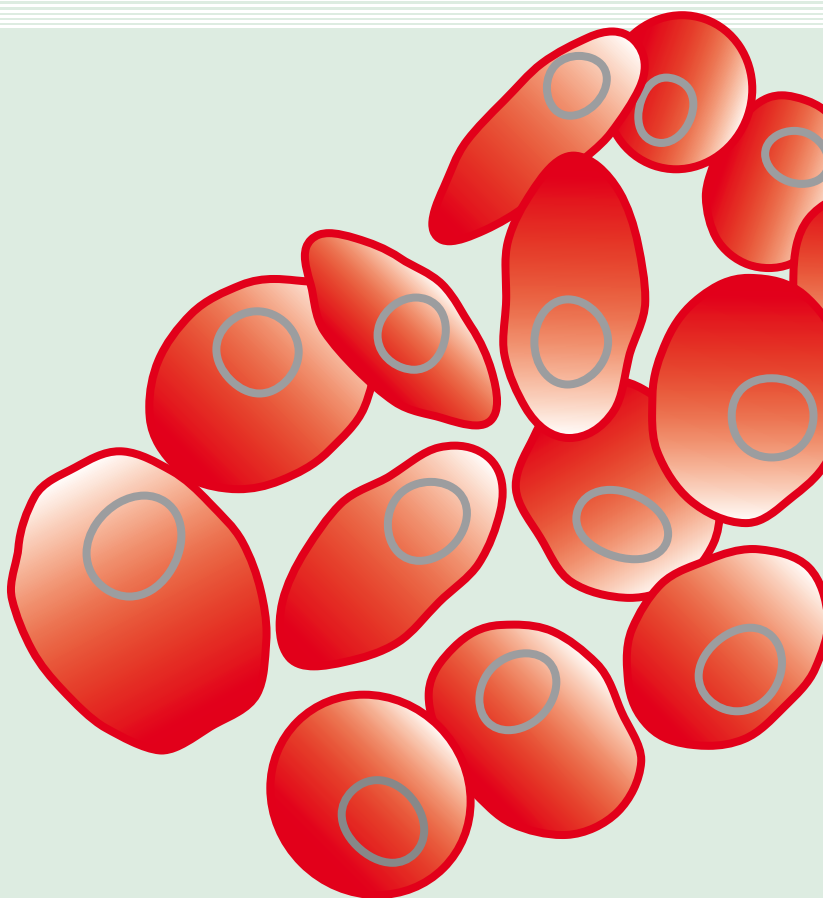


Myelodysplastic Syndromes (MDS)



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 topics 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.

Leukaemia Research, 43 Great Ormond Street, London WC1N 3JJ
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Series compiled by Ken Campbell MSc, revised 2008. A list of advisors can be found at www.lrf.org.uk/advisors

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What are the myelodysplastic syndromes?

The myelodysplastic syndromes (MDS) are a group of diseases in which the production of blood cells by the bone marrow is disrupted. In contrast to leukaemia, in which one specific type of blood cell (the white cell) is produced in excessively large numbers, the production of any, and sometimes of all, types of blood cells is affected.

The myelodysplastic syndromes were formerly referred to by many names including preleukaemia. Although a minority of patients with MDS develop acute leukaemia, most do not. When leukaemic transformation does occur, it is to acute myeloid leukaemia.¹ This form of leukaemia is typically more difficult to treat than de-novo acute myeloid leukaemia (that is cases arising in patients with no previous bone marrow disease).

