UNDERSTANDING MYELODYSPLASTIC SYNDROME (MDS) AND BASIC BLOOD WORK

Saturday, April 23, 2016

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Division of Hematology
London Health Sciences Centre

WELCOME

- Welcome to London, Ontario

London
CANADA

OBJECTIVES

- At the end of this session, participants will be able to:
  - Understand and describe a complete blood count (CBC)
  - Review what myelodysplastic syndrome (MDS) is
  - Describe an overview of how MDS is managed and "newer" therapies

London CANADA

LAB BASICS

What is a CBC?

What are white cells, red cells, and platelets?

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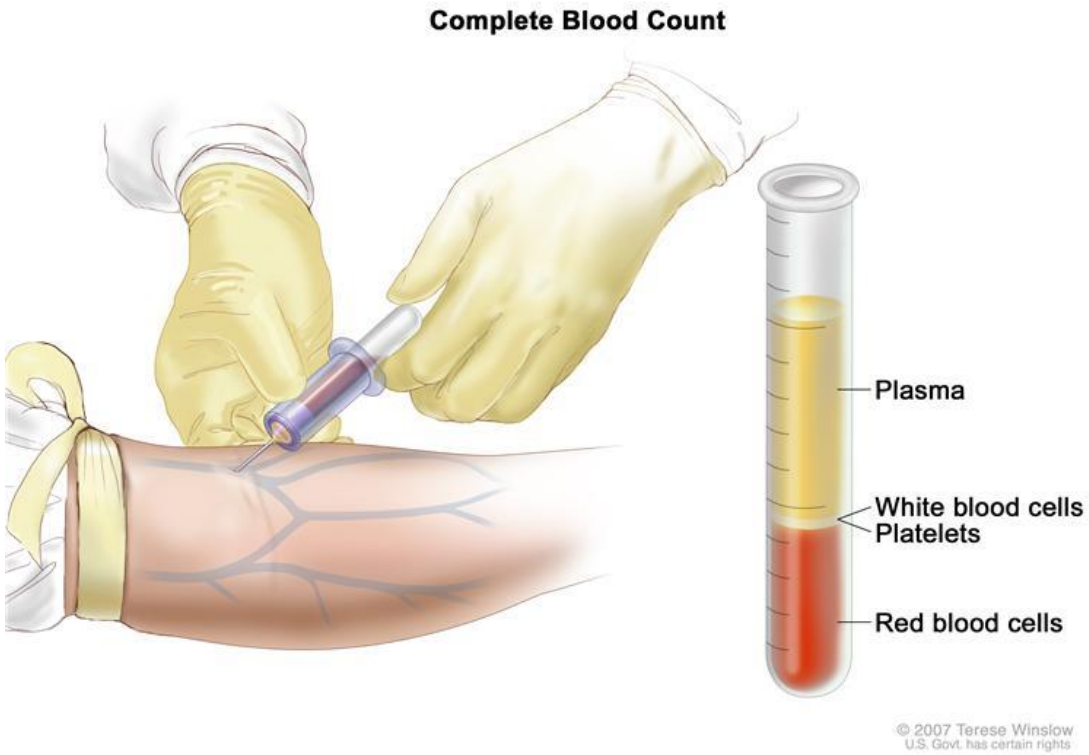
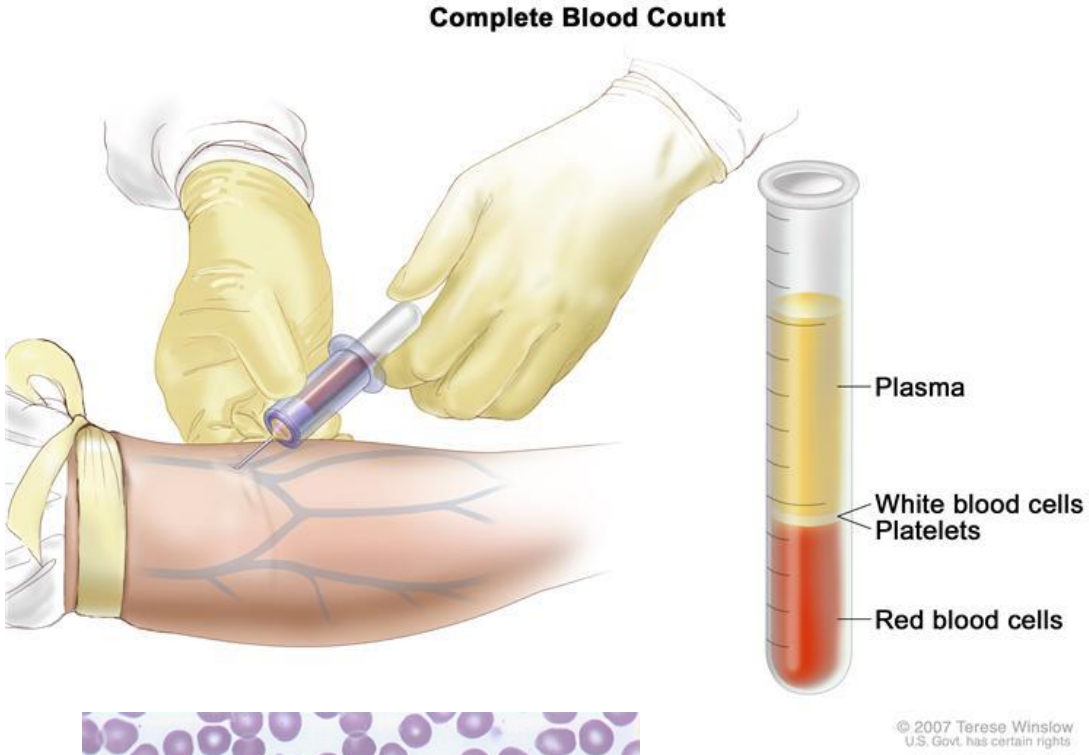
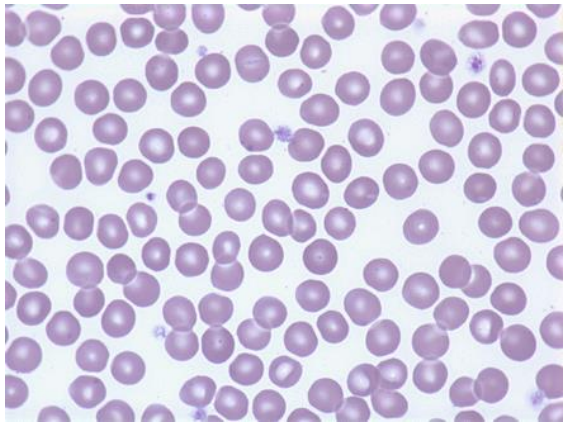


CBC

The complete blood count





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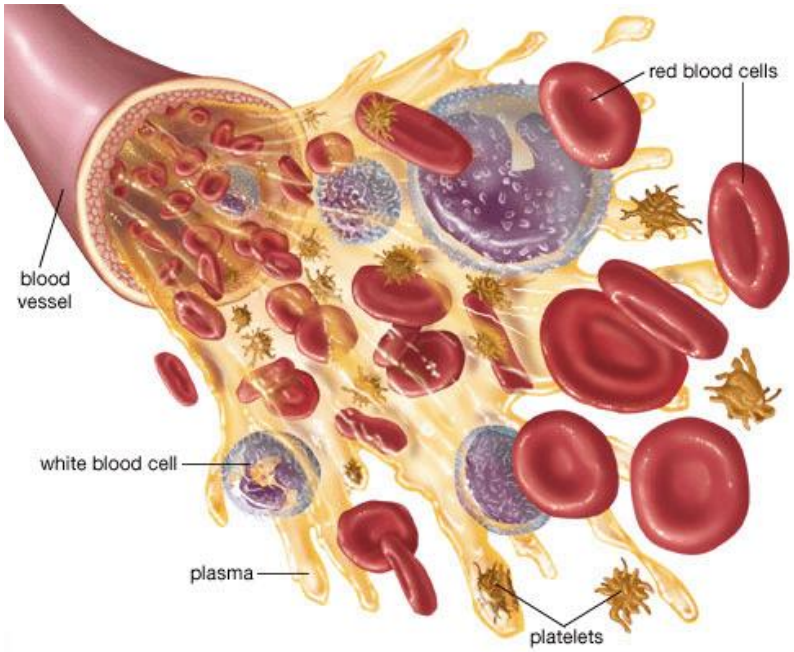
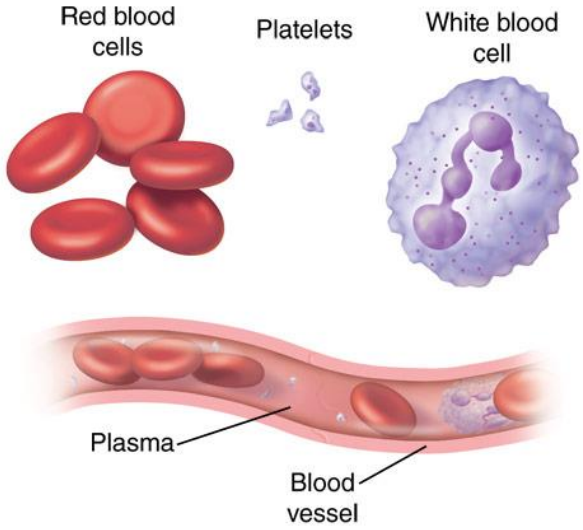
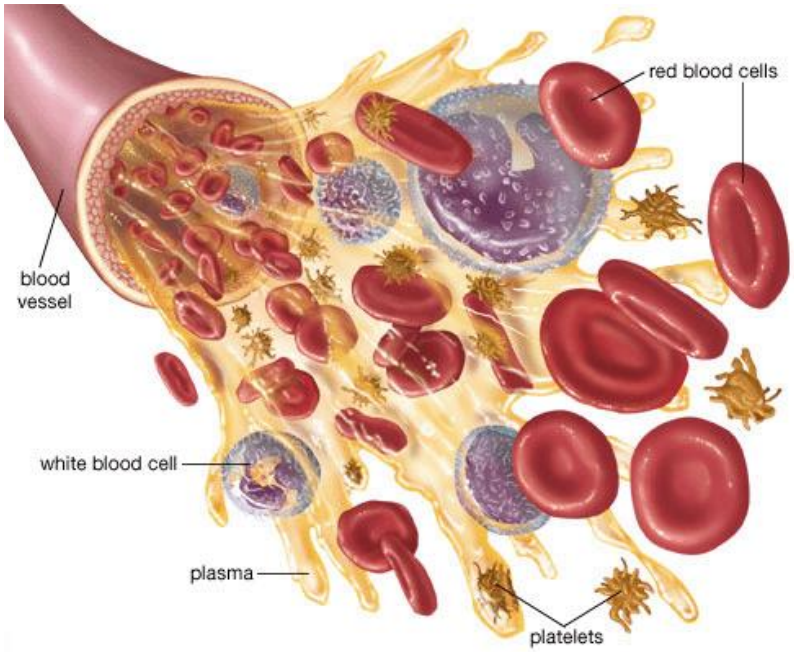




