

# **Myelodysplasia**

## **Diagnosis and Treatment**

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Map

Aerial

Bird's Eye >

Royal Hallamshire Hospital



Sheffield Children's Hospital





# **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

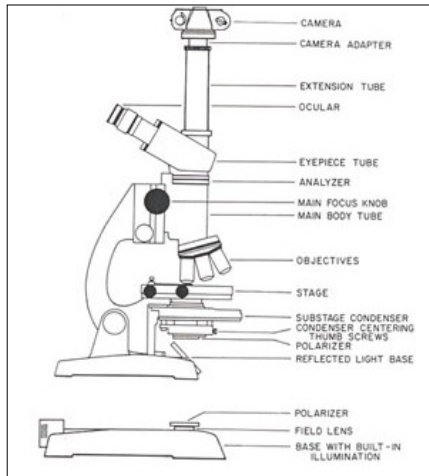
### **Infection**

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

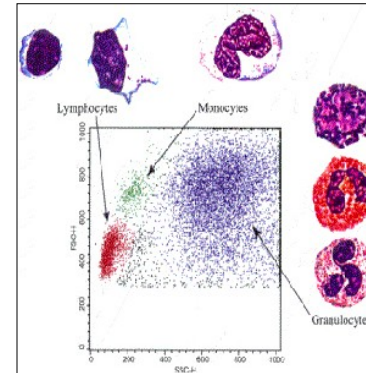


# Diagnosis

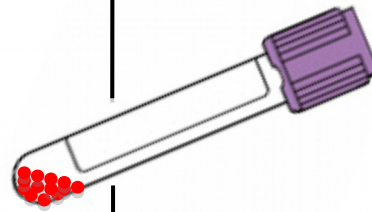
## Specialist tests for myelodysplasia



← Morphology



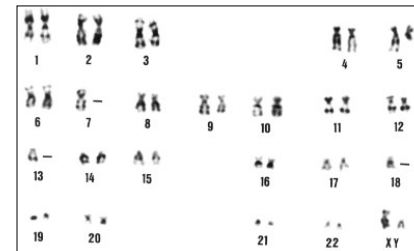
→ Flow cytometry

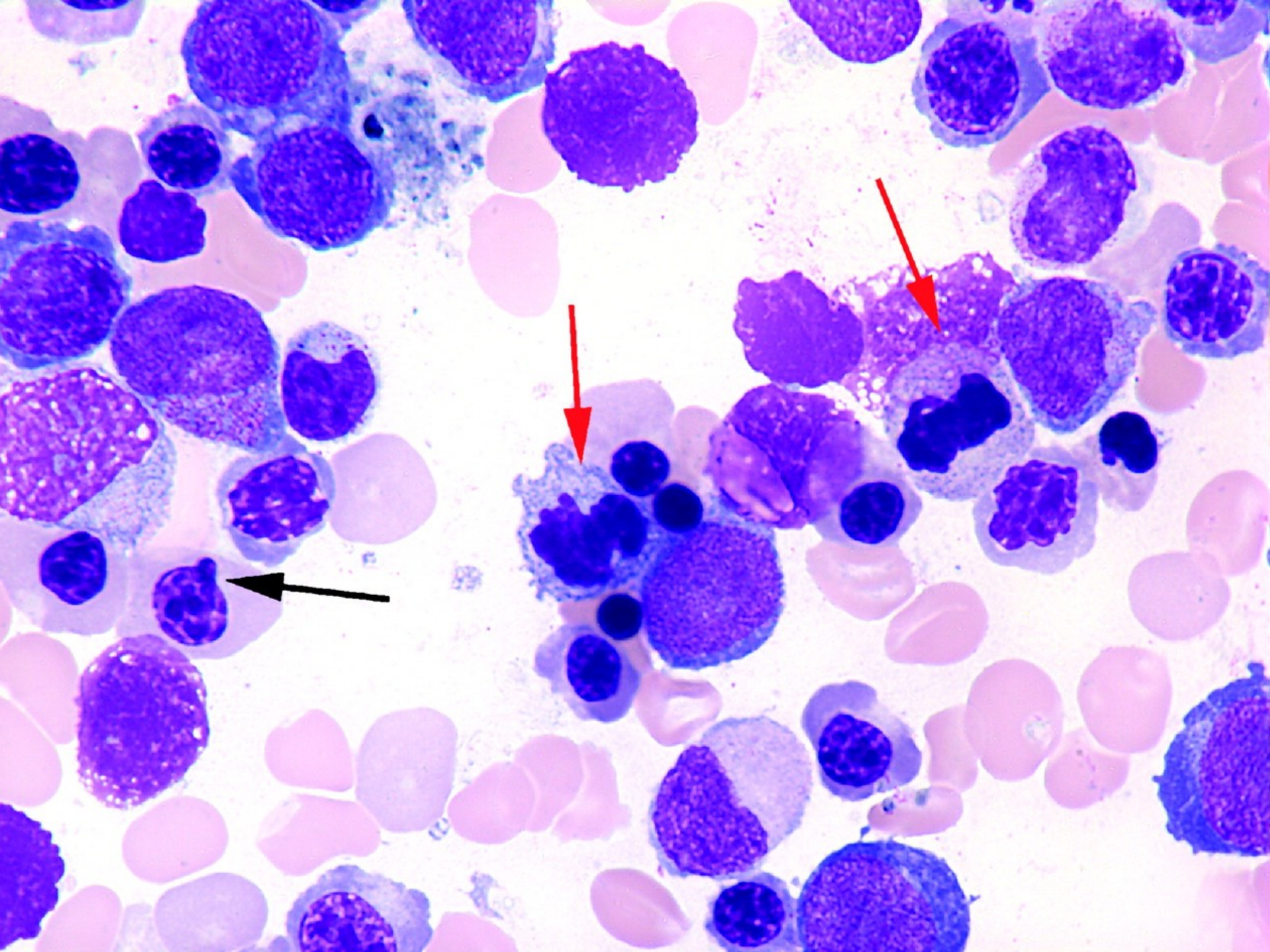


→ Cytogenetics



Bone marrow  
sample



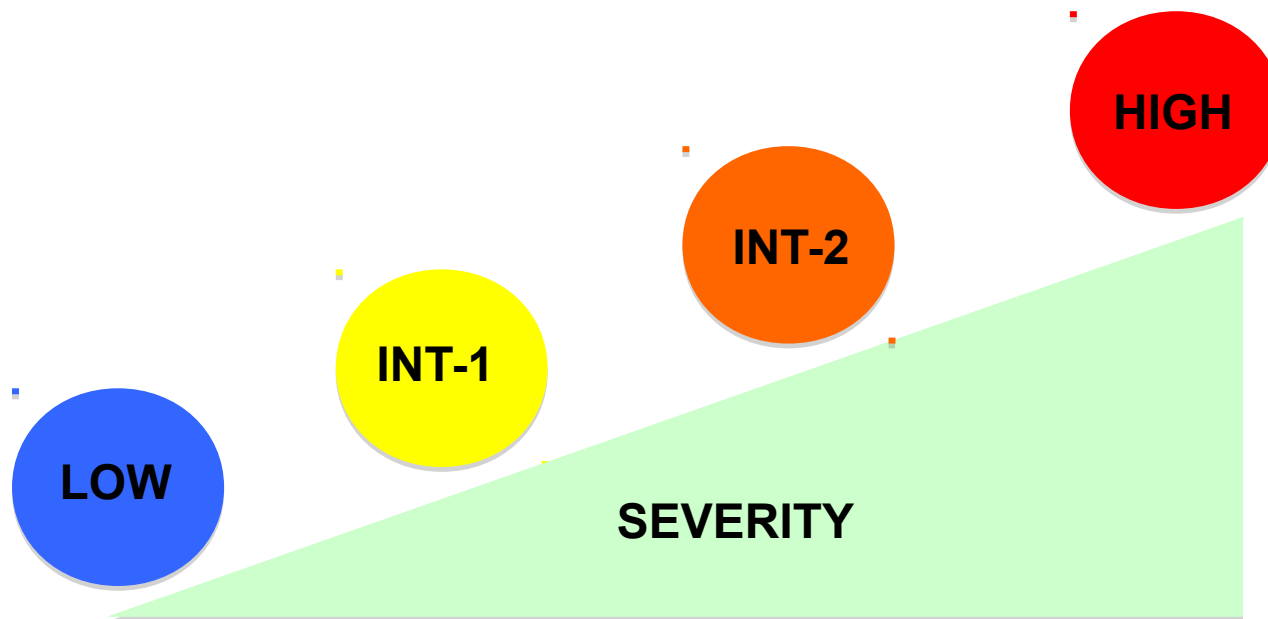


# Diagnosis

## WHO Classification of myelodysplasia

Entity	Bone marrow blasts	Cytogenetics
5q- syndrome	<5%	5q- only
