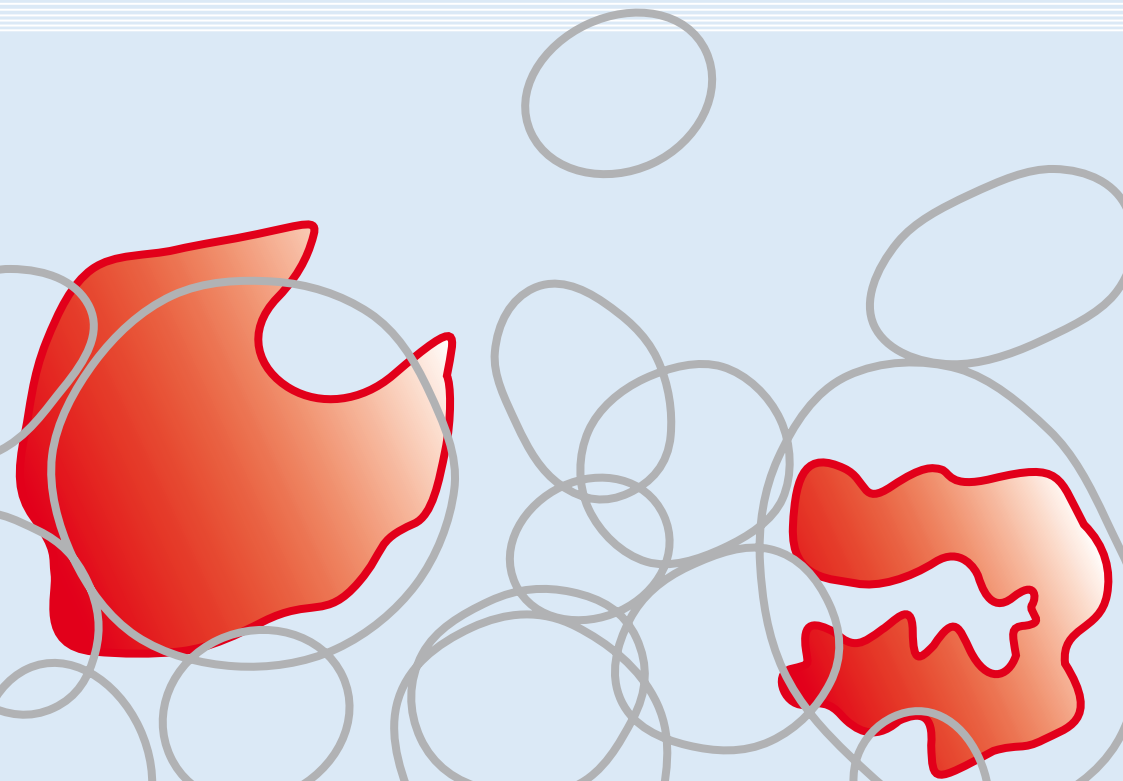


# Childhood Acute Myeloid Leukaemia (AML)



The diagnosis of a blood cancer can be a devastating event for patients, families and friends. It is therefore vital for everyone to have access to reputable and understandable information to help cope with the illness. Whenever possible our booklets are written in line with national guidelines for the treatment of patients with a blood cancer. The information in our booklets is more detailed than in many others but is written in a clear style with all scientific terms explained for the general reader.

We recognise that the amount and level of information needed is a personal decision and can change over time. Particularly at the time of diagnosis, patients may prefer less detailed information. A number of alternative sources of information are available which complement our publications.

The booklets in this series are intended to provide general information about the diseases they describe. In many cases the treatment of individual patients will differ from that described in the booklets.

**At all times patients should rely on the advice of their specialist who is the only person with full information about their diagnosis and medical history.**

**For further advice contact the clinical information team on 020 7269 9060.**

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# What is acute myeloid leukaemia?

**Acute myeloid leukaemia (AML) is sometimes referred to as acute non-lymphocytic leukaemia (ANLL), especially in American publications. AML is a form of cancer that affects the cells producing myeloid blood cells in the bone marrow. Myeloid cells are red blood cells, platelets and all white cells except lymphocytes. The most common forms of AML, in adults and in children, mainly affect the white blood cell production in the bone marrow. The forms that affect red cell and platelet producing marrow cells are less common. They are known as erythroleukaemia and acute megakaryocytic leukaemia respectively.**

Non-lymphocytic white cells include:

- Neutrophils – which mainly combat bacterial infection
- Monocytes – which destroy more resistant bacteria, give rise to tissue immune cells called macrophages and are essential for effective function of antibody producing lymphocytes
- Eosinophils – which are important to defend against parasites and are involved in allergic reactions
- Basophils – which are also involved in allergic reactions and form part of the general immune response initiated by local tissue damage



## Who gets acute myeloid leukaemia?

Unlike acute lymphoblastic leukaemia<sup>1</sup> (ALL), acute myeloid leukaemia is most common in adults, particularly in later life. AML comprises only about 15% of all cases of childhood leukaemia. After childhood the condition is rare until the age of about 40 years when it becomes progressively more common. Boys and girls are affected equally except under the age of two when there is a female preponderance.

<sup>1</sup> There are separate publications on childhood and adult acute lymphoblastic leukaemia available from Leukaemia Research.

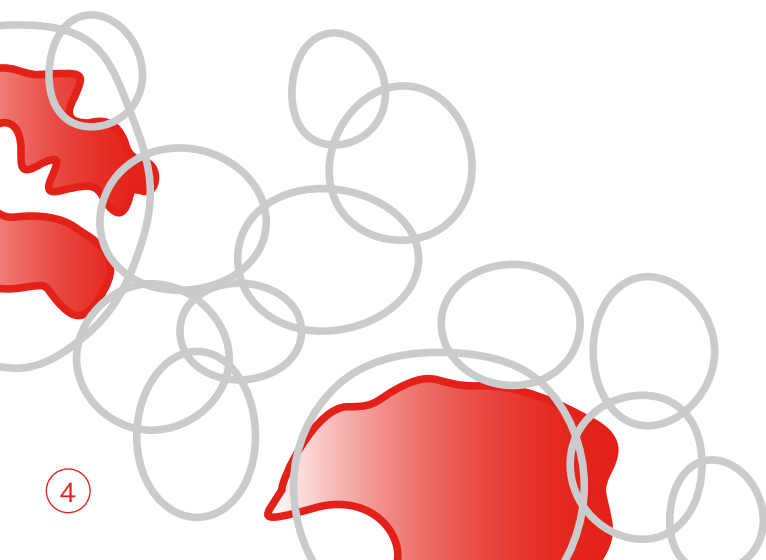
# What are the types of acute myeloid leukaemia?