BLOOD

What is blood made of?



BLOODWORK

This is an example of a complete blood count (CBC) and a white cell differential

Event	Result	Ref. Range	Status
LKC	L 0.9	(4.0 - 10.0)	
ERC	L 2.87	(4.50 - 6.50)	
Hemoglobin	L 83	(135 - 170)	
HCT	L 0.25	(0.40 - 0.51)	
MCV	86.2	(79.0 - 97.0)	
RDW	14.1	(12.0 - 15.0)	
MPV	9.8	(7.1 - 11.1)	
Thrombocytes	* C <10	(150 - 400)	
Neutrophil	* C 0.3	(2.0 - 7.5)	
Lymphs	L 0.5	(1.5 - 4.0)	
Monocyte	L 0.1	(0.2 - 0.8)	
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IS IT COMPLETE?

The complete blood count doesn't measure everything.

Notice that it does not contain other tests of the blood such as kidney function, liver function, thyroid function, sugar levels, cholesterol, calcium, electrolytes..

REF. RANGE

What is a reference range?

How do we come up with this?

Patient Results

Reference Range

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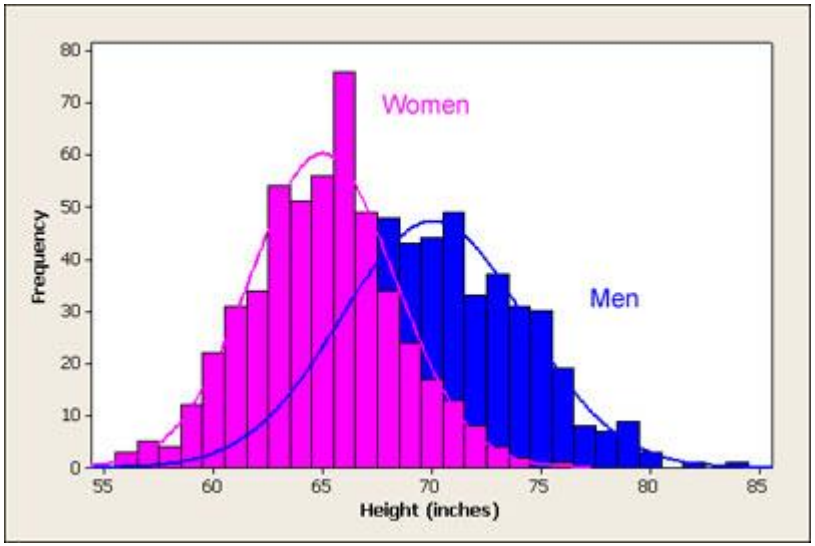

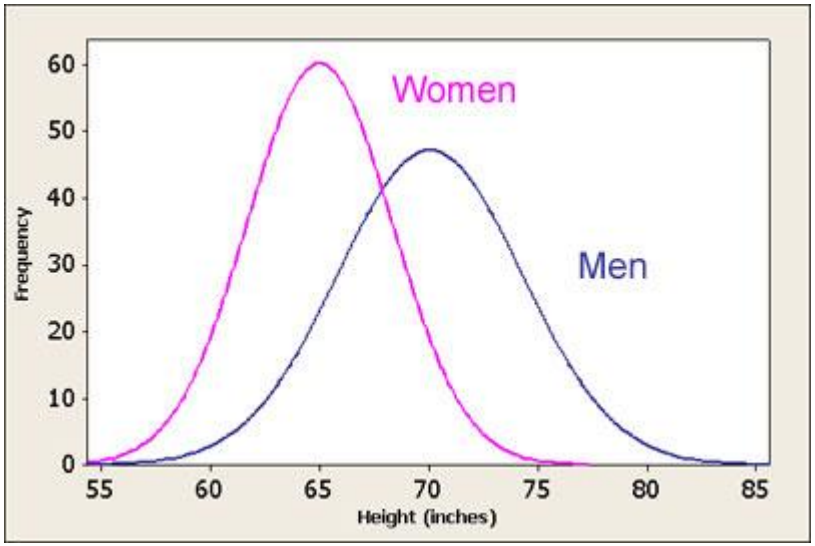

REF. RANGE

Let's talk about height as an example

You have to decide to cut off the range somewhere..

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REF. RANGE

Reference Ranges for each lab value is determined by each individual lab based on their reagents and "normal" controls.

14 WHITE BLOOD CELLS

What are white blood cells?

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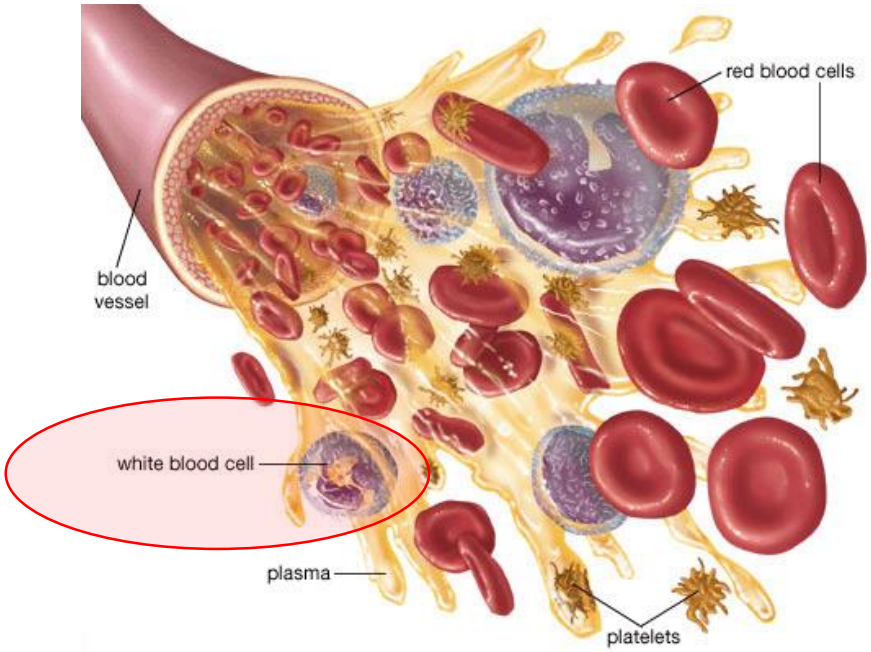

