

Chemotherapy (often abbreviated to chemo and sometimes CTX or CTx) is a type of cancer treatment that uses one or more anti-cancer drugs (chemotherapeutic agents) as part of a standardized chemotherapy regimen.

Chemotherapy may be given with a curative intent (which almost always involves combinations of drugs), or it may aim to prolong life or to reduce symptoms (palliative chemotherapy).

Chemotherapy is one of the major categories of the medical discipline specifically devoted to pharmacotherapy for cancer, which is called medical oncology.

The use of drugs (whether chemotherapy, hormonal therapy or

targeted therapy) constitutes systemic therapy for cancer in that they are introduced into the blood stream and are therefore in principle able to address cancer at any anatomic location in the body.

Traditional chemotherapeutic agents are cytotoxic by means of interfering with cell division (mitosis) but cancer cells vary widely in their susceptibility to these agents.

To a large extent, chemotherapy can be thought of as a way to damage or stress cells, which may then lead to cell death.

Many of the side effects of chemotherapy can be traced to damage to normal cells that divide rapidly and are thus sensitive to anti-

mitotic drugs: cells in the bone marrow, digestive tract and hair follicles.

This results in the most common side-effects of chemotherapy: myelosuppression (decreased production of blood cells, hence also immunosuppression), mucositis (inflammation of the lining of the digestive tract), and alopecia (hair loss).

Chemotherapy may be given with a curative intent or it may aim to prolong life or to palliate symptoms.

Induction chemotherapy is the first line treatment of cancer with a chemotherapeutic drug. This type of chemotherapy is used for curative intent.

Combined modality chemotherapy is the use of drugs with other cancer treatments, such as surgery, radiation therapy, or hyperthermia therapy.

Consolidation chemotherapy is given after remission in order to prolong the overall disease-free time and improve overall survival.

Intensification chemotherapy is identical to consolidation chemotherapy but a different drug than the induction chemotherapy is used.

Combination chemotherapy involves treating a person with a number of different drugs simultaneously.

The drugs differ in their mechanism and side-effects. eloping to any one agent.

Neoadjuvant chemotherapy is given prior to a local treatment such as surgery and is designed to shrink the primary tumor.

It is also given to cancers with a high risk of micrometastatic disease.

Adjuvant chemotherapy is given after a local treatment (radiotherapy or surgery).

It can be used when there is little evidence of cancer present, but there is risk of recurrence.

It is also useful in killing any cancerous cells that have spread to other parts of the body.

Maintenance chemotherapy is a repeated low-dose treatment to prolong remission.

Salvage chemotherapy or palliative chemotherapy is given without curative intent, but simply to decrease tumor load and increase life expectancy.

All chemotherapy regimens require that the recipient be capable of undergoing the treatment.

Because only a fraction of the cells in a tumor die with each treatment (fractional kill), repeated doses must

be administered to continue to reduce the size of the tumor.

Current chemotherapy regimens apply drug treatment in cycles, with the frequency and duration of treatments limited by toxicity.

## Efficacy

The efficacy of chemotherapy depends on the type of cancer and the stage.

The overall effectiveness ranges from being curative for some cancers, such as some leukemias, to being ineffective, such as in some brain tumors, to being needless in others, like most non-melanoma skin cancers.

The dosage of chemotherapy can be difficult: If the dose is too low, it will be ineffective against the tumor, whereas, at excessive doses, the toxicity (side-effects) will be intolerable to the person receiving it.

Drug absorption and clearance are influenced by multiple factors, including age, gender, metabolism, disease state, organ function, drug-to-drug interactions, genetics, and obesity, which has a major impact on the actual concentration of the drug in the person's bloodstream.

The result of this pharmacokinetic variability among people is that many people do not receive the right dose to achieve optimal treatment effectiveness with minimized toxic side effects.

Some people are overdosed while others are underdosed.

One approach that can help clinicians individualize chemotherapy dosing is to measure the drug levels in blood plasma over time and adjust dose according to a formula or algorithm to achieve optimal exposure.

Oncologists are already individualizing dosing of some cancer drugs based on exposure.

