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# Late Effects of Treatment

A Guide for  
Patients

**Leukaemia Care**  
YOUR Blood Cancer Charity

# Introduction

**Your cancer treatment can cause side effects. Some of these will occur at the time of treatment and will normally stop when treatment ends. Some of these side effects may last for a long time after treatment; these are called long term effects. Some side effects do not occur for months or even years after treatment ends; these side effects are called late effects. These late effects can be physical or emotional. Not everyone gets late effects, the risk depends on the type of treatment, the dose of treatment and the patient's age at the time of treatment.**

This booklet is designed to provide you with information about the late effects you may experience, what to expect and how they may be managed. If you need specific advice or are concerned about a particular late effect, please contact your medical team or Clinical Nurse Specialist (CNS).

This booklet has been compiled by Dr Victoria Grandage (UCLH) and peer reviewed by Dr Panos Kottaridis, Royal Free Hospital. The rewrite was put together by Lisa Lovelidge and reviewed by Dr Victoria Grandage. We are also grateful to our patient reviewers, Simon Walker, John Watson and Steve Colbourne and the Brighton support group.

If you would like any information on the sources used for this booklet, please email [communications@leukaemiacare.org.uk](mailto:communications@leukaemiacare.org.uk) for a list of references.

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# About Leukaemia Care

**Leukaemia Care is a national charity dedicated to ensuring that people affected by blood cancer have access to the right information, advice and support.**

## Our services

### Helpline

Our helpline is available 9.00am - 10.00pm on weekdays and 9.30am - 12.30pm on Saturdays. If you need someone to talk to, call **08088 010 444**

### Nurse service

We have two trained nurses on hand to answer your questions and offer advice and support, whether it be through emailing **nurse@leukaemicare.org.uk**, over the phone on **08088 010 444** or via LiveChat.

### Patient Information Booklets

We have a number of patient information booklets like this available to anyone who has been affected by a blood cancer. A full list of titles – both disease specific and general information titles – can be

found on our website at **www.leukaemicare.org.uk/support-and-information/help-and-resources/information-booklets/**

### Support Groups

Our nationwide support groups are a chance to meet and talk to other people who are going through a similar experience. For more information about a support group local to your area, go to **www.leukaemicare.org.uk/support-and-information/support-for-you/find-a-support-group/**

### Buddy Support

We offer one-to-one phone support with volunteers who have had blood cancer themselves or been affected by it in some way. You can speak to someone who knows what you are going through. For more information on how to get a buddy call

**08088 010 444** or email  
**support@leukaemicare.org.uk**

### Online Forum

Our online forum, **www.healthunlocked.com/leukaemia-care**, is a place for people to ask questions anonymously or to join in the discussion with other people in a similar situation.

### Patient and carer conferences

Our nationwide conferences provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support.

### Website

You can access up-to-date information on our website, **www.leukaemicare.org.uk**, as well as speak to one of our care advisers on our online support

service, LiveChat (9am-5pm weekdays).

### Campaigning and Advocacy

Leukaemia Care is involved in campaigning for patient well-being, NHS funding and drug and treatment availability. If you would like an update on any of the work we are currently doing or want to know how to get involved, email **advocacy@leukaemicare.org.uk**

### Patient magazine

Our quarterly magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe go to **www.leukaemicare.org.uk/communication-preferences/**

# A note from our Patient Advocacy team

We know that sometimes the late effects of treatment can be more difficult to manage than the illness itself. Sometimes the effects can be unexpected or more severe than you anticipated.

We know that many patients have lots of questions about the late effects of treatment and how to deal with them and we hope this booklet helps to answer some of them.

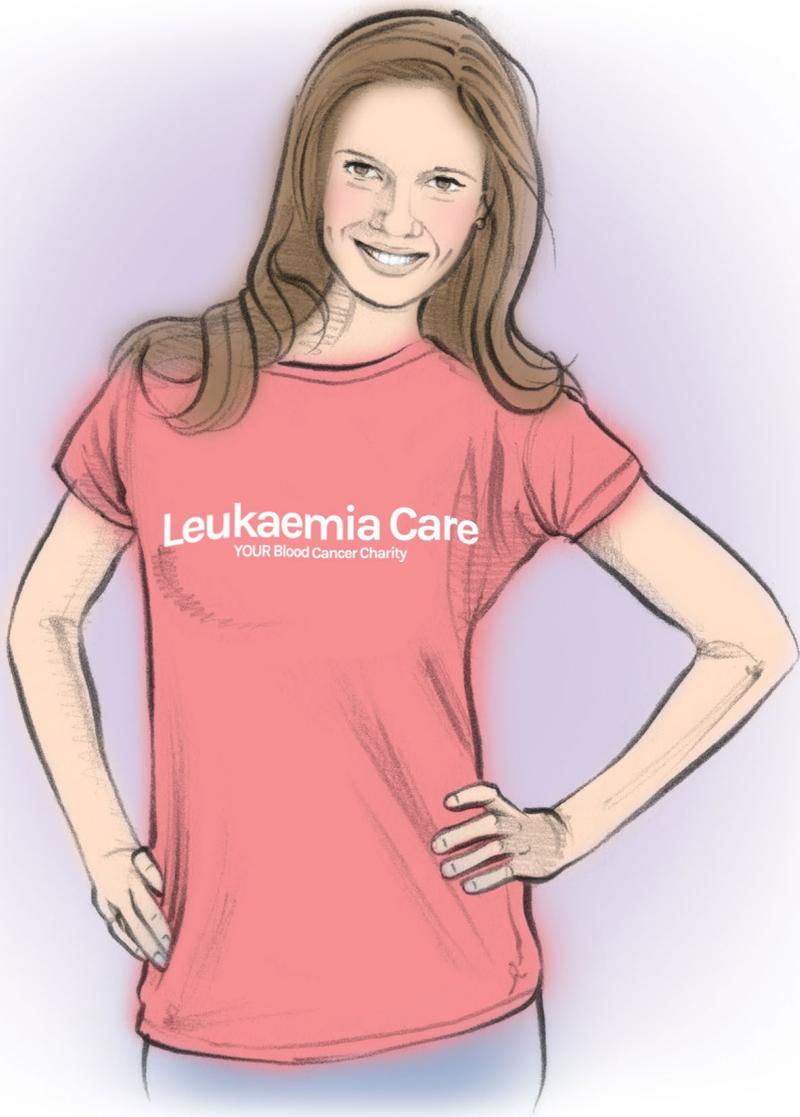
We have included the effects that are most commonly experienced by patients and not all late effects feature in this booklet. This does not mean that what you are experiencing is wrong or not related to your illness or treatment, so if you are at all worried, please speak to your medical team.