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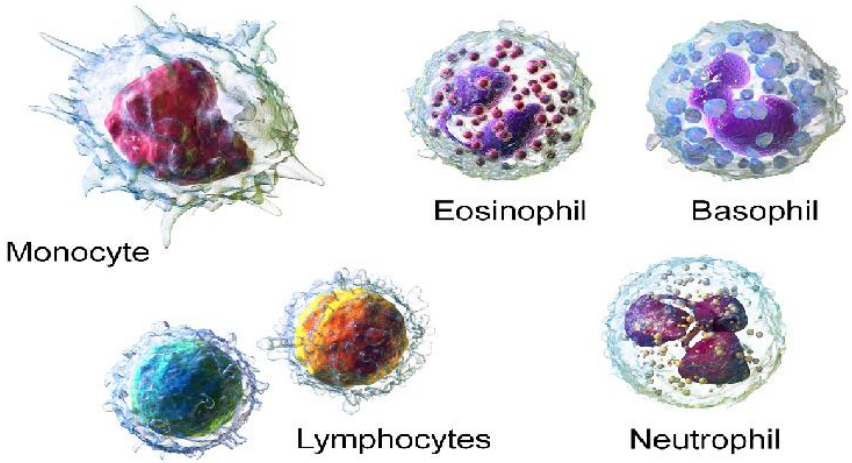
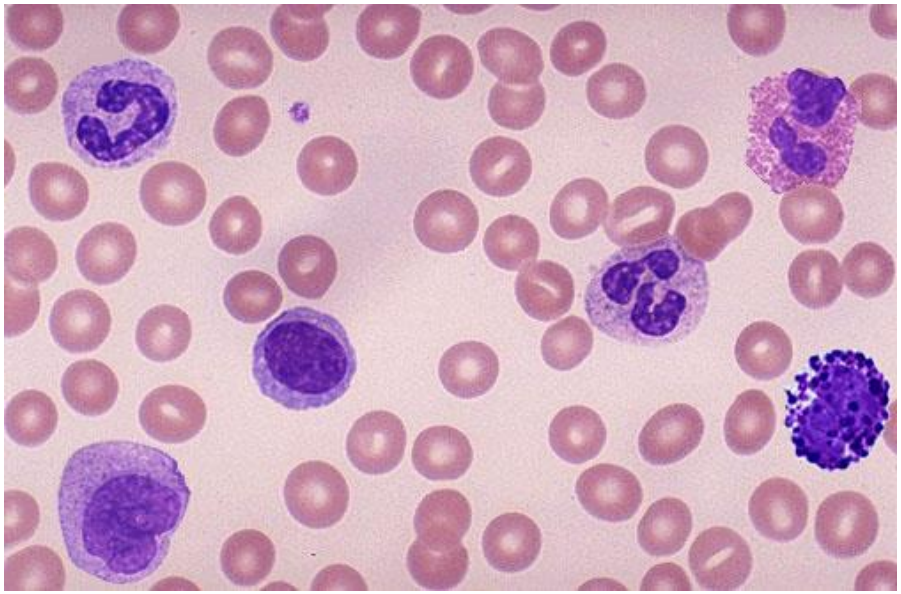
WBC

White blood cells (WBC) are also called leukocytes (LKC)



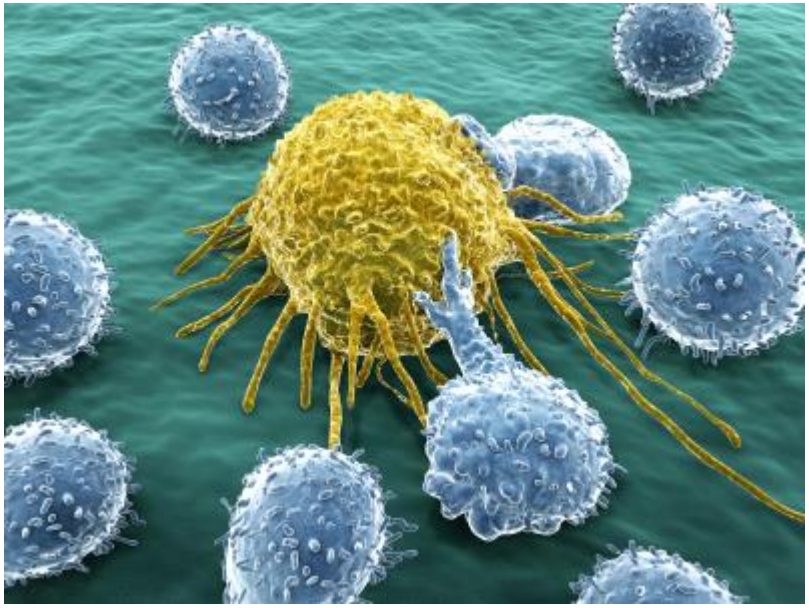
White Blood Cells



BLOOD

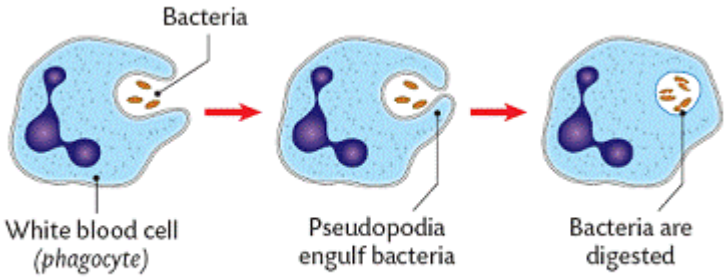
White blood cells are also called leukocytes (LKC)

There are many different types of white blood cells that have different functions.



WBC FUNCTION

What do white blood cells do?



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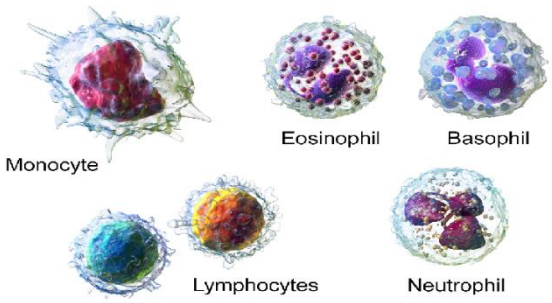
WBC

WBC or LKC is part of the complete blood count (CBC)

WBC is made up of a number of different white blood cells provided in the white cell differential



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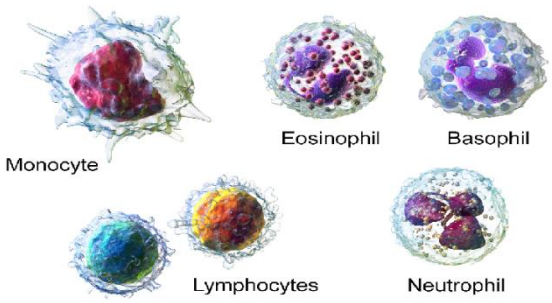

White Blood Cells

- Neutrophils
  - fight bacteria, fungi
- Lymphocytes
  - fight viruses
- Monocytes
  - help fight infections, can migrate to other tissues to engulf infections and debris
- Eosinophils
  - help fight larger parasites, part of allergic response
- Basophils
  - release histamine, part of inflammatory response

WBC

What do these white cells do?

If these blood counts are too low you can have these problems.

Low neutrophils is called (neutropenia)

21 RED BLOOD CELLS

What are red blood cells?

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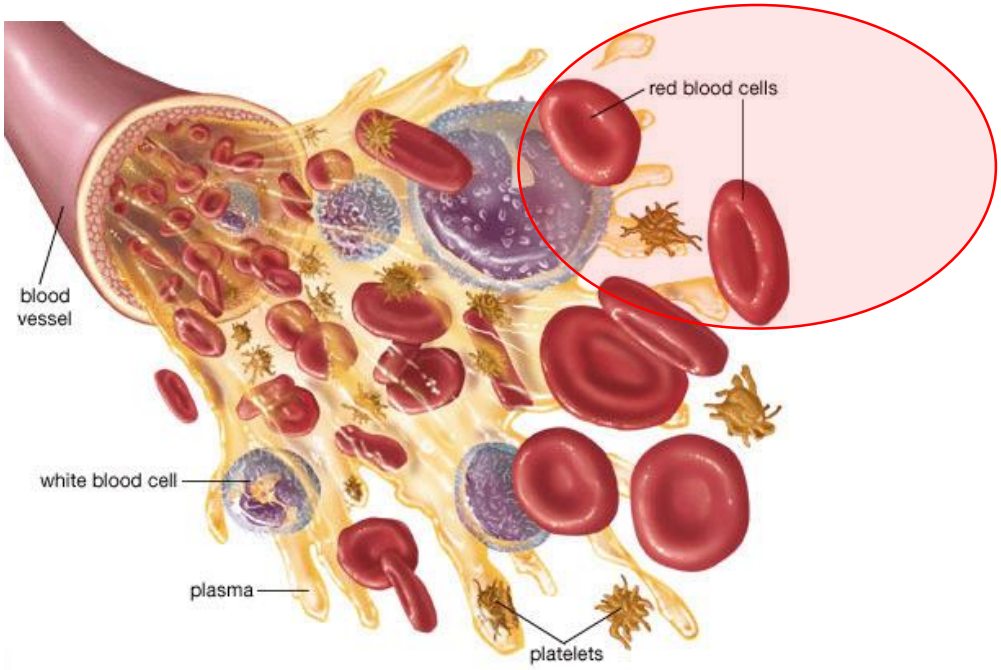

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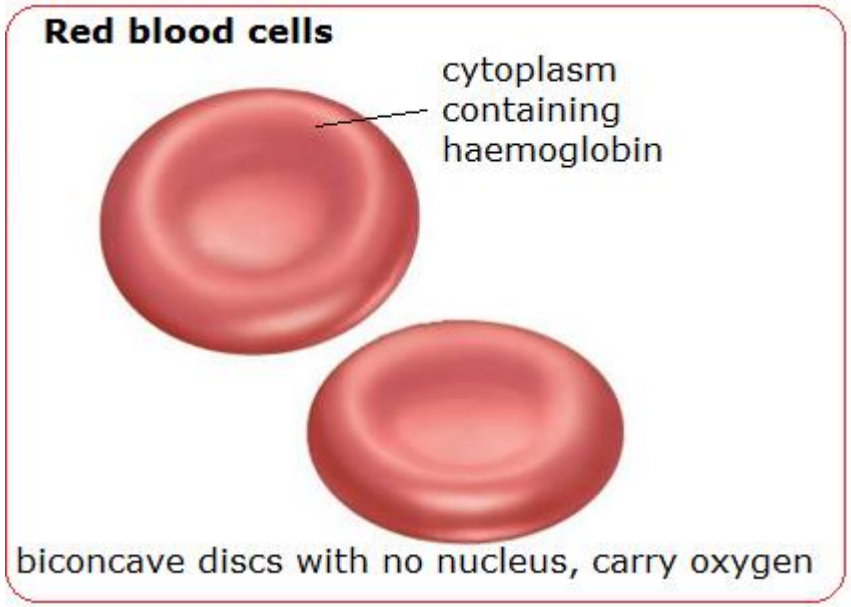
RBC

