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Tracey Murray



Chemotherapy

by **Dr Nick Maisey, Professor David Cunningham, and Lymphoma Clinical Nurse Specialist Tracey Murray**

Introduction

Cytotoxic chemotherapy drugs are drugs that are given to destroy or control cancer cells ('cyto' means cell and 'toxic' means poison). Lymphomas are one of the most sensitive cancers to chemotherapy. The first attempt to treat lymphoma was by the great British surgeon Bilroth, who used arsenic in an attempt to cure his patients! However it was not until after the First World War that the first successful treatment of lymphoma with chemotherapy was achieved, with the use of nitrogen mustard, originally developed as chemical warfare. Since that time literally thousands of chemotherapy drugs have been developed and tested, the vast majority of which

have been found to be either ineffective or too toxic for routine use. Today only a handful of drugs are used.

Chemotherapy drugs work in a number of different ways. Cells go through a 'cycle' which is illustrated in Figure 1 (see page 2). Different chemotherapy drugs act on different parts of this 'cell cycle'. Cancer cells divide rapidly and many of these cells will be at a particular part of the cell cycle at any one time. Chemotherapy drugs that act on different parts of the cell cycle will therefore be effective in killing a large number of cells. However, many 'normal' body cells divide rapidly (such as the bone marrow, the lining of the gut and mouth) and will also be damaged by

chemotherapy drugs. This is part of the reason behind many of the side-effects caused by chemotherapy.

The overall aim of chemotherapy is to give drugs that have a maximal anti-cancer effect, but with the least possible damage to the body's normal cells.

Which chemotherapy?

Lymphoma describes a large family of different diseases that all have one thing in common – they are all cancers of the lymphatic system, part of the normal defence mechanism of the body. It can be divided into Hodgkin and non-Hodgkin lymphoma, but within these subtypes there are several more subdivisions.

Each specific type of lymphoma behaves in a very distinct manner and treatment therefore varies greatly. Some types of lymphoma do not require chemotherapy at all. The patient may require another treatment such as radiotherapy, or may not require any form of therapy if they remain well, without any symptoms. If chemotherapy is required, then the type of chemotherapy depends very much on the

specific type of lymphoma, and the extent to which it may have spread (the 'stage').

The approach to treatment can also vary. It may be treatment intended to completely cure the patient (treatment with 'curative' intent) or, if it is unlikely that the lymphoma is curable, it may be intended to relieve any troublesome symptoms and hold the disease at bay for as long as possible. If this approach is used then the chemotherapy should obviously be as 'non-toxic' to the patient as possible.

Although some chemotherapy drugs are given as tablets, most people with lymphoma are treated with 'intravenous' chemotherapy (chemotherapy given directly into a vein). Drugs are usually given as a 'combination regimen', which means that several drugs are used at the same time. The reason for this is that combinations have been shown to be more effective in many types of lymphoma, and it helps to avoid the

possibility of cancer cells becoming resistant to any one drug. There are several such combinations in routine use (see Figure 2), and certainly too many to describe in detail in this article.

Following the results of recent research most people with either diffuse large B-cell or follicular non-Hodgkin lymphoma will be offered a drug known as rituximab (MabThera®) in addition to their chemotherapy. This drug is not a cytotoxic drug but a monoclonal antibody. This stimulates the body's own immune system to fight the cancer cells. Its combination with chemotherapy has been shown to greatly improve the outcome of treatment without causing any major additional side-effects.

[For further information on rituximab please call our Helpline.](#)

In addition, doctors are constantly trying to improve the treatments and you may be asked if you would like to

take part in a clinical trial. These trials usually compare the standard accepted chemotherapy regimen with one that it is felt may be better.

The vast majority of chemotherapy regimens are given as out-patient treatments, either as a short injection, or as an intravenous drip over an hour or so. They rarely involve coming into hospital overnight. You will usually have an appointment to be seen in the clinic or cancer unit where you will be assessed by a member of the medical team. They will want to know how you have coped with the previous course of chemotherapy, if you have had any side-effects and will often perform a physical examination. In addition, you will usually have a blood test to assess how your bone marrow has been affected by the treatment (see 'Bone marrow suppression' later) and whether it is safe to proceed with the next course.

The frequency and length of different chemotherapy regimens are variable. Most commonly, chemotherapy is given once every 3 to 4 weeks and you will receive 6 to 8 courses of treatment. The usual duration of treatment is therefore around 5 to 6 months. Some treatments may be given on a weekly basis and would involve coming to the clinic once a week for 3 to 4 months. The length of the treatment depends very much on the stage of the disease at presentation, whether you have chemotherapy alone or in combination with radiotherapy and how the lymphoma responds to the chemotherapy. This is assessed by blood tests, physical examination and by a scan.