The major system of classifying AML is based on the appearance of the leukaemic cells. This system is described as the FAB classification after the group of French, American and British haematologists who designed the system. The FAB classification system for AML recognises eight subtypes called M0 to M7. It is important to stress that these categories do not reflect severity of disease, for example M0 is neither better nor worse in outlook than M7.

FAB type	Name	Special Feature	% of cases
M0-M2	AML showing progressively greater maturation of leukaemic cells	Special tests may be needed to distinguish M0 from ALL	45-50
M3	Acute promyelocytic leukaemia	Treated with retinoic acid; haemorrhage risk	10
M4	Acute myelomonocytic leukaemia	May present with gum swelling	15
M5	Acute monoblastic leukaemia	As for M4	Inc. with M4
M6	Acute erythroleukaemia	Red cells affected	1-2
M7	Acute megakaryotic leukaemia	Platelet precursors affected	Rare

Specialist laboratory tests called histochemistry and immunophenotyping may be of value in some instances. There may be particular difficulty in differentiating some cases of M0, M1 and M7-type AML from acute lymphoblastic leukaemia. It is potentially difficult, but very important, to differentiate AML M0 from ALL because the treatment for these two diseases is very different. About 50-60% of children with AML have the M1, M2, M3, M6 or M7 subtypes and only about 15% of children have M4 or M5 subtypes. However, about 80% of children aged less than two years present with the M4 or M5 subtype. The treatment for all subtypes is essentially the same except for M3, this is sometimes known as acute promyelocytic leukaemia (APL) and effective treatment of this type requires the use of a drug called all trans retinoic acid (ATRA) alongside standard chemotherapy.

Detailed examination of chromosomes from leukaemic cells shows distinctive abnormalities in about 75% of cases. The study of these changes is termed cytogenetics and is of value in classifying AML into relative risk groups. The commonest type of change is called a translocation and involves exchange of genetic material between two chromosomes. The implications of such changes are discussed in the section on treatment planning.



# What causes acute myeloid leukaemia?

**The cause(s) of AML is unknown in most instances. One clearly identified risk factor is exposure to very high radiation levels such as experienced after the atom bomb explosions in Japan in 1945. Very few, if any, children in the Western world are exposed to levels of radiation high enough to increase the risk of leukaemia.**

Certain chemical exposures have been clearly shown to increase the risk of AML. In particular, patients who have received chemotherapy for other forms of cancer show a raised incidence of acute myeloid leukaemia (AML). This is often referred to as therapy-related AML, occurring between one and ten years after exposure depending on the drug responsible. It shows certain distinctive features and may be less responsive to standard forms of treatment compared to primary or newly developed (de novo) AML which can arise without any obvious cause. It is thought that this is only relevant to a very few cases of childhood AML.

Benzene levels in exhaust fumes are far below the level known to cause leukaemia but the concentration of this chemical in cigarette smoke is thought to be a significant cause of adult AML. There is no clear evidence implicating benzene as a cause of childhood (paediatric) AML.

A higher incidence of leukaemia in patients with Down's syndrome compared to the general population is observed. AML associated with Down's syndrome is frequently of the FAB M7 type. Although there have been reports of familial AML it is important to stress that the overwhelming majority of cases of childhood AML occur in families with no other affected member.

# What are the signs and symptoms of acute myeloid leukaemia?

## The signs and symptoms seen most often in acute myeloid leukaemia are:

- Anaemia (lack of haemoglobin), causing:
  - ✦ Fatigue and limited capacity for exercise
  - ✦ Breathlessness on exertion
- Low platelet counts, causing:
  - ✦ Bruising within the skin
  - ✦ Bleeding from mucous membranes (e.g. gums) and from wounds and the gut
- Low (normal) white cell counts, high numbers of abnormal cells and high metabolic rate, causing:
  - ✦ Persistent infections
  - ✦ Fever — this is often present even in the absence of clear indications of infection

When first seen by a doctor almost all children with AML will have at least one of these characteristic features and about half of all patients will show all the features — anaemia, bruising/bleeding and persistent infections.

Less frequently symptoms may relate to tissue infiltration. Examples include bone pain, enlarged lymph nodes (glands), enlarged liver or spleen, involvement of the central nervous system and chloromas (masses of leukaemic cells, often within the skin). Certain presenting features are associated with specific FAB subtypes. FAB M3 can sometimes be associated with severe bleeding. Children with FAB M4/M5 subtypes may have swelling of the gums and are particularly likely to have enlargement of the liver, spleen or lymph nodes. They are also more likely to have involvement of the central nervous system and a condition called leukostasis in which blood flow is slowed and even locally blocked by large numbers of leukaemic white blood cells.