If you have any questions about the information in this booklet or you want to know where you can get more information, please call us on **08088 010 444**, where a member of the Patient Advocacy Team or a dedicated trained

volunteer will be ready to answer your questions.

Best wishes,

The Patient Advocacy Team



# The difference between long term and late effects

All methods of treatment for blood cancer can cause side effects. Some of these are acute or early side effects and occur at the time of administration of the treatment, such as nausea and hair loss. These side effects usually stop once the drug is stopped. Certain early side effects persist after treatment, for example reduced fertility, and are permanent. These are long term side effects. Side effects that develop months or years after treatment has stopped are known as late effects, i.e. they have a delayed onset. These side effects may be physical, or emotional, and can include secondary cancers and heart disease.

As treatments for cancer have become more effective and more people survive, our knowledge of late effects has improved. The focus of many newer treatments has moved towards reducing the number and intensity of late effects. Certainly many of the treatments used now are much less likely to cause health problems than those used 20

years ago. Not everyone gets late effects, the risk depends on type of treatment, dose and age when treated.

Because late effects can take many years to appear they may not be known for some of the new drugs being used to treat blood cancer today.

# Treatments for blood cancer

## Chemotherapy

Chemotherapy is the name given to a group of drugs that are used to treat cancer. There are lots of different groups of drugs, all working in different ways to stop the cancer cells growing and dividing and to damage them so that they eventually die. These drugs may be given in the following ways:

- By mouth, as tablets or liquids
- By injection into a vein (intravenous) or muscle (intramuscular) or into the spinal fluid (intrathecal)

A combination of drugs is usually used to treat blood cancer as each drug works in a slightly different way and it allows the maximum number of cancer cells to be killed by a given dose of drug.

Unfortunately, chemotherapy is not cell specific and affects all dividing cells. Thus normal cells are attacked as well, and this is how chemotherapy causes side effects. Chemotherapy works best on the cells that are dividing faster, which

are usually the cancer cells.

Drugs commonly used to treat blood cancers include:

- Vincristine
- Anthracyclines
- Steroids
- Asparaginase
- Cyclophosphamide
- Cytarabine
- Methotrexate
- 6 mercaptopurine

## Monoclonal antibodies

Monoclonal antibodies are antibodies directed at a specific protein on the surface of a cell so that they target cells expressing that protein. Sometimes they have a toxin or a radioactive substance joined onto them so the agent is delivered directly to the cell. Once the antibody has latched onto the cell, the immune system is triggered to destroy it. These are relatively new drugs and some of them are still in clinical trials. You

# Treatments for blood cancer (cont.)

usually have monoclonal antibody treatment through a drip (infusion).

Most side effects occur at the time of the infusion and include fever, rash, feeling sick, wheezing, headaches and faintness. There are not many known late effects, but as they are new drugs some late effects may not yet have become evident.

Common monoclonal antibodies used to treat blood cancer are:

- Rituximab
- Brentuxumab
- Gemtuzumab ozogamicin
- Alemtuzumab

## Radiotherapy

Radiotherapy is the use of high energy radiation to kill cancer cells. It works by damaging the DNA (genetic code) of the cancer cells causing them to die. Normal tissues nearby can be affected, but these have better repair mechanisms and are usually able to repair the DNA damage and grow normally. Modern radiotherapy techniques are aimed at keeping irradiation of normal tissues to a

minimum and aim to limit the risk of permanent side effects, but when given along with chemotherapy, the risk of late effects increases. The dose of radiotherapy, how the dose is divided up into treatment sessions, and the area irradiated will all impact the development of side effects.

Commonly irradiated sites are:

- Cranial irradiation used to be used to prevent the spread of leukaemia to the brain in the treatment of childhood leukaemia which is associated with a high number of late effects. Now it is usually used for treatment of chemotherapy resistant or relapsed leukaemia involving the brain or spinal fluid.
- Involved site radiation is aimed at the lymph nodes that originally contained the cancer and any areas it extended into.
- Extended field radiation was used more commonly in the past and was associated with exposure of a greater proportion of normal lymph node areas and tissues, and thus, greater late

effects.

- Proton Beam radiation - this is a new technique which is thought to reduce the risk of late effects. It is not appropriate for all cancer types. The risk of late effects is part of on-going clinical research.

Common extended fields used are:

- Mantle field lymph node areas in neck, chest and under the arms.
- Inverted Y, which includes the lymph nodes in the upper abdomen, spleen and pelvis.
- Total Body Irradiation (TBI) as the name suggests, means the whole body is irradiated. This is usually used in preparation for a bone marrow transplant.

# Possible late effects:

## Secondary cancers

Secondary cancers are not linked to the original cancer and can occur months to years after the original treatment. The risk is increased by the intensity of treatment you have received and is a result of the cell damage that chemotherapy and radiotherapy can cause. Certain chemotherapy drugs have a higher risk than others, e.g. alkylating drugs have a greater risk of secondary cancers. Furthermore, secondary cancers are more frequent in patients who receive radiation therapy and chemotherapy together compared to either treatment alone.

Because secondary cancers are late effects and can occur many years after treatment has finished, they have been best studied in cancers for which successful treatments have been available for longer, e.g. Hodgkin's Disease.

The secondary cancers most often linked to chemotherapy are myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML). Sometimes, MDS occurs first, and then turns into AML.

Acute lymphoblastic leukaemia (ALL) has also been linked to chemotherapy. Chemotherapy is known to be a greater risk factor than radiation therapy in causing leukaemia. Secondary leukaemia tends to occur between two and ten years after treatment. In many cases it is more difficult to treat than primary leukaemia.

The risk of developing a secondary cancer after radiation treatment goes up as the dose of radiation increases. The area treated is also important, since these cancers tend to develop within the radiation field. Certain organs, such as the breast and thyroid, seem to be more likely to develop cancers after radiation than others.

