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 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.

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. The booklet has since been updated by our Patient Information Writer, Isabelle Leach.

If you would like any information on the sources used for this booklet, please email communications@leukaemiacare.org.uk for a list of references.
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 8:30am – 5:00pm Monday - Friday and 7:00pm – 10:00pm on Thursdays and Fridays. If you need someone to talk to, call **08088 010 444**.

Alternatively, you can send a message via WhatsApp on **07500068065** on weekdays 9:00am – 5:00pm.

**Nurse service**

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

**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.leukaemiacare.org.uk/support-and-information/help-and-resources/information-booklets/](http://www.leukaemiacare.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.leukaemiacare.org.uk/support-and-information/support-for-you/find-a-support-group/](http://www.leukaemiacare.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@leukaemiacare.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.leukaemiacare.org.uk.

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@leukaemiacare.org.uk

Patient magazine
Our magazine includes inspirational patient and carer stories as well as informative articles by medical professionals: www.leukaemiacare.org.uk/communication-preferences/
A note from our Patient Services 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 are aware 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 indicated 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 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 Services team or a dedicated trained volunteer will be ready to answer your questions.

Best wishes,
The Patient Services Team
The different types of side effects

Most of the treatments used for patients with leukaemia (chemotherapies, chemo immunotherapies, radiotherapy and stem cell transplants) can cause side effects. However, not everyone experiences side effects with treatment since people react differently, and some patients do not have any side effects at all.

Side effects from treatment may be acute, late or long-term and are distinguished as follows:

- **Acute side effects**: Side effects that occur during and immediately after treatment. Most side effects are short-lived and reversible, disappearing after treatment ends. For example, nausea and hair loss occur at the time of receiving treatment and usually stop once the drug is stopped.

- **Late side effects**: Side effects that occur after treatment and may continue for a certain period after treatment is finished. These are also known as delayed side effects. Bone loss occurring two years after treatment is an example of a late side effect.

- **Long-term side effects**: Side effects that are permanent and remain long after treatment is finished. The development of lung fibrosis 10 years after treatment is an example of a long-term side effect.

In this booklet, we discuss the late side effects and long-term side effects of treatment for leukaemia. These side effects may be physical or emotional and may not show up for months or years after you have finished treatment. Late and long-term side effects...
vary from patient to patient, ranging from very mild to serious. Not everyone gets late effects; the risk depends on type of treatment, dose and age when treated.

When you receive follow-up care, your haematologist will discuss any possible late or long-term side effects that you may experience because early medical attention often can lessen any issues that can come from late or long-term side effects.

As treatments for leukaemia have become more effective, our knowledge of late and long-term side effects has increased. Many newer treatments have been developed to reduce the number and intensity of late, and particularly long-term, side effects. Certainly, many of the treatments used now are much less likely to cause health problems than those used 20 years ago.

Possible late and long-term side effects of patients receiving cancer treatment include:

• Fatigue

• Eye, hearing and mouth changes

• Skin and nail side effects

• Bone and joint issues

• Endocrine and thyroid changes

• Cognitive or thinking effects

• Lung toxicity

• Heart toxicity

• Nerve side effects

• Kidney and urinary toxicity

• Secondary cancers
Fatigue may be experienced during treatment, but it can also last for years after treatment is finished. It is one of the most common long-term side effects and is experienced by 33% of patients with acute myeloid leukaemia.

Fatigue is a tiredness or feeling of exhaustion which leaves you unable to work or perform your usual activities. Fatigue can be experienced either physically or psychologically, and can affect your ability to do everyday tasks, as well as your mental ability.

The reasons why persistent fatigue occurs following treatment for cancer are not yet fully understood. It is thought that fatigue may be related to chronic inflammation, an imbalance of the autonomic nervous system (nervous system that acts largely unconsciously and regulates body functions such as heart rate), damage to the mitochondria (very small organ within the cells of the body which create more than 90% of the energy that the body needs) or disturbance of the hypothalamic-pituitary-adrenal-axis.

The hypothalamic-pituitary-adrenal-axis is the name for a complex pathway of hormonal interactions between the hypothalamus and pituitary gland in the brain and the adrenal glands situated on top of the kidneys (Figure 1). It is known as the central stress response system and links the central nervous system and endocrine system.

Other more obvious causes of late or long-term fatigue can include:

- Ongoing pain.
- Chemotherapy with drugs such as vincristine, vinblastine, and cisplatin often cause fatigue through and beyond completion of treatment.
- Radiotherapy can cause fatigue that increases over time, irrespective of the site of treatment. Fatigue usually lasts from three to four weeks after treatment stops, but can continue for up to two to three months.
- Bone marrow transplant (stem cell transplant) is an aggressive form of treatment that can cause fatigue lasting for up to one year.
Stress or depression: Fatigue, stress and depression are often linked and it may not be clear as to which started first. Fatigue is one of the major symptoms of depression; however, equally, if you feel fatigued it can lead to low mood. If you are concerned about depression you should discuss with your GP or treating medical team.

Medical conditions: Side effects of cancer can cause hypothyroidism meaning the thyroid gland is under-active. The body's metabolism slows down and food isn't burnt fast enough to provide adequate energy.