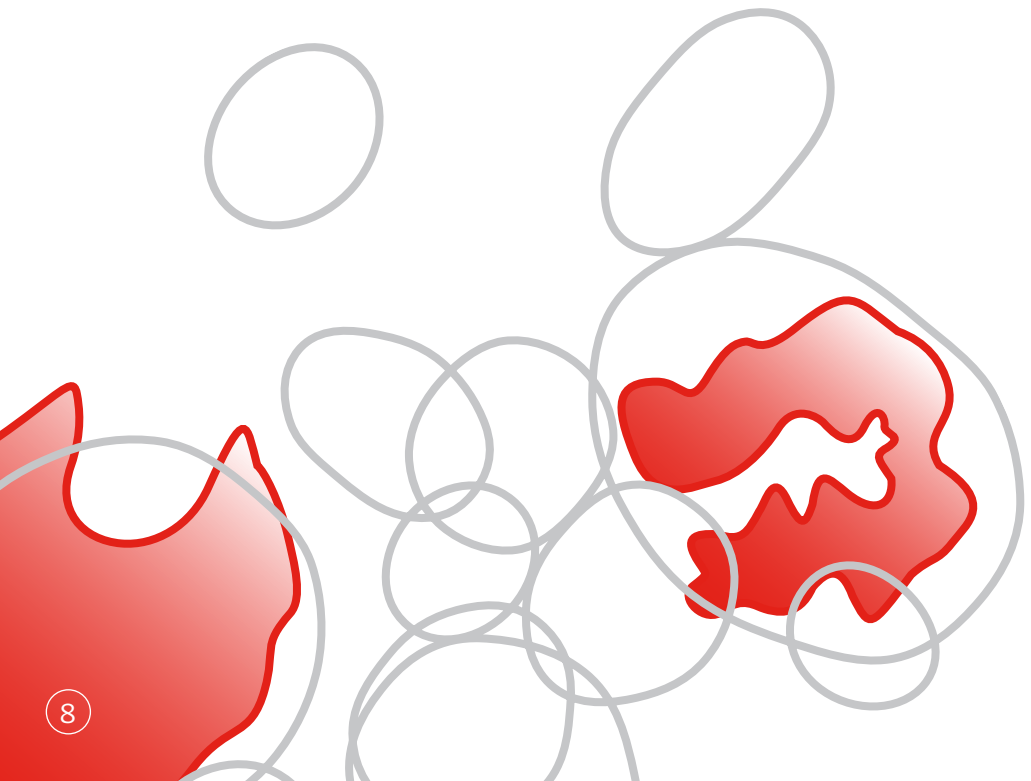
## How is acute myeloid leukaemia diagnosed?

**When a doctor examines a patient with AML there are no specific signs like the rashes seen in some infections. Where gum swelling or chloroma is present this may be strongly suggestive of AML. The median time from a child's first signs or symptoms to diagnosis of AML is six weeks. Leukaemia is not a clinical diagnosis – it requires the results of laboratory tests to confirm the diagnosis.**

The main laboratory tests used in the diagnosis of leukaemia are the full blood count and bone marrow aspirate (a procedure where a small sample of bone marrow is taken). Most children with AML will have a raised white cell count, although this does vary and possibly one fifth will have apparently normal numbers of white blood cells. Even in those cases where the total number of white cells is not raised characteristic abnormal cells called blast cells can almost always be found in the bloodstream. Many patients also have low haemoglobin and red cell counts (anaemia) and/or low platelet counts because the leukaemia cells both crowd-out and actively inhibit the production of normal blood cells in the bone marrow. The red cell and platelet counts can vary from normal to very low levels.

Chromosome analysis is of importance in planning treatment of childhood AML. The analysis is done on bone marrow samples. Patients with AML may require X-rays and other imaging procedures (CAT scan, MRI scan) to determine which organs are affected and to what extent. Lumbar puncture (sampling of the fluid around the spine and brain) is likely to be done especially if symptoms suggest that the central nervous system may be affected. Certain types of AML are associated with significant abnormalities of the blood clotting system so tests for this are routinely included.

Various other tests are performed to assess general health, for example heart, liver and kidney function. These are important to ensure that patients are not particularly prone to side-effects from the planned treatment.



# How is acute myeloid leukaemia treated?

**Without effective treatment, AML can rapidly cause death. The aims of treatment are to achieve a disease-free state called remission and, by further treatment, eradicate the disease and achieve a cure. With modern treatment protocols, including aggressive treatment for children with relatively resistant disease, the cure rate has improved significantly but is still unfortunately well below that achieved in childhood ALL.**

Treatment normally commences within a few days following diagnosis. Although there is a degree of urgency, it is considered better to wait until all the necessary information is available because this allows doctors to offer the appropriate treatment to each individual patient. Virtually all children diagnosed with leukaemia in the UK are treated at specialist paediatric referral centres.

Parents of children with AML may well be asked to consider taking part in a clinical trial.<sup>2</sup>

## Principles of treatment

Treatment of AML is based around a series of short intensive blocks of treatment given over a total period of about four to six months. Although there are gaps of a week or two between blocks of therapy children may have little or no time at home, because they will usually need supportive care between courses, but this will vary. The necessary level of supportive care can only be provided in hospital. It will include barrier-nursing to protect against infection and intensive treatment with intra-venous antibiotics or antifungal drugs if infection occurs. Children will usually require red blood cell transfusions and often in addition require platelet transfusions. The child will usually have a catheter inserted into a blood vessel to allow drugs to be given

<sup>2</sup> There is a separate publication on clinical trials available from Leukaemia Research.

without repeated needle-pricks. There are various types of catheters used and medical or nursing staff will inform parents of the special requirements for care of their child's central venous line. In some instances a child may find it difficult to eat or drink because of the side-effects of chemotherapy. In this case it may be necessary for nutrition to be given by tube or even, in a small number of cases, intravenously.

There are two phases in the treatment of AML, namely remission induction and post-remission treatment, also called consolidation. Unlike childhood ALL, extended maintenance therapy is not given. Remission induction is achieved by using combinations of drugs in high doses given over a few days at intervals of a week or two. This is repeated after a week or two using a different combination of drugs. About four to six such cycles are given over about four to six months. It is normally possible to start this stage of treatment even before all necessary tests have been completed to plan further treatment.

## **Central nervous system directed therapy**

A potential problem in the treatment of AML is central nervous system (CNS) relapse. The cerebro-spinal fluid (CSF), which surrounds the brain and spinal cord, contains a small number of white cells in healthy people. Unfortunately, although leukaemic cells can enter the CSF, administration of drugs by mouth or by injection into a vein does not lead to sufficient accumulation of these drugs in the fluid unless very high doses are applied. There is therefore a risk that leukaemia cells may survive in this site. For this reason it is normal to give central nervous system directed therapy. CNS directed therapy in AML is very much more limited than in ALL and CNS leukaemia appears to be a particular risk for AML M4 and M5 subtypes. It is normal to give only one or two intra-spinal drug treatments for children with AML, using methotrexate, cytarabine and steroids. These drugs are normally given intravenously at the same time. If there are blast (leukaemia) cells in the CSF at the time of diagnosis then more intensive CNS directed therapy may be given. This may include radiotherapy, which is otherwise avoided.

