Myelodysplasia
Diagnosis and Treatment

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Overview

What is myelodysplasia?

Symptoms

Diagnosis and prognosis

Myelodysplasia therapy
  Supportive care
  Non-intensive therapy
  Bone marrow transplant
What is Myelodysplasia?

Myelodysplastic syndrome is a group of clonal stem cell disorders of varying severity typified by low blood counts, dysplasia and a tendency to progress to leukaemia.

Normal bone marrow makes healthy blood cells (red, white and platelet cells)
What is Myelodysplasia?

In MDS, the bone marrow makes the blood cells badly (dysplasia), causing low blood counts and cells that don’t work very well.
Symptoms

Myelodysplasia Symptoms

Fatigue and shortness breath
are caused by anaemia (low red cells)

Bruising and bleeding
are caused by low platelet cell count

Infection
is due to low numbers and/or poorly functioning white cells
Diagnosis

Specialist tests for myelodysplasia

- Bone marrow sample
- Morphology
- Flow cytometry
- Cytogenetics
## Diagnosis

### WHO Classification of myelodysplasia

<table>
<thead>
<tr>
<th>Entity</th>
<th>Bone marrow blasts</th>
<th>Cytogenetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>5q- syndrome</td>
<td>&lt;5%</td>
<td>5q- only</td>
</tr>
<tr>
<td>Refractory anaemia</td>
<td>&lt;5%</td>
<td>various</td>
</tr>
<tr>
<td>Refractory anaemia ring sideroblasts</td>
<td>&lt;5%</td>
<td>various</td>
</tr>
<tr>
<td>Refractory cytopenia multilineage dysplasia (RCMD)</td>
<td>&lt;5%</td>
<td>various</td>
</tr>
<tr>
<td>RCMD-ring sideroblasts</td>
<td>&lt;5%</td>
<td>various</td>
</tr>
<tr>
<td>Refractory anaemia excess blasts-1 (RAEB-1)</td>
<td>5-9%</td>
<td>various</td>
</tr>
<tr>
<td>RAEB-2</td>
<td>10-19%</td>
<td>various</td>
</tr>
<tr>
<td>Chronic myelomonocytic leukaemia -1 (CMML-1)</td>
<td>&lt;10%</td>
<td>various</td>
</tr>
<tr>
<td>CMML-2</td>
<td>10-19%</td>
<td>various</td>
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</tbody>
</table>
International Prognostic Scoring System

- LOW
- INT-1
- INT-2
- HIGH

SEVERITY
Treatment: general concepts

Treatment choices should take into account:

What type of MDS does the patient have?  
How aggressive is their MDS?

Are any symptoms particularly bothersome?  
How does the patient want to be treated?

Is curative therapy appropriate?  
Are clinical trials available?
What is supportive care?

Supportive care is any medicine or device that helps to make symptoms go away, or makes it easier and safer for the patient to receive ‘active’ treatment.....
## Supportive care

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red cell transfusion</td>
<td>Symptomatic anaemia</td>
</tr>
<tr>
<td>Platelet transfusion</td>
<td>Chronic low platelets-bleeding &amp; bruising</td>
</tr>
<tr>
<td></td>
<td>Planned surgical operation</td>
</tr>
<tr>
<td>Granulocyte-colony stimulating factor</td>
<td>Infections associated with low white count</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>Infections</td>
</tr>
<tr>
<td>Iron chelation therapy</td>
<td>Patients with low-risk disease with more than 25 units of red cell transfusion</td>
</tr>
</tbody>
</table>
Supportive care

Red cell transfusion

- Most patients will develop symptoms due to anaemia

- Red cell transfusion is the commonest way anaemia is treated

- The number and frequency may vary, but generally increase over time
Myelodysplasia supportive care

Iron overload
- Long term red cell transfusion can lead to increased iron that the body can’t get rid of
- Increased iron may damage organs like the heart, liver and pancreas

Iron chelation (removal)
- Recommended in transfusion dependent MDS patients with low risk MDS who have received more than 25 units
- Desferral and Exjade are used to remove iron
Myelodysplasia supportive care