If the lymphoma is sensitive to the treatment and is responding well then the chemotherapy will usually continue until the lymphoma is no longer seen. If the chemotherapy has shrunk the lymphoma, but further

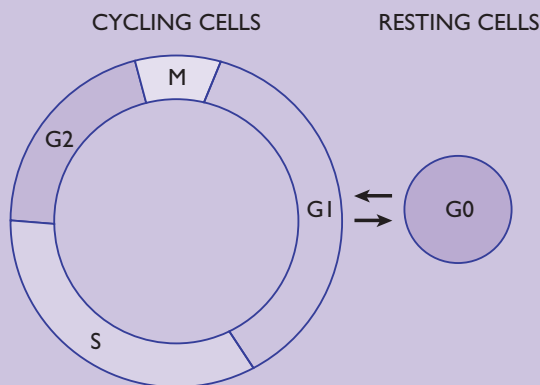


Figure 1: The cell cycle

Cells pass through a number of different stages in their development. After the cell divides it enters the phase known as 'G1' or Growth phase. During this time it increases in size. The next phase is known as the 'S' phase. This is when the cell synthesizes or produces more DNA (the basic genetic information that all cells contain). In the 'G2' phase the cell again continues to grow, until it enters 'M' phase. This is when the cell actually divides into two smaller cells, a process known as Mitosis. The 'daughter' cells can either carry on growing and dividing, or they can enter the 'G0' phase, in which they are simply resting.

Non-Hodgkin lymphoma

Chlorambucil (+/- Prednisolone)

Fludarabine

Fludarabine, Mitozantrone, Dexamethasone **FMD**

Fludarabine/Cyclophosphamide **FC**

Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone **CHOP**

Rituximab (MabThera), Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone **R-CHOP**

Cyclophosphamide, Vincristine, Prednisolone **CVP**

Rituximab, Cyclophosphamide, Vincristine, Prednisolone **R-CVP**

Prednisolone, Mitozantrone, Cyclophosphamide, Etoposide, Bleomycin, Vincristine, (:+/- Methotrexate) **PMitCEBO/M**

Dexamethasone, Cisplatin, Cytarabine **DHAP**

Etoposide, Methylprednisolone, Cytarabine Cisplatin **ESHAP**

Methylprednisolone, Gemcitabine, Cisplatin **GEM-P**

Hodgkin lymphoma

Adriamycin, Bleomycin, Vinblastine, Dacarbazine **ABVD**

Vincristine, Etoposide, Epirubicin, Prednisolone **VEEP**

Chlorambucil, Vinblastine, Procarbazine, Prednisolone **ChIVPP**

Figure 2: some of the commonly used chemotherapy regimens

courses make no difference to the size (i.e. the chemotherapy has achieved a maximal response), then a different treatment may be required. This could be a different chemotherapy regimen, radiotherapy or very occasionally surgery. Possibly no further treatment is necessary if the remaining 'abnormality' on the scan is felt to be scar tissue. A PET (Positron Emission Tomography) scan

may be required to assess for any active lymphoma.

Please call the Helpline if you would like further information on PET scans.

Side-effects – what to expect

The first thing to say is that you may experience no, or very few, side-

effects from the treatment. However, it is important to understand the possible side-effects since it is essential to let your medical team know of any unusual symptoms.

Chemotherapy is given to maximise the anti-cancer activity but every effort is taken to minimise the side-effects. Many chemotherapy drugs give similar side-effects but there may be some side-effects that are very specific to a certain drug. Your medical team will give you details about any of these. Only the more general ones will be discussed here. Side-effects can occur immediately or can be delayed. Most side-effects are temporary and will stop once the treatment is completed.

Immediate side-effects

Nausea and vomiting

Many chemotherapy drugs have the potential to cause nausea and vomiting. This has undoubtedly been a significant problem in the past. However, this has largely been resolved by the introduction of new anti-sickness medications. These can be given as injections or tablets. They are often given prior to the chemotherapy to avoid sickness in the first place, and can be continued for a number of days after the treatment has been given. There are a number of other effective drugs and it has been reported that some people have found it extremely helpful to talk to a psychologist or counsellor if the sickness is a continuing problem.

Skin/nail changes

Skin rashes are uncommon following chemotherapy and, if they do occur, may come in many different forms. In addition, chemotherapy may affect any pre-existing skin condition, either adversely or, as in the case of psoriasis, favourably! Some drugs can generally make your skin more dry, discoloured and sensitive to things like

chlorine in swimming pools and the sun. You should protect your skin in the sun with sunscreens and protective clothing. Any rashes or skin changes should be reported to your medical team. In addition, your nails may change, becoming lighter or darker, slow growing or break more easily.

Medium-term side-effects (Generally lasting for the duration of the chemotherapy)

Lethargy (fatigue)

Lethargy, or tiredness, is one of the most common side-effects of chemotherapy. Often the cause of it is unclear and may be a combination of factors including the chemotherapy, the underlying lymphoma and occasionally anaemia (a low red blood cell count which can be caused by both). If anaemia is the cause then a simple blood transfusion may well correct the problem.

Hair loss (alopecia)

Hair loss is an effect of the chemotherapy on the rapidly dividing cells of the hair follicle. It is by no means universal and many patients have no hair loss at all. The team looking after you will let you know how likely this will be. If this is a side-effect of the treatment, it will only be temporary and the hair will grow back when the chemotherapy course is finished. Many people find that the use of a wig is quite satisfactory during this period, and this is worth organising sooner rather than later so that a wig can be found that is similar to your own hair.