You should report any fatigue to your medical team, so they can find out its cause and provide treatment. If there is not an obvious cause for your fatigue, late or long-term fatigue can still be managed successfully.

Figure 1: Component of the hypothalamic-pituitary-adrenal-axis
Eye changes

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. Cataracts are recognised side effects of cancer treatment. However, they also occur with age in people who have not been treated with cancer treatment.

Chemotherapy, hormone therapy, immunotherapy, radiotherapy and steroid drugs can all lead to an increased risk of cataracts. The risk of cataract formation in patients with radiotherapy increases in line with the radiation dose.

Not all cataracts need treatment and it may be that you just require monitoring by an optician in the first instance. If treatment becomes necessary, the only treatment is surgical. This involves removal of the clouded lens and replacement with an artificial plastic lens. You will normally have local anaesthesia and be able to go home the same day.

Dry eye syndrome

Dry eyes is a common condition which results from inflammation of the cornea, which is the clear outer surface of the eye, and the conjunctiva (membrane covering the eye and eyelids). This leads to reduced tear production.

Certain cancer treatments may predispose to the development of dry eye, especially radiotherapy. Graft-versus-host disease, which can occur after a stem cell 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. Treatments include artificial tears or ointments to lubricate the eye. Alternatively, partially or completely closing your tear ducts with tiny removable silicone plugs can reduce tear loss.
Hearing changes

Some chemotherapy drugs such as cisplatin, high doses of carboplatin, and high doses of radiation can cause hearing loss. This can occur months or years after exposure.

If you or others have noticed any impairment in your hearing, you should speak to your consultant or GP in order to be referred to specialised audiology services. Depending on the type and dose of cancer treatment that you received, you may need to see an audiologist more often.

Mouth changes

If you have had radiation treatment to your head or neck or have received certain chemotherapy drugs, you may notice late side effects such as dry mouth, gum infections, tooth loss, or bone loss of the jaw.

Osteonecrosis (bone death) of the jaw is due to damage to the small blood vessels supplying the bone. The poor supply of oxygen and nutrients as a result of this leads to necrosis of the jawbone. It usually occurs after radiotherapy at doses greater than 40 Gy, usually to the jaw. It can be spontaneous, but usually occurs after dental trauma. Treatment includes pain killers, antibacterial mouth washes, antibiotics, if necessary.

You are normally asked to have a check-up at the dentist every one or two months for at least six months after radiation treatment ends. Your dentist will monitor you for any changes in your mouth, teeth, and jaw. Thorough oral care and regular visits to the dentist can help reduce these symptoms.
Skin side effects
Chemotherapy and radiotherapy can cause several skin problems. The most common ones include dry skin, hyperpigmentation (increased colour) and photosensitivity. Photosensitivity is an enhanced skin response to ultraviolet radiation (sunlight).

In patients who have had a stem cell transplant, graft-versus-host disease (where the donated stem cells react against the patient receiving the stem cells), a number of late side effects are reported such as a rash, blisters on the face, ears, palms, and soles, or sclerosis (hardening) of the skin. These skin conditions are often continuous in patients suffering from chronic graft-versus-host disease.

In immunosuppressed patients, late side effects on skin can include basal and squamous cell carcinomas which are types of skin cancer. They are normally painless and tend to develop slowly. If you notice any changes to your skin, particularly where it is exposed, it is important to let your medical team know.

Dry skin reactions can be effectively improved with moisturising creams and lotions and patients should be encouraged to use them on a regular basis. Photosensitivity is best managed with the use of sun cream, protective clothing and moisturising after-sun creams.

Nail side effects
There are several types of nail changes that may occur in patients receiving chemotherapy. In some patients, chemotherapy changes are only cosmetic, whereas in others, they cause pain and discomfort and impair manual activities.

The most common chemotherapies associated with these changes are taxane chemotherapy drugs such as docetaxel and paclitaxel, anthracyclines such as daunorubicin, monoclonal antibodies such as trastuzumab and tyrosine kinase inhibitors such as imatinib.

Minor changes include alteration of the colour of the nails, single transverse bands of white
discoloration of the nail plate and haemorrhages under the nails. More severe changes include reddening and swelling around the nail, abscesses under the nail, and onycholysis (detachment of the nail plate from the bed). While the appearance of some of these nail changes improves over time, some changes will remain permanent.
Bone and joint issues

Bone changes

Bones reach their maximum density when people are in their early to mid-twenties, and then density subsequently reduces as they get older. In women, this tends to happen after the menopause, and in men, later in life. Thinning of the bones is a known side effect of cancer treatments such as chemotherapy, radiation therapy, steroid drugs and hormonal therapy. With radiation therapy, the thinning of the bone is restricted to the area treated.

Chemotherapy treatments linked to bone loss include methotrexate, docetaxel, paclitaxel, imatinib and steroids.

The effect of chemotherapy on the bone can be direct such as for imatinib which targets various receptors involved in the formation of the bone. Alternatively, for women, the cancer therapy can damage the bone indirectly by affecting the ovarian function and hormonal status. Ovarian failure results in bone loss within two years. Receipt of chemotherapy at a young age can contribute to developing premature ovarian insufficiency, thereby decreasing bone mineral density later in life.

