

# **Myelodysplastic Syndrome (MDS) Basics: What is it? Who gets it? What are the subtypes?**

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UNIVERSITY OF MINNESOTA

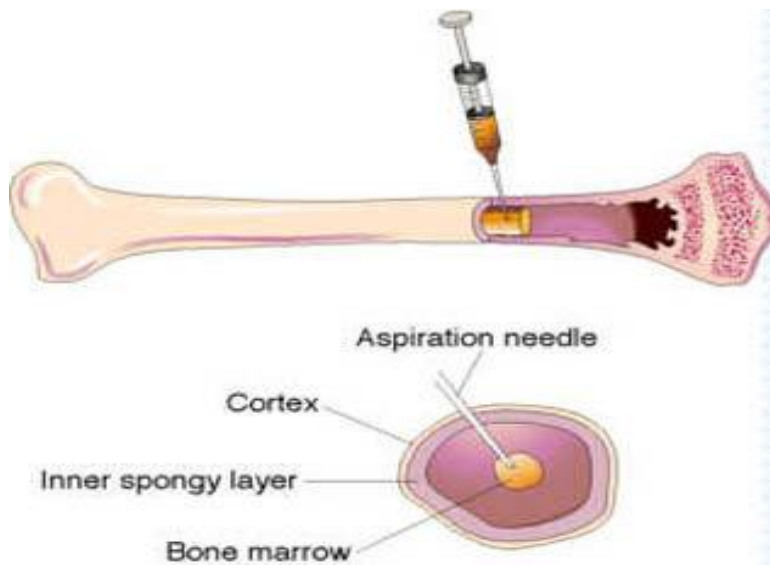
**Driven to Discover<sup>SM</sup>**

**No Disclosures.**

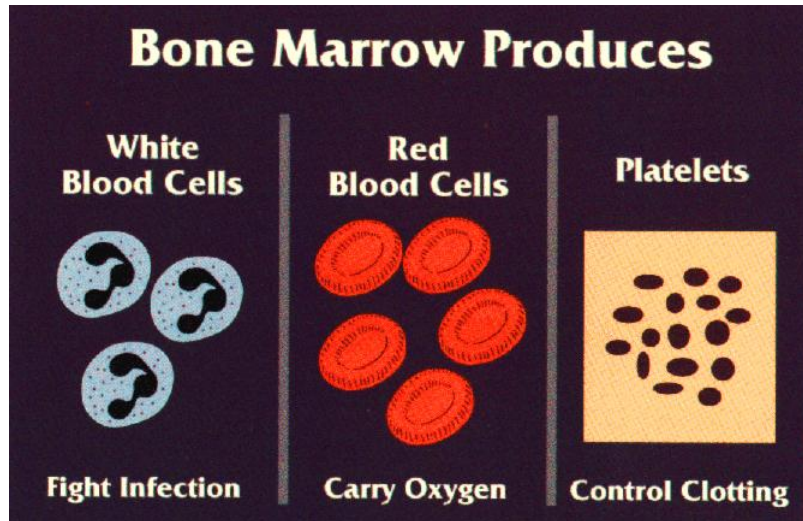
## Overview

- **Bone marrow and blood**
- **What is myelodysplastic syndrome(s)?**
- **Briefly give overview of classification systems for MDS and what this means for treatment approaches**
- **What is currently known about MDS patterns in the United States and why do we think people develop MDS?**
- **Discuss new large study of MDS to help answer questions**

## What is bone marrow?



## What does bone marrow do?



## What is MDS?

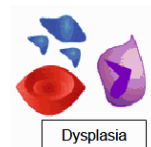
- **MDS** represent a group of blood diseases that can have differences in initial symptoms and treatment approaches
- The hallmark of MDS is a **low** blood cell count (red blood cells, white blood cells, or platelets) in the presence of dysfunctional bone marrow.
- The marrow keeps trying to make more cells to compensate for low counts in the blood. For some reason, many cells die before they make it into the blood stream...



