near the treatment field. When the simulation is complete, the radiation therapy team meets to decide how much radiation is needed, how it should be delivered, and how many treatments the patient should have.

Radiosensitizers and radioprotectors are chemicals that modify a cell's response to radiation. Radiosensitizers are drugs that make cancer cells more sensitive to the effects of radiation therapy. Several compounds are under study as radiosensitizers. In addition, some anticancer drugs, such as 5-fluorouracil and cisplatin, make cancer cells more sensitive to radiation therapy. Radioprotectors (also called radioprotectants) are drugs that protect normal (noncancerous) cells from the damage caused by radiation therapy. These agents promote the repair of normal cells that are exposed to radiation. Amifostine (trade name Ethyol) is the only drug approved by the U.S. Food and Drug Administration as a radioprotector. It helps to reduce the dry mouth that can occur if the parotid glands (which help to produce saliva and are located near the ear) receive a large dose of radiation. Additional studies are under way to determine whether amifostine is effective when used with radiation therapy to treat other types of cancer. Other compounds are also under study as radioprotectors.

Radiopharmaceuticals, also known as radionucleotides, are radioactive drugs used to treat cancer, including thyroid cancer, cancer that recurs in the chest wall, and pain caused by the spread of cancer to the bone. The most commonly used radiopharmaceuticals are samarium 153 (Quadramet) and strontium 89 (Metastron). These drugs are approved by the FDA to relieve pain caused by bone metastases. Both agents are given intravenously, usually on an outpatient basis. Sometimes they are given in addition to external beam radiation. Other types of radiopharmaceuticals, such as phosphorous 32, rhodium 186, and gallium nitrate, are not used as frequently. Still other radiopharmaceuticals are under investigation. (3)

Chemotherapy

Chemotherapy uses medicines to attack the cancer cells. Just the word "chemotherapy" can cause a lot of fear because the side effects can be severe. However, not all people experience severe side effects. The side effects of chemotherapy can often be reduced with other

medicines. Chemotherapy is usually used when the cancer has spread to other areas in the body. Chemotherapy can also be used in combination with surgery and radiation. Sometimes the tumor is surgically removed and then chemotherapy is used to make sure all the cancer cells are killed. Chemotherapy drugs are often called "anticancer" drugs.

Normal cells grow and die in a controlled way. When cancer occurs, cells in the body that are not normal keep dividing and forming more cells without control. Anticancer drugs destroy cancer cells by stopping them from growing or multiplying. Healthy cells can also be harmed, especially those that divide quickly. Harm to healthy cells is what causes side effects. These cells usually repair themselves after chemotherapy. Because some drugs work better together than alone, two or more drugs are often given at the same time. This is called "combination chemotherapy".

Depending on the type of cancer and how advanced it is, chemotherapy can be used for different goals:

- To cure the cancer. Cancer is considered cured when the patient remains free of evidence of cancer cells.
- To control the cancer. This is done by keeping the cancer from spreading; slowing the cancer's growth; and killing cancer cells that may have spread to other parts of the body from the original tumor.
- To relieve symptoms that the cancer may cause. Relieving symptoms such as pain can help patients live more comfortably.

Sometimes chemotherapy is the only treatment a patient receives. More often, chemotherapy is used in addition to surgery, radiation therapy, and/or biological therapy to:

- Shrink a tumor before surgery or radiation therapy. This is called neo-adjuvant therapy.
- Help destroy any cancer cells that may remain after surgery and/or radiation therapy. This is called adjuvant chemotherapy.
- Make radiation therapy and biological therapy work better.
- Help destroy cancer if it recurs or has spread to other parts of the body from the original tumor.
- Relieve symptoms cause by the cancer.
- In some cases, with specific cancers, cure the disease.

Some chemotherapy drugs are used for many different types of cancer, while others might be used for just one or two types of cancer. The doctor recommends a treatment plan based on:

- What kind of cancer the patient has.
- What part of the body the cancer is found.
- The effect of cancer on the patient's normal body functions.
- The patient's general health.

There are more than 100 chemotherapy drugs used in various combinations for the treatment of cancer. Although a patient might receive a single chemotherapy drug to treat cancer, generally the chemotherapy drugs are more powerful when used in combination with other drugs. Chemotherapy drugs are divided into several categories based on how they affect specific chemical substances within cancer cells, which cellular activities or processes the drug interferes with, and which specific phases of the cell cycle the drug affects. Knowing this helps oncologists decide which drugs are likely to work well together and, if more than one drug will be used, plan exactly when each of the drugs should be given and in which order and how often.

