Chemotherapy Principles

An In-depth Discussion of the Techniques and Its Role in Cancer Treatment

The thought of having chemotherapy frightens many people. Almost everyone has heard stories about someone who was “on chemo.” But knowing what chemotherapy is, how it works, and what to expect can often help calm your fears. It can also give you a better sense of control over your life during your experience with cancer.

What is chemotherapy?

The word *chemotherapy* means the use of any drug (such as aspirin or penicillin) to treat any disease, but to most people chemotherapy refers to drugs used for cancer treatment. It’s often shortened to “chemo.” Two other medical terms used to describe cancer chemotherapy are *antineoplastic* (meaning anti-cancer) therapy and *cytotoxic* (cell-killing) therapy.

History of chemotherapy

The first drug used for cancer chemotherapy did not start out as a medicine. Mustard gas was used as a chemical warfare agent during World War I and was studied further during World War II. During a military operation in World War II, a group of people were accidentally exposed to mustard gas and were later found to have very low white blood cell counts.

Doctors reasoned that something that damaged the rapidly growing white blood cells might have a similar effect on cancer. So, in the 1940s, several patients with advanced lymphomas (cancers of certain white blood cells) were given the drug by vein, rather than by breathing the irritating gas. Their improvement, although temporary, was remarkable.

That experience led researchers to look for other substances that might have similar effects against cancer. As a result, many other drugs have been developed.

Why chemotherapy is different from other treatments

Treatments like radiation and surgery are considered *local treatments*. They act only in one area of the body such as the breast, lung, or prostate and usually target the cancer directly. Chemotherapy differs from surgery or radiation in that it's almost always used as a *systemic treatment*. This means the drugs travel throughout the body to reach cancer cells wherever they are. (There are ways to use chemotherapy to treat one part of the body. This is discussed in the section called "How is chemotherapy given?")

Chemotherapy is used to treat many cancers. More than 100 chemotherapy drugs are used today — either alone or in combination with other drugs or treatments. As research continues, more drugs are expected to become available. These drugs vary widely in their chemical composition, how they are taken, their usefulness in treating specific forms of cancer, and their side effects.

New drugs are first developed through research in test tubes and animals. Then the drugs are tested in clinical trials in humans to find out how safe they are and how well they work.

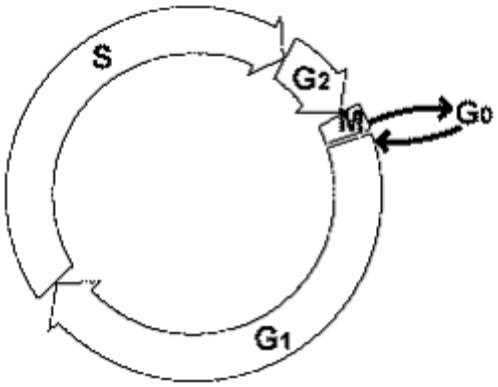
How chemotherapy works

To understand how chemotherapy works, it helps to understand the normal life cycle of a cell, or the *cell cycle*. All living tissue is made up of cells. Cells grow and reproduce to replace cells lost through injury or normal "wear and tear." The cell cycle is a series of steps that both normal cells and cancer cells go through in order to form new cells.

This discussion is somewhat technical, but it can help you understand how doctors predict which drugs are likely to work well together and how doctors decide how often doses of each drug should be given.

The cell cycle has 5 phases which are labeled below using letters and numbers. Since cell reproduction happens over and over, the cell cycle is shown as a circle. All the steps lead back to the resting phase (G0), which is the starting point.

After a cell reproduces, the 2 new cells are identical. Each of the 2 cells made from the first cell can go through this cell cycle again when new cells are needed.



The Cell Cycle

G0 phase (resting stage): The cell has not yet started to divide. Cells spend much of their lives in this phase. Depending on the type of cell, G0 can last from a few hours to a few years. When the cell gets a signal to reproduce, it moves into the G1 phase.

G1 phase: During this phase, the cell starts making more proteins and growing larger, so the new cells will be of normal size. This phase lasts about 18 to 30 hours.

S phase: In the S phase, the chromosomes containing the genetic code (DNA) are copied so that both of the new cells formed will have matching strands of DNA. The S phase lasts about 18 to 20 hours.

G2 phase: In the G2 phase, the cell checks the DNA and gets ready to start splitting into 2 cells. This phase lasts from 2 to 10 hours.

M phase (mitosis): In this phase, which lasts only 30 to 60 minutes, the cell actually splits into 2 new cells.

The cell cycle is important because many chemotherapy drugs work only on cells that are actively reproducing (not cells that are in the resting phase, G0). Some drugs specifically attack cells in a particular phase of the cell cycle (the M or S phases, for example). Understanding how these drugs work helps oncologists predict which drugs are likely to work well together. Doctors can also plan how often doses of each drug should be given based on the timing of the cell phases.

Chemotherapy drugs cannot tell the difference between reproducing cells of normal tissues (those that are replacing worn-out normal cells) and cancer cells. This means normal cells are damaged and this results in side effects. Each time chemotherapy is given, it involves trying to find a balance between destroying the cancer cells (in order to cure or control the disease) and sparing the normal cells (to lessen unwanted side effects).

The goals of chemotherapy

There are 3 possible goals for chemotherapy treatment:

Cure: If possible, chemotherapy is used to cure the cancer, meaning that the cancer disappears and does not return. However, most doctors do not use the word “cure” except as a possibility or intention. When giving treatment that has a chance of curing a person’s cancer, the doctor may describe it as treatment with *curative intent*. But there are no guarantees, and though cure may be the goal, it doesn’t always work out that way. It often takes many years to know if a person’s cancer is actually cured.

Control: If cure is not possible, the goal may be to control the disease — to shrink any cancerous tumors and/or stop the cancer from growing and spreading. This can help someone with cancer feel better and possibly live longer. In many cases, the cancer does not completely go away but is controlled and managed as a chronic disease, much like heart disease or diabetes. In other cases, the cancer may even seem to have gone away for a while, but it’s expected to come back.