Age at the time of treatment also affects the risk of solid tumours. For example, the risk of developing breast cancer after radiation is higher in those who were treated when they were young compared with those given radiation as adults. Risk decreases as the age at the time of radiation increases, with

little or no increase in breast cancer risk among women who had radiation after the age of 40. Other factors can also affect the risk of radiation-related cancers. Smoking, for example, increases the risk of lung cancer after radiation even more than smoking on its own. Early menopause, which can be caused by chemotherapy, can lower the risk of radiation-related breast cancer.

## Management of the risk

All cancer survivors will be advised to live a healthy lifestyle, exercise regularly and reduce known risk factors for cancer such as smoking or excess sun exposure. They should be self-aware and report new symptoms in a timely manner, especially symptoms that could be indicative of a secondary cancer such as new lumps, bleeding, weight loss etc. Women should be encouraged to be breast aware and men should know how to examine their testicles. Patients should be encouraged to enter a screening program where there

is one available, e.g. cervical screening and breast screening. Patients should discuss their exact risks of secondary cancer with their treating team.

# Possible late effects: Heart problems

The heart sits between the lungs on the left side of your chest within a fibrous sack called the pericardium. The heart is essentially a muscle that contracts and relaxes in a coordinated way to pump blood throughout the body to deliver oxygen and nutrients to the tissues. The heart beat is initiated and coordinated by the electrical conduction system. The heart itself is supplied by special blood vessels known as the coronary arteries, and damage to these vessels means that the heart muscle may not get enough oxygen and can be damaged.

The heart can be affected by a number of chemotherapy drugs used to treat blood cancers, as well as by radiotherapy if the heart is in the radiotherapy field. This effect is often referred to as cardiotoxicity. It may be acute at the time of administration of the drug or may develop as a late effect many years after the end of treatment.

## How might chemotherapy affect the heart?

Drugs such as daunorubicin, may have a direct toxic effect on the heart muscle, affecting the way the heart pumps. This may be called cardiomyopathy or left ventricular dysfunction and can lead to heart failure.

The pericardium, which is the sack that the heart sits in, can be affected by drugs. It can be inflamed, which is known as pericarditis, or thickened, which is known as pericardial fibrosis.

Drugs such as ifosfamide and gemcitabine, may affect the heart rhythm leading to the heart beating either too fast, too slow or irregularly.

The blood vessels supplying the heart can become hardened or blocked and this may affect oxygen getting to the heart. This is known as coronary artery disease and is more usual after radiotherapy.

The most common drugs implicated in late cardiotoxicity

are anthracyclines. These drugs are included in many chemotherapy regimens used to treat cancer. They include doxorubicin (adriamycin), daunorubicin, idarubicin and epirubicin. They are often administered as part of combination chemotherapy. Mitoxantrone has a similar effect, although it is from a different group of drugs. These drugs can affect the heart muscle and, in turn, the ability of the heart to pump. Usually these effects are associated with higher doses of the drug but not always, and some people will be more susceptible than others. Lifestyle factors such as smoking, obesity, high cholesterol and high blood pressure will also have an impact.

## How can radiotherapy affect the heart?

Radiotherapy can have a number of effects on the heart. Although modern radiotherapy fields will try and avoid the heart where possible, it might still be exposed.

### Pericarditis

Inflammation of the pericardium, or pericarditis, usually occurs

early after radiotherapy and presents with a fever and sharp chest pain that is worse on breathing in and may be relieved by sitting forward.

### Coronary artery disease

Radiotherapy may lead to proliferation of the cells lining the blood vessels leading to narrowing of the artery and a reduction in blood flow. It can occur many years after radiotherapy and, depending on age at treatment, it is likely to occur at a younger age than in the normal population.

## Management of the risk

As a patient it is important that you understand the treatment that you have received. Ideally you will have an end of treatment summary or care plan that outlines problems of which you are at risk. Your consultant should inform you if you are at risk of heart problems after treatment and let you know if any surveillance is necessary.

This is a list of symptoms associated with heart disease. These are not specific to heart disease, but you should be

# Possible late effects: Heart problems (cont.)

checked out if you develop any of them:

- Shortness of breath
- Feeling short of breath when lying flat
- Fatigue
- Chest pain or jaw pain (pain that classically radiates to the arm or neck)
- Nausea or vomiting
- Swollen feet and ankles
- Coughing or wheezing
- A sensation that your heart is racing or missing a beat

If you received anthracyclines in childhood or adolescence you should be on a screening programme. Usually echocardiograms are used to monitor your heart function and size. The usual screening frequency is five yearly unless an abnormality is detected. Screening is also more frequent during pregnancy due to the strain put on the heart. If you were treated at an older age, your consultant will decide what

screening is necessary based on your history and any other risk factors. It is important to highlight if you have a family history of stroke or heart disease. With aging the risk of heart problems increases in the general population and the incidence of high blood pressure, coronary artery disease, diabetes and other risk factors also increase.

## What you can do to help yourself

It is always worrying to know that you have a risk of heart disease, but there are things that you can do to keep yourself well. If you are a smoker it is advisable to give up and your GP may have some resources to help you do that successfully.

A healthy balanced diet and exercise are also important. Current guidelines are that we should all have at least 30 minutes of moderate exercise daily or at least 150 minutes each week.

If you have high blood pressure, diabetes or high cholesterol, these should all be controlled as well

as possible as they are also risk factors for cardiovascular disease. In case of severe heart damage, medications such as beta blockers and ACE inhibitors might offer some delay in progression and also reverse part of the damage. These drugs might have to be continued for life.

# Possible late effects: Bone problems

Normal bones are made up of a hard outer layer known as the cortex and a softer inner layer made of spongy bone. The cells that form bone are known as osteoblasts and the cells that resorb and remodel the bone, e.g. after injury or to maintain bone mass, are known as osteoclasts.

## Osteopenia/ osteoporosis

The bone matrix is predominantly made of collagen. The hardness of the bone relates to its salt mineral content, which is made up of calcium and phosphate. Our bones reach maximum density in our early to mid-twenties and as we get older the density reduces. In women this tends to happen after the menopause and in men later in life.

Weight bearing exercise, calcium and vitamin D are all important for maintaining bone density. Immobility, some hormone deficiencies, certain drugs and radiotherapy can lead to a reduction in bone density.

A reduced bone density is known

as osteopenia, a severe reduction leading to fractures is known as osteoporosis.