Red blood cells (RBC) are also called erythrocytes

ERC is the erythrocyte count



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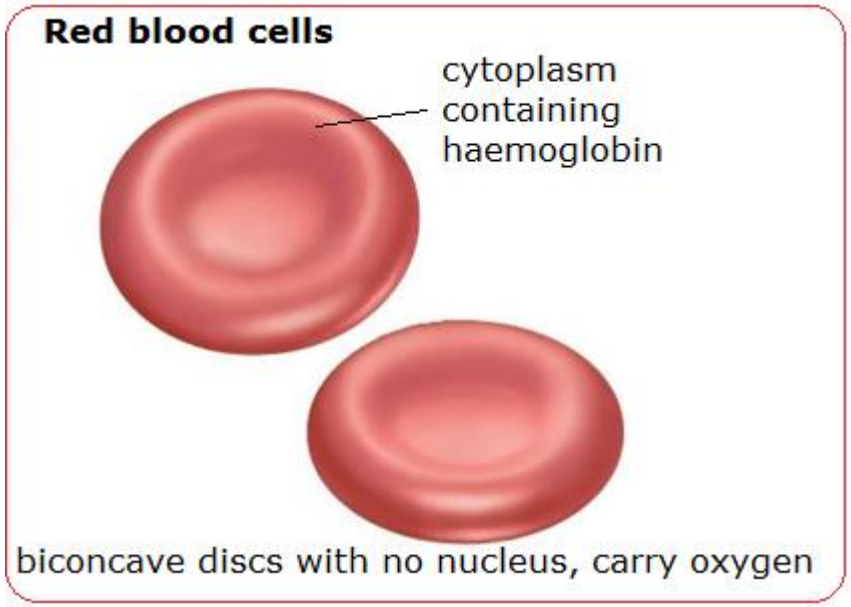
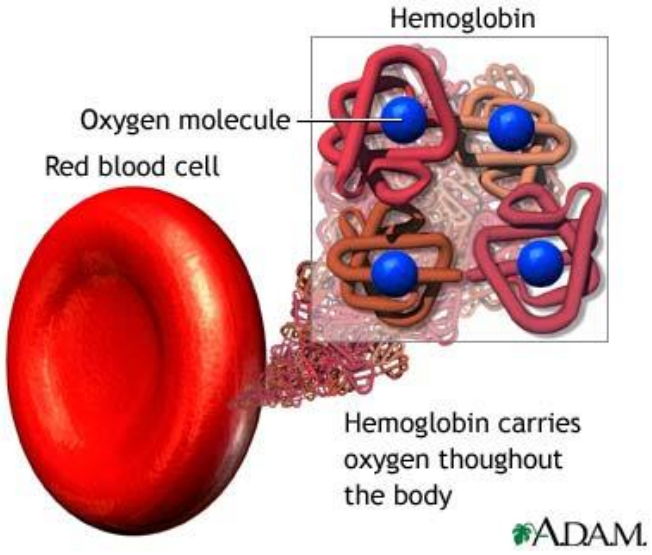
RBC

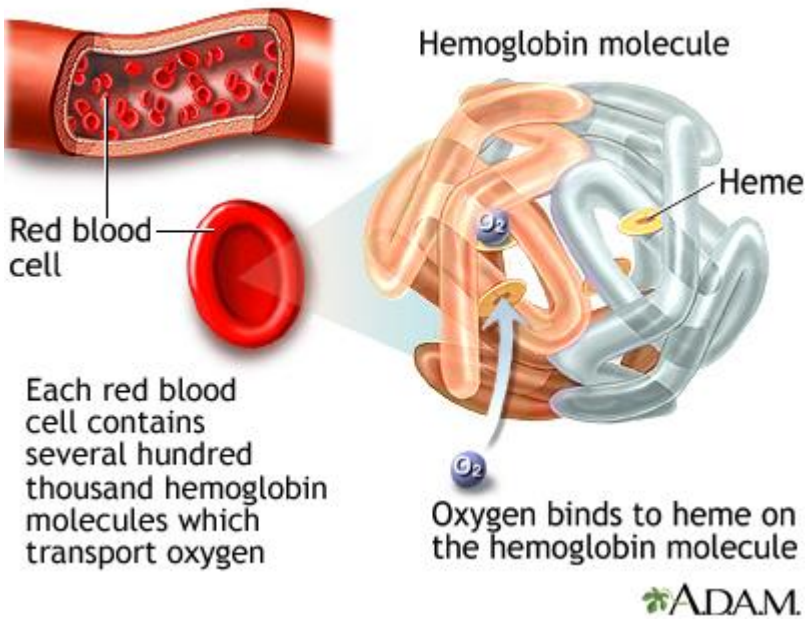
There are different measures that involve red blood cells such as hemoglobin, hematocrit, MCV and RDW.





HEMOGLOBIN

Hemoglobin molecules are essential.. They carry oxygen in the red blood cells.



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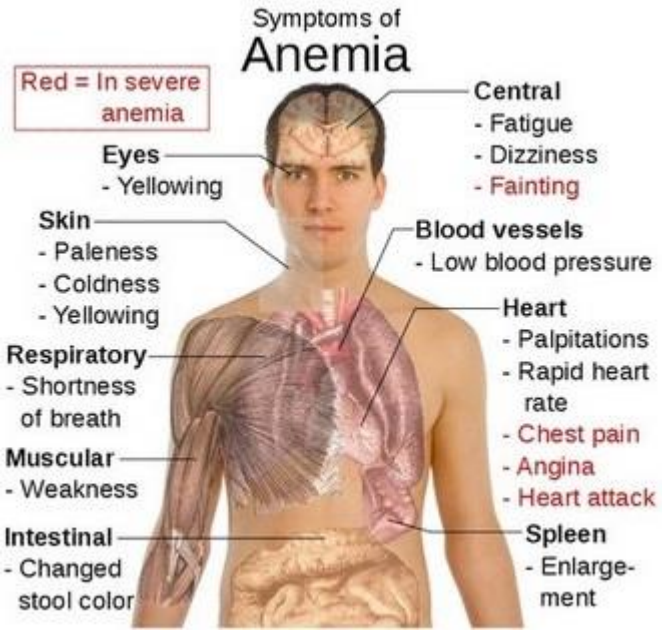

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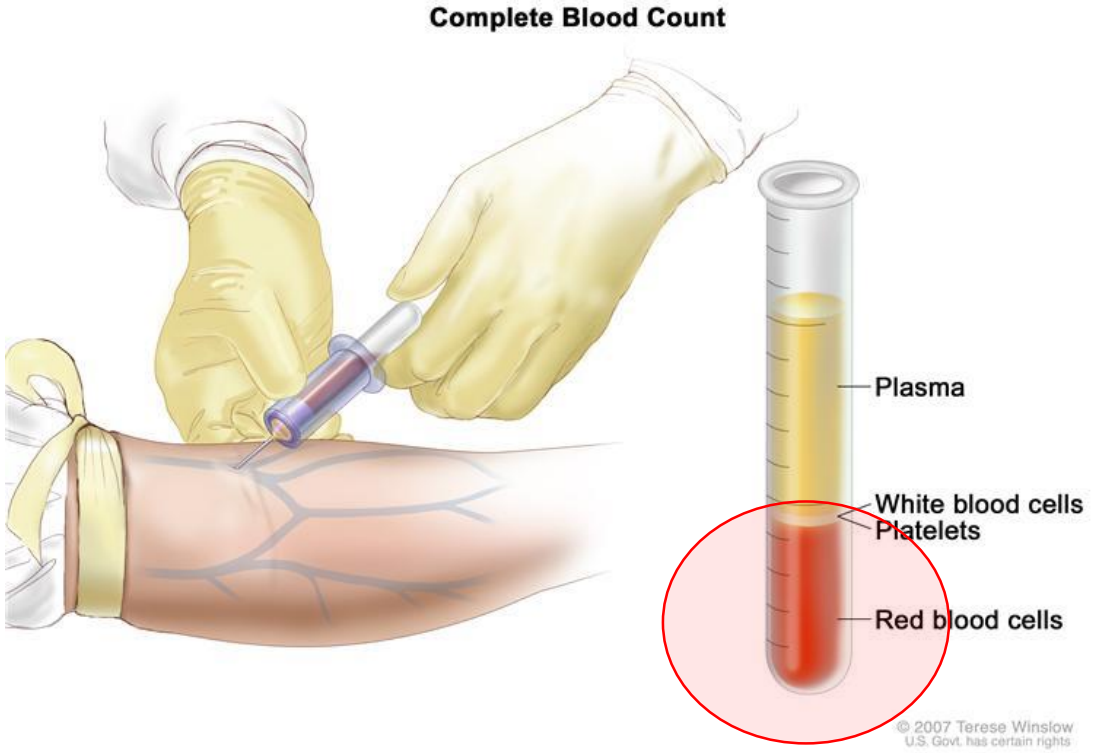
ANEMIA

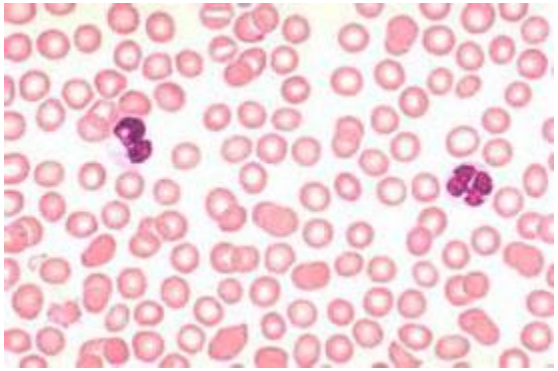
Anemia means low hemoglobin.