Palliation: When the cancer is at an advanced stage, chemotherapy drugs may be used to relieve symptoms caused by the cancer. When the only goal of a certain treatment is to improve the quality of life but not treat the disease itself, it’s called *palliative treatmen*t or palliation.

Chemo that’s given with other treatments

Sometimes, chemotherapy is the only treatment used. In other cases, chemotherapy may be given along with other treatments. It may be used as *adjuvant therapy* or *neoadjuvant therapy*.

Adjuvant chemotherapy: After surgery to remove the cancer, there may still be some cancer cells left behind that cannot be seen. When drugs are used to kill those unseen cancer cells, it’s called adjuvant chemotherapy. Adjuvant treatment can also be given after radiation. An example of this would be adjuvant hormone therapy after radiation for prostate cancer.

Neoadjuvant chemotherapy: Chemotherapy can be given before the main cancer treatment (such as surgery or radiation). Giving chemotherapy first can shrink a large cancerous tumor, making it easier to remove with surgery. Shrinking the tumor may also allow it to be treated more easily with radiation. Neoadjuvant chemotherapy also can kill small deposits of cancer cells that cannot be seen on scans or x-rays.

Different types of chemotherapy drugs

Chemotherapy drugs can be divided into several groups based on factors such as how they work, their chemical structure, and their relationship to another drug. Because some drugs act in more than one way, they may belong to more than one group.

Knowing how the drug works is important in predicting side effects. This helps oncologists decide which drugs are likely to work well together. If more than one drug will be used, this information also helps them plan exactly when each of the drugs should be given (in which order and how often).

Alkylating agents

Alkylating agents directly damage DNA to prevent the cancer cell from reproducing. As a class of drugs, these agents are not phase-specific; in other words, they work in all phases of the cell cycle. Alkylating agents are used to treat many different cancers, including leukemia, lymphoma, Hodgkin disease, multiple myeloma, and sarcoma, as well as cancers of the lung, breast, and ovary.

Because these drugs damage DNA, they can cause long-term damage to the bone marrow. In rare cases, this can eventually lead to acute leukemia. The risk of leukemia from alkylating agents is "dose-dependent," meaning that the risk is small with lower doses, but goes up as the total amount of the drug used gets higher. The risk of leukemia after getting alkylating agents is highest about 5 to 10 years after treatment.

There are different classes of alkylating agents, including:

- Nitrogen mustards: such as mechlorethamine (nitrogen mustard), chlorambucil, cyclophosphamide (Cytoxan®), ifosfamide, and melphalan
- Nitrosoureas: which include streptozocin, carmustine (BCNU), and lomustine
- Alkyl sulfonates: busulfan
- Triazines: dacarbazine (DTIC) and temozolomide (Temodar®)
- Ethylenimines: thiotepa and altretamine (hexamethylmelamine)

The **platinum** drugs (cisplatin, carboplatin, and oxalaplatin) are sometimes grouped with alkylating agents because they kill cells in a similar way. These drugs are less likely than the alkylating agents to cause leukemia later on.

Antimetabolites

Antimetabolites are a class of drugs that interfere with DNA and RNA growth by substituting for the normal building blocks of RNA and DNA. These agents damage cells

during the S phase. They are commonly used to treat leukemias, cancers of the breast, ovary, and the intestinal tract, as well as other types of cancer.

Examples of antimetabolites include:

- 5-fluorouracil (5-FU)
- 6-mercaptopurine (6-MP)
- Capecitabine (Xeloda®)
- Cladribine
- Clofarabine
- Cytarabine (Ara-C®)
- Floxuridine
- Fludarabine
- Gemcitabine (Gemzar®)
- Hydroxyurea
- Methotrexate
- Pemetrexed (Alimta®)
- Pentostatin
- Thioguanine

Anti-tumor antibiotics

Anthracyclines

Anthracyclines are anti-tumor antibiotics that interfere with enzymes involved in DNA replication. These drugs work in all phases of the cell cycle. They are widely used for a variety of cancers. A major consideration when giving these drugs is that they can permanently damage the heart if given in high doses. For this reason, lifetime dose limits are often placed on these drugs.

Examples of anthracyclines include:

- Daunorubicin
- Doxorubicin (Adriamycin®)

- Epirubicin
- Idarubicin

Other anti-tumor antibiotics

Anti-tumor antibiotics that are not anthracyclines include:

- Actinomycin-D
- Bleomycin
- Mitomycin-C

Mitoxantrone is an anti-tumor antibiotic that is similar to doxorubicin in many ways, including the potential for damaging the heart. This drug also acts as a topoisomerase II inhibitor (see below), and can lead to treatment-related leukemia. Mitoxantrone is used to treat prostate cancer, breast cancer, lymphoma, and leukemia.

Topoisomerase inhibitors

These drugs interfere with enzymes called topoisomerases, which help separate the strands of DNA so they can be copied. They are used to treat certain leukemias, as well as lung, ovarian, gastrointestinal, and other cancers.

Examples of topoisomerase I inhibitors include topotecan and irinotecan (CPT-11).

Examples of topoisomerase II inhibitors include etoposide (VP-16) and teniposide. Mitoxantrone also inhibits topoisomerase II.

Treatment with topoisomerase II inhibitors increases the risk of a second cancer — acute myelogenous leukemia (AML). With this type of drug, a secondary leukemia can be seen as early as 2 to 3 years after the drug is given.

Mitotic inhibitors

Mitotic inhibitors are often plant alkaloids and other compounds derived from natural products. They can stop mitosis or inhibit enzymes from making proteins needed for cell reproduction.