Chemotherapy Agents

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| <u>Alkylating Agents</u> | work directly on DNA to prevent the cancer cell from reproducing. As a class of drugs, these agents are not phase-specific. They work in all phases of the cell cycle. These drugs are active against chronic leukemias, non-Hodgkin's lymphoma, Hodgkin's disease, multiple myeloma, and certain cancers of the lung, breast, and ovary. Examples of alkylating agents include busulfan, cisplatin, carboplatin, chlorambucil, cyclophosphamide, ifosfamide, dacarbazine (DTIC), mechlorethamine (nitrogen mustard), and melphalan. |
| <u>Antimetabolites</u> | are a class of drugs that interfere with DNA and RNA growth. These agents work during the S phase and are used to treat chronic leukemias as well as tumors of the breast, ovary, and the gastrointestinal tract. Examples of antimetabolites include 5-fluorouracil, capecitabine, methotrexate, gemcitabine, cytarabine (ara-C), and fludarabine. |
| <u>Antitumor Antibiotics</u> | interfere with DNA by stopping enzymes and mitosis or altering the membranes that surround cells. They are not the same as antibiotics used to treat infections. These agents work in all phases of the cell cycle. Thus they are widely used for a variety of cancers. Examples of antitumor antibiotics include dactinomycin, daunorubicin, doxorubicin (Adriamycin), idarubicin, and mitoxantrone. |
| <u>Mitotic Inhibitors</u> | are plant alkaloids and other compounds derived from natural products. They can inhibit or stop, mitosis or inhibit enzymes for making proteins needed for reproduction of the cell. These work during the M phase of the cell cycle. Examples of mitotic inhibitors include paclitaxel, docetaxel, etoposide (VP-16), vinblastine, vincristine, and vinorelbine. |
| <u>Nitrosoureas</u> | act in a similar way to alkylating agents. They interfere with enzymes that help repair DNA. These agents are able to travel to the brain so they are used to treat brain tumors as well as non-Hodgkin's lymphomas, multiple myeloma, and malignant melanoma. Examples of nitrosoureas include carmustine and lomustine. |

Drugs used in chemotherapy regimens can be given in many ways. The most common routes of administration include:

- Oral
- Topical
- Intravenous
- Intramuscular

- Subcutaneous

The IV route is the most common form of administration. The IV route gets the drug dispersed quickly throughout the body. IV therapy may be given through a vein in the arm or hand or through a vascular access device (VAD), which includes a catheter implanted into a larger vein in the chest, neck or arm. The advantages of the VADs include: to give several drugs at one time, for long-term therapy, for continuous infusion chemotherapy, and more stable access in a larger vein thus reducing the risk of drug leaking outside of the vein.

Side effects are different for each person, for each chemotherapy drugs, and they also differ based on the dosage, the route the drug is given, and how the drug affects a person individually. The most common side effects of chemotherapy include: nausea and vomiting, hair loss, fatigue, an increased chance of bruising and bleeding, and getting an infection. Most side effects gradually disappear after treatment ends because the healthy cells recover quickly. The time it takes to get over some side effects and regain energy varies from person to person and depends on many factors, including the overall health and the specific drugs the person received. (4)

Other Treatments

Targeted therapy/Monoclonal Antibodies: Targeted cancer therapies are drugs that block the growth and spread of cancer by interfering with specific molecules involved in carcinogenesis (the process by which normal cells are transformed into cancer cells) and tumor growth. Monoclonal antibodies have been developed for the treatment of cancer. Monoclonal antibodies are different from traditional chemotherapy. Chemotherapies are chemicals that kill rapidly dividing cells. Both chemotherapies and monoclonal antibodies can kill good cells as well as cancer cells, the effect on the normal cells cause side effects. The side effects associated with monoclonal antibody therapies are generally considered to be more manageable than side effects associated with chemotherapy and radiation. There is the potential for allergic or anaphylactic reactions that can be severe or even life threatening. Monoclonal antibodies are not available for all types of cancer and are currently being used for treatment of colon, breast, lung, Non-Hodgkin's lymphoma and some forms of leukemia. Hopefully in the future this kind of treatment will be available to ovarian, pancreas and other solid tumors.

Corticosteroid Hormones: Steroids are natural hormones and hormone-like drugs that are useful in treating some types of cancer (lymphoma, leukemias, and multiple myeloma) as well as other illnesses. When these drugs are used to kill cancer cells or slow their growth, they are considered chemotherapy drugs. They are often combined with other types of chemotherapy drugs to increase their effectiveness. Examples include prednisone and dexamethasone.