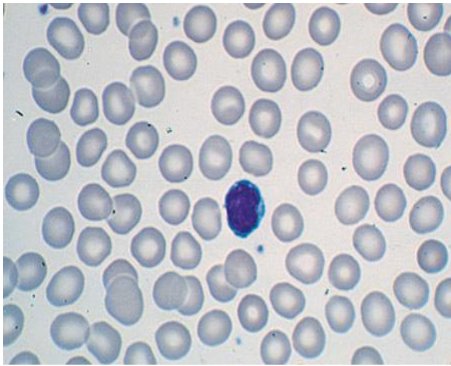
## MDS Summary

**All people with MDS have 2 things in common:**

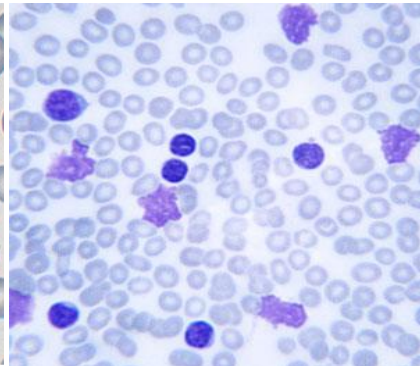
- **Low blood cell count for at least 1 blood cell type such as red blood cells, white blood cells, or platelets (low cell count is called cytopenia)**
- **Blood cells in bone marrow and blood have an abnormal shape, size or look (dysplasia) and are immature (blasts)**



Normal blood smear



MDS blood smear



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~ 33% of MDS patients can develop acute myeloid leukemia

## Blasts are not fun –

**Blasts are very immature cells - People with MDS may have too many blasts in their bone marrow**

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- **Lower-risk MDS** → **≤ 5% wbc in marrow are blasts**
- **Higher-risk MDS** → **5-19% wbc in marrow are blasts**
- **AML** → **20% or more wbc are blasts**

## How is MDS classified?

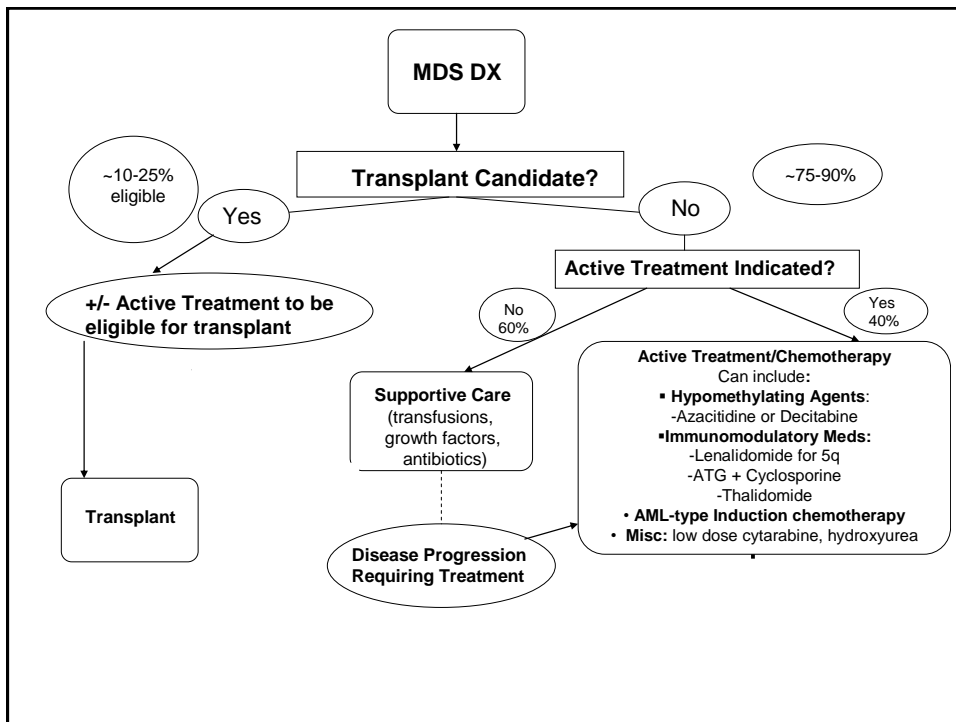
### MDS classification-many subtypes

French-American-British	World Health Organization	International Classification for Diseases-Oncology-3 (ICDO3 codes) (used by SEER)
Refractory anemia (RA)	RA	9980 (RA)
RA with sideroblasts (RARS)	RARS	9982 (RARS)
RA with excess blasts (RAEB)	Refractory cytopenia with multilineage dysplasia (RCMD)	9983 (RAEB, RAEB-1, RAEB-2)
RA with excess blasts in transformation (RAEB-T)	RCMD with ringed sideroblasts (RCMD-RS)	9984 (RAEB-T)
Chronic myelomonocytic leukemia (CMML), WBC <12,000	RAEB-1	9985 (RCMD)
	RAEB-2	9986 MDS + 5q deletion
	MDS with isolated 5q deletion	9987 therapy-related MDS
	MDS NOS	9989 (MDS NOS)