These drugs work during the M phase of the cell cycle but can damage cells in all phases. They are used to treat many different types of cancer including breast, lung, myelomas, lymphomas, and leukemias. These drugs are known for their potential to cause peripheral nerve damage, which can be a dose-limiting side effect.

Examples of mitotic inhibitors include:

- Taxanes: paclitaxel (Taxol®) and docetaxel (Taxotere®)
- Epothilones: ixabepilone (Ixempra®)
- Vinca alkaloids: vinblastine (Velban®), vincristine (Oncovin®), and vinorelbine (Navelbine®)
- Estramustine (Emcyt®)

Corticosteroids

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.

Corticosteroids are also commonly used as *anti-emetics* to help prevent nausea and vomiting caused by chemotherapy. They are used before chemotherapy to help prevent severe allergic reactions (hypersensitivity reactions), too. When a corticosteroid is used to prevent vomiting or allergic reactions, it's not considered chemotherapy.

Examples include prednisone, methylprednisolone (Solumedrol®), and dexamethasone (Decadron®).

Miscellaneous chemotherapy drugs

Some chemotherapy drugs act in slightly different ways and do not fit well into any of the other categories.

Examples include drugs like L-asparaginase, which is an enzyme, and the proteosome inhibitor bortezomib (Velcade®).

Other types of cancer drugs

Other drugs and biological treatments are used to treat cancer, but are not usually considered chemotherapy. While chemotherapy drugs take advantage of the fact that cancer cells divide rapidly, these other drugs target different properties that set cancer cells apart from normal cells. They often have less serious side effects than those commonly caused by chemotherapy drugs because they are targeted to work mainly on cancer cells, not normal, healthy cells. Many are used along with chemotherapy.

Targeted therapies

As researchers have learned more about the inner workings of cancer cells, they have begun to create new drugs that attack cancer cells more specifically than traditional

chemotherapy drugs. Most attack cells with mutant versions of certain genes, or cells that express too many copies of a particular gene. These drugs can be used as part of the main treatment, or they may be used after treatment to maintain remission or decrease the chance of recurrence.

Examples of targeted therapies include imatinib (Gleevec®), gefitinib (Iressa®), sunitinib (Sutent®) and bortezomib (Velcade®). Targeted therapies are a huge research focus and probably many more will be developed in the future. You can learn more about them in our separate document, *Targeted Therapy*.

Differentiating agents

These drugs act on the cancer cells to make them mature into normal cells. Examples include the retinoids, tretinoin (ATRA or Atralin®) and bexarotene (Targretin®), as well as arsenic trioxide (Arsenox®).

Hormone therapy

Drugs in this category are sex hormones, or hormone-like drugs, that change the action or production of female or male hormones. They are used to slow the growth of breast, prostate, and endometrial (uterine) cancers, which normally grow in response to natural hormones in the body. These cancer treatment hormones do not work in the same ways as standard chemotherapy drugs, but rather by preventing the cancer cell from using the hormone it needs to grow, or by preventing the body from making the hormones.

Examples include:

- The anti-estrogens: fulvestrant (Faslodex®), tamoxifen, and toremifene (Fareston®)
- Aromatase inhibitors: anastrozole (Arimidex®), exemestane (Aromasin®), and letrozole (Femara®)
- Progestins:megestrol acetate (Megace®)
- Estrogens
- Anti-androgens: bicalutamide (Casodex®), flutamide (Eulexin®), and nilutamide (Nilandron®)
- Gonadotropin-releasing hormone (GnRH), also known as luteinizing hormone-releasing hormone (LHRH) agonists or analogs: leuprolide (Lupron®) and goserelin (Zoladex®)

Immunotherapy

Some drugs are given to people with cancer to stimulate their natural immune systems to recognize and attack cancer cells. These drugs offer a unique method of treatment, and are often considered to be separate from chemotherapy. Compared with other forms of cancer treatment such as surgery, radiation therapy, or chemotherapy, immunotherapy is still fairly new.

There are different types of immunotherapy. *Active immunotherapies* stimulate the body's own immune system to fight the disease. *Passive immunotherapies* do not rely on the body to attack the disease; instead, they use immune system components (such as antibodies) created outside the body.

Types of immunotherapies and some examples include:

- Monoclonal antibody therapy (passive immunotherapies), such as rituximab (Rituxan®) and alemtuzumab (Campath®)
- Non-specific immunotherapies and adjuvants (other substances or cells that boost the immune response), such as BCG, interleukin-2 (IL-2), and interferon-alfa
- Immunomodulating drugs, for instance, thalidomide and lenalidomide (Revlimid®)
- Cancer vaccines (active specific immunotherapies). In 2010, the FDA approved the first vaccine to treat cancer (the Provenge® vaccine for advanced prostate cancer); other vaccines for many different types of cancer are being studied

For more specific information on these types of drugs see our document called *Immunotherapy*.

Deciding which chemotherapy drugs to use

In some cases, the best choice of doses and schedules for giving each drug are clear, and most oncologists would recommend the same treatment. In other cases, less may be known about the single best way to treat people with certain types and stages of cancer. In these situations different cancer doctors might choose different drug combinations with different schedules.

Factors to consider in choosing which drugs to use for a chemotherapy regimen include:

- The type of cancer
- The stage of the cancer (how far it has spread)
- The patient's age
- The patient's general state of health

- Other serious health problems (such as heart, liver, or kidney diseases)
- Types of cancer treatments given in the past

Doctors take these factors into account, along with information published in medical journals and textbooks describing the outcomes of similar patients treated with chemotherapy.

Chemotherapy regimens or treatment plans may use a single drug or a combination of drugs. Oncologists recommend a combination of drugs for most people with cancer. This is typically more effective than a single drug, as the cancer cells can be attacked in several different ways. Doctors must also consider side effects of each drug and any potential interactions among the drugs.

Side effects

Different drugs have different side effects. It's often better to use moderate doses of 2 drugs that will cause bearable side effects, rather than very high doses of a single drug that might cause severe side effects and maybe permanently damage an important organ. But there are exceptions to this rule, and a single chemotherapy drug may be the best option for some people with certain types of cancer.