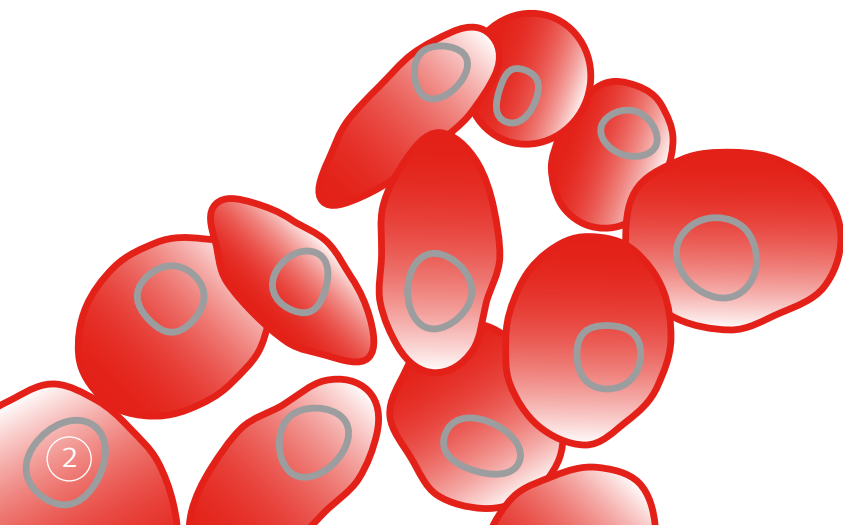
The bone marrow in myelodysplastic syndrome is typically more active than normal and yet the numbers of blood cells in the circulation are reduced. This is because most of the cells being produced in the bone marrow are defective and are destroyed before they leave the bone marrow. The hallmark of the myelodysplastic syndromes is the combination of a hyperactive marrow with low blood cell counts. A reduction in numbers of all the types of blood cell is called pancytopenia.

The other common feature of the myelodysplastic syndromes is abnormality in the appearance of the bone marrow and blood cells. These abnormalities (e.g. white cells lacking normal granules) are characteristic of the condition.

¹ There is a separate publication on adult acute myeloid leukaemia available from Leukaemia Research.

The myelodysplastic syndromes are difficult to treat because of the unusual combination of hyperactive marrow but inadequate blood cell production. The only treatment considered potentially curative is a donor stem cell transplant in younger and fitter patients. Unfortunately most patients are too old for this to be an option.

There is a degree of overlap between MDS and aplastic anaemia. It may sometimes be difficult to distinguish between aplastic anaemia and a subtype of MDS in which the marrow is underactive. This form of MDS is called hypoproliferative or hypoplastic myelodysplastic syndrome. Fortunately, discrimination between these conditions is not critical for treatment planning.

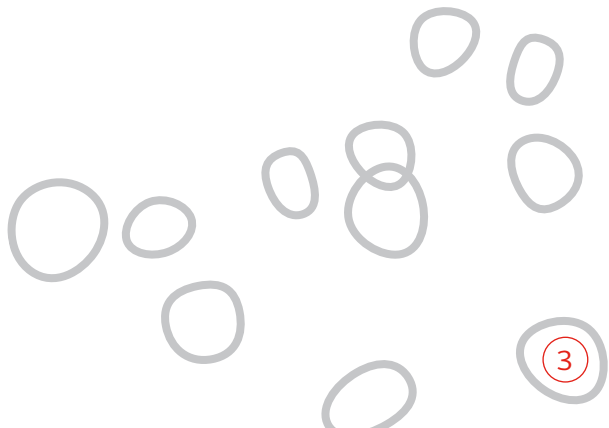


Who gets MDS?

The myelodysplastic syndromes may be diagnosed at any age but they are rare in childhood and very uncommon in young adults. It is likely that all childhood cases would be referred to a nationally recognised centre of excellence. This booklet deals with the adult disease.

The median age at diagnosis is between 65 and 75 years. Over 90% of patients are over 50 years at the time of diagnosis.

Men are more likely than women to be diagnosed with MDS. This is most marked in the typical older patient group. Cases occurring in younger patients are more evenly distributed between men and women.



What are the types of myelodysplastic syndrome?

The International Prognostic Scoring System (IPPS) has been developed to classify the different types of MDS and has some value in predicting the outcome (i.e. prognosis).

About 10% of cases arise in patients who have received either chemotherapy or radiotherapy as part of their treatment for another disease. This is known as secondary or treatment related MDS. This is more often the case with patients who develop MDS at a relatively young age.

There is a generally accepted classification system for myelodysplastic syndrome which is based on the appearance of the bone marrow and the blood findings. This system is called the FAB system in recognition of the group of French, American and British haematologists who designed the system. The World Health Organization has proposed a newer classification system but the current *UK Guidelines for Management of MDS* use the FAB classification as there is limited experience of use of the new classification. The treatment sections of this booklet are based on the UK guidelines. The accepted subtypes in the FAB system are listed below.

There are five types of myelodysplastic syndrome in the FAB system as it is currently used, these are:

- Refractory anaemia
- Refractory anaemia with ring sideroblasts
- Refractory anaemia with excess blasts
- Refractory anaemia with excess blasts in transformation
- Chronic myelomonocytic leukaemia.