## Further Classification: WPSS versus IPSS

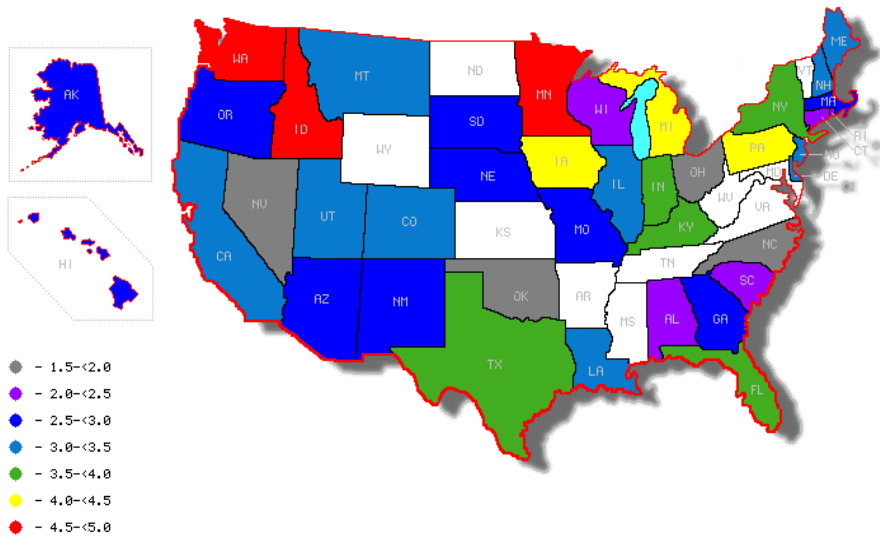
WPSS variable	Variable Score				Risk Group	Total Score	
	0	1	2	3			
WHO category	RA/RARS/5q-	RCMD/RCMD-RS	RAEB-1	RAEB-2	Very low	0	
Cytogenetic Risk	Good	Intermediate	Poor		Low	1	
Transfusion Requirement	No	Yes			Intermediate	2	
					High	3 – 4	
					Very high	5 – 6	
IPSS variable	Variable Score					Risk Group	Total Score
	0	0.5	1	1.5	2.0		
Bone marrow blast (%)	<5	5-10	-	11-20	21-30	Low	0
Cytogenetic risk	Good	Intermediate	Poor			Intermediate-1	0.5 – 1
Cytopenia*	0/1	2/3				Intermediate-2	1.5 – 2
						High	2.5–3.5

\*Hemoglobin <10 g/dL, neutrophils < 1500/μl, platelets < 100,000/μ



# MDS in the United States

## MDS Incidence Rates



Derived from Rollison DE et al, Cancer 112; 45-52, 2008

## **Incidence**

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- **First reportable as 'cancer' in 2001**
- **More than 10,000 cases per year (similar to glioma, a brain tumor)**
- **Incidence rate 3.3/100,000; varies by geography**
- **White > Hispanic > Black > Asian**
- **Male > female (60%)**
- **Median age of 76 years (most cases over 60)**

## **Epidemiology: Risk Factors**

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- **Cause is unknown in >80% of patients**
- **Prior exposure to chemotherapy and/or radiation**
- **Advancing age**
- **Congenital diseases (Fanconi anemia, congenital neutropenia, rare, familial MDS)**
- **? Environmental toxins**

## **MDS Risk Factors**

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<b>Risk Factor</b>	<b>Evidence</b>
Increasing Age	++++
Male Gender	++++
Chemotherapy Agents/XRT	++++
Benzene/Solvents	+++
Smoking	++
Pesticides/Herbicides/Fertilizers	++
Ionizing Radiation	+

Slide Courtesy of S. Strom, MD Anderson  
Cancer Center

**Sometimes MDS ---→ AML**

**Can we learn from studies  
of AML as well?**

# Risk Factors for Adult Myeloid Leukemia

- **Benzene:** occupational exposures
- **Ionizing radiation:** radium workers, atomic bomb
- **Prior chemotherapy:** up to 5% of AML
- **Cigarette smoking:** modest but consistent
- **Others?**