Fixed risk factors for osteoporosis are:

- Female gender
- Age
- Menopause/hysterectomy
- Ethnicity (Caucasian and Asian people are more at risk than those of African descent)
- Family history

## Drugs that can affect bone density

Corticosteroids (prednisolone or dexamethasone) are commonly used to treat acute lymphoblastic leukaemia (ALL), lymphoma, myeloma and chronic graft versus host disease (GVHD) that can occur after a bone marrow transplant. Their effect on bone density will depend on your age at treatment and the length of time they are taken. If you are prescribed them at a younger age before you have reached peak bone mass, your bone density will

not be reduced as much as those who are prescribed them later in life. Continuous steroids are more damaging to bone mass than pulses (intermittent dosing).

Bone loss is most rapid in the first few months of therapy and bone mineral density (BMD) should be considered in anyone that is intended to continue therapy for three months continuously. The fracture risk increases rapidly after the onset of treatment and declines rapidly after stopping therapy.

Other treatments that can affect bone density include methotrexate, ciclosporin and radiotherapy.

Some conditions that may occur after cancer treatment that increase the likelihood of osteoporosis are:

- Low levels of female/male hormones
- Growth hormone deficiency
- Immobility

Risk factors for osteoporosis that you can do something about:

- Smoking

- High alcohol intake
- Low body mass index
- Nutritional state
- Low vitamin D levels

## How might osteoporosis be picked up?

Osteopenia and osteoporosis are unlikely to produce any symptoms unless a fracture has occurred. Your clinical team will decide if you are at high risk and if you require investigation/screening. The most usual method for screening is via a dual X-ray absorptiometry or DEXA scan, which is a low radiation X-ray that can detect small changes in the bone density at the spine and hip.

## How is osteoporosis treated?

During osteoporosis treatment, any underlying hormone deficiencies will be corrected and your calcium and vitamin D levels will be maximised. Young females with premature ovarian failure (POF) should be considered for hormone replacement treatment

# Possible late effects: Bone problems (cont.)

(HRT) up to the age of 50. HRT should be prescribed with caution in patients with previous history of clotting events or strong family history of breast cancer.

## Risk factors for osteoporosis

Weight bearing exercise is good for your bone density and immobility may make it worse. Smoking also has an effect on bone density and should be avoided. Whether you are offered medical treatment or not will depend on your gender, age, whether you have had a fracture already or your risk of fracture.

## Osteoradionecrosis

Osteoradionecrosis (ORN) is a condition of poor bone repair due to damage to the small blood vessels supplying the bone, and therefore, poor supply of oxygen and nutrients. Osteoradionecrosis can be picked up by X-Ray or MRI.

It occurs usually after radiotherapy at high doses (greater than 40 Gy), usually to the jaw. It can be spontaneous but usually occurs after dental trauma, such as an extraction,

but can occur after trauma as minimal as irritation from dentures. If you have received radiotherapy to the head or neck above the collar bones or mouth and throat you are at risk.

## Treatment of ORN

Treatment is symptomatic in most cases. If there is evidence of infection, pain killers and antibiotics will be given. Hyperbaric oxygen and surgery are sometimes used.

## What can you do to prevent ORN?

- Good dental hygiene is essential
- Artificial saliva if you have a dry mouth
- Fluoride treatment may be helpful
- See a dentist every six months and make sure they are aware of your history, especially if they feel an extraction is necessary
- Healthy balanced diet

## Osteonecrosis (avascular necrosis)

Osteonecrosis (avascular necrosis)

[AVN]) is a disorder caused by temporary or permanent interruption to the blood supply to the bone. The bone tissue loses its oxygen and nutrient supply and dies. The bones commonly involved are the long bones in the leg, involving the hip and knee joints. Other common sites include the shoulder and ankles. One or more bones can be affected at the same time. It can be symptomless or cause significant pain. The amount of disability will depend on the bones/joints involved.

## Causes of AVN

- Steroids: The mechanism by which steroids cause AVN is not clear. It seems to be more common when you receive these medicines during adolescence than in childhood or adulthood, possibly relating to the hormones and bone growth occurring at that time.
- Alcohol
- Injury

## Diagnosis of AVN

Diagnosis of AVN is made using X-ray and MRI.

## Treatments

The goal of treatment for AVN is to improve the use of the bone by good pain relief and physiotherapy, to prevent any further damage to the bone, and to aim for joint survival.

Treatments for AVN are:

- Pain relief
- Reduced weight bearing that may slow the damage and allow natural healing
- Physiotherapy
- Surgery
- Decompression that involves removing a core of bone and allowing a better blood supply, useful for early AVN
- Osteotomy that involves reshaping the bone to reduce stress on an affected area
- Joint replacement

## Osteonecrosis of the jaw

Osteonecrosis of the jaw is a rare side effect of bisphosphonate that is caused by poor bone healing.

# Possible late effects: Bone problems (cont.)

It is most common with the drug zoledronic acid, usually when it is given in high doses. It is often related to tooth extraction or dental surgery and affected patients may present with pain and swelling, bad breath or spasm of the jaw muscles.

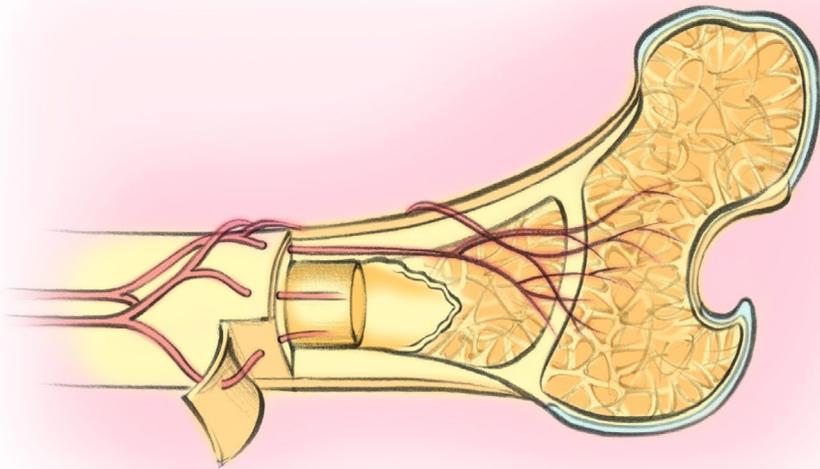
## Diagnosis of osteonecrosis

Diagnosis for osteonecrosis is the same as for AVN.