Supportive care

Platelet transfusion

• Platelet transfusion should be reserved for patients with bruising or bleeding symptoms

• Planned surgery, dental extraction may also need to be covered by platelet transfusion
Myelodysplasia supportive care

Erythropoietin

- May improve anaemia in patients with MDS
- May reduce red cell transfusion need
- Seems to work best when given with white cell growth factor G-CSF
- Has to be given by injection
### Table 4. Trials of erythropoietin alone in MDS

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hellström-Lindberg 1995</td>
<td>205 from 17 trials</td>
<td>16% overall response</td>
<td>Higher response if: a) Serum EPO &lt; 200 U/L b) Non-RARS c) Non Transfusion dependent</td>
</tr>
<tr>
<td>Rodríguez et al 1994</td>
<td>115 from 10 studies</td>
<td>23.5%</td>
<td>Higher response for RAEB No relation to EPO level</td>
</tr>
<tr>
<td>Terpos et al 2002</td>
<td>281</td>
<td>45% at 26 weeks (18% at 12 weeks)</td>
<td>Prolonged therapy increased response</td>
</tr>
<tr>
<td>Italian Cooperative</td>
<td>87</td>
<td>14/38 vs 4/37 responders</td>
<td>Low risk MDS pts only (double blind)</td>
</tr>
<tr>
<td>Rose et al 1995</td>
<td>116</td>
<td>28%</td>
<td>Serum EPO &lt; 100 predicted response (54% of RA with low EPO responded)</td>
</tr>
</tbody>
</table>
Myelodysplasia
Non-intensive therapy

**Lenolidomide**
Should be considered for 5q- syndrome

**Oral medication**
Eliminates need for transfusion in 67% of patients

**5q- Syndrome MDS**
5% of MDS patients have 5q- MDS

- Usually female
- ‘Good’ platelet count
- Anaemia
- Chromosome 5q missing
- Good prognosis

Not yet licensed in Europe
Myelodysplasia
Non-intensive therapy

Azacytidine in high-risk myelodysplasia

Significant benefit to patients with aggressive MDS when treated with Azacytidine on clinical trials (USA and Europe)

Benefits include:
- Reduced red cell transfusion
- Improvement in survival
- Less chance of MDS deteriorating
- Results not influenced by patient age, blast cells, karyotype

Drug administered by injection (but oral preparation in development)

Well tolerated
Myelodysplasia therapy

NICE appeal 1st June 2010

“Appraisal committee to reconsider guidance by taking into account both best supportive care and low dose chemotherapy as comparators”

“Examine data on quality of life”
Myelodysplasia therapy

Cancer Drug Fund—From April 2011

Interim funding from October 2010

Fund to cover treatments not currently funded by NHS:

Treatments rejected by NICE

Treatments yet to be appraised by NICE
Myelodysplasia Immuno-therapy

Anti-thymocyte Globulin (ATG)
May be indicated in low-risk MDS
(with reduced bone marrow cells)

Requires admission to hospital, and haematology team experienced in its use

Improves blood counts in 30-50% of cases
Myelodysplasia
Intensive treatment

Bone marrow transplant

Why should it be considered?

Who should have it?

How do you do it?
Myelodysplasia
Intensive treatment

Bone marrow transplant should be considered when ‘curative’ therapy is thought to be appropriate.

Key issues for patients:
Motivated, and deemed fit for BMT
‘High-risk’ MDS, with disease under control

Appropriate counselling regarding outcomes, risks, and intensive long-term follow-up
Myelodysplasia
Bone marrow transplantation

Donor
Bone marrow collection

Patient
Chemotherapy

Bone marrow transplant team

Inpatient
Long term follow up
Myelodysplasia
Bone marrow transplantation

BMT is not for everyone
It is complicated, and not with risks

BMT is applicable in ‘selected’ older adults
Summary

1. **MDS** is not one disease, but a group of disorders that cause the bone marrow to fail.

2. **Diagnosis** may require a number of special tests on bone marrow and blood, and may need repeating before a firm diagnosis can be made!

3. **Treatments** range from ‘supportive’ to the ‘intensive’. Modern treatments, including BMT, are increasingly relevant to the majority of patients with MDS.