Refractory anaemia (RA)

The marrow cells that produce red cells appear abnormal. The white cell and platelet producing cells may also appear abnormal but the proportion of primitive cells (blast cells) is not significantly increased. The main clinical feature is anaemia, which is usually mild to moderate but can be severe; often the red cells have a larger average size (mean cell volume or MCV) than normal, this is called macrocytosis. The numbers of white cells and/or platelets may be lower than normal.

RA accounts for about 30-45% of cases. About 10% of cases of RA will transform to acute leukaemia.

Refractory anaemia with ring sideroblasts (RARS)

The same changes are seen as in RA but there are additional abnormalities in the red cell population. The red cell precursors are unable to use iron normally and instead the iron is deposited in characteristic rings in the red cell precursors. These cells are called ring sideroblasts. If there are more than 15% ring sideroblasts in the bone marrow the disease is classified as RARS. While anaemia is again the most common clinical problem, the numbers of white cells and/or platelets may also be lower than normal. The rate of transformation to acute leukaemia is lower than for RA at about 8% of cases. This form of MDS makes up approximately 15% of cases.

Refractory anaemia with excess blasts (RAEB)

In this form there is an increase in precursor blood cells (called blasts) in the marrow. Normal bone marrow contains up to about 5% blast cells.

Patients with RAEB have between 5-20% blast cells in their bone marrow. Patients with this form are more likely to have reduced numbers of platelets and/or white cells as well as red cells in their blood. This form accounts for about 15% of cases - about 40% of patients with RAEB will go on to develop acute leukaemia.

The following subtypes are currently included in the FAB scheme but a new proposed classification of cancers of the blood and bone marrow produced by the World Health Organization (WHO) has suggested that they be moved to other categories.

Refractory anaemia with excess blasts in transformation (RAEB-t)

The findings in these patients are similar to those in RAEB but with a higher proportion of blasts (20-30%) in the marrow. This form accounts for about 5-15% of cases. It has recently been proposed that these patients should now be classified as having acute myeloid leukaemia. The rate of conversion to overt leukaemia (over 30% blasts in the marrow) is high (between 60-75%) and the treatment is similar to that used for acute myeloid leukaemia.

The median survival tends to be poorer than for other forms of refractory anaemia but chemotherapy, with or without stem cell transplantation, produces prolonged survival in some cases.

Chronic myelomonocytic leukaemia (CMML)²

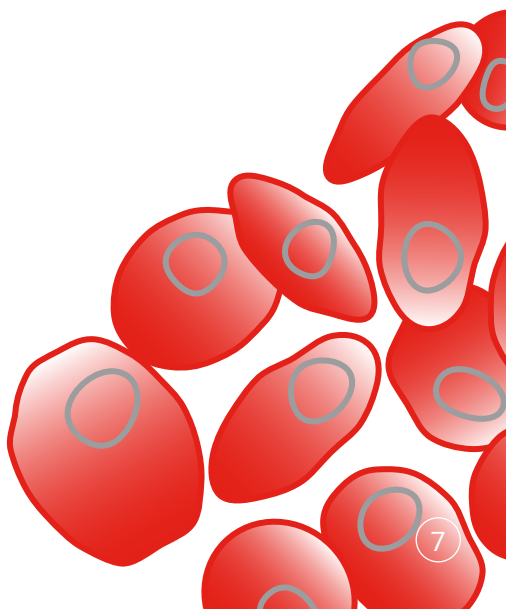
In CMML the red cell precursors usually appear abnormal. The defining feature of CMML is that the number of one type of white cells (monocytes)

²A separate publication on CMML is available from Leukaemia Research.

in the blood is increased to more than 1×10^9 /litre. The marrow may or may not contain an increased proportion of blast cells. There may be anaemia and/or low platelets.

CMML is considered to be a form of myelodysplastic syndrome because the bone marrow shows features similar to those seen in other forms of the disease, but it also shows features of the related diseases known as the myeloproliferative disorders. The new WHO classification moves CMML into a separate category called the Myelodysplastic/Myeloproliferative Disorders.

CMML accounts for approximately 15% of myelodysplastic syndromes. Transformation of CMML to acute leukaemia happens in a similar way to other forms of myelodysplastic syndrome. Median survival is of the order of 12-18 months. Between 15-30% of patients progress to acute leukaemia.



What causes MDS?