Most of the knowledge of the late effects of cancer treatment for bone loss is based on data from childhood cancer patients, whereas current knowledge concerning late effects in adult cancer survivors is not as evident.

Severe reduction in bone mineral density is known as osteoporosis and may lead to bone fractures, particularly in patients who received chemotherapy at a young age. In these patients, treatment with substitution sex hormones is recommended to avoid decreased bone mineral density which could lead to early onset osteoporosis. Low levels of female/male hormones, growth hormone deficiency and immobility are all risk factors for osteoporosis. Hormone replacement therapy should be prescribed with care in patients with a family history of breast cancer or clotting events.

Following treatment, it is essential to have regular check-ups, where tests for bone mineral density will be performed. The most usual method for screening bone
mineral density is using a dual X-ray absorptiometry (DEXA) scan, which is a low radiation X-ray that can detect small changes in the bone density at the spine and hip. In premenopausal females and younger men, Z-scores should be assessed. Z-scores compare your bone density with that of other people your same age and sex. You can also minimise the risk of bone loss by limiting your alcohol intake and not smoking. In addition, weight bearing exercise, calcium and vitamin D are useful for preserving bone density.

**Joint Changes**

Cancer treatments including chemotherapy drugs, steroids and radiotherapy can lead to muscle weakness, scar tissue and bone loss. This may cause a loss of motion in joints. If you are at risk because of your previous cancer treatment, you will be monitored for early signs of joint changes in order to address them before they worsen. Examples of joint changes include difficulty in opening your mouth wide and pain performing certain movements which involve the affected joint.

Osteonecrosis is a disease resulting in the death of bone cells caused by temporary or permanent interruption to the blood supply to the bone. Radiation therapy or chemotherapy are the treatments most commonly associated with osteonecrosis. The bone tissue loses its oxygen and nutrient supply and dies. It is most common in the hip and shoulder, but can affect other large joints such as the knee, elbow, wrist and ankle. One or more bones can be affected at the same time. It can cause significant pain and the amount of disability will depend on the bones/joints involved.

Diagnosis of joint osteonecrosis is made by X-Ray and magnetic resonance imaging (MRI). Treatment consists of improving the use of the bone involved with physiotherapy and good pain relief. Surgery and joint replacement can be used if required.

Hormone replacement therapy should be prescribed with caution in patients with previous history of clotting events or strong family history of breast cancer.
Endocrine changes

The endocrine system is a network of glands that creates hormones to control several important body functions including growth, how the body generates energy, sleep, sexual development and reproduction. The main glands in the endocrine system involve the hypothalamus and pituitary in the brain and the adrenal glands on the kidneys.

Radiation to the head and neck area and the use of some chemotherapies can result in temporary or permanent damage to these components of the endocrine system. This damage can lead to early menopause, infertility, underactive thyroid and weight gain.

Thyroid changes

The thyroid gland is a small gland based in the lower neck (Figure 1). 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 as part of treatment to prepare the bone marrow for a stem cell transplant or in patients where cranial/craniospinal radiotherapy is necessary.

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. If the body’s metabolism slows down, it does not burn food fast enough to provide adequate energy and heat. Patients experience fatigue, feelings of being cold, slow pulse rate, weight gain, and sometimes hoarseness. Because an underactive thyroid is a permanent side effect, you will be prescribed thyroxine tablets for life and you should have your thyroid function monitored yearly.

Thyroid nodules/thyroid cancer

After radiotherapy to the neck, thyroid nodules/cancer can occur. These late side effects will be picked up during your yearly thyroid test. If your doctor 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. If the result is not cancerous, your nodule will be monitored by yearly ultrasounds.

If the cells become indicative of thyroid cancer, you will be referred to a surgeon to discuss removing part or all of the thyroid gland. Symptoms and signs of thyroid cancer are a painless hard lump, hoarseness, difficulty swallowing, enlarged lymph nodes in your neck and difficulty breathing.

Decreased fertility and early menopause

Both chemotherapy and radiotherapy can result in premature ovarian failure and early menopause in women, and low testosterone levels and sperm counts in men. These changes result in a permanent decrease in fertility for both genders. Fertility is the ability to have children and it can be affected by treatment with both chemotherapy and radiotherapy.

Male fertility

In 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.

Chemotherapy drugs most commonly implicated in affecting sperm production are carmustine, busulphan, chlorambucil, cyclophosphamide, ifosfamide, cisplatin and cytarabine. The specific effect on sperm production, and whether it is temporary or permanent, will depend on which drug is used and its dose. Recovery can take many years.

Testosterone secretion is usually much less affected by these chemotherapies. Testosterone is the male hormone secreted mainly in the testes, with a small amount being made in the adrenal glands. Testosterone regulates sex drive and sperm production, muscle mass, bone mass, fat distribution and the production of red blood cells. Male patients who have gone through puberty should be offered the opportunity to store sperm before
Female fertility

The ovaries are very sensitive to chemotherapy. Some drugs may cause either rapid and permanent ovarian failure or a period of normal fertility followed by an early menopause. Some drugs, particularly alkylating agents, are more damaging to the ovaries than others. Chemotherapy drugs used in the treatment of leukaemia and commonly implicated in affecting ovarian function are similar to those affecting sperm production, and include carmustine, busulphan, chlorambucil, cyclophosphamide, ifosfamide, cisplatin and cytarabine. The impact of a given treatment will depend on the total dose of drugs received and the age at which they are administered.