## Treatment

Treatments for osteonecrosis of the jaw are:

- Pain killers
- Antibacterial mouth washes
- Antibiotics, if necessary
- Surgery



# Possible late effects: Eye and ear problems

Some cancer treatments may have an effect on your vision. Some of these are acute and occur at the time of receiving the drugs, while others may develop over time. As deterioration in your vision can significantly impact your quality of life, it is important that if you are at risk you have your eyes monitored regularly. As you age other factors may compound the problem as age related visual changes occur. Diseases such as diabetes, if not well controlled, may also impact your vision. This is important to remember as some therapies may increase your risk of developing diabetes.

## Cataracts

Cataracts are areas of clouding of the lens of the eye that interfere with light passing through it. Cataracts generally cause blurred vision, sensitivity to light and glare. It may also cause double vision and poor vision at night. If you have them already, you may need a change to your glasses or contact lens prescriptions.

## Risks factors for cataracts

Risk factors for cataracts include:

- Steroids
- Radiotherapy (the risk of cataract formation rises with increasing radiation dose)
- Total radiation dose of 10 Gy or higher
- Age

Not all cataracts need treatment and it may be that your vision requires monitoring in the first instance. If treatment becomes necessary the only treatment is surgical removal of the lens and replacement with an artificial lens.

## Dry eye syndrome (keratoconjunctivitis sicca)

Dry eyes is a common condition in the general population, especially over the age of 65 years, and results from inflammation of the cornea, which is the clear outer surface of the eye and the

conjunctiva (membrane covering the eye and eyelids), leads to reduced tear production.

Certain cancer treatments may predispose the development of dry eye, especially radiotherapy. Graft versus host disease (GVHD), which can occur after a bone marrow transplant, can affect any part of the eye, but typically causes inflammation of the conjunctiva and tear glands.

Dry eyes are also more prone to eye infection. Symptoms of dry eye include dry gritty eyes, pain, light sensitivity and excessive watering of your eyes.

## Treatment

Treatments for dry eye syndrome are:

- Artificial tears or ointments to lubricate the eye
- Surgery

## Hearing Problems

Several chemotherapy drugs such as cisplatin, as well as certain antibiotics such as aminoglycosides, can affect

your hearing. This can happen a few days, months or years after exposure to these medications. If you feel that your hearing is impaired you will need to speak to your consultant or GP in order to be referred to specialised services.

# Possible late effects: Skin and nail problems

Chemotherapy can cause several skin problems; the most common ones include dry skin, hyperpigmentation, nail changes and photosensitivity.

In immunosuppressed patients, skin problems can include basal and squamous cell carcinomas (skin cancer). They are normally painless and tend to develop slowly. If you notice any changes to your skin, particularly where it is exposed, speak to your doctor.

## Treating dry skin

Creams and lotions are effective ways of restoring moisture following dry skin reactions and patients should be encouraged to use them on a regular basis.

Photosensitivity is an enhanced skin response to ultraviolet radiation (sunlight). Things you can do to manage photosensitivity include the use of sun cream, protective clothing and moisturising creams and lotions.

## Nail problems

There are several types of nail changes that may occur in

patients receiving chemotherapy. The most common of these, particularly in dark-skinned persons, is hyperpigmentation, vertical or horizontal bands, or general darkening of the nails.

## Management of nail problems

There are several things that you can do to prevent further damage:

- Nails should be trimmed and kept clean.
- Gloves should be worn for housecleaning and gardening to minimise damage and prevent infection.
- Nail polish and imitation fingernails should not be worn until the nails have grown out and returned to normal.

# Possible late effects: Fertility problems

Fertility is the ability to have children and can be affected by treatment with both chemotherapy and radiotherapy.

All patients who may be considering having children in the future and require anti-cancer treatment, should be fully informed about the potential effects on fertility at the time of diagnosis and prior to starting potentially sterilising treatment. When children are having treatment, their parents should be given this information.

## Male fertility

For men, fertility can be affected by anything that interferes with sperm production, including the hormones necessary for sperm production and the ability to have an erection and ejaculate. Chemotherapy can slow down or stop sperm production either temporarily or permanently. It depends very much on the chemotherapy drug and the doses used. Testosterone secretion is usually much less affected.

Male patients who have gone through puberty should be offered

the opportunity to store sperm before treatment starts so that this can be used in the future for assisted conception. It may not always be possible to store sperm if the man has a very low sperm count due to cancer or may be too unwell. Sometimes your doctor may want to start your treatment very quickly. In this case it may not be possible to store sperm or to store more than one sample.

Chemotherapy drugs (alkylating agents) commonly implicated in affecting sperm production are:

- BCNU (carmustine)
- Busulphan
- CCNU (Lomustine)
- Chlorambucil
- Cyclophosphamide
- Ifosfamide
- Melphalan
- Cisplatin
- Cytarabine
- Dacarbazine
- Procarbazine

# Possible late effects: Fertility problems (cont.)

Whether the sperm count is affected and whether this effect is temporary or permanent depends on the drug and the dose used. Recovery can take many years.

Pelvic radiotherapy can affect sperm production, testosterone secretion and also affect the nerves necessary for sustained erection. If pelvic radiotherapy is being given and the testes do not need to be irradiated, they can be protected by taping them away from the radiotherapy beam or by using lead shielding.

The testes may need to be irradiated if involved with leukaemia or during total body irradiation (TBI) in preparation for transplant. At these doses the treatment usually results in permanent sterility. Despite the fact that the cells that produce sperm are sensitive to chemotherapy/radiotherapy, those that produce testosterone are pretty resistant and males therefore rarely require hormone replacement treatment.

After cancer treatment it can be difficult to know whether you are fertile or not. When you are well enough you should be

given the opportunity to assess this. Fertility is most effectively assessed by a semen analysis. Deciding when to undertake this test is a personal decision. Some men wish to know straight away and others would rather wait until they begin actively trying for a child. It is important to consider how the results may affect you and to discuss this with your partner and family. You should be supported in this by your clinical team. It is important to bear in mind that if you are undertaking this test soon after treatment the results may improve with subsequent tests. Your clinical team will be able to inform you of the likelihood of that happening.