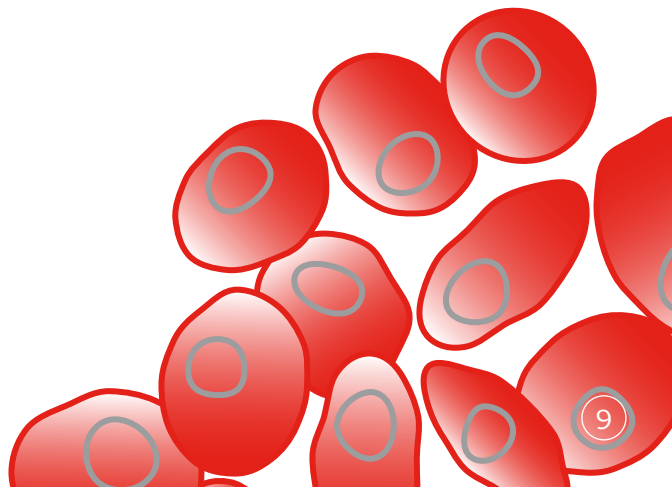
Although most patients have no obvious cause for their disease there are several possible environmental risk factors. Exposures to high levels of certain chemicals (particularly benzene) and ionising radiation are both considered potential causes of MDS. A slightly increased incidence of MDS has been reported among smokers and ex-smokers and may be associated with specific chemicals present in tobacco smoke.

The use of certain chemotherapy drugs and radiation as part of the treatment for another disease, usually a cancer, may (rarely) lead to subsequent development of MDS. This is a definite cause of MDS, unlike the environmental risk factors, which remain unproven. Both therapy-related MDS and AML have been reported most frequently after treatment for Hodgkin's lymphoma, non-Hodgkin's lymphoma, multiple myeloma, polycythaemia vera, ovarian cancer, testicular cancer and breast cancer. Therapy-related MDS usually develops three to seven years after exposure to chemotherapy. Approximately 80% of cases of AML occurring after exposure to chemotherapy drugs are preceded by MDS. More than 85% of patients who develop chemotherapy-related leukaemia or MDS have been previously treated with a class of drugs called alkylating agents.

What are the signs and symptoms of MDS?

About one-fifth of MDS patients have no signs or symptoms and are diagnosed by chance as a result of a routine blood test. Those patients who do have symptoms present with clinical features due to bone marrow failure. In about 80% of patients this is anaemia, whilst about 20% present with infections or bleeding.

Anaemia tends to lead to fatigue and shortness of breath even on light exertion. Infections can occur at any site in the body and are usually caused by bacteria or fungi. About 10% of patients will have an enlarged spleen, especially those who have CMML.



British Committee for Standards in Haematology MDS Guidelines

A group of expert haematologists, with a specialist interest in MDS, has prepared guidelines for the diagnosis and therapy of adult myelodysplastic syndromes. The content of the following section of the booklet is based on the BCSH guidelines, the full version of which can be found on the web at www.bcsguidelines.com

It is important to understand that, although guidelines represent the collected opinions of a group of experts on best clinical practice based on best available evidence, they are only guidelines. In most cases treatment will be based on these but a clinician may decide that it is not in the best interests of a specific patient to be treated exactly, or even broadly, according to the guidelines.



How are the myelodysplastic syndromes diagnosed?

Assessing the appearance of blood and bone marrow cells under the microscope is called morphological examination. The BCSH guidelines state that: ‘The diagnosis and classification of MDS remain dependent on the morphological examination of blood and bone marrow cells’.

Under the microscope affected cells show characteristic abnormalities both in the blood and in the bone marrow. This is the defining feature of the disease. In the majority of cases there will also be anaemia (reduced haemoglobin and red cell numbers). The white cell and platelet counts may also be reduced below normal numbers. When a patient is found to have cells on the blood film suggestive of MDS a full clinical history will be taken to rule out other causes and bone marrow samples will be obtained. The BCSH guidelines point out that a bone marrow sample may not be necessary in the case of patients whose care is unlikely to be affected by the result, for example an elderly patient or a very ill patient who is unfit to receive active treatment. In all other cases it is recommended that bone marrow samples are obtained to confirm diagnosis and to provide prognostic information including cytogenetics. Cytogenetics is the study of the changes in genetic structure of the chromosomes in the affected cells; information from cytogenetic studies is of value in predicting the likely outcome of disease. In the case of MDS it may also be helpful to confirm the diagnosis.