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. In addition, the effect on the uterus with high doses of radiotherapy is a decrease in the functional lining of the uterus, which can lead to an increased risk of early pregnancy loss.

Fertility preservation before treatment is not as simple for women as it is for men; however, the onset of regular periods is encouraging. Blood tests to look at certain hormone levels may suggest your level of fertility and the levels of eggs in your ovary. As soon as possible after you are informed that you will be receiving treatment, you should seek information from both your oncologist and fertility specialists in order to make informed decisions about fertility. For an acute leukaemia, treatment normally starts relatively quickly after the diagnosis, so speak to your medical team about timeframes.

In order to give you the option of having biological children in the future, in the event your fertility does not recover after treatment, it is sensible to freeze your eggs prior to receiving treatment.

All patients who may be considering having children in the future and require anticancer 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.
Cognitive function is a collective name for all the mental processes that allow us to carry out any task. While receiving chemotherapy, patients commonly notice that their short-term memory and concentration are diminished. Although this usually settles shortly after their treatment ends, it can occasionally be a long-term effect for some patients.

Radiation therapy to areas that include the brain can cause difficulties in the months or years after treatment ends. These late effects may include verbal memory loss, issues with concentration, speed of processing of information, and personality changes.

Following cancer treatment, you will have regular check-up appointments. If you have experienced any symptoms of brain changes, you will be assessed to determine if these are late side effects of your treatment or are related to the cancer itself. Referral for physical, occupational, or speech therapy should be made for late side effects.
Patients who have had radiation treatment as part of the conditioning regimen for a stem cell transplant (radiation of the bone marrow) are at risk of lymphoedema which occurs as a late effect.

Lymphoedema is a condition where the lymph fluid from the lymphatic system does not drain into the blood vessels as it should because of damage by radiation to the lymphatic vessels. The lymphatic fluid builds up in the tissues causing swelling. Lymphoedema can develop many years after treatment.

The degree and severity of lymphoedema varies among patients, even in patients receiving similar treatment. Lymphoedema may range from causing mild discomfort to pain with severe swelling and disfiguration. Lymphoedema may increase the risk for cellulitis and should be treated with lymphatic drainage massage and physiotherapy, compression garments, exercise and diet.
Chemotherapies such as bleomycin, busulphan, carmustine, high doses of cyclophosphamide and radiation therapy to the chest are associated with lung damage. Chronic graft-versus-host disease after a stem cell transplant is also known to affect lung function.

Lung damage can cause shortness of breath, wheezing, fever, dry cough, congestion, and feeling tired. In general, these symptoms usually begin to improve after around two to three weeks. However, months or years after radiotherapy, patients may develop serious side effects, including pneumonitis and fibrosis. Pneumonitis is an inflammation of the walls of the alveoli (air sacs) in the lungs and pulmonary fibrosis is a build-up of scar tissue in the lungs. It is not usually associated with a bacterial infection.

Pulmonary fibrosis generally occurs following pneumonitis due to radiation therapy. It commonly occurs six to 24 months after the pneumonitis, especially if this has not been diagnosed or treated adequately. However, pulmonary fibrosis may develop several years after radiation therapy is completed.

Pulmonary fibrosis can lead to chronic pulmonary insufficiency, when the lungs cannot take in enough oxygen or expel enough carbon dioxide to keep the body healthy. This condition depends on the proportion of the lung treated with radiation, because fibrosis is limited to the area of the lung that has been irradiated. When a large area of the lung has been subjected to radiotherapy, the extensive pulmonary fibrosis leads to pulmonary hypertension and cor pulmonale can develop. Cor pulmonale is an abnormal enlargement of the right side of the heart due to the pulmonary hypertension. Symptoms of cor pulmonale include shortness of breath and fainting on exertion, fatigue, lethargy and chest pain.

Oxygen therapy can be given for serious trouble in breathing, and is normally administered through nasal prongs or a mask that fits over your mouth and nose.

Risk of lung damage is increased
by smoking, pre-existing lung problems such as asthma, young age of onset of treatment and administration of cancer drugs anthracyclines that increase the effect of radiotherapy.
Heart toxicity

Acute side effects of chemotherapy or radiation on the heart occur during and shortly after treatment. Most side effects are short-lived and reversible, disappearing after treatment. However, some side effects of cancer treatment only develop months or years after the treatment has stopped.

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.

Cardiotoxicity and chemotherapies

The most common drugs implicated in late cardiotoxicity are the anthracyclines. These drugs are used in many treatment combinations for patients with leukaemia. They include doxorubicin (adriamycin), daunorubicin, idarubicin and epirubicin. They are often administered as part of combination chemotherapy. However, their use is limited by their toxic effects on the heart (cardiotoxicity) which depends on the dose (dose-dependent).