## Treatment planning

A high proportion of children (that is up to 75-85%) with AML will achieve remission (clearance of leukaemia cells from blood and bone marrow). In order to achieve this and a good long-term survival it has been found that remission induction must involve very aggressive drug treatment. Results are continually being improved, especially with better control of infection, and about 95% of children can be expected to survive the remission induction phase using current treatment protocols.

With the exception of children with the FAB M3 subtype, all children with AML receive very similar treatment. Children with FAB M3 (APL) receive a drug called all trans retinoic acid (ATRA) as part of the remission induction phase of their treatment.

It has been difficult to establish which factors of the disease affect the likelihood of a good long-term outcome. Certain specific chromosome abnormalities are associated with better than average chances of obtaining complete remission and long-term disease free survival. Other chromosome changes are found to be linked with either failure to achieve remission or with poorer survival. It is increasingly being recognised that response to treatment within the first one or two weeks is an important predictor of long-term outcome.

Certain translocations are typically seen in specific FAB subtypes and are associated with relatively good responses to treatment. Such translocations are called good-risk cytogenetics. These include FAB M2 with t(8;21), FAB M3 with t(15;17) and a change called an inversion seen in some cases of FAB M4 in which part of chromosome 16 has flipped end-to-end. Children in the good-risk group have a 70% chance of long-term survival with standard chemotherapy alone. Children without these changes, but who respond promptly to initial

treatment, are classed as having standard-risk disease while all other children are considered to have poor-risk disease. About 20% of children with AML are classed as good-risk patients, about 70% are classified as standard-risk and the remaining 10% as having poor-risk disease. In the latter two groups the chances of long-term survival are significantly lower than in good-risk patients with chemotherapy alone.

When a sibling donor is available it is commonly recommended that children in the poor-risk group should receive a stem cell transplant in first remission. Stem cell transplants are not commonly performed in first complete remission for children with standard-risk disease. These children are assessed on a case-by-case basis.

There are limited data available on the value of stem cell transplants from unrelated or mis-matched related donors for children with AML. At present such transplants tend to be given only to children who have relapsed and who therefore have a poor chance of long-term survival with conventional chemotherapy. Further information on this aspect of treatment is given overleaf.

## Remission induction phase

This involves the use of several drugs in combination to clear all detectable leukaemia cells from the blood and bone marrow. In children it has been found that the speed of response at this stage of treatment (time to achieve complete remission) is a strong predictor of final outcome. Children who achieve complete remission after one course of treatment are regarded as having standard-risk disease, whereas children who take longer are considered

to have poor-risk AML. Remission induction normally employs cytarabine plus an anthracycline (daunorubicin, adriamycin, buridazone or idarubicin). These combinations can be expected to achieve remission in most children. It is common practice to also give one or more additional drugs such as etoposide or thioguanine in the expectation that this will further increase the number of children who will achieve complete remission. The intensity of treatment needed to achieve this normally causes severe bone marrow suppression. During this period there are significant risks of haemorrhage or infection and expert supportive care is essential. CNS-directed therapy during this phase includes one or two injections of chemotherapy directly into the fluid around the spine. This is called an intrathecal injection.

A drug called allopurinol is given to prevent children developing kidney damage as a result of the amount of uric acid released when tumour cells are killed. Allopurinol treatment is normally started as soon as a child is diagnosed and before any specific anti-leukaemia treatment. An alternative drug sometimes use for this purpose is called Rasburicase.

The major short-term side-effects during this period are related to bone marrow suppression. Low neutrophil and platelet counts increase the risk of infection and bleeding respectively. Platelet transfusions can be given to reduce the risk of haemorrhage. Infection must be guarded against by good sterile precautions and prompt treatment must be given if infection occurs. There is some evidence that the use of growth factors to stimulate neutrophil production may reduce the duration and severity of infection risk but does not improve overall survival. Occasionally, the destruction of cells is so rapid that a condition called tumour-lysis occurs which affects the kidneys. This may require temporary use of an artificial kidney. Hair loss is almost inevitable but is temporary.

The long-term side-effects of this phase of treatment are largely dependent on the administered drugs and will be discussed with parents by the specialist. Because of the risks of infection and haemorrhage children are likely to spend all or part of this stage of treatment as in-patients.

## Consolidation

This phase of treatment may be referred to as post-induction or post-remission therapy or as intensification. Disappearance of leukaemia cells from the blood and bone marrow, examined by microscope, does not mean that all the leukaemia cells in the body have been killed. In order to optimise the outcome of treatment it has been found necessary to give further blocks of treatment soon after completion of remission induction. Consolidation refers to further blocks of treatment with the same drugs as used in remission induction at the same, or possibly lower, dosage. Intensification therapy either uses additional drugs or higher doses of the same drugs as were used in the first treatment phase. Some regimens include both. The clearest evidence of benefit from intensification is for the use of high-dose cytarabine. A special case of intensification is the use of stem cell transplantation. This is discussed in detail below. A high proportion of clinical trials in childhood AML are directed at establishing the optimum consolidation regimen to apply, and to determine exactly which children should be considered for a stem cell transplant.

## Stem cell transplantation<sup>3</sup>

A high proportion of children with AML will have no added survival benefit from a stem cell transplant. Stem cell transplants are not recommended in first remission for children with good-risk disease. For children with standard-risk disease the decision is made essentially on a child-by-child basis. Children with high-risk disease may be considered for a donor stem cell transplant whilst in first remission. Other than this the place of stem cell transplantation is primarily in the treatment of children who have experienced a relapse.

<sup>3</sup> There is a separate publication on bone marrow and stem cell transplantation available from Leukaemia Research.