In the majority of cases the bone marrow will be more active than normal (hyperplastic) and this feature, combined with the characteristic abnormalities in appearance of the cells and the low blood cell numbers, will make the diagnosis straightforward. There is no specific test for MDS. It is, in some cases, a diagnosis by exclusion made when a patient has typical features of MDS with no obvious underlying cause. Sometimes cytogenetic results will allow a definite diagnosis.

Prognosis

For the majority of patients the choice of treatment will be based on the International Prognostic Scoring System³ (IPSS) risk category, age and general fitness of the patient. The IPSS includes information on the proportion of blast cells in the bone marrow, the number of cell types affected and cytogenetics (the chromosome changes usually seen in MDS). These have all been found to be relevant in predicting the outcome (prognosis) and in selecting the optimal treatment.

³ The IPSS system is described in detail in the Appendix.

Treatment

Principles of treatment

Not all patients will receive active treatment straight away because in most cases there is no evidence that early treatment influences overall survival duration. Patients who are not commencing treatment will have regular check-ups. This is often referred to as 'watch and wait'.⁴

The guidelines recommend that, whenever possible, treatment decisions should be based on the patient's IPSS score. It is important that this should be determined when the clinical condition is stable, not for example during an infection which may be present when the patient is first diagnosed.

The only treatment approach considered to be potentially curative is a donor stem cell transplant. Unfortunately only a small minority of patients with MDS will be candidates for this form of treatment. Patients who are candidates for a stem cell transplant are identified early so that a search for donors can be initiated and a transplant performed at an early stage. In all cases supportive care is of great importance, this includes measures to prevent and to treat infections and, in many cases, blood (and/or platelet) transfusions.

Treatment planning

The central elements of treatment planning are the age of the patient, the IPSS score and whether the patient has primary or secondary myelodysplastic syndrome.

All patients require supportive care, that is treatment aimed at controlling symptoms and preventing or treating complications, at some stage. The

⁴ A separate publication on 'watch and wait' is available from Leukaemia Research.

nature and extent of supportive care required would depend on the severity of cytopenias, that is which cell types are low in number and to what level they fall.

Treatment extending beyond supportive care can be classed as either low-intensity, high-intensity or high-intensity with stem cell transplant.

Supportive care⁵

Supportive care is directed not at the underlying disease but rather at control of the symptoms and the complications caused by the disease. Almost all patients will require red cell transfusions at some stage.

Anaemia

About 80% of patients with MDS will have a haemoglobin level below 10g/dl when they are diagnosed. This is mainly due to the inability of the marrow to produce blood cells but other factors, such as poor diet, bleeding, excess breakdown of red cells and infection may contribute. Where such additional causes are present they should be treated as appropriate. Chronic anaemia is seldom life-threatening but it does affect quality of life and requires treatment as follows:

- Transfusion (and iron chelation)
 - ✦ The use of red cell transfusions should be considered in any MDS patient with symptomatic anaemia. There is no set level at which transfusion is indicated. Each patient's needs will be assessed individually.
 - ✦ Some patients, who are expected to need many transfusions over a long period, may need treatment to prevent accumulation of excess iron in the body. This is called iron chelation. There are several possible approaches to iron chelation and the specialist will select the appropriate one, usually after discussion with the patient.

⁵A separate publication on supportive care is available from Leukaemia Research.

○ EPO and G-CSF

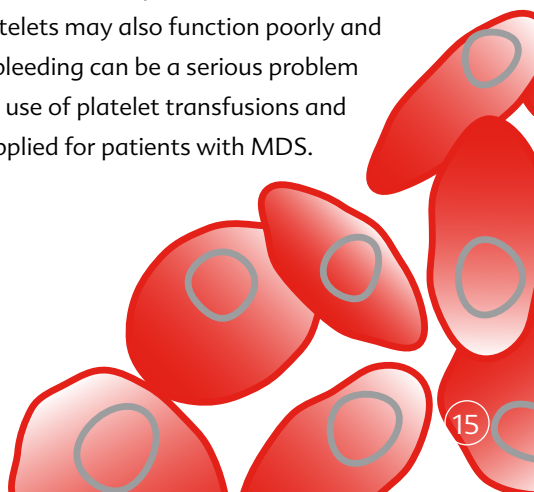
- ✦ Normal blood cell production is regulated by growth factors. Erythropoietin (EPO) specifically stimulates production of red cells whereas G-CSF stimulates production of certain types of white blood cell. There is clear evidence that selected MDS patients may benefit from treatment with EPO. Unfortunately, erythropoietin used alone appears to only benefit about 15-20% of patients with MDS. These are mainly patients with RA or RAEB who are not dependent on blood transfusions; a proportion of patients with these subtypes will benefit from addition of G-CSF. Patients with the RARS subtype are more likely to respond to the combination of EPO and G-CSF. The specialist will assess whether a patient is likely to benefit from EPO, with or without G-CSF.