Doctors try to give chemotherapy at levels high enough to cure or control the cancer, while keeping side effects at a minimum. They also try to avoid multiple drugs that have similar side effects.

Drug interactions

In addition to considering how to best combine 2 or more chemotherapy drugs, doctors must also consider potential interactions between chemotherapy drugs. They have to look at interactions between chemo drugs and other medicines, too, including vitamins and non-prescription medicines. In some patients, these interactions may make side effects worse. In others, they may interfere with the effectiveness of the chemotherapy.

It's important that you tell your doctor about all medicines you are taking, including vitamins, herbal or dietary supplements, and non-prescription medicines.

For example, platelets are the blood cells that cause blood to clot and prevent bleeding. Many chemotherapy drugs temporarily slow down the bone marrow's production of platelets. Taking aspirin or other related drugs can also weaken blood platelets. This is not a problem for healthy people with normal platelet counts. But if a person has low platelet counts from chemotherapy, this combination may put them at risk of a serious bleeding problem.

Vitamins

Many people want to take an active role in improving their general health to help their body's natural defenses fight the cancer and speed up their recovery from the side effects of chemotherapy.

Because most people think of vitamins as a safe way to improve health, it's not surprising that many people with cancer take high doses of one or more vitamins. But few realize that some vitamins might make their chemotherapy less effective.

Certain vitamins, such as A, E, and C act as antioxidants. This means that they can prevent formation of ions (free radicals) that damage DNA. This damage is thought to have an important role in causing cancer. There is some evidence that getting enough of these vitamins (through a balanced diet and, perhaps, by taking vitamin supplements) may help reduce the risk of developing some types of cancer.

On the other hand, some chemotherapy drugs (as well as radiation treatments) work by producing these same types of free radical ions. These ions severely damage the DNA of cancer cells so the cells are unable to grow and reproduce. Some scientists believe that taking high doses of antioxidants during treatment may make chemotherapy or radiation less effective. Few studies have been done to thoroughly test this theory.

Until we know more about the effects of vitamins on chemotherapy drugs, many oncologists recommend the following during chemotherapy:

- If your doctor has not prescribed vitamins for a specific reason, it's best not to take any.
- A simple multivitamin is probably OK for people who want to take a vitamin supplement, but always check with your doctor first.
- It's safest to avoid taking high doses of antioxidant vitamins during cancer treatment. Ask your doctors if and when it might be safe to start such vitamins after treatment is finished.
- If you are concerned about nutrition, you can usually get plenty of vitamins by eating a well-balanced diet.

Planning drug doses and schedules

Some drugs, especially those available without a prescription, have a fairly wide *therapeutic index*. This means that wide ranges of doses can be used effectively and safely. For example, the label on a bottle of aspirin may suggest taking 2 tablets for a mild headache. But one tablet (half the dose) is likely enough to help many people.

Most chemotherapy drugs, on the other hand, are strong medicines that have a fairly narrow range of safe and effective doses. Taking too little of a drug will not effectively treat the cancer and taking too much may cause life-threatening side effects. For this reason, doctors must calculate chemotherapy doses very precisely.

Doses

Depending on the drug(s) to be given, there are different ways to determine chemotherapy doses. Most chemotherapy drugs are measured in milligrams (mg).

The overall dose may be based on a person's body weight in kilograms (1 kilogram is 2.2 pounds). For instance, if the standard dose of a drug is 10 milligrams per kilogram (10 mg/kg), a person weighing 110 pounds (50 kilograms) would receive 500 mg (10 mg/kg x 50 kg).

Some chemotherapy doses are determined based on body surface area (BSA), which doctors calculate using your height and weight. BSA is expressed in meters squared (m^2).

Dosages for children and adults differ, even after BSA is taken into account. This is because children's bodies process drugs differently. They may have different levels of sensitivity to the drugs, too. For the same reasons, dosages of some drugs may also be adjusted for people who:

- Are elderly
- Have poor nutritional status
- Are obese
- Have already taken or are currently taking other medicines
- Have already had or are currently receiving radiation therapy
- Have low blood cell counts
- Have liver or kidney diseases

Schedule (cycles)

Chemotherapy is generally given at regular intervals called *cycles*. A chemotherapy cycle may involve a dose of one or more drugs followed by several days or weeks without treatment. This gives normal cells time to recover from the drug's side effects. Sometimes, doses may be given several days in a row, or every other day for several days, followed by a period of rest. Some drugs work best when given continuously over a set number of days.

Each drug is given on a schedule that is carefully set up to make the most of its anti-cancer actions and minimize side effects. If more than one drug is used, the treatment plan will specify how often and exactly when each drug should be given. The number of cycles you receive may be decided before treatment starts, based on the type and stage of cancer. In some cases, the number is flexible, and will take into account how the treatment affects the cancer and your overall health.

Changes in doses and schedules

In most cases, the most effective doses and schedules of drugs to treat specific cancers have been found by testing them in clinical trials. It's important, when possible, to get the full course of chemotherapy and to keep the cycles on schedule. This will give you the best chance to get the maximum benefit from treatment.

There may be times, though, when serious side effects require doctors to adjust the chemotherapy plan (dose and/or schedule) to allow your body time to recover. In some cases, supportive medicines such as growth factors may be used to help the body recover more quickly. Again, the key is to give enough medicine to affect the cancer cells without causing other serious problems.

Where is chemotherapy given?

Chemotherapy treatments can be given in the following locations:

- Hospital
- Doctor's office
- Outpatient clinic
- Home
- Workplace

The type of health insurance you have, your personal preference, convenience, the type of drugs to be used, and how the drugs are to be given must all be considered when choosing the best place to get chemotherapy. For example, a chemotherapy regimen that requires placement of a special intravenous catheter and infusion over 24 hours or longer may need to be done in a hospital. Or, this drug may be given through a small, portable pump that you can wear at home or work. The specific drugs and their doses, as well as your general state of health, will determine the expected side effects and how closely you need to be monitored during treatment.