## Female fertility

The ovaries are very sensitive to chemotherapy. Some drugs may have no effect on fertility, while others may lead to an early menopause but with a period of normal fertility or permanent and rapid ovarian failure.

Some drugs, particularly alkylating agents, are more damaging to the ovaries than others. The impact of a given treatment will depend on the

total dose of drugs and the age at which they are administered. Younger women have more eggs so ovarian toxicity may appear less severe than in older women since their ovaries still support regular menstrual cycles despite a decreased egg cell reserve.

Chemotherapy drugs (alkylating agents) commonly implicated in affecting ovarian function are:

- BCNU
- Busulphan
- CCNU
- Chlorambucil
- Cyclophosphamide
- Ifosfamide
- Melphalan
- Cisplatin
- Cytarabine
- Dacarbazine
- Procarbazine

Radiotherapy produces severe dose-related damage to the ovarian tissue, both the egg producing and hormone producing cells. It may cause

immediate permanent sterility, temporary cessation of the periods or lead to an early menopause. The probability of infertility from a given dose of radiotherapy increases with age and simultaneous use of chemotherapy.

Pelvic radiation is most likely to be used to treat lymphomas involving pelvic lymph nodes and in the bone marrow transplant setting as TBI. From a fertility point of view it is also important to consider the effect of radiation on the uterus. High doses of radiotherapy can affect the function of the lining of the uterus (endometrium) and lead to an increased risk of early pregnancy loss.

Fertility preservation before treatment is not as simple for women as it is for men. The best methods would be storage of embryos, but lack of a partner and time constraints often make this quite difficult. Eggs can also be frozen, and results with this technique are improving all the time. Freezing (cryopreservation) of embryos or eggs require hormonal manipulation and

## Possible late effects: Fertility problems (cont.)

invasive egg retrieval and takes between two to four weeks. The majority of patients with a new diagnosis of blood cancer will not have time to go through this procedure before their cancer treatment begins.

Assessing fertility after treatment in a woman is difficult but the onset of regular periods is encouraging. Blood tests to look at certain hormone levels may give an idea of fertility and ovarian reserve. If you have been told you are at risk of an early menopause then it is important to start your family as early as possible. If you do not have a partner and are at risk of a reduced ovarian reserve, freezing your eggs may be an option at least six months after cancer treatment; you should have an opportunity to discuss this with a fertility expert. The best way to assess fertility is to combine blood tests (looking at several hormone levels) with an internal ultrasound around the third day of your period. Within the last few years a hormone called AMH can give a good indication of fertility.



# Possible late effects: Thyroid problems

The thyroid gland is a small gland based in the lower neck. It produces the hormone thyroxine that helps regulate the body's metabolism. The thyroid gland is not usually affected by chemotherapy but is very sensitive to the effects of radiotherapy to the neck. This is often given to treat lymphoma involving the lymph nodes in the neck or as part of TBI in preparation for a bone marrow transplant. Occasionally it may happen in some patients who have received cranial/ craniospinal irradiation.

## Underactive thyroid (hypothyroidism)

The most common effect of radiation is for the thyroid gland to become underactive. This leads to a reduction of thyroid hormone production and a slowing of the body's metabolism.

Common symptoms include:

- Fatigue/lethargy
- Hoarseness
- Difficulty concentrating
- Feeling cold

- Low mood
- Constipation
- Weight gain
- Slow pulse rate
- Brittle hair

An underactive thyroid is diagnosed by a blood test. This will show a low thyroxine and a high thyroid stimulation hormone (TSH). If you have received radiotherapy to the neck you should have your thyroid function monitored yearly.

## Treatment of underactive thyroid

An underactive thyroid is easily treated with thyroxine tablets. Once you are on replacement thyroxine you will require regular testing to make sure you are on the correct dose.

## Thyroid nodules/ thyroid cancer

Thyroid nodules/cancer can occur after radiotherapy to the neck. If you have received radiotherapy to that area you should have your neck examined every year. It is not unreasonable to supplement

this with regular ultrasounds of your neck every three years or so; this is a decision to be made between patient and clinician. If your clinician feels a nodule, he will arrange an ultrasound of the thyroid gland to assess it. Usually a fine needle aspiration is carried out so that the cells in the nodule can be examined.

## **Management of thyroid nodules/thyroid cancer**

If the cells collected by the aspiration are benign, the nodules will most likely be monitored for any change by yearly ultrasounds. If the cells become indicative of thyroid cancer, you will most likely be referred to a surgeon in this area to discuss removing part or all of the thyroid gland.

Symptoms and signs of thyroid cancer are:

- Usually a painless hard lump in the thyroid gland
- Hoarseness
- Difficulty swallowing
- Enlarged lymph nodes
- Difficulty breathing

# Possible late effects: Lung problems

The lungs are essential organs that supply oxygen to the body. A normal lung is spongy and full of tiny air sacks that are important for passing oxygen from the lungs into the blood.

The lungs can be affected by:

- Radiation to the chest in isolation or as part of TBI
- Chemotherapy – bleomycin, busulphan, CCNU, BCNU, high dose cyclophosphamide
- Chronic graft versus host disease (GVHD) after a bone marrow transplant
- Severe infection during your treatment

Your risk of problems will be increased by smoking, pre-existing lung problems (such as asthma), younger age of treatment and administration of drugs (anthracyclines) that increase the effect of radiotherapy.

Problems that can occur with the lungs include:

- Reduced lung capacity
- Lung tissue which is stiffer than normal (fibrosis)

- Increased risk of infections
- Increased risk of lung cancer

Symptoms of lung problems are:

- Shortness of breath
- Long standing cough
- Tiredness on mild exercise
- Recurrent chest infections

## Management of the risk of developing lung problems

If you have received any of the above treatments it is essential that you do not smoke as this will increase your risk of developing lung problems. You should try to exercise regularly and have a healthy diet. If you have evidence of lung problems, you should consider having the yearly flu pneumococcal vaccines. If you have received bleomycin and are having an operation, you should tell your anaesthetist as it is important to avoid breathing high concentrations of oxygen for long times. It is also important to discuss this with the British Diving Association if you plan to go scuba diving.