○ Immunosuppression

- ✦ Use of drugs which selectively reduce the activity of the immune system may be helpful in relieving anaemia in patients with hypoplastic MDS. This form of the disease is uncommon; it resembles aplastic anaemia which also may respond to this form of treatment. Immunosuppression may also be effective in some younger patients, predominantly with refractory anaemia.

Thrombocytopenia

About 40 to 60% of MDS patients will have a reduced platelet count (thrombocytopenia) at diagnosis. The platelets may also function poorly and these factors, taken together, mean that bleeding can be a serious problem in MDS. There are standard guidelines for use of platelet transfusions and it is recommended that these should be applied for patients with MDS.



Infection

- Prophylaxis (prevention)
 - ✦ There is no evidence to support the use of anti-bacterial or anti-fungal drugs to prevent infection in MDS patients with low neutrophil counts. Low-dose G-CSF therapy may be considered to maintain the neutrophil count above $1 \times 10^9/l$ in patients with very low neutrophil counts and repeated infections.
- Therapeutic
 - ✦ Patients with low neutrophil counts (neutropenia) are at increased risk of developing potentially severe infections. When infection does occur in MDS patients it will be treated in the same way as for other neutropenic patients; if the infection is severe a patient may require intravenous antibiotic therapy given as an inpatient.

Non-intensive chemotherapy

There is no clear evidence to support the routine use of low-dose chemotherapy in any patients with MDS. At present, the guidelines recommend that such treatment should only be given as part of a clinical trial.⁶

Chronic myelomonocytic leukaemia

In CMML it is commonly necessary to treat with cytotoxic drugs (anti-leukaemia drugs). Hydroxyurea is considered the standard treatment in this situation.

Intensive chemotherapy/stem cell transplantation

Intensive chemotherapy uses high doses of cytotoxic (cell-killing) drugs to clear the diseased cells from the marrow (remission induction). In appropriate

⁶ A separate publication on clinical trials is available from Leukaemia Research.

cases, and where a donor is available, a stem cell transplant may follow.⁷ A donor stem cell transplant may be feasible for a small minority of patients. For 30-50% of such eligible patients it may result in long-term disease-free survival. Autologous transplant (using a patient's own cells) is at present only considered in the context of a clinical trial. There is also a small group of patients for whom intensive chemotherapy alone may be beneficial which is discussed below.

There are four IPSS risk categories. These are low, intermediate-1, intermediate-2 and high. To consider each category in turn:

○ IPSS low

- ✦ Neither intensive chemotherapy nor stem cell transplantation is recommended for this group of patients as they have a comparatively long median survival with supportive care only.

○ IPSS Intermediate-1

- ✦ Patients under 65 years and fit for transplant should be assessed for fitness and eligibility for a donor transplant as soon as possible after diagnosis. This is because transplants are more likely to be successful if carried out early in the course of the disease. The ideal donor for a stem cell transplant is a well-matched sibling donor. The recommendations in this group depend on age and on availability of a donor as follows:

Sibling donor available for a patient under 50 years

Standard stem cell transplant with full conditioning

Sibling donor available for a patient between 50-65 years

Reduced intensity stem cell transplant ('mini-transplant') as part of a clinical trial if a transplant arm is available

Non-sibling donor for a patient under 40 years

Standard stem cell transplant with full conditioning as part of a clinical trial if a transplant arm is available

⁷ A separate publication on stem cell transplantation is available from Leukaemia Research.