Hormonal Therapies: Hormonal therapies, or hormone-like drugs, alter the action or production of female or male hormones. They are used to slow the growth of breast, prostate, and endometrial (lining of the uterus) cancers, which normally grow in response to hormone levels in the body. These hormones do not work in the same ways as standard chemotherapy drugs. Examples include anti-estrogens (tamoxifen, fulvestrant), aromatase inhibitors (anastrozole, letrozole), progestins (megestrol acetate), anti-androgens (bicalutamide, flutamide), and LHRH agonists (leuprolide, goserelin).

Immunotherapy or Biological Therapy (also called biological response modifier therapy): Some drugs are given to people with cancer to stimulate their immune systems to more effectively recognize and attack cancer cells. These drugs offer a unique method of treatment, and are often considered to be separate from chemotherapy. The patient and doctor decide which drug or combination of drugs, dosages, route of administration, frequency and length of treatment that is best. All of the decisions would depend on the specific type of cancer, the location, the

extent of its growth, how it is affecting the normal body functions, and the person's overall general health. Biological therapies include interferons, interleukins, colony-stimulating factors, monoclonal antibodies, vaccines, gene therapy, and nonspecific immunomodulating agents. Immune system cells include the following:

- Lymphocytes are a type of white blood cell found in the blood and many other parts of the body. Types of lymphocytes include B cells, T cells, and Natural Killer cells.
 - B cells (B lymphocytes) mature into plasma cells that secrete proteins called antibodies (immunoglobulins). Antibodies recognize and attach to foreign substances known as antigens, fitting together much the way a key fits a lock. Each type of B cell makes one specific antibody, which recognizes one specific antigen.
 - T cells (T lymphocytes) work primarily by producing proteins called cytokines. Cytokines allow immune system cells to communicate with each other and include lymphokines, interferons, interleukins, and colony-stimulating factors. Some T cells, called cytotoxic T cells, release pore-forming proteins that directly attack infected, foreign, or cancerous cells. Other T cells, called helper T cells, regulate the immune response by releasing cytokines to signal other immune system defenders.
 - Natural Killer cells (NK cells) produce powerful cytokines and pore-forming proteins that bind to and kill many foreign invaders, infected cells, and tumor cells. Unlike cytotoxic T cells, they are poised to attack quickly, upon their first encounter with their targets.
- Phagocytes are white blood cells that can swallow and digest microscopic organisms and particles in a process known as phagocytosis. There are several types of phagocytes, including monocytes, which circulate in the blood, and macrophages, which are located in tissues throughout the body.

Bone marrow Transplantation and Peripheral Blood Stem Cell Transplantation: These are used to treat a variety of different cancers. They are sometimes called bone marrow rescue or stem cell rescue. This is because the bone marrow or stem cells are used to replace the cells in the bone marrow that have been killed off by high dose chemotherapy or total body radiotherapy. Receiving the bone marrow is just like having a blood transfusion. The stem cells or bone marrow drips into the patient's blood stream through an IV or central line. The cells find their way back into the bones and start to grow again. Soon they would be making new blood cells. The side effects for bone marrow and stem cell transplants are the same as for chemotherapy. The main side effects are risk of infection, anemia, risk of bleeding, nausea and vomiting, diarrhea, sore mouth, difficulty eating and drinking and fatigue.

Photodynamic therapy (PDT): combines a drug (called a photosensitizer or photosensitizing agent) with a specific type of light to kill cancer cells. When photosensitizers are exposed to a specific wavelength of light, they produce a form of oxygen that kills nearby cells. Each photosensitizer is activated by light of a specific wavelength. This wavelength determines how far the light can travel into the body. Doctors use specific photosensitizers and wavelengths of light to treat different areas of the body with PDT.

Angiogenesis Inhibitors: Angiogenesis means the formation of new blood vessels. Angiogenesis is a process controlled by certain chemicals produced in the body. These chemicals stimulate blood vessels or form new ones. Other chemicals, called angiogenesis inhibitors, signal the process to stop. Angiogenesis plays an important role in the growth and spread of cancer. New blood vessels "feed" the cancer cells with oxygen and nutrients, allowing these cells to grow, invade nearby tissues, spread to other parts of the body, and form new colonies of cancer cells. Because cancer cannot grow or spread without the formation of new blood vessels, scientists are trying to find ways to stop angiogenesis. They are studying natural and synthetic angiogenesis inhibitors, also called anti-angiogenesis agents, in the hope that these chemicals will prevent the growth of cancer by blocking the formation of new blood vessels. In animal studies, angiogenesis inhibitors have successfully stopped the formation of new blood vessels,

causing the cancer to shrink and die.