## BMI and Leukemia

Meta-analysis: Larsson et al Int J Cancer 2008

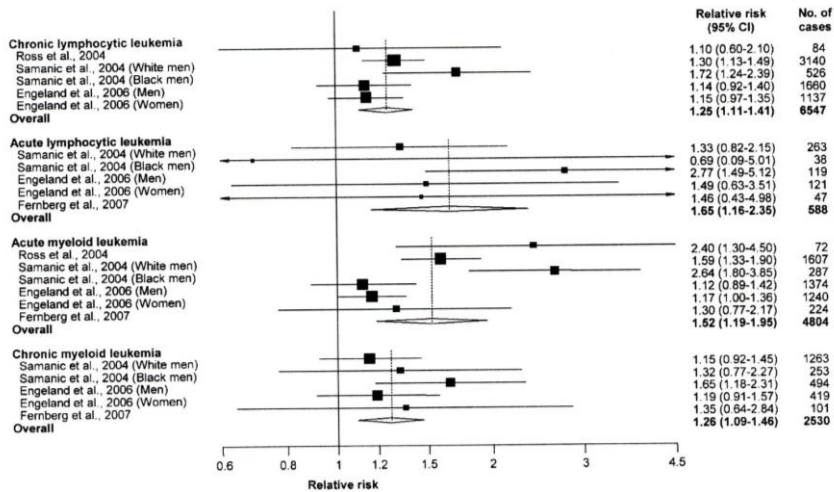


FIGURE 2 – Association of obesity with incidence of leukemia subtypes. Tests for heterogeneity: chronic lymphocytic leukemia,  $p = 0.21$ ,  $I^2 = 31.2\%$ ; acute lymphocytic leukemia,  $p = 0.37$ ,  $I^2 = 6.8\%$ ; acute myeloid leukemia,  $p < 0.001$ ,  $I^2 = 79.3\%$ ; chronic myeloid leukemia,  $p = 0.51$ ,  $I^2 = 0\%$ .

## **Non-steroidal anti-inflammatory drugs (NSAIDs) and malignancy**

- **Regular use of aspirin and other non-aspirin NSAIDs has been associated with a decreased risk of cancer of the colon.**
- **Recent reports also suggest a reduction in risk of esophageal, lung, pancreatic, and breast cancer.**

**Could aspirin or non-aspirin NSAID-use be associated with a reduction in risk of adult leukemia?**

## NSAIDs and Leukemia

The Iowa Women's Health Study  
(Kasum C et al, Cancer Epi Biom Prev 2003; 12:534-537)

FREQUENCY	MULTIVARIATE MODEL RR (95% CONFIDENCE INTERVAL)
<b>Aspirin-use</b>	
None	1.0 (reference)
<1-1 week	0.37 (0.21-0.66)
≥ 2 times/week	0.45 (0.27-0.75)
	p trend=0.002
<b>Non-asp NSAID-use</b>	
None	1.0 (reference)
<1-1 week	1.11 (0.62-2.00)
≥ 2 times/week	1.30 (0.77-2.21)
	p trend=0.33

**So... it seems reasonable  
to explore these other  
factors (body mass index,  
aspirin use) in a study of  
MDS**



**Adults in Minnesota with MDS  
Funded by the National Cancer Institute 2010-2014**

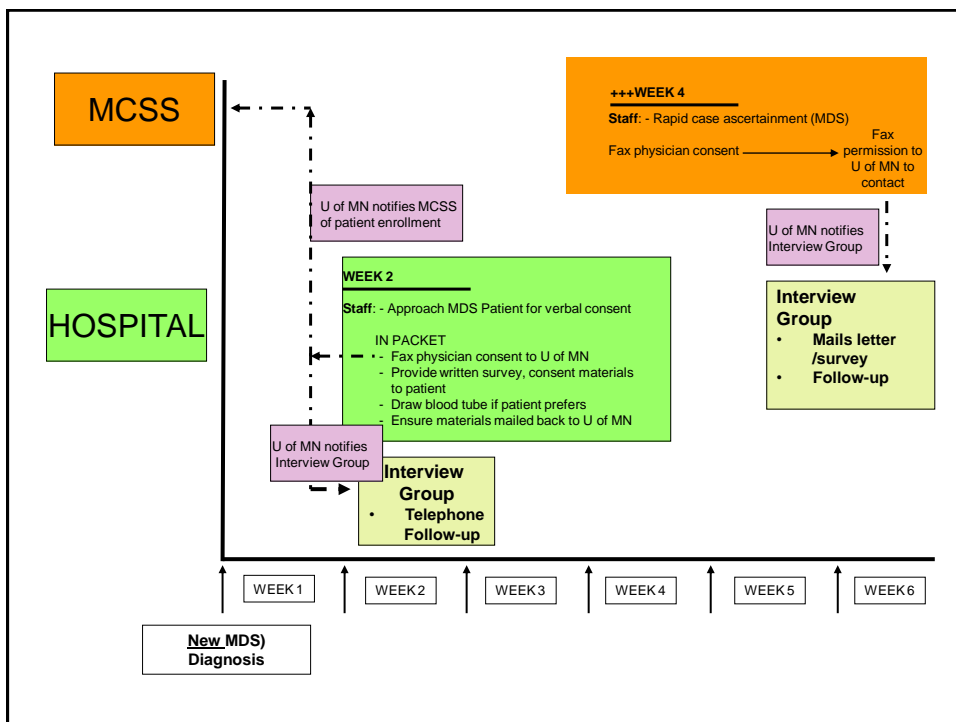
## **MDS study goals**

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- **Recruit ~700 cases and 700 controls over a 4 1/2 year period; aged 20-85 years**
- **Investigate risk factors for MDS in Minnesota by comparing to controls**
- **Are there risk factors more common in MDS that progress to AML?**
- **Examine genes that may contribute to the development of MDS**