How is chemotherapy given?

Systemic chemotherapy

Drugs used for systemic (total body) chemotherapy can be given in these ways:

- Oral (PO) — taken by mouth (usually as pills)
- Intravenous (IV) — infused through a vein
- Intramuscular (IM) — injected into a muscle
- Subcutaneous (SQ) — injected under the skin

Some chemotherapy drugs are never taken by mouth because the digestive system can't absorb them or because they irritate the digestive system. Even when a drug is available in an oral form (such as a pill or liquid), this method may not be the best choice. For example, some people with certain symptoms (like severe nausea, vomiting, or diarrhea) can't swallow liquids or pills; other people may have trouble remembering when or how many pills to take. Still, chemotherapy drugs are powerful treatments, regardless of their form and the way they are administered.

The term *parenteral* is used to describe drugs given into a vein (intravenously or IV), muscle (intramuscularly or IM), or under the skin (subcutaneously or SQ). The IV route is the most common. IM and SQ injections are less often used because many drugs can irritate or even damage the skin and muscle tissue.

The IV route gets the drug quickly throughout the body. IV therapy may be given through a catheter placed in a vein in the arm or hand, which is called a "peripheral line." IV drugs can also be given through a catheter placed into a larger vein in the chest, or neck which is known as a *central venous catheter* (CVC) or "central line."

Central venous catheters (CVCs) or vascular access devices (VADs) may be needed.

Central venous catheters are also known as *vascular access devices*. Some types of catheters are put into the arm (so they're inserted peripherally), but are threaded into a larger vein in the chest. They are used for these reasons:

- To give several drugs at one time
- For long-term therapy (to reduce the number of needle sticks)
- For frequent treatments (using a CVC won't cause as much wear and tear to the veins, potential scarring, and discomfort as numerous IVs that go into the small veins of the arms or hands)

- For continuous infusion chemotherapy
- To give drugs that can cause serious damage to skin and muscle tissue if they leak outside of a vein (these drugs are known as *vesicants*). Delivering these through a CVC provides more reliable access to a vein than a short-term IV, reducing the risk that the drug will leak outside the vein and damage tissues.

Many different types of CVCs can be used to allow an easier route for IV medicines. These CVCs have different types of catheters and ports. The type of CVC used is based on how long you'll be getting treatment, how long it takes to infuse each dose of chemotherapy, your preferences, your doctor's preferences, the care required to maintain the CVC, and its cost. Before you consent to a vascular access device, find out more from the doctor about the type he or she recommends and why. Devices are placed in different parts of the body and require different levels of care. Some can restrict certain activities that you normally do, and safety can be a concern as well. Each type comes with its own potential problems and complications. Ask about other options to be sure that you get the type that will work best for you while still meeting your treatment needs. Also find out if your health insurance will cover the costs of the CVC.

Types of central venous catheters or vascular access devices

Type of device and some brand names	**Comments**
PICC (peripherally inserted central catheter) (pronounced "pick") (Per-Q-Cath, Groshong PICC)	Inserted in a vein in the arm and threaded up near the heart. An intermediate-term catheter which allows for continuous access for several weeks to months. No surgery is needed. Care of the external catheter and regular flushing is needed.
Midline catheter (Per-Q-Cath Midline, Groshong Midline)	Also placed in a vein in the arm, but the catheter is not threaded as far as a PICC. This catheter is used for intermediate length therapy when a regular short-term IV is not advisable or available. No surgery is needed. Care of the external catheter and regular flushing is needed.
Tunneled central venous catheter (Hickman, Broviac, Groshong, Neostar)	The catheter can have multiple separate lumens (channels or tubes) and is surgically placed in a large central vein in the chest. The catheter is tunneled under the skin, but the openings to the lumens remain outside the body. This is a long-term catheter that's good for months to years. Site care of external catheter and

	regular flushing is needed.
Implantable venous access port (Port-A-Cath, BardPort, PassPort, Medi-port, Infusaport)	A drum-shaped port of plastic, stainless steel, or titanium with a silicone septum across the top. This device is surgically placed under the skin of the chest or upper arm. The attached catheter extends into a large or central vein. The port is accessed through the skin and into the septum with a non-coring needle. It's intended for long-term use. No routine care is needed when there's no needle in the port, but it may need to be flushed if not used for more than a month at a time.
Implantable pump	A titanium pump with an internal power source surgically implanted to give continuous infusion chemotherapy, usually at home. There is a refillable reservoir for continuous infusions that is accessed by sticking a needle through the skin.

Most of the time, these catheters or ports are put in while you are awake. The port or catheter insertion may be done in the treatment center, clinic, or hospital. You can check with your doctor or nurse about whether you need to limit your food and fluid intake before the procedure, and if medicine will be used to keep you comfortable. Inserting some of the vascular access devices is more involved than others, and may require medicine that lessens pain and makes you sleepy. Check with your doctor to find out if you need a friend or relative to drive you home after the procedure.

Potential problems with central venous catheters or vascular access devices that may happen when the catheter is put in:

- Anything that's put inside a blood vessel might damage the vessel, cause bruising or bleeding at the puncture site, or cause infection.
- Bleeding — the doctor will do blood tests before the catheter is put in to be sure that your blood clots normally. Even with normal clotting, blood can leak out of the vein and cause bruising, pressure on other blood vessels or organs, and other problems.
- Sometimes a condition called a *pneumothorax* may develop when a CVC is placed in the chest or neck. This happens when a lung is punctured and air collects in the chest outside the lung. It may cause one of the lungs to collapse. If placement is guided by ultrasound or fluoroscopy, it greatly decreases this risk.