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 result in heart failure in the long-term. Ultimately, the chambers of the heart become dilated and do not pump the blood correctly. Cardiotoxicity with anthracyclines may become apparent within one year of the completion of treatment.

In addition to the dose and length of your anthracycline treatment, risk factors for having cardiotoxicity are being younger (especially less than seven years old), female and previously treated with chest radiotherapy or other cardiotoxic drugs.

Mitoxantrone, which is a type II topo-isomerase inhibitor that acts by disrupting the formation and repair of the DNA of leukaemia cells as well as healthy cells, is used in the treatment of acute myeloid leukaemia and in treatment combination for chronic myeloid leukaemia. Mitoxantrone can affect the
heart muscle and, in turn, the ability of the heart to pump blood effectively. Usually these effects are associated with higher doses of the drug but not always, and some people will be more susceptible than others.

In case of severe heart damage, the use of medications such as beta-blockers and angiotensin converting enzyme inhibitors might offer some delay in progression of your cardiotoxicity, and also reverse part of the damage. These drugs might have to be continued for life.

**Cardiotoxicity and radiation**

Cardiotoxicity related to previous radiation therapy can have significant consequences years after treatment, but the exact cause of it is not clear. Although modern radiotherapy fields try and avoid the heart where possible, it might still be exposed.

Radiotherapy can have a number of effects on the heart. It may lead to acute inflammation within the heart blood vessels. It can cause cardiomyopathy, coronary artery disease, valvular disease (damage to one of the four heart valves), and disease of the heart conduction system and pericardium (membrane enclosing the heart). Radiotherapy also causes proliferation of the cells lining the blood vessels leading to narrowing of the artery and a reduction in blood flow. The blood vessels supplying the heart may become hardened or blocked, which is known as coronary artery disease, affecting the supply of oxygen getting to the heart. 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.
Kidney toxicity

Certain chemotherapy drugs are known to damage kidney function. This may last for several months or years after treatment with these drugs, or even for life. Long-term kidney toxicity has been reported after as long as 35 years in patients who have received ifosfamide, cisplatin, carboplatin, tacrolimus, methotrexate, cyclophosphamide and radiotherapy as children. Patients with the highest risk for kidney damage were those receiving ifosfamide and cisplatin.

When the kidneys are not functioning properly, filtration of the blood through the glomeruli (small filtering unit of tiny blood vessels in the kidney) is reduced, and urea (breakdown product of proteins normally excreted in the urine), builds up in the blood. In addition, the chemicals and water extracted from this fluid as it passes along the kidney’s tubules (small tubes) cannot be regulated properly, resulting in a build-up of potassium, sodium and fluid. This predisposes the kidney to damage and infection.

In children and adolescents treated with ifosfamide, chronic glomerular nephrotoxicity was reported in up to 50% of patients and chronic tubular nephrotoxicity was reported in up to 25%. For those receiving cisplatin, chronic glomerular nephrotoxicity was reported in up to 80% of patients and chronic tubular nephrotoxicity was reported in up to 30%. Carboplatin nephrotoxicity is similar to cisplatin but less common and usually much less severe.

Long-term renal toxicity caused by the calcineurin inhibitor tacrolimus, which is sometimes used in chronic lymphocytic leukaemia, can cause interstitial fibrosis and tubular atrophy leading to chronic kidney disease.

Methotrexate is used in the treatment of acute lymphoblastic leukaemia; however, at high doses, it is known to crystallise in the renal tubules and is also associated with tubulointerstitial nephritis that can lead to chronic kidney disease.

Cyclophosphamide can cause haemorrhagic cystitis, but it is also reported to cause renal tubular necrosis. Interferon-alpha can cause glomerulonephritis, which can be occasionally seen in patients with chronic myeloid leukaemia treated with high

Kidney and liver toxicity
doses of interferon-alpha over long periods of time.

Early detection of side effects of chemotherapy on the kidney is important to prevent progression to end stage renal disease. Patients who have received ifosfamide should be monitored yearly.

Liver toxicity

Hepatotoxicity is the injury of liver cells as a result of impaired liver function caused by exposure to a drug. Certain chemotherapy drugs can damage cells in the liver by interfering with the production of their DNA, as well as the process of their cell division. Of these drugs, those that are used in patients with leukaemia include the anti metabolites drugs (methotrexate, 6 mercaptopurine and cytarabine) and alkylating drugs (cisplatin, carboplati n and chlorambucil).

Methotrexate has been associated with steatosis, steatohepatitis, fibrosis and cirrhosis. Steatosis, also known as non-alcoholic fatty liver, is an accumulation of fat in the liver cells, and steatohepatitis occurs where the steatosis is associated with an area of inflammation and swelling of the liver cells. However, these chronic liver complications may be reversed within months after treatment is stopped if recognised early enough.

Following the use of 6-mercaptopurine as maintenance treatment for acute lymphoblastic leukaemia, hepatocellular toxicity and cholestatic toxicity, can lead to obstruction of the bile duct. The risk of hepatotoxicity is related to the cumulative dose of methotrexate. Early portal fibrosis is found only in patients with prolonged therapy.

Cytarabine can cause hepatotoxicity which is dependent on the total dose received. Mild elevation of liver enzyme levels are seen in 5% to 10% of patients, but higher doses can cause liver abnormalities. Severe cholestatic toxicity related to cytarabine therapy has been reported.