# Possible late effects: Kidney and liver problems

Some chemotherapy drugs can damage the kidney function, which might remain impaired for several months, years or for life after exposure. When the kidneys are not functioning properly, filtration is reduced and urea builds up in the blood. In addition, the balance of electrolytes and water cannot be regulated properly, resulting in a build-up of potassium, sodium and fluid. Kidney damage may also result in increased excretion of protein in the urine. Protein is an important component in our blood that carries food, hormones, and many other things through the body.

## Management of kidney damage

In order to prevent further damage to the kidneys, patients should be encouraged to drink plenty of fluids daily and avoid nephrotoxic drugs (drugs that are damaging to the kidneys) that potentially can deteriorate the already impaired function.

## Liver problems

The liver breaks down many chemotherapy drugs. Certain chemotherapy drugs can damage

cells in the liver (hepatotoxicity), although some drugs are more likely to cause liver damage than others, especially when higher doses are used. History of hepatitis can speed up the development of cirrhosis and therefore patients should be followed for life in specialised centres.

# Managing late effects

## Managing physical late effects

Your treating clinician should have informed you before you started treatment about the acute and long-term effects of your treatment. The pressure at this point is to get on and treat the cancer as delay could have a detrimental effect on outcome.

Your risk of late effects depends on your age at treatment, your diagnosis and the treatment you have received. You may not be able to stop late effects from happening but you can work towards reducing the risk of them developing and catching them early. It is important to have a frank discussion with your clinical team about your risks for late effects. Ideally you should have this information written down. You should understand what monitoring is necessary and attend your follow up appointments. You should also be mindful of what symptoms to look out for.

Be self-aware; know what is normal for you, so that when you develop a new symptom you can report it as soon as

possible. For women this includes examining your breasts and for men examining your testicles. Know your skin and your moles so that you can report any changes. Follow a healthy lifestyle, have a balanced diet, exercise regularly, avoid risk factors such as smoking and excess sun exposure.

Sensitivity to sunlight is a common side effect of many treatments. Wear a hat and high factor sun cream whenever you are outside to protect your skin.

## Exercise

If you've experienced different side effects after finishing treatment, regular physical activity can help you manage these. For example:

- Regular activity can help to alleviate fatigue: even a small increase in activity can help to improve your energy levels.
- During exercise the brain produces chemicals called

endorphins that can help to manage stress, anxiety, low mood or depression.

- Exercise can help build muscle strength that can often be affected following treatment. Low intensity weight training may help to build strength.
- If you have gained weight during treatment due to inactivity, exercise can help to maintain a healthy weight, which can help reduce the risk of getting other health problems.
- Exercise promotes better sleep. Being more active during the day helps you to relax and sleep better at night.

## Healthy eating

A balanced diet is eating the correct amount of the seven nutrients to give you enough energy for daily activity. The seven nutrients are: protein; carbohydrates; fats; fibre; minerals; vitamins and water.

A daily diet for most people should include varying portions of:

- Fruit and vegetables
- Starchy, carbohydrate-rich

foods such as bread, rice, pasta, and potatoes

- Foods high in protein such as meat, poultry, fish, nuts, eggs and pulses like beans and lentils
- Some milk and dairy foods such as cheese, yoghurts and cream
- A small amount of food high in fat, salt and sugar
- Plenty of water

You can find more information about diet and exercise in the *Living Well with Leukaemia* section on our website: <https://www.leukaemiacare.org.uk/support-and-information/information-about-blood-cancer/living-well-with-leukaemia/>

If you develop a late effect it is likely you will be referred to a clinician with expertise in that area. Most late effects are managed the same way whether they occur after cancer therapy or not. There will be special considerations as it is likely they will be occurring at a younger age, such as heart failure or coronary artery disease.

Certain treatments are associated

# Managing late effects (cont.)

with a significant number of late effects and so you may find yourself seeing a number of different clinicians at different hospitals, which can be stressful and have an impact on your education or work. This in turn may have a financial impact. You will need to talk to your employer with regard to your working arrangements.

You may need to negotiate a reduction in working hours or need to make an arrangement with your employer for times when you may need to go to hospital, or for those times when you may not be well enough to work.

Your consultant or GP can arrange letters to your employer to confirm that you are suffering late effects of cancer treatment and the effect it may have on your work life.

It is important for you to know that people who have had any form of cancer are covered by law by the Equality Act. This means that legally your employer cannot discriminate against you and must make reasonable adjustments relating to the late effects you are suffering.

## Managing emotional and psychological late effects

Late effects may have a negative effect on your quality of life. You may feel that you are not the same person, that your experience of cancer has changed you and perhaps those closest to you as well. They can affect your body image and your confidence. This may lead to difficulties in forming relationships and a feeling of isolation. It is important that you discuss your feelings with your clinical team, so they can assess your needs for support and intervention and point you in the right direction for advice on social and financial issues.

Not everything about having cancer is bad. Many people find a renewed sense of purpose or value in life. Relationships can become closer and more meaningful. Look for the positives and learn from your experience of cancer. Manage uncertainty by taking control and making positive choices about the rest of your life. Fears of cancer recurrence can be very troubling, but they usually fade with time. Think about your priorities and

make plans for the future you want. This could be making more time for hobbies and interests, or with the people you love. Or it can be bigger things like a change of occupation, or a new direction in life. Find a new normal, based on your priorities now, and build your life into what you want it to be. Be kind to yourself, make time for yourself and the things you want to do.

## **What support should I look for?**

Most of the services for people with blood cancers are focused on the earlier stages of diagnosis and treatment, so patients may feel lonely or even abandoned when treatments are over. This later period, often described as survivorship, involves many challenges. It can feel hard to get back to normal, as so many things will have changed. This is a time when uncertainty can be a prominent feature of life, and most people have an ongoing fear of the cancer coming back. Though uncommon, severe psychological reactions like depression can have a very negative effect on quality of life.

It is important as you go through life after treatment to have someone to listen and be there for you. This may be your partner, another family member, or a friend. Many people also find support groups helpful, sharing experiences with people who know what they have been through. For others it is better to move on, and seek a new identity after cancer. Most people cope with this informal support, but others will need professional psychological help, especially if they are depressed.

Places to seek this include your local health centre or cancer centre, or there are some private or charitable services that offer support. See if your local cancer services have a directory or recommendations of who can help. Mindfulness has emerged as a way that people can learn to live with long term challenges and periods of uncertainty, by cultivating a balanced and non-judgemental approach to their experience of life. It is often taught in groups but can be learned and practiced alone.