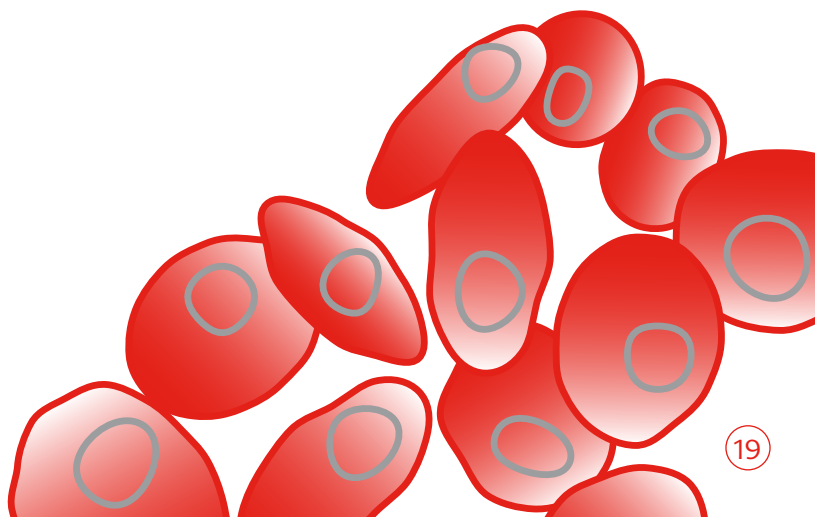
- ❖ Patients either over 65 years, or under 65 years, who are unfit for a transplant (e.g. other illness) receive supportive care and/or growth factor therapy (EPO/G-CSF)
- IPSS Intermediate-2/high
 - ❖ The recommendations in this group are essentially the same as the intermediate-1 group above but only if patients respond well to their initial (remission induction) chemotherapy. Patients who are not eligible for a transplant and who have RAEB-t subtype with no other risk factors may be offered intensive treatment with the same type of chemotherapy that is given for acute myeloid leukaemia (AML). However, fewer courses of treatment may be given for MDS than for AML. In other high risk patients intensive chemotherapy should not be offered if a stem cell transplant is not intended.

❖ **Supportive care/Investigational therapy**

- If patients are not in the IPSS low category but do not fit any of the groups for whom intensive chemotherapy, with or without SCT, is indicated they may be recommended to receive supportive care or asked to consider entering a clinical trial. These options will be discussed in detail by the specialist.

Follow up

The most important aspects of the follow-up of patients with MDS are regular checks for evidence of disease progression or of transformation to acute myeloid leukaemia.



Summary

The myelodysplastic syndromes (MDS) are a group of diseases in which the production of blood cells is severely disrupted. In contrast to leukaemia (in which one type of blood cell is produced in excessively large numbers) the production of any, and sometimes of all, types of blood cells is affected in myelodysplastic syndrome. The myelodysplastic syndromes result from production of large numbers of defective cells in the bone marrow which leads to the paradox of a very active marrow but with reduced numbers of healthy cells in the circulating blood.

The conditions are seen most commonly in older patients, with a male excess, although the minority of cases seen in young people affect men and women equally.

Those patients who do not have symptoms may require no treatment at all. Virtually all patients will require supportive treatment including red cell transfusions at some stage during their illness.

For patients who require treatment, the choice of therapy is based on their age, general fitness and on a system called the International Prognostic Scoring System. Most patients with mild forms of the disease are given supportive therapy only.

Intensive drug treatment may induce remission in patients with more advanced disease but these are not usually durable and over 90% of patients will experience relapse. The only potentially curative treatment is a stem cell transplant from a tissue-matching donor. Unfortunately, most patients with MDS are not able to receive this form of treatment.

Other resources

Other useful sources of information include:

The Myelodysplastic Syndromes Foundation

www.mds-foundation.org

e-mail: patientliaison@mds-foundation.org

The MDS Foundation, 36 Front Street PO Box 353

Crosswicks, NJ 08515 USA

Aplastic Anemia and MDS International Foundation

www.aplastic.org

e-mail: help@aamds.org

Aplastic Anemia & MDS International Foundation, Inc. PO Box 613

Annapolis, MD 21404-0613 USA

There are currently three UK centres with a specialist interest in treating patients with MDS, and which The Myelodysplastic Syndromes Foundation recognises as ‘Centres of Excellence’.

These are:

King’s College Hospital, London

(Contact: Professor Ghulam Mufti,

ghulam.mufti@kcl.ac.uk, 020 7346 3080)

Ninewells Hospital, Dundee

(Contact: Dr David Bowen

d.t.bowen@dundee.ac.uk, 01382 660111 ext. 33893/35247)

Royal Bournemouth Hospital, Bournemouth

(Contact: Dr Sally Killick, 01202 704783)

Appendix – International prognostic scoring system

The International Prognostic Scoring System (IPSS) was developed by analysing information on almost 1,000 MDS patients, who mostly received only supportive care, and determining which factors best predicted disease progression and outcome. This was then used to create a scoring system based on percentage of blasts in the bone marrow, cytogenetics and the number of cell types affected in the circulating blood.