## Types

### Alkylating agents

Alkylating agents will work at any point in the cell cycle and thus are

known as cell cycle-independent drugs.

For this reason, the effect on the cell is dose dependent; the fraction of cells that die is directly proportional to the dose of the drug.

## Antimetabolites

Anti-metabolites are a group of molecules that impede DNA and RNA synthesis.

These drugs exert their effect by either blocking the enzymes required for DNA synthesis or becoming incorporated into DNA or RNA.

By inhibiting the enzymes involved in DNA synthesis, they prevent mitosis

because the DNA cannot duplicate itself.

## Anti-microtubule agents

Anti-microtubule agents are plant-derived chemicals that block cell division by preventing microtubule function.

## Topoisomerase inhibitors

### Topoisomerase I and II Inhibitors

Topoisomerase inhibitors are drugs that affect the activity of two enzymes.

## Cytotoxic antibiotics

The cytotoxic antibiotics are a varied group of drugs that have various mechanisms of action.

Most chemotherapy is delivered intravenously, although a number of agents can be administered orally.

There are many intravenous methods of drug delivery, known as vascular access devices.

The devices have different applications regarding the duration of chemotherapy treatment, a method of delivery and types of chemotherapeutic agent.

Depending on the person, the type of cancer, the stage of cancer, the type of chemotherapy, and the dosage, intravenous chemotherapy may be

given on either an inpatient or an outpatient basis.

## Adverse effects

Chemotherapeutic techniques have a range of side-effects that depend on the type of medications used.

The most common medications affect mainly the fast-dividing cells of the body, such as blood cells and the cells lining the mouth, stomach, and intestines.

Chemotherapy-related toxicities can occur acutely after administration, within hours or days, or chronically, from weeks to years.

Virtually all chemotherapeutic regimens can cause depression of the

immune system, often by paralyzing the bone marrow and leading to a decrease of white blood cells, red blood cells, and platelets.

Although people receiving chemotherapy are encouraged to wash their hands, avoid sick people, and take other infection-reducing steps, about 85% of infections are due to naturally occurring microorganisms in the person's own gastrointestinal tract (including oral cavity) and skin.

Sometimes, chemotherapy treatments are postponed because the immune system is suppressed to a critically low level.

Neutropenic enterocolitis

Due to immune system suppression, neutropenic enterocolitis (typhlitis) is a "life-threatening gastrointestinal complication of chemotherapy.

Typhlitis is an intestinal infection which may manifest itself through symptoms including nausea, vomiting, diarrhea, a distended abdomen, fever, chills, or abdominal pain and tenderness.

Typhlitis is a medical emergency. It has a very poor prognosis and is often fatal unless promptly recognized and aggressively treated.

Gastrointestinal distress

Nausea, vomiting, anorexia, diarrhea, abdominal cramps, and constipation are common side-effects of

chemotherapeutic medications that kill fast-dividing cells.

## Anemia

Anemia can be a combined outcome caused by myelosuppressive chemotherapy, and possible cancer-related causes such as bleeding, blood cell destruction (hemolysis), hereditary disease, kidney dysfunction, nutritional deficiencies or anemia of chronic disease.

## Fatigue

Fatigue may be a consequence of the type of cancer or its treatment and can last for months to years after treatment.

One physiological cause of fatigue is anemia, which can be caused by chemotherapy, surgery, radiotherapy, primary and metastatic disease or nutritional depletion.

## Nausea and vomiting

Nausea and vomiting are two of the most feared cancer treatment-related side-effects for people with cancer and their families.

## Hair loss

Hair loss (Alopecia) can be caused by chemotherapy that kills rapidly dividing cells; other medications may cause hair to thin.

These are most often temporary effects: hair usually starts to regrow

a few weeks after the last treatment, and can sometimes change color, texture, thickness and style.

## Secondary neoplasm

Development of secondary neoplasia after successful chemotherapy or radiotherapy treatment can occur.

## Infertility

Some types of chemotherapy are gonadotoxic and may cause infertility.