Stem cell transplantation (SCT) is the term now used in place of bone marrow transplantation (BMT). A bone marrow transplant is one form of SCT but for many patients the source of stem cells is now the circulating blood. An SCT may be either allogeneic (from a donor) or autologous (the patient's own stem cells). A stem cell transplant involves the use of very high-dose chemotherapy (and possibly whole body radiotherapy) to destroy the child's bone marrow and immune system. This is termed myeloablation. The destroyed marrow must then be replaced with stem cells from a donor or, less frequently in childhood AML, the child's own stem cells. The major hazard of this procedure is infection during the period when blood cell production is essentially absent. Improved supportive care, especially nursing, during this period has reduced the infection risk and decreased transplant-related mortality from 20% to 10% over the last 15 years.

Stem cell transplants from a donor, other than an identical twin, contain functioning cells from the donor's immune system. These may recognise the recipient's cells as foreign and will attack them. Certain tissues within the body seem more likely to provoke such an attack than others. An immune attack by donor cells on the host's body is called graft versus host disease (GvHD). There is a beneficial aspect to the immune response caused by the donor's cells — a similar process tends to destroy leukaemic cells very effectively. This is known as the graft versus leukaemia effect (GvL). Many clinical trials are seeking to achieve the maximum GvL-effect with the minimum of GvHD. Graft versus host disease and recurrence of the original disease (relapse) are hazards of stem cell transplantation. Unfortunately measures to reduce the risk of GvHD, such as the use of a drug called cyclosporin, appear to increase the risk of relapse.



Allogeneic transplants carry a higher chance of eliminating the leukaemia but they also carry a higher risk of graft rejection and of GvHD. The preferred donor, where available, is a sibling with a closely matched tissue type. If not available an unrelated donor from a volunteer panel may be considered. The risks of rejection and of graft versus host disease are both greater with an unrelated donor. In acute leukaemia, for many children it will not be possible to find a matched unrelated donor in time from the various panels of volunteer donors. This is a particular problem for children from ethnic minorities as tissue types differ in their frequencies between ethnic populations and because most volunteer donors are Caucasians.

Autologous transplants are safer in terms of graft failure or graft versus host disease but there is a greater risk of return of the original leukaemia. It is a little surprising that graft versus host disease, or a very similar clinical picture, can occur in the context of an autologous transplant but this does happen, although at a lower rate than for donor transplants.

## **Treatment of acute promyelocytic leukaemia<sup>4</sup>**

APL is rare in childhood, possibly about 1% of cases of leukaemia. In APL there is a characteristic chromosome abnormality and the cell does not respond normally to a substance called retinoic acid. It has been shown that high doses of all trans-retinoic acid, called ATRA, can cause APL cells to mature and then to die off by a process called apoptosis. Clinical trials of ATRA alongside conventional induction therapy in childhood APL have led to improved survival compared to standard chemotherapy or ATRA alone. Patients with APL who do not respond to retinoic acid (refractory disease), or who relapse, may show a good response to a drug called arsenic trioxide.

<sup>4</sup> There is a separate publication on acute promyelocytic leukaemia available from Leukaemia Research.

## Treatment of relapse

Although a high proportion of children with AML will achieve a remission a significant proportion (20-25%) will eventually relapse. This is to say their disease will return. Relapse is most likely in children in the poor-risk group, with a lower incidence in the standard-risk group. Around 70% of children with AML have standard-risk disease which means that most relapses will occur in this group of patients. Relapsed AML tends to be more resistant to treatment than the original disease. One reason for this may be that the leukaemia cells have become resistant to drug treatment. This drug resistance is often not specific to a particular drug, it may affect all or virtually all, anti-leukaemia drugs. This is known as multi drug resistance (MDR). A number of drugs are being studied which may be capable of preventing or reversing MDR. The timing of relapse is significant. Children who relapse a long time after treatment has finished have a better chance of responding to re-treatment and tend to have a higher incidence and duration of second remissions. During this period they will be considered for a transplant if they have not already received one. In children who have received a donor transplant it may be possible to use immune cells from the original donor to treat a relapse. This is known as donor lymphocyte infusion (DLI).

Unfortunately, for children with AML who experience a relapse the chances of long-term survival are poor at present. Patients with good-risk disease who have not had a transplant but who have a matched sibling donor available probably have the best chance of success. If it is not feasible to give further aggressive therapy it may be possible to achieve reasonable control of the disease for a short period with low-dose chemotherapy given on an outpatient basis.

Although the chance of relapse becomes progressively less with time, particularly once all treatment has been completed, late relapses do occur and typically appear to result, not from development of drug resistance, but because not all leukaemia cells have been eradicated by the initial therapy.

## Long-term effects of treatment

Long-term survival of children with AML has improved dramatically although the overall outlook is not as good as that for the more common form of leukaemia in childhood (ALL). Unfortunately, there are long-term adverse effects from certain aspects of treatment. Although efforts continue to improve survival still further, a major secondary aim of current clinical trials is to reduce the incidence and severity of adverse effects of treatments.

Radiotherapy is rarely used in AML except for a small number of cases of children with blast cells in their cerebro-spinal fluid (CSF) or as part of preparation for a stem cell transplant.<sup>5</sup>

Long-term effects related to chemotherapy clearly depend on the drugs used, the intensity of treatment and, in the case of some drugs, on the total amount of the drug received. It is more difficult to establish which drugs are responsible for which long-term effects in situations like childhood AML where combinations of drugs are administered in high doses over several blocks of treatment. There are known long-term adverse effects of certain drugs. A detailed discussion of these is not possible as they depend on interactions between drugs and may even vary between individuals. Some specific examples of concerns include the potential effects of anthracycline drugs on the heart and the risk of deafness in children treated intensively with certain antibiotics. Detailed advice will be available from the specialist before a child starts treatment.

<sup>5</sup> There is a separate publication on bone marrow and stem cell transplantation available from Leukaemia Research.