- Normal heart rhythm may be disturbed when the catheter is put in. This is usually only temporary and stops when the catheter position is changed. It rarely causes serious problems.
- In rare cases, the catheter will go into an artery instead of a vein. If this happens, the catheter will have to be taken out. If there are no other complications, the artery usually heals by itself.
- Infection may develop at the incision that is made to put in the catheter. Be sure to follow any instructions about caring for the incisions as they heal.

Potential problems with central venous catheters or vascular access devices that may happen sometime later:

- Infection — skin infection can start where the catheter or port goes into the body. More serious bloodstream infections can also happen in some cases. The chance of infection can be minimized if you (and anyone else who handles the catheter) wash your hands before using it, change the dressing carefully, check the skin each time the dressing is changed, and use careful sterile technique when using the catheter.
- A hole or break in the catheter may lead to a fluid leak. It's important to not always clamp the catheter in the same spot, which can weaken that area. Never use too much force when flushing it.
- Any type of catheter may become blocked by clotted blood. You can minimize this risk by carefully flushing the catheter as instructed. Once a catheter becomes blocked off (occluded), it sometimes can be opened by injecting certain medicines, but in some cases it may need to be removed or replaced.
- The catheter may move or be pulled out if it's not taped or sutured to the skin.
- The catheter should always be clamped when not in use, and caps should be screwed on tightly to keep air from getting in the bloodstream. A large amount of air in the catheter may create an emergency that causes chest pain or shortness of breath.
- If the vein the catheter is in gets blocked (closed off) a blood clot may develop and the arm, shoulder, neck, or head may swell. The clot may be treated with blood thinners, but in some cases, the catheter will have to be removed.

Be sure you understand the benefits and risks of having a CVC or other VAD. Know what problems to watch for, what to do about them, and when to call your doctor.

Regional chemotherapy

When there's a need to get high doses of chemotherapy to a specific area of the body, it may be given by a regional method. Regional chemotherapy directs the anti-cancer drugs

into the part of the body where the cancer is. The purpose is to get more of the drug to the cancer, while trying to minimize side effects on the whole body. Side effects will often still happen because the drugs can be partly absorbed into the bloodstream and travel throughout the body. Examples of regional chemotherapy include drugs given into these parts of the body:

- Intra-arterial — injected into an artery that goes to a certain area of the body
- Intravesical — infused into the bladder
- Intrapleural — infused into the chest cavity between the lung and chest wall
- Intraperitoneal — infused into the abdomen around the intestines and other organs
- Intrathecal — infused into the central nervous system via spinal fluid
- Intralesional/intratumoral — injected directly into the tumor
- Topical — applied to the skin as a cream or lotion

Intra-arterial chemotherapy

An intra-arterial infusion allows a chemotherapy drug to be given directly to the cancerous tumor through a catheter placed in the artery that supplies blood to the tumor. This method is used to treat disease in an organ such as the liver (isolated hepatic perfusion), or to treat an extremity such as the leg (isolated limb perfusion).

The goal is to concentrate the drug in the area of the tumor and decrease systemic side effects. The catheter is attached to an implanted or portable pump. Although this approach sounds like a good idea for better effectiveness and fewer side effects, most studies have not found it to be as useful as expected. This approach is being studied for many types of cancer in clinical trials. Except for these clinical trials, it’s rarely available outside of specialized cancer centers.

Intracavitary chemotherapy

Intracavitary is a broad term used to describe chemotherapy given directly into a body cavity. The chemo drug is given through a catheter placed into one of these areas as described below.

Intravesical chemotherapy is often used for early stage bladder cancer. The chemotherapy is usually given weekly for 4 to 12 weeks. For each treatment, a urinary catheter is placed into the bladder to give the drug. The drug is kept in the bladder for about 2 hours and then drained. The urinary catheter is removed after each treatment.

Intrapleural chemotherapy is not used very often but may be helpful for some people with mesothelioma (cancer that develops in the lining of the lung), and those with lung or

breast cancers that have spread to the pleura (the membrane around the lungs and lining the chest cavity). Intrapleural chemotherapy is given through chest catheters that may be connected to an implantable port. These catheters can be used to give drugs and to drain fluid that can build up in the pleural space when cancer has spread to that area.

Intraperitoneal chemotherapy has become one of the standard treatments for certain stages of ovarian cancer. It may also be used to treat some recurrent colon cancers, as well as cancers of the appendix or stomach that have spread extensively within the abdomen. Intraperitoneal chemotherapy is given through a Tenckhoff catheter (a catheter specially designed for removing or adding large amounts of fluid from or into the abdominal cavity) or through an implanted port attached to a catheter. Chemotherapy injected into the port travels through the catheter into the abdominal cavity where it's absorbed into the affected area before entering the bloodstream. This approach can work very well, but it can also have more severe side effects than regular IV chemotherapy. The higher doses that are used, along with more gradual absorption of the drug into the body, may be part of why the side effects may be worse.

Intrathecal chemotherapy is given directly into the fluid surrounding the brain and spinal cord (the cerebrospinal fluid or CSF) to reach cancer cells in the fluid and the central nervous system (brain and spinal cord). Most chemotherapy drugs that are put into the bloodstream are unable to cross the barrier between the bloodstream and the central nervous system, called the *blood-brain barrier*. Intrathecal chemotherapy gets the drug directly to the central nervous system.

Intrathecal chemotherapy is given in 1 of 2 ways:

- The chemotherapy can be given by a *lumbar puncture* (spinal tap) done daily or weekly. This is when a thin needle is placed between the bones of the lower spine and into the space through which the CSF flows around the spinal cord.
- A special device called an *Ommaya reservoir* can be used. It's a small, drum-like port which is placed under the skin of the skull. An attached catheter goes through the skull into a ventricle (a space inside the brain filled with CSF). A special needle is put through the skin and into the port to give the chemotherapy.