Gene Therapy: is an experimental treatment that involves introducing genetic material into a person's cells to fight or prevent disease. A gene can be delivered to a cell using a carrier known as a "vector". The most common types of vectors used in gene therapy are viruses. The viruses used in gene therapy are altered to make them safe. Some risks still exist with gene therapy. A clinical trial using gene therapy must be approved by at least two review boards at the scientists' institution, as well as by the U.S. Food and Drug Administrations and the National Institutes of Health Recombinant DNA Advisory Committee.

Lasers in Cancer Treatment: Laser light is a light of such high intensity and narrow beam that it can be used to do precise surgery to remove cancer or precancerous growths or to relieve symptoms of cancer. It is used most often to treat cancers on the surface of the body or the lining of internal organs. Laser therapy is often given through a thin tube called an endoscope. An endoscope can be inserted in openings in the body to treat cancer or precancerous growths inside the trachea, esophagus, stomach, or colon. Laser therapy causes less bleeding and damage to normal tissue than standard surgical tools, and there is a lower risk of infection. Laser therapy is extremely expensive and the effects of the surgery may not be permanent, so the surgery may have to be repeated.

Hyperthermia: is a type of cancer treatment in which body tissue is exposed to high temperatures (up to 113 degrees F.) to damage and kill cancer cells. Hyperthermia is almost always used with other forms of cancer therapy, such as radiation therapy and chemotherapy. Several methods of hyperthermia are currently under study, including local, regional, and whole-body hyperthermia. Many clinical trials are being conducted to evaluate the effectiveness of hyperthermia. (5)

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Course Exam

1. Monocytes circulate in the blood.
 True False
2. There are no longer risks involved when using gene therapy.
 True False

3. Some drugs are given to people with cancer to stimulate their immune systems to more effectively recognize and attack cancer cells.
 True False
4. Steroids are natural hormones and hormone-like drugs that are useful in treating some types of cancer.
 True False
5. Targeted cancer therapies are drugs that block the growth and spread of cancer by interfering with specific molecules involved in carcinogenesis.
 True False
6. Types of lymphocytes include B cells, Natural Killer cells and Phagocytes.
 True False
7. Radiation therapy uses ionizing radiation to kill cancer cells and shrink tumors.
 True False
8. Internal radiation is the type most often used.
 True False
9. Radiation therapy may be used to treat almost every type of solid tumor.
 True False
10. Intraoperative radiation therapy is a form of internal radiation that is given during surgery.
 True False
11. Prophylactic cranial irradiation is external radiation given to the brain.
 True False
12. External radiation therapy is also called brachytherapy when it is placed very close to or inside the tumor.
 True False
13. Proton beam therapy is a type of particle beam radiation therapy.
 True False
14. Stereotactic radiosurgery is mostly used in the treatment of small benign and malignant brain tumors.
 True False
15. The areas of the body to receive radiation are marked with a temporary or permanent marker, tiny dots or a 'tattoo' showing where the radiation should be aimed.
 True False
16. Anticancer drugs destroy only cancer cells.
 True False

17. Goals of chemotherapy include curing the cancer, controlling the cancer and relieving symptoms that the cancer may cause.
- True False
18. Chemotherapy is never the only treatment that a cancer patient would receive.
- True False
19. Mitotic inhibitors work during the M phase of the cell cycle.
- True False
20. Alkylating agents work directly on the RNA to prevent the cancer cell from reproducing.
- True False
21. Nitrosoureas act in a similar way to alkylating agents.
- True False
22. The IM route is the most common form of administration for chemotherapy.
- True False
23. The most common side effects of chemotherapy include nausea and vomiting, hair loss and fatigue.
- True False
24. Surgery is one of the main treatments for cancer.
- True False
25. Different cancer types are more likely to spread to particular parts of the body.
- True False
26. Hormone therapy works the same way as standard chemotherapy drugs.
- True False
27. A system called 'staging' is used to describe the size of a tumor and whether it has spread.
- True False
28. Lymphedema happens to all breast cancer patients.
- True False
29. Metastasis is when a new tumor forms in another area of the body.
- True False
30. Cancer can be inherited.
- True False