A common concern of parents and older children is the effect on fertility. Alkylating agents, nitrosureas and cyclophosphamide may all adversely affect the reproductive system. Cyclophosphamide and cytarabine, in particular, may affect sperm production in males causing sterility but without serious effects on sexual maturation. It is very important that those treated as children should be aware that fertility may return after very long periods of no sperm production. For this reason it would be unwise for a sexually active male who has been sterile as a consequence of chemotherapy, to assume that this will always continue to be the case. In females, chemotherapy without radiotherapy is less likely to lead to sterility. There are certain long-term consequences seen only in children who have received stem cell transplants that are discussed in detail in the booklet on stem cell transplantation. An important consideration for both males and females is whether there is a risk of adverse effects on offspring from treatment received during childhood. A number of large studies in Britain and abroad have confirmed that there is no increased risk of cancer or of an abnormality in children whose parents received treatment for cancer during childhood.

Secondary cancers are a well established, although thankfully uncommon, consequence of drug and radiation therapy for childhood leukaemia. The overall incidence of this is probably less than 2-3% at 20 years. Modern treatment regimens, that drastically minimise the use of drugs and radiotherapy known to cause secondary tumours, mean that the incidence will probably be significantly lower for children being currently treated. Although there are significant long-term adverse effects of treatment for childhood leukaemia, a major study recently concluded that most children achieve their life goals.

## Follow-up

The main purposes of follow-up for children treated for AML are detection of relapse and treatment complications. During the first year following completion of chemotherapy children are normally checked every two to three months. Checks will then gradually become less frequent until they are given annually at five years and beyond. Long-term follow-up is particularly important for those children who have received treatment that may affect reproductive maturation. For this group of children hormone therapy may be necessary at an appropriate age to ensure that they achieve puberty. Neglect of such therapy may cause severe psychosocial distress to the child and peer group rejection. It can be expected that all paediatric specialist referral centres will have a programme in place to ensure such follow-up.



## Prognosis

**As discussed in the treatment sections, most children can expect to achieve a good first remission. The major prognostic factor for long-term survival is the risk group – good-risk, standard-risk or poor-risk. Children in the good-risk group have about a 70% chance of long-term survival when treated with chemotherapy alone. For children in this group who relapse, a stem cell transplant in second remission may be feasible. For children in the poor-risk group the availability of a matched sibling donor may be of significance to the prognosis. Children who have a donor available and who receive a transplant have about a 50% chance of long-term survival. In the standard-risk group, stem cell transplants in first complete remission are used infrequently and decisions are made on a case-by-case basis. The decision on what treatment is preferred will be discussed with parents. Where children have relapsed the prognosis is poor with the possible exception of those children who have not previously been transplanted and have a matched sibling donor. Clinical trials currently have three main aims; to reduce the proportion of children who relapse, to improve the management of relapsed disease and to minimise the impact of side-effects of treatment on those who are successfully treated for childhood AML.**

It is important to remember that statistics for survival are based on how a group of patients may respond to treatment. For individual patients survival is all or nothing. The data are valuable in guiding treatment choices and in giving patients or relatives some indications of the likely progression of the condition. Parents should guard against becoming dispirited (or unduly complacent) based solely on their child's risk group.

## Summary

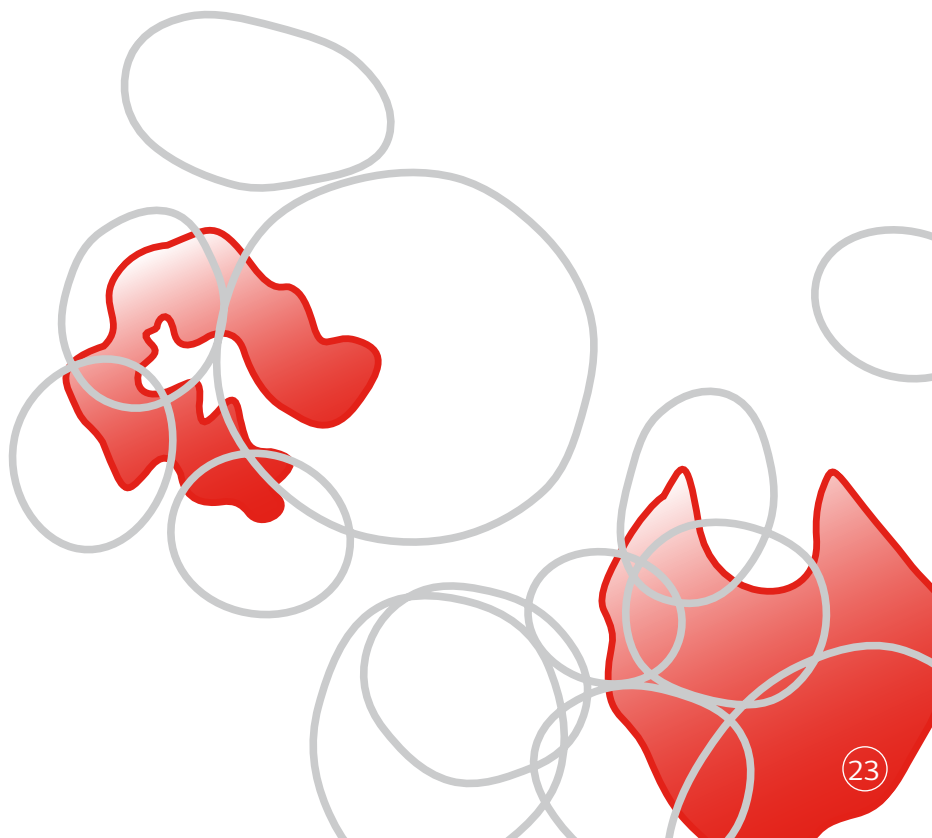
**Childhood acute myeloid leukaemia is a form of cancer that affects blood producing cells in the bone marrow. Although childhood AML is a very serious disease that is almost uniformly fatal if not treated it is potentially curable with intensive chemotherapy, with or without stem cell transplantation. Patients in the good-risk group have about a 70% chance of being long-term survivors with chemotherapy alone. For those who relapse a stem cell transplant may be an option.**

Treatment is based on the use of drugs in various combinations. The treatment of childhood AML is based around a series of short blocks of treatment given over about four to six months, most or all of which is spent as an in-patient. A special case is acute promyelocytic leukaemia in which a drug called retinoic acid is used in remission induction.