Refractory anaemia	<5%	various
Refractory anaemia ring sideroblasts	<5%	various
Refractory cytopenia multilineage dysplasia (RCMD)	<5%	various
RCMD-ring sideroblasts	<5%	various
Refractory anaemia excess blasts-1 (RAEB-1)	5-9%	various
RAEB-2	10-19%	various
Chronic myelomonocytic leukaemia -1 (CMML-1)	<10%	various
CMML-2	10-19%	various

# International Prognostic Scoring System



# 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?



# **Treatment supportive care**

**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

<b>Red cell transfusion</b>	Symptomatic anaemia
<b>Platelet transfusion</b>	Chronic low platelets-bleeding & bruising  Planned surgical operation
<b>Granulocyte-colony stimulating factor</b>	Infections associated with low white count
<b>Antibiotic</b>	Infections
<b>Iron chelation therapy</b>	Patients with low-risk disease with more than 25 units of red cell transfusion

# Myelodysplasia

## supportive care

### 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



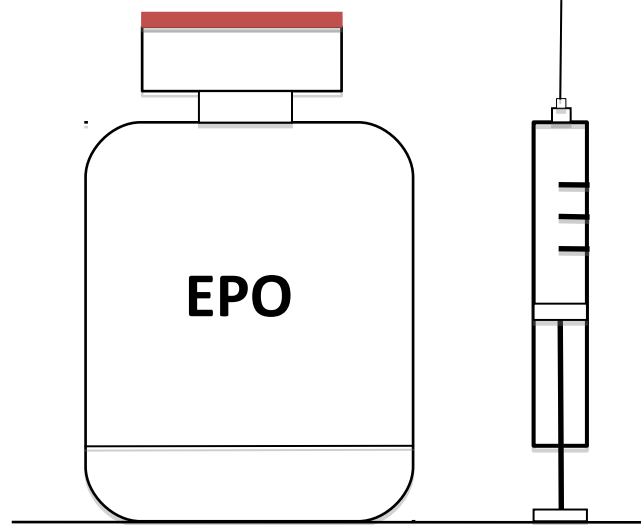
## Platelet transfusion

- 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**

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

# Myelodysplasia

## Non-intensive therapy

### Lenolidomide

Should be considered for  
5q- syndrome

Oral medication

Eliminates need for  
transfusion in 67% of  
patients

Not yet licensed in  
Europe

### 5q- Syndrome MDS

5% of MDS patients have 5q-  
MDS

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

# **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 1<sup>st</sup> 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:**