Bone marrow suppression

The cells that are produced in the bone marrow divide very rapidly and so they are often affected by the chemotherapy. If your blood count gets too low you are at risk of:

- becoming anaemic
- being prone to bleeding (a low platelet count)



Chemotherapy nurse administering an intravenous injection of chemotherapy drugs

- neutropenia (a low white blood cell count) which means you are prone to infections.

The medical team will be monitoring your blood count carefully and may give you blood transfusions or platelets if they feel it is necessary. There are also drugs that can help boost your white blood count if this becomes a problem.

Please call the Helpline if you would like further information on blood counts.

You will be given advice about ways to protect yourself or minimise the risks of infection including foods to avoid and initially staying away from crowded public places. You are advised to have a thermometer at home. You will be given contact telephone numbers for your medical team. It is essential that you call with any signs of infection or any bruising or bleeding.

Diarrhoea and constipation

The chemotherapy could cause either of these two side effects. You should report any changes in your bowel

habits as early as possible so that advice can be given on dietary changes. It may be necessary for the medical team to prescribe some medication to help resolve the problem.

Mouth changes

Some chemotherapy drugs can make your mouth sore. You will be given advice on good hygiene for the mouth to try and prevent this and possibly some mouthwashes may be given. If your mouth does become sore or painful and ulcers appear these could cause problems with infections and should be reported so that appropriate advice can be given. In addition chemotherapy can affect the way food and drink tastes. This should resolve once treatment is completed.

Peripheral neuropathy (effects on the nerves)

Many of the chemotherapy combinations used in the treatment for lymphoma contain a drug which can cause damage to the nerve endings in the hands and feet. This can cause a sensation of pins and needles or numbness. This usually

improves slowly after chemotherapy is completed but in some severe cases can be permanent. Therefore it is important to report any early signs so that the drug dosage can be reduced or a different drug used if necessary.

Hearing changes

Another drug, Cisplatin, used in certain treatment regimens for lymphoma can cause tinnitus (a continuous noise in the ears) or hearing loss associated particularly with high pitched noises or sounds. You may require a hearing test before receiving the drug. Again it is important to report any changes you notice while you are receiving chemotherapy.

Sexuality/Contraception

Some chemotherapy can affect your mood, level of physical ability and general feelings about having sex. If you are worried or concerned about any issues relating to your sex-life please discuss this with your doctor or nurse. In addition, it is advised to avoid pregnancy during chemotherapy and for sometime after chemotherapy. A barrier method of contraception is advisable as this will prevent any small risk of problems for your partner during the first few days after you have had your chemotherapy.

Long-term side-effects

Sterility

Many chemotherapy agents are known to affect fertility. This may be temporary while you are having chemotherapy, and female patients may stop having periods during this time. However, in some patients who receive specific types of drugs, chemotherapy may cause permanent sterility. This can also be related to your age and whether you are male or female. You should discuss the

risk of this happening to you before starting treatment. If there is a risk then male patients should be offered the possibility of sperm banking. Women may be offered the possibility of having their eggs 'harvested' and then fertilised by a partner's sperm. These can then be stored for future use, although this will mean some delay before treatment can be started. A more recent technique, although still experimental, is to have part of the ovary removed and frozen or eggs harvested and frozen without being fertilised. The outcome of any of these techniques, however, cannot be guaranteed. In addition to permanent sterility in some women, chemotherapy may bring on an early menopause. Your doctor will be able to inform you of the risk of this happening to you.

[Please call the Helpline for further information on fertility.](#)

Heart problems

Anthracycline drugs are used in many of the chemotherapy regimens for lymphoma treatment. It is known that these drugs can cause serious side-effects to the heart, even years after the treatment has ended. However, the effect on the heart very much depends on the total dose that you receive over the whole course of treatment and any heart problems you already have prior to starting treatment. Your heart function may be tested prior to using these drugs and a careful assessment will be made to avoid you receiving too much.

Lung problems

Problems affecting the lungs caused by chemotherapy are much less common. Some drugs, however, are well recognised as having the potential to cause damage. If these drugs are to be used the medical

team will be aware of this potential problem and, if necessary, perform specialised lung function tests to monitor the effects of treatment.

Second cancers

Rarely some chemotherapy can increase your risk of developing other cancers such as leukaemia later in life. Modern treatment aims to reduce this risk while still maintaining the benefits of treatment to the lymphoma you currently have.

[Please call the Helpline for further information on late effects.](#)

Other side-effects

There are many other potential side-effects that are specific to particular chemotherapy drugs. Before starting your chemotherapy the medical team looking after you should inform you fully about these side-effects.

What should you tell us?

It is impossible to predict how a patient will respond to chemotherapy. There are a number of potential side-effects but each patient is an individual and so may well have unique problems. The safest approach is to inform your medical team if you are unwell in any way or have any specific worries. They will be very happy to discuss this with you, either over the phone or in the hospital.

We hope that this article has taken away some of your worries about chemotherapy. If you have any questions regarding your own treatment, your medical team will be more than happy to answer your questions.