Cyclophosphamide, chlorambucil and 6-mercaptopurine are known to cause a condition known as sinusoidal obstructive syndrome of the liver. Sinusoidal obstruction syndrome is the blockage of the very small (microscopic) veins in the liver. It is a potentially fatal
form of hepatic injury which can present in an acute, subacute or chronic form. It is usually accompanied with abdominal pain and swelling, portal hypertension and elevations of liver enzyme levels.

Lenalidomide is an immunomodulatory drug used in the treatment of relapsed chronic lymphocytic leukaemia which has been associated with rare, but severe, hepatotoxicity. Side effects of toxic hepatitis and cholestatic hepatitis have been reported approximately eight weeks after starting lenalidomide. Re-activation of viruses such as herpes zoster, which causes shingles, or hepatitis B have also been reported with lenalidomide treatment.

Recognising the early patterns of hepatotoxicity by means of regular liver function tests can allow for early management of these side effects. Patients who have received 6-mercaptopurine or methotrexate as part of their treatment for leukaemia should have liver function tests every one to three years.
Certain anticancer drugs can cause temporary or permanent peripheral neuropathy, which is the damage or dysfunction of one or more nerves resulting in numbness, tingling, muscle weakness and pain in the area supplied by the nerves. Peripheral neuropathy can develop weeks after starting chemotherapy, and may last from months to years after chemotherapy is finished.

Several anticancer drugs used to treat leukaemia are known to cause peripheral neuropathy such as platinum-based drugs (cisplatin and carboplatin), vinca alkaloids drugs (vincristine) and taxane drugs (docetaxel and paclitaxel). About 58% of patients who receive taxane based chemotherapy develop peripheral neuropathy.

Peripheral neuropathy caused by docetaxel can persist for up to three years after treatment is finished and significantly affects patients' quality of life. Long-term peripheral neuropathy is related with high levels of disease including disorders of coordination, balance and speech, insomnia and depression.

It is important to let your doctor know immediately if you experience any of these symptoms so your medication can be adjusted to relieve the condition. Peripheral neuropathy can last for many years after the end of treatment and dramatically reduce quality of life.
Secondary cancers have become one of the most serious late side effects of cancer treatments in recent years, both for children and adults. A secondary cancer is the development of a new primary cancer of a different type to the original cancer often years after treatment. For example, patients who have had treatment for acute lymphoblastic leukaemia may develop a thyroid cancer 15 years after their treatment.

Secondary cancers are often mistakenly considered to be related to the first cancer, or thought to be the spread of the first cancer to other areas in the body. These should more appropriately be called metastasis. Analysis of the thyroid cancer will show thyroid cancer cells, and not leukaemia cells that have travelled to the thyroid gland. Secondary cancers often occur years or decades after the original treatment of radiotherapy or chemotherapy.

Any chemotherapy whose anticancer action is to damage DNA of cells may result in secondary cancers in the future. Chemotherapies that are most likely to cause this damage are alkylating drugs (cyclophosphamide), platinum drugs (cisplatin), and anthracycline drugs (daunorubicin and doxorubicin). Radiotherapy is also known to break DNA strands leading to gene mutation and subsequently cancer transformation in the new cell.

The risk factors for a secondary cancer are:

**Type of treatments:**

- Patients who receive radiotherapy and chemotherapy together are at greater risk than those on either treatment alone.
- Chemotherapy is known to be a greater risk factor than radiation therapy in causing leukaemia.
- Alkylating chemotherapy drugs have a greater risk of causing secondary cancers.

**Intensity of treatment (number of cycles) and doses received.**

For patients who received radiotherapy, the area treated is also important.
Age at the time of treatment, particularly radiation.

Since emerging new treatments are allowing patients with childhood cancers to survive well into adulthood, the incidence of secondary cancers is rising.

It is important to discuss with your doctor the types of secondary cancers you may be at risk of, following the treatment for leukaemia you received. You should have regular check-ups for the rest of your life to catch any recurrence of your leukaemia and any new cancer that may occur. In addition, it is important to be self-aware and report new symptoms as soon as possible. Patients should be encouraged to enter a screening program where one is available.
Managing late effects

Awareness of physical late and long-term effects

Your doctor will have made you aware of any potential late and long-term side effects before starting treatment. However, the main priority after diagnosis is treating your leukaemia as soon as possible. Since your risk of late effects depends on your age, diagnosis and treatment you received, you may not be able to prevent them happening, but you can work towards catching them early and reducing the risk of them progressing.

It is important to discuss risks for late effects with your clinical team. Ideally you should have a written list of them. You should understand how essential monitoring is and that attending your follow-up appointments is important. You should be aware of the symptoms to look for. Be self-aware of your skin, especially moles and any new lumps, so you can report any changes as soon as possible. Regular self-examination of breasts and testicles is advisable.

Patients are encouraged to enter a screening program where one is available, as well as following a healthy lifestyle, a balanced diet and a regular exercise program. It is important to avoid risk factors such as smoking and excess sun exposure.