Chemotherapy is given this way when it's needed to treat cancer cells that have entered the central nervous system (this is called *leptomeningeal spread*). This is seen most commonly in leukemias, but also may happen with some lymphomas and advanced solid tumors like breast and lung cancers. Intrathecal chemotherapy does not help when tumors have already started growing in the brain or spinal cord.

Intralesional chemotherapy

Intralesional chemotherapy refers to the drug being injected directly into the cancerous tumor. It may be used for tumors that are in or under the skin, and rarely for tumors that

are on an organ inside the body. It's only possible when the tumor can be safely reached by a needle, and is most often used when surgery is not an option.

Topical chemotherapy

In this use, chemotherapy is applied to the skin in the form of a cream or lotion. Most often, it's put onto skin cancers such as the basal cell or squamous cell types. It's also used to treat pre-cancerous growths on the skin. The patient or a family member usually puts on the chemotherapy cream. It's important to understand the schedule, know exactly how to use these potent drugs, and know what kinds of precautions to use.

Safety precautions

For health professionals

Many chemotherapy drugs are considered hazardous to healthy people. That's why the nurses and doctors who give chemotherapy will take precautions to avoid direct contact with the drugs while giving them to you.

Chemotherapy drugs can be dangerous to others in these ways:

- They can cause abnormal changes in DNA. (They are *mutagenic.*)
- They may be able to alter development of a fetus or embryo, leading to birth defects. (They are *teratogenic*.)
- They may be able to cause another type of cancer. (They are *carcinogenic*.)
- Some may cause skin irritation or damage.

Nurses may wear special gloves, goggles, and gowns when preparing and giving you chemotherapy. Pharmacists or nurses prepare the drugs in areas with special ventilation systems to avoid spattering and/or inhaling the droplets that can form while mixing.

If you're in the hospital, the health care professionals caring for you may use special precautions when they handle your urine and stool for a few days after treatment. This is because your body waste may contain the drugs. If you get chemotherapy at home, you will be given special instructions and precautions to ensure the safety of your caregivers and those living with you.

Special procedures are used to dispose of materials that were used to mix and give the drugs. There are separate plastic containers to dispose of sharp items, syringes, IV tubing, and medicine bags. Gowns and gloves are disposed of in special bags. If there are any visible leaks or spills, special precautions are used to clean up the drugs.

For patients and their loved ones

There are many things you can do during and after chemotherapy to keep yourself and your loved ones from being affected by the drugs while your body is getting rid of them. It takes about 48 hours for your body to break down and/or get rid of most chemo drugs.

Most of this comes out in your body fluids — urine, stool, tears, saliva, and vomit. The drugs are also found in your blood. When these drugs leave your body as waste, they can harm or irritate skin — even other people's skin. Keep in mind that for this reason, toilets can be a hazard for children and pets and it's important to be careful. Talk to your doctor about these and any other precautions you should follow.

During and for 48 hours after you finish getting chemotherapy:

- Flush the toilet twice after you use it. Put the lid down before flushing to avoid splashing. If possible, you might want to use a separate toilet during this time.
- Both men and women should sit on the toilet to use it. This cuts down on splashing.
- Always wash your hands with warm water and soap after using the toilet. Use paper towels to dry your hands.
- If you vomit into the toilet, clean off all splashes and flush twice. If you vomit into a bucket or basin, carefully empty it into the toilet without splashing the contents and flush twice. Wash out the bucket with hot soapy water and rinse it, emptying the wash and rinse water into the toilet, then flushing it. Dry the bucket with paper towels and throw them away.
- Caregivers should wear throw-away waterproof gloves if they need to touch any of your body fluids. (These can be bought in most drug stores.) They should always wash their hands with warm water and soap afterward — even if they wore gloves.
- If a caregiver does come in contact with any of your body fluids they should wash the area very well with warm soap and water. Although this isn't likely to cause any harm, try to take extra care to avoid this. At your next visit, let your doctor know this happened. Being exposed frequently may lead to problems.
- Use a condom during sex. The drugs can be found in semen and vaginal secretions.
- Drugs might also be found in saliva, so avoid deep kissing and sharing food or drinks with others. Clean flatware and dishes thoroughly with soap and warm water and rinse well before washing a second time with the other dishes.
- Any clothes or sheets that have body fluids on them should be washed in your washing machine — not by hand. Wash them twice in hot water with regular laundry detergent. Do not wash them with other clothes. If they cannot be washed right away seal them in a plastic bag.

- If using throw-away adult diapers, underwear, or sanitary pads, seal them in plastic and throw them away with your regular trash.

Adapted from The Cleveland Clinic Foundation. Chemotherapy Precautions During and After Treatment. 2012. Available at http://my.clevelandclinic.org/services/Bone_Marrow_Transplantation/hic_Chemotherapy_Precautions_During_and_After_Treatment.aspx

Chemotherapy side effects

Although chemotherapy is given to kill cancer cells, it also damages normal cells. The normal cells most likely to be damaged are those that divide rapidly, for instance:

- Bone marrow/blood cells
- Cells of hair follicles
- Cells lining the digestive tract
- Cells lining the reproductive tract

Damage to these cells accounts for many of the side effects of chemotherapy drugs. Side effects are different for each chemotherapy drug. They also differ based on the dose, the way the drug is given, and how the drug affects you individually.

If you would like more information on chemotherapy side effects and how to manage them, please call us at 1-800-227-2345, read our booklet called *Understanding Chemotherapy: A Guide for Patients and Families*, or find more on our Web site at www.cancer.org. You can also find more on side effects in the “To learn more” section.

Questions to ask about chemotherapy

Your doctor will recommend a chemotherapy plan based on your medical history, type of cancer, extent of cancer, current state of health, and the current research.

You may want to ask your doctor or nurses the following questions about your chemotherapy treatment plan:

- What is the goal of this course of chemotherapy? Cure? Control? To ease symptoms?
- What chemotherapy drugs will I be given?
- How will I take these drugs (by mouth, as a shot, or through a vein)?
- How often will I need to get chemotherapy?
- How long will I be getting chemotherapy treatments?