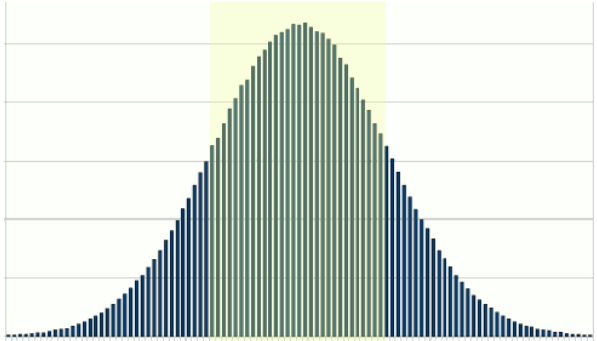


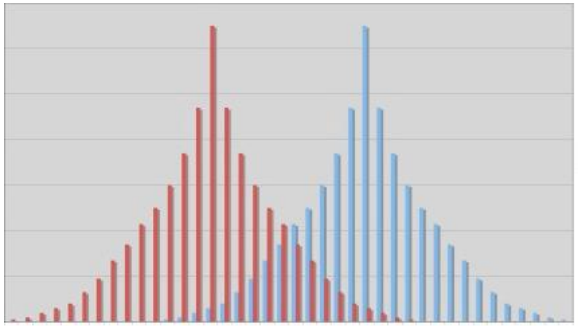
HCT	L 0.25	(0.40 - 0.51)

HEMATOCRIT

Hematocrit is the volume of blood occupied by red blood cells.







MCV	86.2	(79.0 - 97.0)
RDW	14.1	(12.0 - 15.0)

RBC INDICES

MCV = mean cell volume. This is the average size of red blood cells.

RDW = red cell distribution width. This is how variable the size of red cells are.

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PLATELETS

What are platelets?

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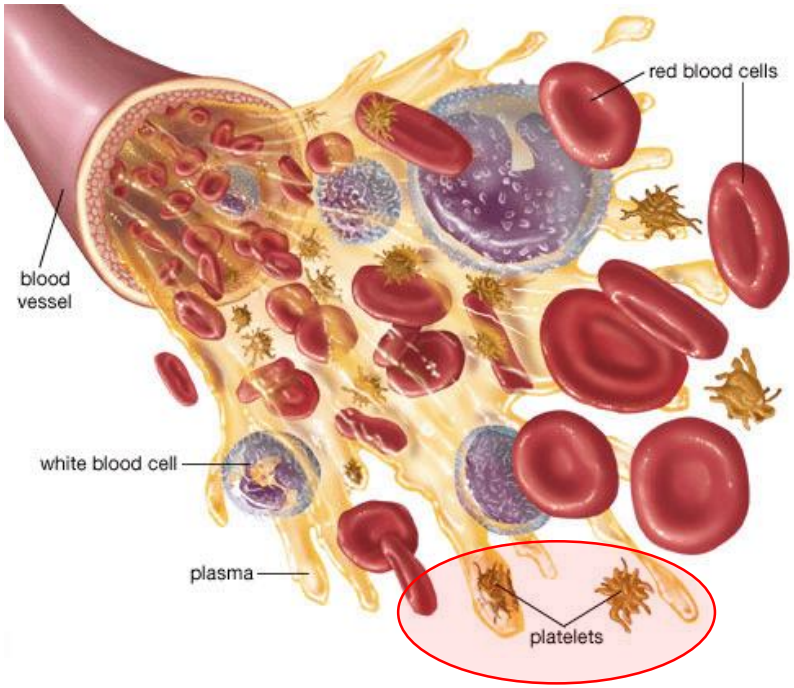
April 23, 2016



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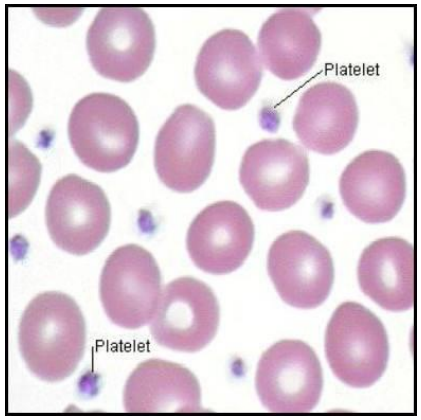
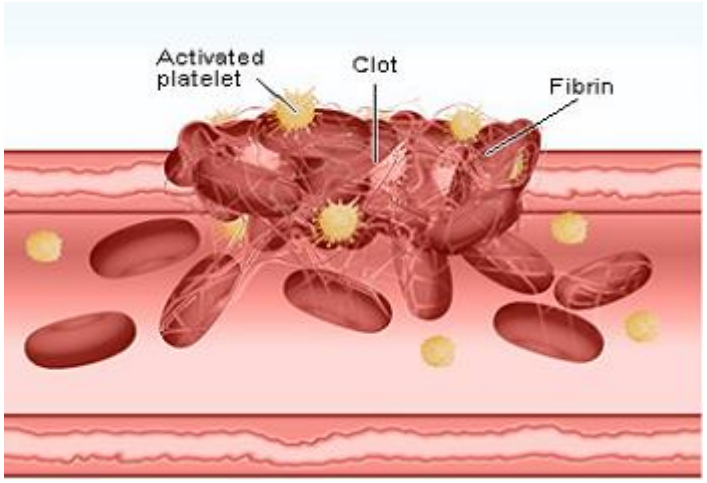
BLOOD

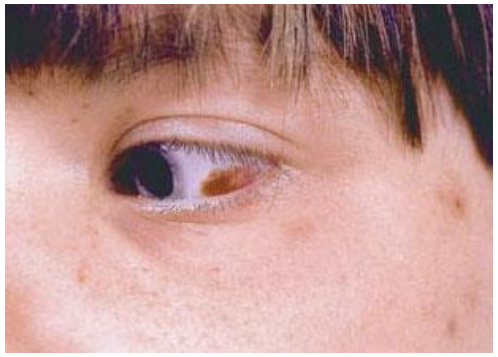
Platelets are also called thrombocytes





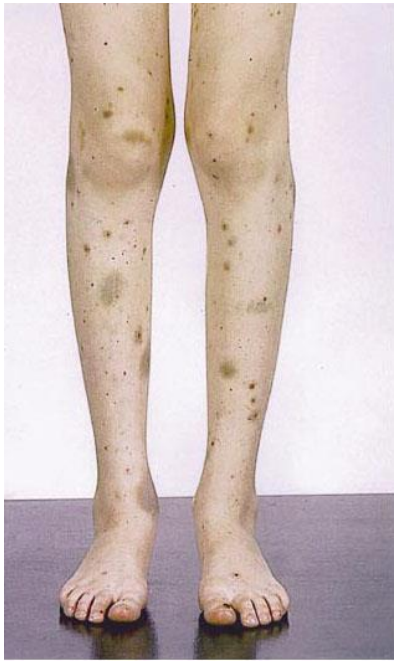
PLATELETS

Function to form a clot along with clotting factors



LOW PLATELETS

Low platelets lead to easy bleeding and bruising



WHERE DO ALL THESE BLOOD CELLS COME FROM?

The factory..

34 BONE MARROW

Where do all of our blood cells come from?