Exercise

If you have experienced side effects after finishing treatment, regular physical activity can help you manage these:

- Regular activity can help alleviate fatigue. Even a small increase in activity can help to improve your energy levels.
- During exercise, the brain produces chemicals called endorphins that help to manage stress, anxiety, low mood or depression.
- Exercise can help build muscle strength that is often affected during treatment. Low intensity weight training may help to build strength.
- If you have gained weight during treatment due to inactivity, exercise can help you reach a healthy weight. This will reduce
the risk of getting other health problems.

- Exercise promotes better sleep. Being more active during the day helps you relax and sleep better at night.

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.

Healthy eating

A balanced diet is eating the correct amount of the seven nutrients required to give you enough energy for daily activity. These seven nutrients are: protein, carbohydrates, fats, fibre, minerals, vitamins and water. A daily diet 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 booklets on our website at www.leukaemiacare.org.uk/supportand-information/information-booklets/.

Managing your work commitments

If you develop a late effect, it is likely that you will be referred to a clinician with expertise in that area. Most late effects are managed as they would whether they are a result of leukaemia treatment or not. Because some treatments are associated with a significant number of late effects, you may find yourself seeing several clinicians at different hospitals, which can be stressful and have an impact on your education or work.
Managing late effects (cont.)

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 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.

It is important to know that people who have had any form of cancer are covered by the Equality Act. This means that legally employers cannot discriminate against you and must make reasonable adjustments relating to the late effects that you are suffering. Your consultant or GP can arrange letters to your employer to confirm that you are suffering late effects of leukaemia treatment and its impact on your work.

Managing with 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 leukaemia has changed you, and perhaps those closest to you as well. This can affect your body image and your confidence and lead to a feeling of isolation and difficulties in your relationships. 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.

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 leukaemia.

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 leukaemia are focused on the earlier stages of diagnosis and treatment, so patients may feel lonely or even abandoned when treatment is over. This period often 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 leukaemia coming back.

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 leukaemia. 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)
A leukaemia in which lymphocytes start multiplying uncontrollably in the bone marrow, resulting in high numbers of abnormal, immature lymphocytes. Lymphocytes are a type of white blood cell involved in the immune response.

Acute Myeloid Leukaemia (AML)
A rapid and aggressive cancer of the myeloid cells in the bone marrow.

Alkaloid
Naturally occurring organic nitrogen-containing compounds. Some synthetic compounds of similar structure may also be termed alkaloids.

Anaemia
A condition where the number of red blood cells are reduced. Red blood cells contain haemoglobin and transport oxygen to body cells. This may be due to a lack of iron, leukaemia, or sickle cell disease.

Anthracycline
Antibiotic derived from the bacteria Streptomyces peucetius which was found to be an effective anticancer drug.

Antibiotic
A drug used to treat or prevent bacterial infections.

Blood Cancer
Cancer of blood cells from the bone marrow or lymphatic system. There are three main types of blood cancer:

- Leukaemia begins in the bone marrow and is classified according to the type of blood cell it affects (either myeloid or lymphoid) and whether it grows quickly (acute) or slowly (chronic).
- Lymphoma starts in the lymphocyte white blood cells within the lymphatic system.
- Myeloma is a cancer of the plasma cells and starts in the bone marrow. Plasma cells are a type of white blood cell that makes antibodies.

Blood Cells
Cells present in the blood and bone marrow which include red blood cells, white blood cells and platelets. These three types of blood cell make up 45% of the blood volume, with the remaining 55% being plasma, the liquid component of blood.
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 Failure
The bone marrow is unable to keep up with the body’s need for white and red blood cells and platelets.

Bone Marrow Relapse
The presence of greater than 25% of leukaemia cells in a bone marrow aspirate following the first complete remission.

Chemo-immunotherapy
Chemotherapy to which an immunotherapy drug has been added.

Chemotherapy
Drugs that work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

Chronic Lymphocytic Leukaemia (CLL)
A leukaemia in which the B-lymphocytes (B-cells) in the bone marrow start multiplying excessively leading to large numbers of small, mature lymphocyte cells, which are unable to fight infection, and their presence prevents the bone marrow from producing healthy blood cells of all types.

Chronic Myeloid Leukaemia (CML)
A leukaemia in which the myeloid cells start multiplying in the bone marrow leading to large numbers of abnormal, immature myeloid cells called blasts, which prevent the bone marrow from producing enough healthy blood cells of all types.

Conditioning Regimen
This treatment regimen consists of chemotherapy or total body irradiation to eliminate the cancer cells and prevent the immune system rejecting the new stem cells prior to an allogeneic stem cell transplant.

Corticosteroids (Steroids)
Hormones normally produced by the adrenal glands which are two small glands found above the kidneys. Corticosteroids reduce inflammation (redness and swelling) and the activity of the immune system. They are used for inflammatory conditions such as asthma and eczema and autoimmune diseases such as
rheumatoid arthritis.

**Cytarabine**
Antimetabolite drug which works by disrupting the DNA of cancer cells, thereby slowing or stopping their growth.

**Graft-versus-Host Disease**
A serious complication that occurs with allogeneic stem cell transplants. It happens when the graft (donated marrow or stem cells) reacts against the host (patient receiving the stem cells).