# Glossary

## Acute Lymphoblastic Leukaemia (ALL)

ALL is a cancer of the white blood cells that would become lymphocytes. Normal white blood cells divide and grow in an orderly and controlled way; however, in leukaemia this process is disrupted. This means signals that stop the body making too many cells are ignored. Cells continue to divide but do not mature into normal lymphocytes (white blood cells).

## Bone marrow

The soft blood-forming tissue that fills the cavities of bones and contains fat, immature and mature blood cells, including white blood cells, red blood cells and platelets.

## Bone marrow transplant

A procedure to replace damaged or destroyed bone marrow with healthy bone marrow cells (stem cells).

## Cancer

A group of diseases involving abnormal cell growth with the

potential to invade or spread to other parts of the body.

## Chemotherapy

A form of cancer treatment that uses one or more anticancer drugs as part of a standardised chemotherapy regime.

## Chronic

A human health condition or disease that is persistent or otherwise long-lasting in its effects. The term chronic is usually applied when the course of the disease lasts for more than three months.

## Deoxyribonucleic Acid (DNA)

A molecule that carries the genetic instructions used in the growth development, functioning and reproduction of all living organisms.

## Fatigue

Extreme tiredness, which is not alleviated by rest or sleep. Fatigue can be acute and come on suddenly or chronic and persist.

## Graft Versus Host Disease (GVHD)

A condition that might occur after an allogeneic transplant. In GVHD, the donated bone marrow or peripheral blood stem cells view the recipient's body as foreign.

### Immunosuppression

The partial or complete suppression of the immune response of an individual. It is induced to help the survival of an organ after a transplant operation.

### Late Effects

Late effects are health problems that occur months or years after treatment has ended. Late effects are governed by the treatment received e.g. chemotherapy, radiotherapy and surgery, as well as the intensity of that treatment.

### Lymph node or gland

An oval-shaped organ of the lymphatic system that catches viruses and bacteria. It contains white blood cells that fight infections.

## Myelodysplastic Syndromes (MDS)

A disorder in which the bone marrow does not make enough healthy blood cells. The maturation of the cells is abnormal and there may be blasts visible in the marrow. It may be a precursor to the development of acute leukaemia.

### Monoclonal antibodies

Antibodies that are made by identical immune cells that are all clones of a unique parent cell. They therefore all bind to the same epitope (the part of an antigen that is recognised by the antibody).

### Mucositis

Oral mucositis is a common complication of chemotherapy. It begins five to ten days after the start of chemotherapy and lasts 7-14 days. Chemotherapy-induced mucositis cause the mucosal lining of the mouth and gut to atrophy (waste away) and break down, forming ulcers, leading to a sore mouth and diarrhoea.

# Glossary (cont.)

## Radiotherapy

The use of high energy X-Rays to treat cancer. The radiotherapy field is the area of the body being treated. Cancer cells are killed within the radiotherapy field.

## Secondary leukaemia

A collective term used to describe a group of patients with acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS) who have a history of environmental, occupational or therapeutic exposure to hematotoxins or radiation.

## Spleen

The largest organ of the lymphatic system. Similar in structure to a

large lymph node, it acts primarily as a blood filter and defends the body against infection.

## Stem cell transplant (SCT)

A stem cell transplant involves the administration of chemotherapy plus or minus radiotherapy as conditioning followed by infusion of stem cells. The stem cells engraft and form a new immune system.

## Tell us what you think!

If you would like to give us some feedback about this patient information booklet, please hover over the code to the right using your phone or tablet's camera. Click the link as it appears and this will take you to a short web form to fill in.

Suitable for Android, iPhone 7 and above.



# Useful contacts and further support

There are a number of helpful sources to support you during your diagnosis, treatment and beyond, including:

- Your haematologist and healthcare team
- Your family and friends
- Your psychologist (ask your haematologist or CNS for a referral)
- Reliable online sources, such as Leukaemia Care
- Charitable organisations

There are a number of organisations, including ourselves, who provide expert advice and information.

## Leukaemia Care

We are a charity dedicated to supporting anyone affected by the diagnosis of any blood cancer.

We provide emotional support through a range of support services including a helpline, patient and carer conferences, support group, informative website, one-to-one buddy service and high-quality patient information. We also have a nurse on our help line for any medical queries relating to your diagnosis.

Helpline: **08088 010 444**  
**[www.leukaemicare.org.uk](http://www.leukaemicare.org.uk)**  
**[support@leukaemicare.org.uk](mailto:support@leukaemicare.org.uk)**

## Bloodwise

Bloodwise is the leading charity into the research of blood cancers. They offer support to patients, their family and friends through patient services.

**020 7504 2200**  
**[www.bloodwise.org.uk](http://www.bloodwise.org.uk)**

## Cancer Research UK

Cancer Research UK is a leading charity dedicated to cancer research.

**0808 800 4040**  
**[www.cancerresearchuk.org](http://www.cancerresearchuk.org)**

## Macmillan

Macmillan provides free practical, medical and financial support for people facing cancer.

**0808 808 0000**  
**[www.macmillan.org.uk](http://www.macmillan.org.uk)**

## Maggie's Centres

Maggie's offers free practical, emotional and social support to people with cancer and their families and friends.

**0300 123 1801**  
**[www.maggiescentres.org](http://www.maggiescentres.org)**

## Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

**08444 111 444**  
**[www.adviceguide.org.uk](http://www.adviceguide.org.uk)**

Leukaemia Care is a national charity dedicated to providing information, advice and support to anyone affected by a blood cancer.

Around 34,000 new cases of blood cancer are diagnosed in the UK each year. We are here to support you, whether you're a patient, carer or family member.

## Want to talk?

Helpline: **08088 010 444**

(free from landlines and all major mobile networks)

Office Line: **01905 755977**

**[www.leukaemiacare.org.uk](http://www.leukaemiacare.org.uk)**

**[support@leukaemiacare.org.uk](mailto:support@leukaemiacare.org.uk)**

Leukaemia Care,  
One Birch Court,  
Blackpole East,  
Worcester,  
WR3 8SG

Registered charity  
259483 and SC039207

**Leukaemia Care**  
YOUR Blood Cancer Charity