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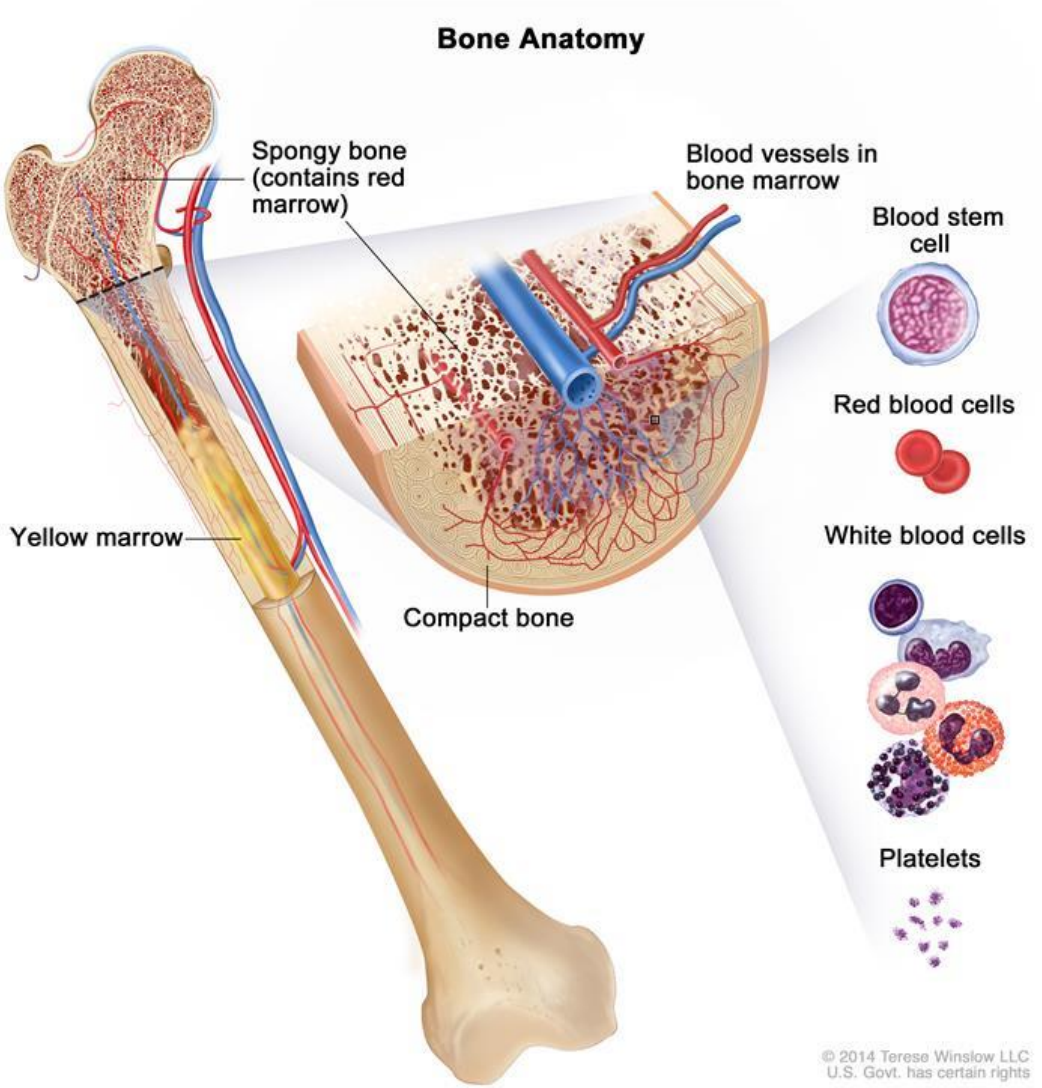
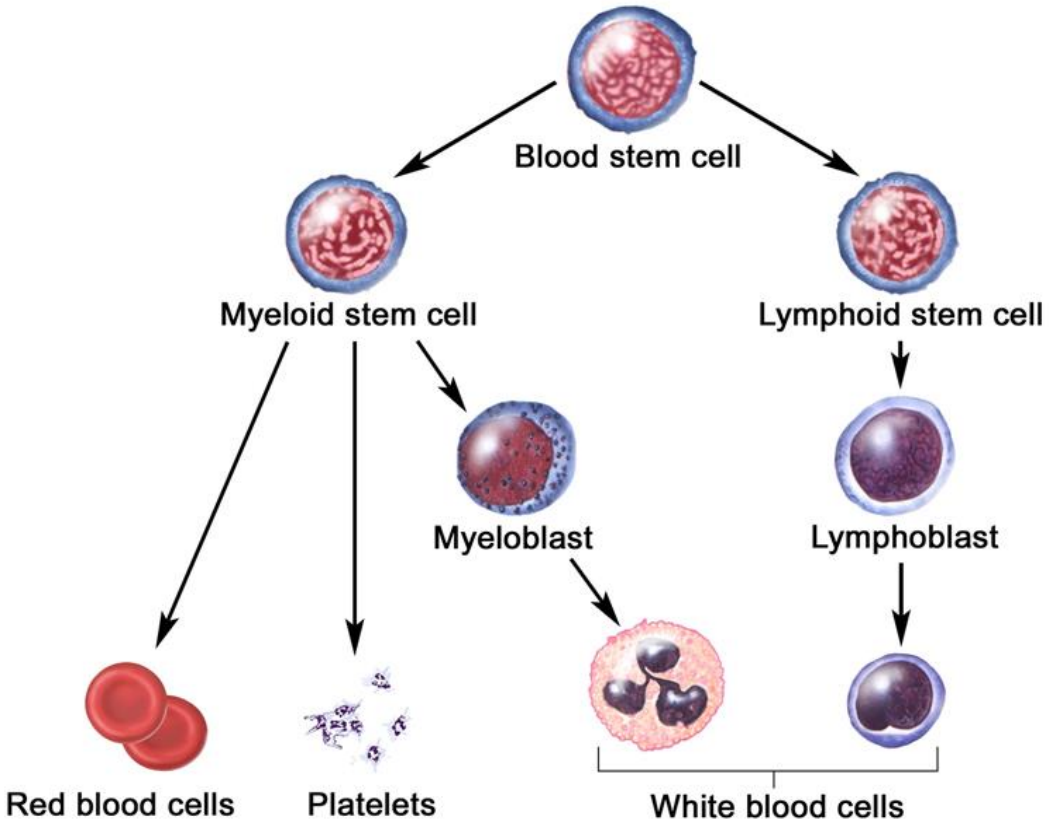


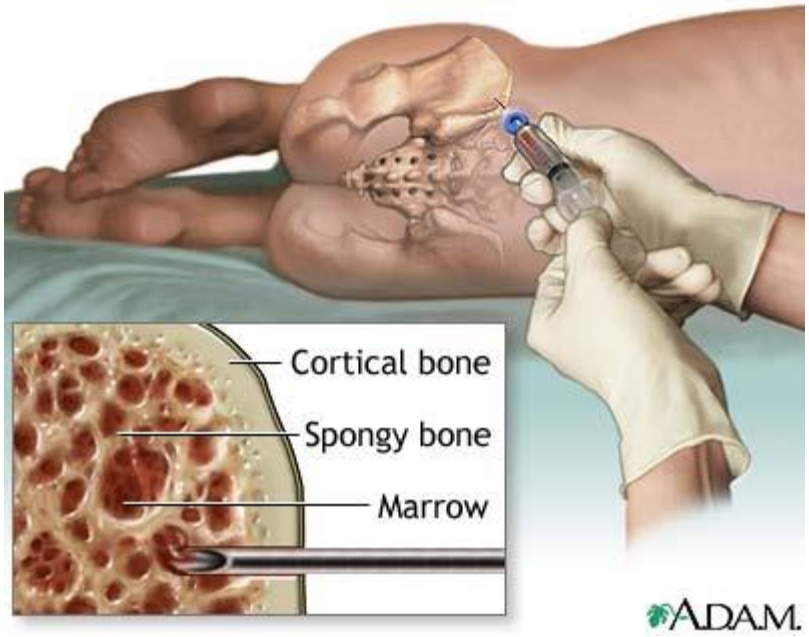
BONE MARROW

This is the factory that makes all of our blood cells..



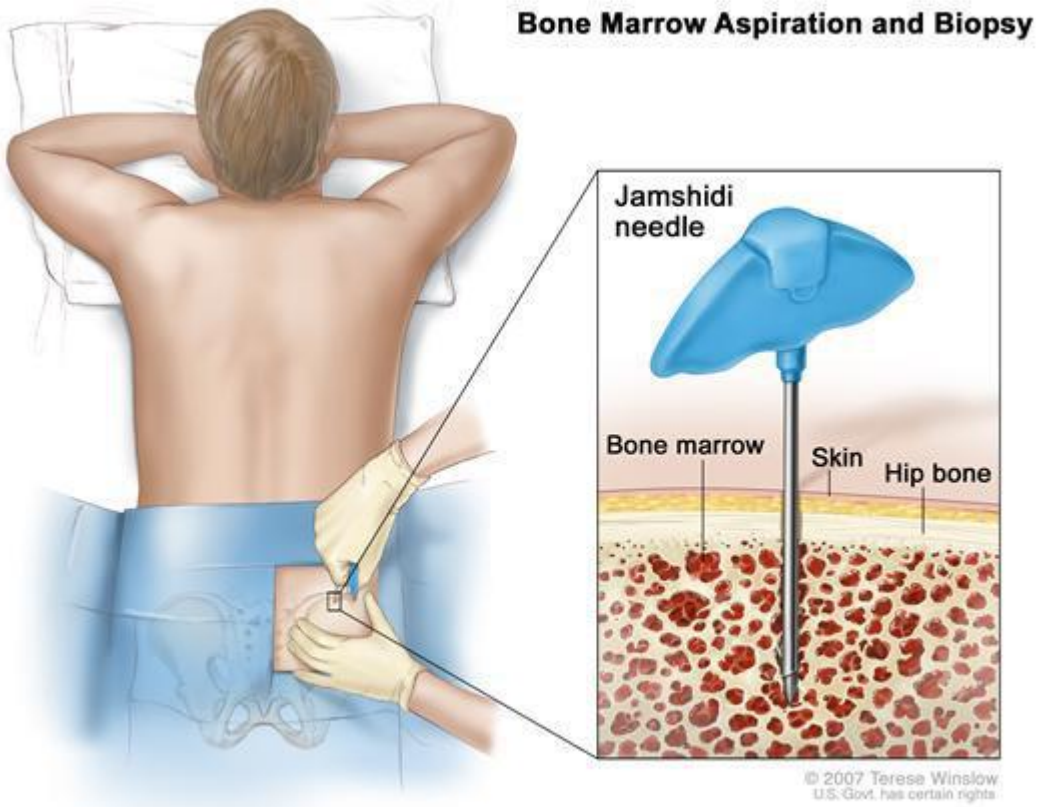
THE STEM CELL

In the bone marrow factory, all of our blood cells come from a stem cell. Stem cells divide and grow and eventually become these different blood cells.