- Where will I get my treatments?
- Are there ways to help me prepare for treatment and decrease the chance of side effects?
- How will we know if treatment's working?
- What side effects might I have?
- What activities should I do or not do to take care of myself?
- Can I keep working (or going to school) during treatment?
- What long-term effects might I expect?
- What problems should I call you about, even at night or on the weekends?
- How can I contact you after office hours if I have problems that you need to know about?
- How much will chemotherapy cost? Will it be covered by my insurance or health plan?
- If the insurance company requests a second opinion, or if I would like one, how do I go about doing that?

What's new in chemotherapy research?

Over the years, many people have been successfully treated with chemotherapy thanks to ongoing research into the use of these drugs. Yet despite the best treatments, some cancers are very difficult to control, and some will come back.

Several exciting new uses of chemotherapy and other agents hold even more promise for curing or controlling cancer. New drugs, new combinations of drugs, and new delivery techniques will help doctors cure or control cancer and improve the quality of life for people with cancer. There are many expected advances in coming years; here are just a few:

- New classes of chemotherapy medicines and combinations of medicines are being developed.
- New ways to give the drugs are being studied, such as using smaller amounts over longer periods of time or giving them continuously with special pumps.
- Some newer medicines, called *targeted therapies*, are designed to attack a particular target on cancer cells. These drugs may have fewer side effects than standard

chemotherapy drugs and may be used along with them. Several are now being studied, and many are already being used.

- Other approaches to targeting drugs more specifically at the cancer cells — such as attaching drugs to *monoclonal antibodies* — may make them work better and cause fewer side effects. Monoclonal antibodies, which are special types of proteins made in the lab, can be designed to guide chemotherapy drugs directly to the cancer cells. A number of these are being studied and some are available through clinical trials. A couple of monoclonal antibodies that deliver radiation to the cancer cells have already been approved.

- Monoclonal antibodies (without attached chemotherapy) can also be used as immunotherapy drugs, to strengthen the body's immune response against cancer cells. A number of these types of drugs have been approved, and more are being studied. For more on these drugs, see our document called *Immunotherapy*.

- *Liposomal therapy* uses chemotherapy drugs that have been packaged inside liposomes (synthetic fat globules). The liposome helps the drug penetrate the cancer cells more selectively and decreases possible side effects (such as hair loss and nausea and vomiting). Examples of liposomal medicines already being used are Doxil® (the encapsulated form of doxorubicin) and DaunoXome® (the encapsulated form of daunorubicin).

- Chemoprotective agents are being developed to protect against specific side effects of certain chemotherapy drugs. For example, dexrazoxane (Zinecard®) helps prevent heart damage, amifostine (Ethyol®) helps protect the kidneys, and mesna protects the bladder.

- Some new agents may be given along with chemotherapy to help overcome drug resistance. Cancer cells often become resistant to chemotherapy by developing the ability to pump the drugs out of the cells. These new agents inactivate the pumps, which allows the chemotherapy to remain in the cancer cells longer, which might make it more effective.

Chemotherapy in clinical trials

Chemotherapy drugs are still being developed and tested, and approved drugs are being studied in new ways. Clinical trials are studies of new or experimental drugs or other new treatment methods (including new regimens that use older drugs) in human volunteers. These studies are done when there's a reason to believe a new drug or a new combination of drugs may be valuable in curing or controlling cancer.

If you wish to take part in a clinical trial, the researchers will fully explain the requirements to you and your family. You can always refuse to take part in the study, or

leave the study at any time if you change your mind. Being in a clinical trial does not keep you from getting other medical or nursing care that you need.

People who volunteer to take part in clinical trials make an important contribution to medical care because the study results will also help future patients. At the same time, they may be among the first to benefit from these new treatments. To learn more about clinical trials, please see our document called *Clinical Trials: What You Need to Know*.

The American Cancer Society offers a clinical trials matching service for patients, their families, and friends. You can reach this service by calling 1-800-303-5691, or online at www.cancer.org. Based on the information you provide about your cancer type, stage, and previous treatments, the service will compile a list of clinical trials that match your medical needs. To help find a center more convenient for you, the service can also take into account where you live and whether you are willing to travel.

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

To learn more

More information from your American Cancer Society

The following related information may also be helpful to you. These materials may be read on our Web site or ordered from our toll-free number, 1-800-227-2345.

More on chemotherapy

Chemo - What It Is, How It Helps (also in Spanish)

Oral Chemotherapy: What You Need to Know

Understanding Chemotherapy: A Guide for Patients and Families (also in Spanish)

More on certain types of chemotherapy

Immunotherapy

Targeted Therapy

We also have information on individual chemotherapy drugs and almost any other drug used in cancer treatment

More on chemotherapy side effects

Chemotherapy Side Effects Worksheet

Anemia in People With Cancer

Chemo Brain

Distress in People With Cancer

Fatigue in People With Cancer

Fertility and Women With Cancer

Fertility and Men With Cancer

Infections in People With Cancer

Nausea and Vomiting

Peripheral Neuropathy Caused by Chemotherapy

Sexuality for the Man With Cancer (also in Spanish)

Sexuality for the Woman With Cancer (also in Spanish)

Second Cancers Caused by Cancer Treatment

Childhood Cancer: Late Effects of Cancer Treatment

National organizations and Web sites*

Along with the American Cancer Society, other sources of information and support include:

CancerCare
Toll-free number: 1-800-813-4673
Web site: www.cancercare.org

> Provides free information, counseling, and support services to anyone affected by cancer.

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

Provides accurate, up-to-date information about cancer to patients, their families, health professionals, and the general public. Offers a clinical trials matching service. The Web site is also available in Spanish.

**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 **1-800-227-2345** or visit www.cancer.org.

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