## Peripheral neuropathy

Between 30 and 40 percent of people undergoing chemotherapy experience chemotherapy-induced peripheral neuropathy (CIPN), a progressive, enduring, and often irreversible

condition, causing pain, tingling, numbness, and sensitivity to cold, beginning in the hands and feet and sometimes progressing to the arms and legs.

## Cognitive impairment

Some people receiving chemotherapy report fatigue or non-specific neurocognitive problems, such as an inability to concentrate.

## Tumor lysis syndrome

In particularly large tumors and cancers with high white cell counts, such as lymphomas, teratomas, and some leukemias, some people develop tumor lysis syndrome.

The rapid breakdown of cancer cells causes the release of chemicals from the inside of the cells.

Following this, high levels of uric acid, potassium, and phosphate are found in the blood.

High levels of phosphate induce secondary hypoparathyroidism, resulting in low levels of calcium in the blood.

This causes kidney damage and the high levels of potassium can cause cardiac arrhythmia.

Organ damage

Cardiotoxicity (heart damage)

Hepatotoxicity (liver damage) can be caused by many cytotoxic drugs.

The liver damage can consist of damage to liver cells, hepatic sinusoidal syndrome (obstruction of the veins in the liver), cholestasis (where bile does not flow from the liver to the intestine) and liver fibrosis.

Nephrotoxicity (kidney damage) can be caused by tumor lysis syndrome and also due direct effects of drug clearance by the kidneys.

Ototoxicity (damage to the inner ear) is a common side effect of platinum-based drugs that can produce symptoms such as dizziness and vertigo.

Chemotherapy does not always work, and even when it is useful, it may not completely destroy the cancer.

People frequently fail to understand its limitations.

The blood-brain barrier poses an obstacle to the delivery of chemotherapy to the brain.

This is because the brain has an extensive system in place to protect it from harmful chemicals.

Blood vessels in tumors are very different from those seen in normal tissues.

As a tumor grows, tumor cells furthest away from the blood vessels become low in oxygen (hypoxic).

To counteract this they then signal for new blood vessels to grow.

The newly formed tumor vasculature is poorly formed and does not deliver an adequate blood supply to all areas of the tumor.

This leads to issues with drug delivery because many drugs will be delivered to the tumor by the circulatory system.

## Resistance

Resistance is a major cause of treatment failure in chemotherapeutic drugs.

## Cytotoxics and targeted therapies

Targeted therapies are a relatively new class of cancer drugs that can overcome many of the issues seen with the use of cytotoxics.

Cancer is the uncontrolled growth of cells coupled with malignant behavior: invasion and metastasis (among other features).

It is caused by the interaction between genetic susceptibility and environmental factors.

In the broad sense, most chemotherapeutic drugs work by impairing mitosis (cell division), effectively targeting fast-dividing cells.

As these drugs cause damage to cells, they are termed cytotoxic.

As chemotherapy affects cell division, tumors with high growth rates (such as acute myelogenous leukemia and the aggressive lymphomas, including Hodgkin's disease) are more sensitive to chemotherapy, as a larger proportion of the targeted cells are undergoing cell division at any time.

Chemotherapy drugs are also used in conditioning regimens prior to bone marrow transplant (hematopoietic stem cell transplant).

Conditioning regimens are used to suppress the recipient's immune system in order to allow a transplant to engraft.

## Electrochemotherapy

Electrochemotherapy is the combined treatment in which injection of a chemotherapeutic drug is followed by application of high-voltage electric pulses locally to the tumor.

The treatment enables the chemotherapeutic drugs, which otherwise cannot or hardly go through the membrane of cells to enter the cancer cells.

This allows for greater effectiveness of antitumor treatment being achieved.

## Hyperthermia therapy

Hyperthermia therapy is heat treatment for cancer that can be a

powerful tool when used in combination with chemotherapy (thermochemotherapy) or radiation for the control of a variety of cancers.

The heat can be applied locally to the tumor site, which will dilate blood vessels to the tumor, allowing more of chemotherapeutic medication to enter the tumor.

Additionally, the tumor cell membrane will become more porous, further allowing more of the chemotherapeutic medicine to enter the tumor cell.