BONE MARROW

This is how we take a bone marrow sample..



BONE MARROW

This is how we take a bone marrow sample..

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LET'S TALK MDS

What is MDS?

MYELODYSPLASTIC SYNDROMES

- Definition
  - Myelodysplastic syndromes (MDS) form a group of clonal hematopoietic stem cell malignancies characterized by ineffective hematopoiesis in one or more cell lineages, associated peripheral cytopenias, and risk of transformation to acute myeloid leukemia

Sloand EM. Myelodysplastic syndromes: introduction. Semin Hematolo. 2008;45:1-2. Valent P, Horny HP, Bennett JM, et al. Leuk Res 2007;31:72-36.

Dr. Robert Barr and the Ford Pinto

MYELODYSPLASTIC SYNDROMES

- In other words..
  - MDS is a group of blood and bone marrow disorders (cancers) where the blood cells are made with defects and don't survive as long as it should.
  - This leads to low blood counts in 1 or more of the blood cells.
  - It is NOT leukemia, but can be considered pre-leukemic.
  - It is NOT 1 disease and behaves differently in different people.

HOW COMMON IS MDS?

- Actual incidence very difficult to determine
  - Approx 3-4 per 100,000, much more common in elderly, approx 1 in 1000
  - Median age at diagnosis 65 – 70 years

World Health Organization Classification of Tumours. Pathology & Genetics: Tumours of Haematopoietic and Lymphoid Tissues. Edited by Elaine S. Jaffe, Nacy Lee Harris, Harald Stein, James W. Vardiman. IARC Press Lyon 2001. Silverman, LR. Modulation of the Clone: Altering the Course of Myelodysplastic Syndrome. Blood & Bone Marrow Transplantation Reviews 2006; 16(3):5-8.

WHAT CAUSES MDS?

- Causes?
  - idiopathic (meaning we don't know)
  - can be secondary to toxic exposures such as chemotherapy, radiation, environmental toxins
  - may be associated with some hereditary disorders but MDS is NOT hereditary

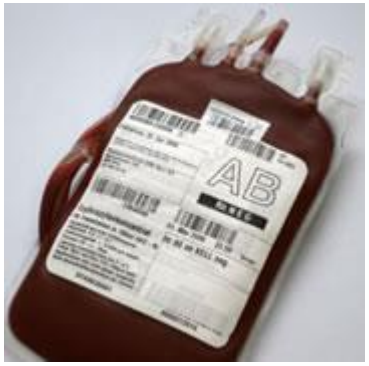
World Health Organization Classification of Tumours. Pathology & Genetics: Tumours of Haematopoietic and Lymphoid Tissues. Edited by Elaine S. Jaffe, Nacy Lee Harris, Harald Stein, James W. Vardiman. IARC Press Lyon 2001. Silverman, LR. Modulation of the Clone: Altering the Course of Myelodysplastic Syndrome. Blood & Bone Marrow Transplantation Reviews 2006; 16(3):5-8.

IMPACT OF MDS

- Patient
  - Poor quality of life - time and commitment to transfusions
  - Complications of Iron Overload
  - Cardiorespiratory symptoms
  - Hospitalizations for cardiac complications, infections, bleeding, increased risk of leukemic transformation
  - Increased risk of shorter survival
- Society
  - Transfusion burden
  - Hospitalizations for cardiac complications, infections, complications of iron overload, bleeding, leukemia

MANAGEMENT FOR MDS PATIENTS

- The mainstay of management is supportive
- Transfusions, antibiotics
  - No specific transfusion threshold, rather patient dependent based on level of hemoglobin associated with symptoms of anemia



Steensma DP and Bennett JM. The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

MANAGEMENT FOR SELECT MDS PATIENTS

- There are medications that may be useful in select MDS patients
- Erythropoietin (EPO)
  - A growth hormone that stimulates red blood cell production
- Iron chelation therapy
  - Medication to help remove excess iron if there is too much
- Revlimid (lenalidomide)
  - Useful for individuals with the 5q deletion
- Vidaza (azacytidine)
  - A medication for patients considered to be in the "higher" risk category

Steensma DP and Bennett JM. The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

MANAGEMENT: WHAT ABOUT TRANSPLANT?

- A bone marrow (or stem cell) transplant
  - High risk
  - Reserved for the "younger" patient (age <= 50-55) with severe disease

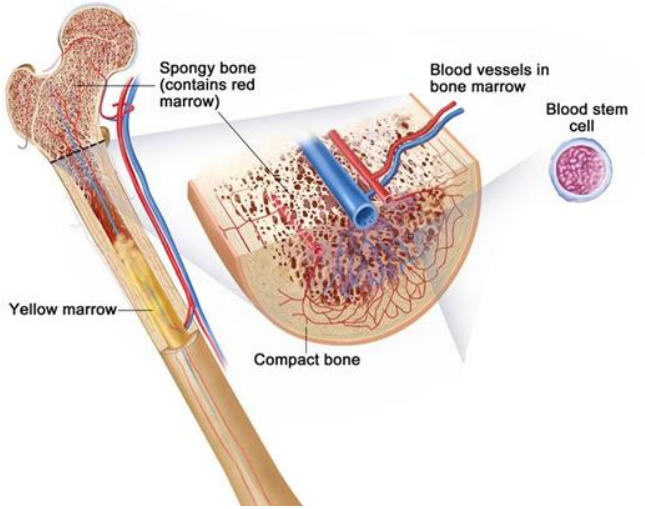
Steensma DP and Bennett JM. The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

MANAGEMENT: HOW DO WE SELECT TREATMENT?

- It depends on the type of MDS you have and how fit you are
- Lower risk MDS
  - Transfusions and other supportive care
  - Erythropoietin (EPO) – if your body is not producing enough
  - Iron chelation therapy – if you have too much iron from transfusions
  - Revlimid (lenalidomide) – if you have the 5q deletion
- Higher risk MDS
  - Transfusions and other supportive care
  - Stem Cell Transplant - Reserved for the "younger" patient (age <= 50-55) with severe disease
  - Vidaza (azacytidine) – For patients who can come to the cancer centre 7 days every 28 days

Steensma DP and Bennett JM. The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

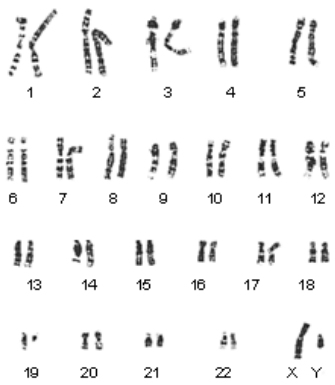
IPSS – International Prognostic Staging System



1) Number of blasts

2) Number of cells low

Event	Result	Ref. Range	Status
LKC	L 0.9	(4.0 - 10.0)	
ERC	L 2.87	(4.50 - 6.50)	
Hemoglobin	L 83	(135 - 170)	
HCT	L 0.25	(0.40 - 0.51)	
MCV	86.2	(79.0 - 97.0)	
RDW	14.1	(12.0 - 15.0)	
MPV	9.8	(7.1 - 11.1)	
Thrombocytes	* C	(150 - 400)	