**Immunotherapy**
A treatment that uses the body’s own immune system to fight the cancer.

**Incidence**
The number of new cases of disease which are reported as an incidence rate or a risk.

**Intravesical**
In the bladder (injection, cancer).

**Lymph Nodes**
Component of the lymphatic system (part of the body’s immune system) that contain lymphocytes which produce antibodies and macrophage cells which digest dead cells. Lymph nodes are swollen with cell fragments in the event of infection or cancer. They are located mainly in the spleen but also in the neck, armpit and groin.

**Lymphocytes**
A type of white blood cell that is vitally important to the immune response. There are three types of lymphocytes: B-cells, T-cells and natural killer (NK)-cells. B-cells produce antibodies that seek out invading organisms. T-cells destroy the organisms that have been labelled by the B-cells, as well as internal cells that have become cancerous. NK-cells attack cancer cells and viruses.

**Lymphoedema**
A condition that causes swelling in the body’s tissues affecting any part of the body, but usually develops in the arms or legs. It develops when the lymphatic system is blocked or does not work properly.

**Metastases**
A development in another part of the body of cancer cells related to the primary cancer. For example, a patient with lung cancer can have metastases in the liver which have often travelled to the liver through the blood.

**Mutation (gene)**
A permanent alteration in the
DNA sequence of a gene, so that it differs from what is found in most people.

**Neuropathy**
Damage or dysfunction of one or more nerves that can result in numbness, tingling, muscle weakness and pain in the affected area.

**Nodule**
A rounded lump with a distinct border.

**Portal Hypertension**
A high pressure in the portal vein which carries blood from the digestive organs to the liver. It is caused by a blockage to the blood flow in the liver.

**Pulmonary Hypertension**
A high pressure in the pulmonary arteries which supply blood to the lung to be oxygenated. It is caused by hardened pulmonary arteries or disease in the lung.

**Secondary Cancers**
Second primary cancer that often appears after a number of years following chemotherapy or radiation treatment for a previous different primary cancer. Secondary cancer is not a re-occurrence or spread of the primary cancer in another part of the body which is called a metastatic cancer. Secondary cancers are often other blood cancers, lung cancer and skin cancers.

**Spleen**
The largest organ of the lymphatic system whose function is to help clear the body of toxins, waste and other unwanted materials. The spleen is located under the ribs on the left of the abdomen.

**Splenomegaly**
Enlarged spleen.

**Stem Cell Transplant**
A transplant of stem cells derived from part of the same individual or a donor.

**Targeted Therapy**
Drugs that specifically interrupt the leukaemia cells from growing in the body. However, these drugs do not also harm the body’s healthy cells the way conventional drugs do.

**Total Body Irradiation (TBI)**
Radiation treatment to the whole body to prepare a patient for a stem cell transplant. Irradiation is the term used when radiation falls onto a surface (e.g., radiation waves on the surface of the skin). Total body irradiation is
used to destroy or suppress the patient’s immune system in order to prevent rejection of the donor’s stem cells. In addition, it can eliminate any residual cancer cells in the patient’s body to increase the chances of a successful transplant.

**Tyrosine Kinase Inhibitors (TKIs)**

Drugs that inhibit the tyrosine kinase enzyme which controls the function of a cell. Tyrosine kinase inhibitors can switch ‘off’ tyrosine kinase enzymes that are permanently active due to a mutation.

**Tyrosine Kinase Receptors**

Receptors present in the membranes of all of the body’s cells which can be activated by the enzyme tyrosine kinase.

**Urea**

A breakdown product of proteins in the body which is excreted in the urine.

**Uric Acid**

A product of the metabolic breakdown of purine nucleotides which are the chemical building blocks of DNA. Uric acid is a normal component of urine.

**Vasculitis**

Inflammation of the blood vessels.

**Watch and Wait**

A management approach for slow growing blood cancers. Also called active monitoring, the Watch and Wait approach is the current standard of care for patients with slow growing blood cancers who do not have any symptoms. Treatment is usually started either once symptoms appear or when test results suggest the blood cancer is progressing.

**White Blood Cells**

White blood cells are one of the types of cells found in the blood and bone marrow, along with red blood cells and platelets. White blood cells create an immune response against both infectious disease and foreign invaders. Granulocyte white blood cells include the neutrophils (protect against bacterial infections and inflammation), eosinophils (protect against parasites and allergens) and basophils (create the inflammatory reactions during an immune response). Other white blood cells include the lymphocytes (recognise bacteria, viruses and toxins, to which they produce antibodies) and monocytes (clear infection products from the body).
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.leukaemiacare.org.uk
support@leukaemiacare.org.uk

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

0808 2080 888
www.bloodcancer.org.uk

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

0808 800 4040
www.cancerresearchuk.org

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

0808 808 0000
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

Citizens Advice Bureau (CAB)
Offers advice on benefits and financial assistance.

08444 111 444
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
support@leukaemiacare.org.uk

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

Leukaemia Care is registered as a charity in England and Wales (no.1183890) and Scotland (no. SCO49802). Company number: 11911752. Registered office address: One Birch Court, Blackpole East, Worcester, WR3 8SG.