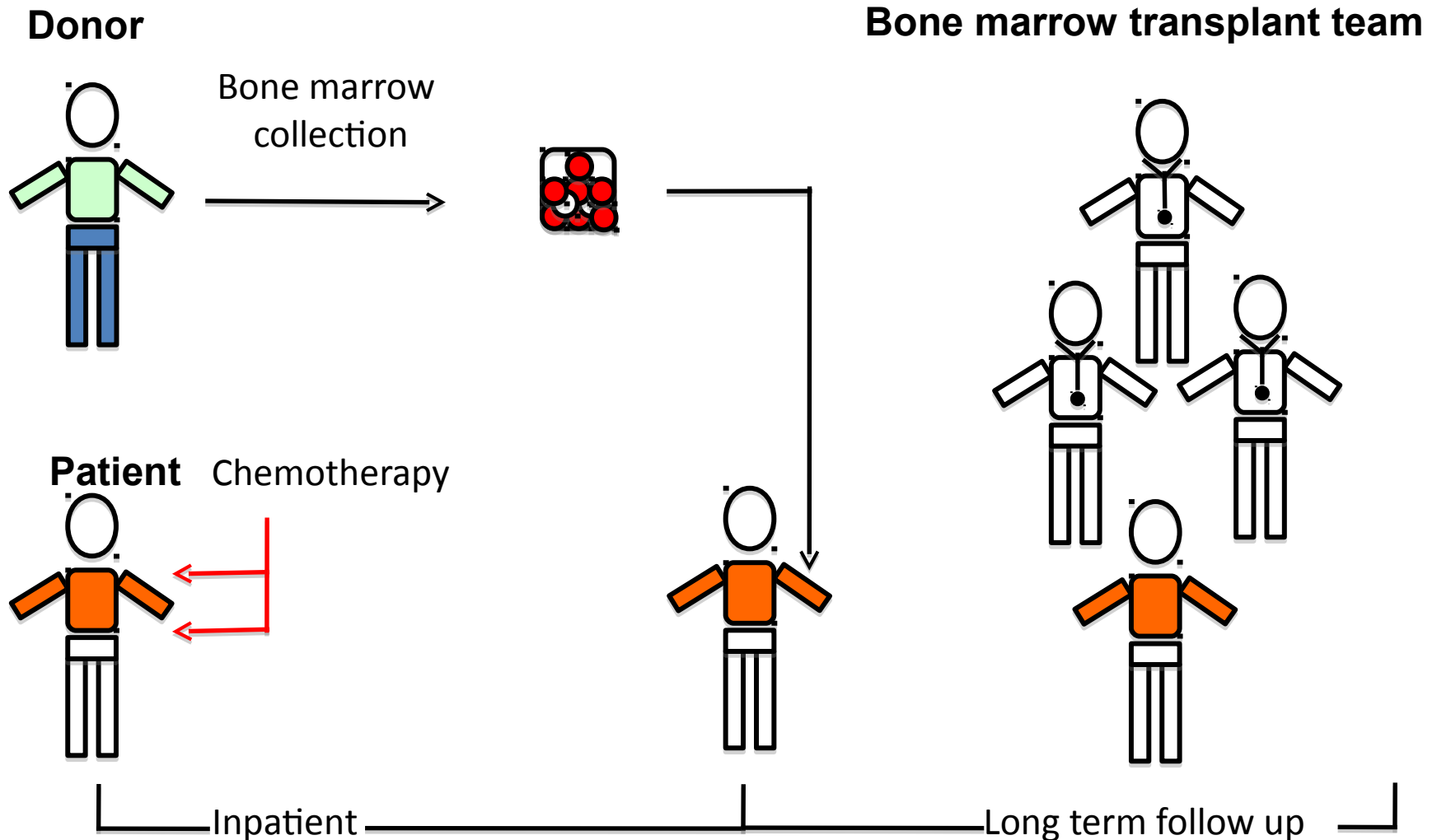
Motivated, and deemed fit for BMT

'High-risk' MDS, with disease under control

Appropriate counselling regarding outcomes, risks, and intensive long- term follow-up

# Myelodysplasia

## Bone marrow transplantation





# 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