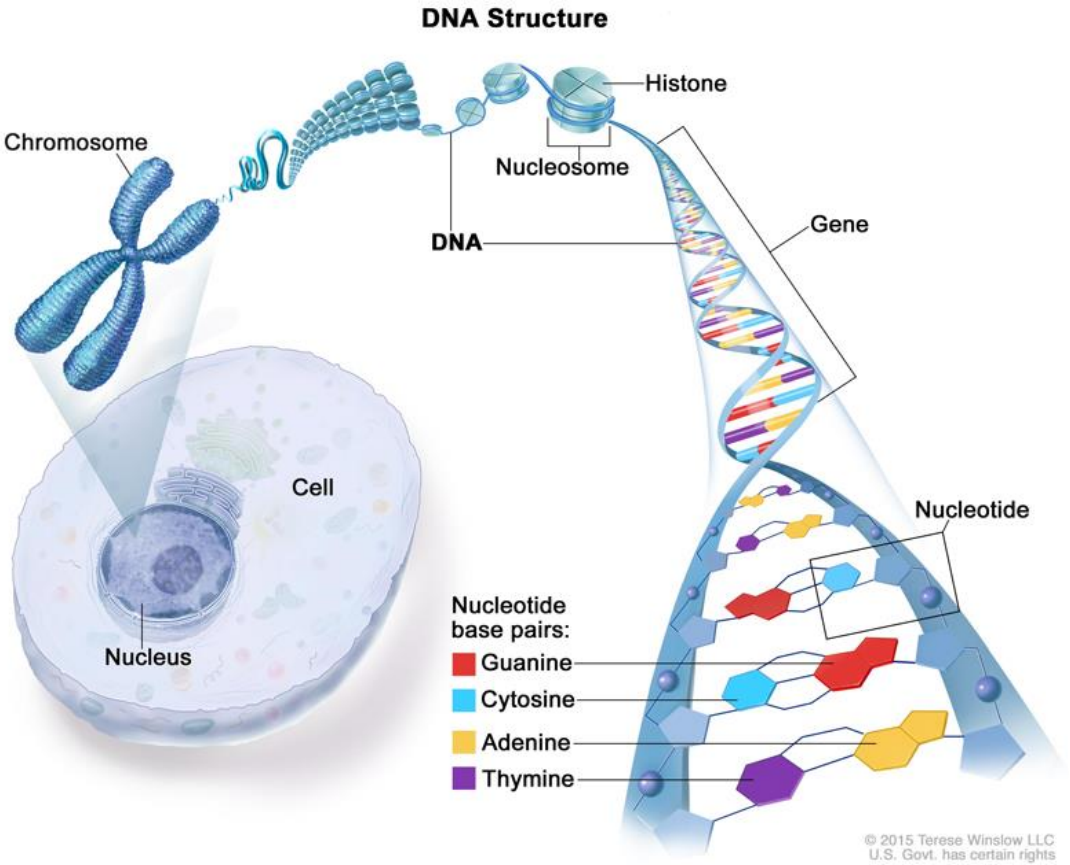


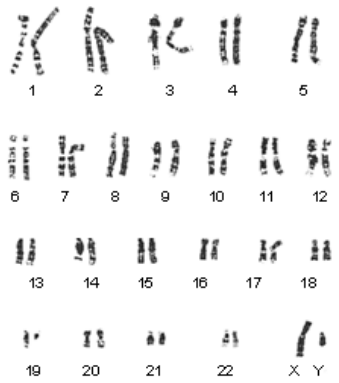
3) Cytogenetics

MDS RISK SCORE

How do we determine what type of MDS you have?

Most often use a scoring system called the IPSS: It is based on 3 factors – the number of blasts in the bone marrow, the number of blood counts that are low and the cytogenetics.



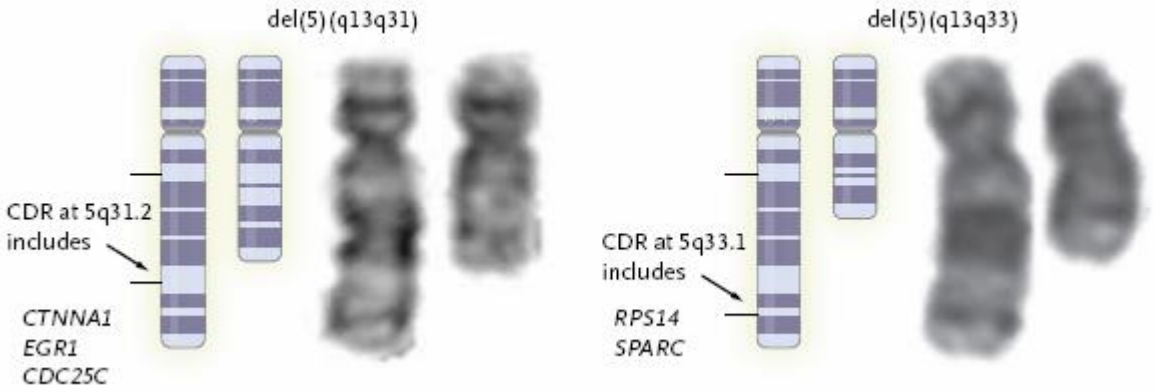


CYTOGENETICS

Each cell contains genetic material packaged in chromosomes.

Normally, we have 23 pairs of chromosomes.

We can tell if there are any abnormalities in these chromosomes.



CYTOGENETICS

This is an example of a cytogenetic abnormality.

The 5q deletion is found in some patients with MDS and they may respond to Revlimid (lenalidomide).

Tefferi A, Vardiman JW. Myelodysplastic syndromes. N Engl J Med. 2009 Nov 5;361(19):1872-85.

IPSS – International Prognostic Staging System

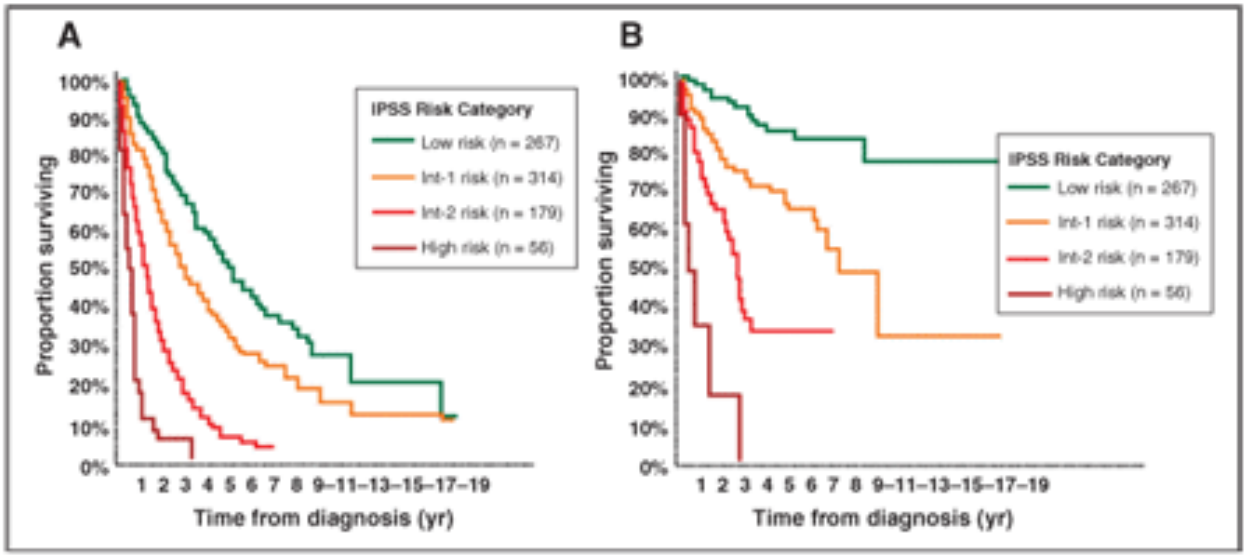


Figure 1: IPSS Category and Outcome—(A) Kaplan-Meier analysis of overall survival (n = 816) and **(B)** time until acute myeloid leukemia (AML) progression (n = 759) for patients with de novo myelodysplastic syndrome, according to risk category as determined by the 1997 International Prognostic Scoring System (IPSS, see Tables 1 and 2). Int = intermediate. Figures redrawn and modified from Greenberg et al.[10]

MDS RISK SCORE

How do we determine what type of MDS you have?

Most often use a scoring system called the IPSS: It is based on 3 factors – the number of blasts in the bone marrow, the number of blood counts that are low and the cytogenetics.

MANAGEMENT: HOW DO WE SELECT TREATMENT?

- It depends on the type of MDS you have and how fit you are
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MANAGEMENT: FOLLOW-UP

- How will you be followed?
  - Patients with MDS should be followed by a Hematologist or a Hematogist/Oncologist.
  - Depending on the severity of your disease and the treatments you have received or are receiving, your Hematologist will determine how frequently to see you.
  - You will have a face-to-face clinic visit with your Hematologist and typically have bloodwork done regularly
  - Occasionally, you may require a bone marrow aspirate and biopsy

Steensma DP and Bennett JM. The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

MANAGEMENT: FOLLOW-UP

- **Looking for support?**
  - Seek out support from family, friends, your doctor(s), nurse(s), social worker, and Support Groups

Aplastic Anemia & Myelodysplasia Association of Canada

Steensma DP and Bennett JM. The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

MANAGEMENT: NEW THERAPIES?

- Other genetic modifying drugs
  - Vidaza (azacytidine) is the first of the available drugs
  - Dacogen (decitabine) – may be similar to azacytidine
  - Vorinostat – may also modify MDS genetics
- Targetted therapies
  - Understanding the genetics of MDS is leading to a number of potential targeted drugs all still in development
- Drugs that boost blood cells
  - Romiplostim or Eltrombopag – stimulate platelet production
- Potential cure?

Steensma DP and Bennett JM. The Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2006;81(1):104-130.

SUMMARY

- Blood is made up of white blood cells, red blood cells, and platelets in a fluid called plasma
- The laboratory tests – complete blood count (CBC) and white cell differential give us information about these cells
- These laboratory tests help you and your doctors diagnose diseases, assess how severe it is, when to transfuse, and to follow your disease
- Myelodysplastic syndromes (MDS) are a group of different types of blood and/or bone marrow disorders (cancers)
- Transfusions are the mainstay of treatment/management in most patients with MDS
- Medication therapies in MDS are tailored to the type of disease that a patient has

Bone marrow factory - The future