Children in the poor-risk group may have an improved chance of survival if they have a matched sibling who can act as a donor for a stem cell transplant. Treatment decisions for standard-risk children are made on a case-by-case basis but do not usually include a stem cell transplant in first complete remission. The outlook for patients whose disease has relapsed tends to be poor.

Stem cell transplantation is not appropriate for all children with AML. It is often recommended in first remission for selected patients in either the standard- or poor-risk groups but not for patients in the good-risk group. Good-risk patients have a high chance of a good response to re-treatment after relapse so the risks of stem cell transplantation in first remission are not justified.

The prognosis for childhood AML varies and is dependent in part on characteristics of the patient and in part on the features of their disease. Parents should seek individual advice on prognosis from their child's specialist. There has been a marked improvement in outcome for children with AML. Comparative studies are seeking to build on that improvement.



# Coping with childhood leukaemia

This section offers advice to try to help you as a family cope with the stresses and problems of having a child with leukaemia.

**Not all of the difficulties discussed will necessarily apply to you but they may be important factors for other members of your family or other similar families.**

This information has been divided into four sections. We would like to suggest that you read the first two sections within a few days of hearing the diagnosis, as they will help you through the first weeks. The remaining two are more concerned with the future and are best left a little while. They deal with practical problems and the help that is available and how to set about getting this help.

They also discuss possible long term difficulties and how to handle them.

## The diagnosis and the first few days

**You have recently suffered a very severe shock because you have learned that your child has leukaemia. You may have suspected this diagnosis but naturally hoped that you were wrong. Now that you know the truth you are besieged by many bewildering thoughts and feelings. It is important for you to know that this is natural and that you are not unusual in having these thoughts.**

The doctor in charge of your child's treatment will by now have talked to you and tried to explain to you what leukaemia is and how it is likely to affect your child. You will probably have taken in very little of what was said and will have forgotten a great deal. Do not worry about this. The doctor understands this and will be prepared to explain everything again. If he/she does not suggest this then do not be afraid to ask for the opportunity of another talk. It is often a good idea to write down the questions which keep coming to your mind – you can then go through them with the doctor, otherwise you might forget them.

It is hard at first not to be very depressed or angry about the news but you must remember that so much can be done today for children with leukaemia and you must have hope. Children have as good as an 70% chance of treatment being successful and these children will go on to lead completely normal lives. It is never possible for your doctor to be absolutely certain about the outlook for your child but what you are told will be a fair assessment and, even if there is some uncertainty, the doctor is being honest. No-one knows at the time of diagnosis which children will survive. The doctor can only talk of risks and chances.

The doctor will explain to you what the treatment for your child is likely to entail. While it will sound very complicated and frightening to you, remember that the doctors and nurses are carrying out these treatments every day and for them it is as much a routine as it is, for example, a policeman to direct traffic, a mechanic to find and mend a fault in a car engine or a lawyer to draw up complicated legal documents. The people treating your child are experts in their field. While this should give you confidence it may also make you feel inadequate.

Remember that you are very important to your child and by remaining calm and giving encouragement you can help him/her with the numerous tests and investigations which have to be done.

The doctors and nurses are aware of your feelings and they will want you to help nurse your child and assist in other ways. If you feel able to stay with your child while tests are being done then that should be possible, but if you find it upsetting then it is probably better for you to wait close by. If you are yourself agitated and upset you will convey this to your child and make the situation more frightening. You must not feel ashamed of these feelings; most people not used to hospitals are on edge when they first go to one and you are naturally even more anxious because of your child's serious illness. You are probably much better waiting so that you can comfort your child and play with him/her after the procedure is over.

These days most children's centres treating leukaemia give the patients an anaesthetic to do the more painful tests. In this case you will probably be allowed to stay with your child until he/she is asleep and will be able to sit at the bedside waiting for him/her to wake.

## Visiting and living in hospital with your child

**Children's hospitals always have free visiting for parents and this should also be the case in all children's units of district general hospitals. This means that parents can come at any time and stay until the evening. Obviously the nurses have to settle the young in their beds and cots in the early evening, but they will encourage you to see your child settled and it is best to follow your usual routine. Lots of other visitors are not welcomed because the children get tired quickly and are easily overwhelmed. They are also prone to have too many infections and it is not a good thing to have too many people around the bed. The ward sister will however usually allow brothers and sisters to visit at weekends and this is important so that the family can get together.**

Most children's hospitals have facilities to allow you to live in with your child. Many of you will wish to do this but it is important to give it some thought especially if you have other children at home.

The nature of your child's illness means that repeated hospital visits and further admissions are likely in the future and the rest of the family may feel rather neglected. Parents have a great need to talk with each other about this shock which has struck the family and to discuss their feelings, reactions and worries. You both need comfort and support and it is easier to give this to each other if you have time alone together. This is very difficult if mother is living in at the hospital and father trying to keep the rest of the family together. Some parents find that the most sensible solution is to spend as much time as possible with your child in the day and go home in the evenings. The circumstances are different from those of a short-lived acute illness where the child soon recovers and the usual family routine can be quickly restored.

The family can cope for a few days in these cases but with a disease like leukaemia the ongoing treatment, although mostly on an outpatient basis, will last for months and it is important from the onset to work out a method for your family so that no one feels neglected or put upon.

No-one will think the less of you for spending some time away from your child. We all need some time to ourselves especially at periods like this when we need to 'refuel'. The staff all realise how stressful it is to be on a busy ward for long hours with little to do yourself.



## Coping with the problems of treatment

**In the majority of cases the child with leukaemia responds quickly to treatment and returns to an active normal life. The period of time in hospital will vary according to the type of leukaemia and treatment programme, but most children have a first stay in hospital for about three to six weeks. Your doctor will be able to give you some advice as to how long the child is likely to remain in hospital.**

On your return home and despite the resumption of normal health and activity there will be constant reminders to you of your child's illness, for example loss of hair, variable appetite, moodiness and sometimes a more dependent attitude. The majority of these symptoms are due to the effects of the drugs which your child has to take and it is important not to pay too much attention to them.