Definitions used in the IPSS

∴ Karyotype

- Good – normal, deletion of Y chromosome, del(5q), del(20q)
- Poor – complex (more than 3 abnormalities), chromosome 7 abnormalities
- Intermediate – all other abnormalities

∴ Cytopenias

- Haemoglobin – less than 10g/dl
- Neutrophils – less than $1.8 \times 10^9/l$
- Platelets – less than $100 \times 10^9/l$

IPSS score table

Score	0	0.5	1	1.5	2
BM blasts %	<5	5-10		11-20	21-30
Karyotype	Good	Intermediate	Poor		
Cytopenias	0/1	2/3			

The individual scores for bone marrow blast percentage, karyotype and cytopenias are added together to give the IPSS score. The scores for the risk groups are as follows:

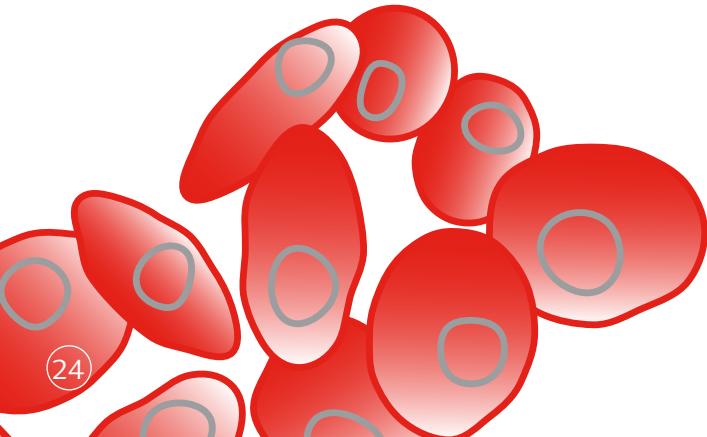
Low	0
INT-1	0.5-1.0
INT-2	1.5-2.0
High	>2.5

Median survival by IPSS score (by age group)

Median Survival (yrs)	≤ 60 yrs	>60 yrs	≤ 70 yrs	>70 yrs
Low	11.8	4.8	9	3.9
Int-1	5.2	2.7	4.4	2.4
Int-2	1.8	1.1	1.3	1.2
High	0.3	0.5	0.4	0.4

NB: Median survival is often misunderstood by patients and family to mean the maximum expected lifespan. In fact, it is the time at which one would expect half of a group of patients diagnosed at the same time to still be alive – many of those still alive will live for many more years, decades even. It is also important to realise that not all patients who die after being diagnosed with MDS die from MDS. Particularly in the case of elderly patients, many will die from other diseases. Finally, one should always remember that survival data is historical and may not reflect improvements based on newer drugs or treatments.

Notes



Typical normal values for blood test results

	WBC x 10⁹/l	RBC x 10¹²/l	Hb g/dl	ANC x 10⁹/l	Platelets x 10⁹/l
Adult male	3.7 to 9.5	4.3 to 5.7	13.3 to 16.7	1.7 to 6.1	143 to 332
Adult female	3.9 to 11.1	3.9 to 5.0	11.8 to 14.8	1.7 to 6.1	143 to 332
West Indian	2.8 to 9.8			1.0 to 6.5	122 to 374
African	2.8 to 7.8			0.9 to 4.2	115 to 342
Child 2-5 yrs	5 to 13	4.2 to 5.0	11 to 14	1.5 to 8.5	143 to 332
Child 6-9 yrs	4 to 10	4.3 to 5.1	11 to 14	1.5 to 6.0	143 to 332
Child 9-12 yrs	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.



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**Adult Acute
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**Childhood Acute
Lymphoblastic Leukaemia (ALL)**

**Childhood Acute
Myeloid Leukaemia (AML)**

**Chronic Lymphocytic
Leukaemia (CLL)**

Chronic Myeloid Leukaemia (CML)

Aplastic Anaemia (AA)

**The Myelodysplastic
Syndromes (MDS)**

**The Myeloproliferative
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