On returning home it is essential that you try to return to the normal day-to-day life of your family and also maintain your usual routine. You will of course have to make regular visits to hospital, but these will usually occur on average every two to three weeks, and the doctors will not expect serious complications or deterioration to occur in a sudden way. You will be warned of the symptoms to look out for which should alert you to contact the doctor. Do not hesitate to discuss problems with the doctor who can advise you how to handle them.

Some children who have received a lot of attention while in hospital continue to be demanding while at home. This must be discouraged as it is detrimental to normal family relationships – brothers and sisters will feel neglected and then they will also play up to gain attention. Your child with leukaemia will be happier and better able to deal with the disease if you accept it as something which you all have to try to overcome. While it cannot be ignored, it should not become the centre of all attention and conversation. Everyone in the family must remain important, with their special needs and requirements.

Your doctor will tell you when your child is fit to return to school, nursery or playgroup. This may be up to six months after diagnosis but it depends on the treatment schedule. If the child has to be readmitted for further drug treatment or for radiotherapy then return to school may be delayed. Return to normal activities should be a goal to look forward to as should family holidays.

In the early days following diagnosis a patient will probably have had time off work. This should not be prolonged unless your child's life is in immediate danger, which is very rarely the case, and if it is the doctor will have told you. Cutting yourselves off as a family from workmates, friends and other contacts leads to isolation and this makes coping more difficult.



## The people who can help you

**There are several groups of people whose job it is to provide help and support to families in your circumstances. In addition there may be relatives and friends who would like to help in practical ways as well as sitting talking with you about your child's illness. Within the hospital, as well as doctors treating your child, the sisters and staff nurses on the ward and in the clinic will have had a lot of experience of the way you are feeling and the kind of difficulties you may have. Most of the large children's units have nurses, social workers and health visitors specially appointed to provide assistance. It is wrong to think that these people are only there to help 'problem families', people with financial difficulties or people who cannot cope on their own. There may be a simple solution to the problem which is worrying you and even if there isn't discussing it will always help. Many Regional Centres also now have parent self-help groups. You may find it very valuable to meet other parents who have 'been through it all' themselves, so that you can share your experiences. Your local group's organiser will help to put you in touch with appropriate other parents.**

Your general practitioner will be happy to listen to your personal fears and anxieties — your feelings of guilt and anger. Your neighbours and friends will be pleased to look after other children, do some shopping and maybe drive you to the hospital. Grandparents often feel lost and do not know what attitude to adopt. Family discussions can be helpful so that they too understand what is to be expected. In their young days leukaemia was almost invariably a fatal disease and they may need the reassurance of a talk with the doctor before they can believe that your more optimistic attitude is realistic.

This booklet has tried to cover many aspects. It is not intended to imply that every family will experience all the difficulties mentioned. We all have different circumstances and our response to anxiety, stress and illness is a very individual thing. It is hoped that you will be helped by those comments which seem to apply to you and if there are other problems not dealt with then mention them to the doctor or social worker. They will also be interested to hear from you about your own method of coping and how you have been helped.



## Typical normal values for blood test results

	WBC x 10 <sup>9</sup> /l	RBC x 10 <sup>12</sup> /l	Hb g/dl	ANC x 10 <sup>9</sup> /l	Platelets x 10 <sup>9</sup> /l
<b>Adult male</b>	3.7 to 9.5	4.3 to 5.7	13.3 to 16.7	1.7 to 6.1	143 to 332
<b>Adult female</b>	3.9 to 11.1	3.9 to 5.0	11.8 to 14.8	1.7 to 6.1	143 to 332
<b>West Indian</b>	2.8 to 9.8			1.0 to 6.5	122 to 374
<b>African</b>	2.8 to 7.8			0.9 to 4.2	115 to 342
<b>Child 2-5 yrs</b>	5 to 13	4.2 to 5.0	11 to 14	1.5 to 8.5	143 to 332
<b>Child 6-9 yrs</b>	4 to 10	4.3 to 5.1	11 to 14	1.5 to 6.0	143 to 332
<b>Child 9-12 yrs</b>	4 to 10	4.3 to 5.1	11.5 to 15.5	1.5 to 6.0	143 to 332

Normal ranges vary slightly between laboratories so you may wish to ask your doctor to enter your normal values below:

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WBC	White blood cell count
RBC	Red blood cell count
Hb	Haemoglobin concentration
ANC	Absolute neutrophil count

Separate ranges are quoted for West Indian and African populations as these groups have different normal ranges for white cell counts, absolute neutrophil counts and platelet counts.

This information is adapted, with permission, from *A Beginner's Guide to Blood Cells*, Dr Barbara Bain. Pub. Blackwell, Oxford, 1996.

**The following patient information booklets are available free of charge from Leukaemia Research. You can download them from our website or request copies by phone or post (see form inside):**

Leukaemia and Related Diseases

Acute Promyelocytic Leukaemia

Adult Acute Lymphoblastic Leukaemia (ALL)

Adult Acute Myeloid Leukaemia (AML)

Aplastic Anaemia (AA)

Bone Marrow and Stem Cell Transplantation (BMT)

Childhood Acute Lymphoblastic Leukaemia (ALL)

Childhood Acute Myeloid Leukaemia (AML)

Chronic Lymphocytic Leukaemia (CLL)

Chronic Myeloid Leukaemia (CML)

Hodgkin's Lymphoma (HL)

Multiple Myeloma (MM)

Non-Hodgkin's Lymphoma (NHL)

The Myelodysplastic Syndromes (MDS)

The Myeloproliferative Disorders (MPD)

Clinical Trials

Chemotherapy – what do I need to know?

Donating stem cells – what's involved?

The Seven Steps – Blood & Bone Marrow Transplantation

Young Adults with a blood cancer – what do I need to know?

Jack's Diary: an illustrated children's book to help young patients understand and deal with blood cancers, treatment and life changes

**Leaflets on a range of associated blood disorders are also available**

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