# AIMMS Study

- **Self-administered survey (demographics, farming, NSAIDs, other lifestyle, family history)**
- **Saliva samples (or blood sample if patients prefer)**
- **Medical/pathology records from the time of diagnosis**
- **Slide specimen for pathology review**

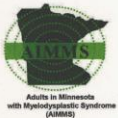


# AIMMS Study

## Case-control study in Minnesota

- Investigate the role of NSAIDs
- Examine smoking, farming practices and related exposures
- Investigate obesity
- Explore genes involved in metabolism of above

**LETTERS TO THE SUPER MINNESOTA**



Adults in Minnesota with Myelodysplastic Syndrome (AIMMS)

Dear Fellow Minnesotan,


Thank you for taking part in the Minnesota study being done by researchers at the University of Minnesota Masonic Cancer Center, Mayo Clinic, Minnesota Department of Health, and several local area hospitals. The purpose of this study is to identify environmental and genetic factors related to the development of a leukemia-like blood disorder called myelodysplastic syndrome (MDS) in adults.

The study includes two parts: (1) filling out this survey and (2) giving us a sample of saliva. You may choose to fill out the survey and not give us a saliva sample. This survey asks for general information about you as well as information about your personal habits, such as smoking and alcohol use, medical history, and environmental and chemical exposures you may have had on the job or in your everyday life. It will take about twenty minutes to fill out. Please answer every question as best you can. If you do not know the answer to a question, please provide your best guess.

In order to obtain the most valid information possible, it is important that this survey is answered by the person it was given or addressed to. If that person is not able to fill in the survey, he/she can call us to take the survey over the telephone. To set up a time to take the survey over the telephone, please call the interviewers at the University of Minnesota at (612) 625-3910. If you are calling long distance, please call our toll-free number at 1-866-434-9879.

If you have any other questions as you fill out this survey, please call us at the same numbers; (612) 625-3910 for local calls, 1-866-434-9879 for long distance calls.

Warm regards,



Julie A. Ross, Ph.D.  
Professor  
University of Minnesota

**AIMMS Study  
Future Contact**

*To maintain your confidentiality, this page will be stored separately from your responses to the survey.*

A. How was the survey completed?

1  I filled it out myself

2  Someone helped me fill it out

3  Spouse

4  Child

5  Other, please specify: \_\_\_\_\_

B. What is your date of birth?

Month Day Year

C. To thank you for filling out this survey, we would like to send you a \$10 gift card. Please select your favorite:

1  Target

2  Cub Foods

3  Cenex: Please name location (town): \_\_\_\_\_

4  Dairy Queen

D. Would you like to receive any updates or study results?

1  No

2  Yes

E. We would like to know if it would be okay to contact you in the future to see if you have learned anything more about your family health history and to update our records. This would be in the next year or so. Would this be okay?

1  No

2  Yes

**Please turn to the next page.**

**Medical History**

31. Not including the past two years, did you regularly take any of the following medications?  
(Do not include occasional use of less than once per month)

Medication	Average days per month used	On days used, number of pills taken	Total number of years taken
<p>a. <b>Aspirin</b> (regular or extra strength, 163 mg or more, e.g., Bufferin, Anacin, Bayer, Excedrin, Ecotrin, etc.)</p> <p>1 <input type="checkbox"/> No                  2 <input type="checkbox"/> Yes                  3 <input type="checkbox"/> Not sure</p>	<p>□□ days per month</p>	<p>□□ number of pills</p>	<p>□□ years</p>
<p>What was your main reason for using this? _____</p>			
<p>b. <b>Aspirin</b> (baby or low dose, 162 mg or less)</p> <p>1 <input type="checkbox"/> No                  2 <input type="checkbox"/> Yes                  3 <input type="checkbox"/> Not sure</p>	<p>□□ days per month</p>	<p>□□ number of pills</p>	<p>□□ years</p>
<p>What was your main reason for using this? _____</p>			
<p>c. <b>Ibuprofen</b> (e.g., Motrin, Advil, Nuprin, Mediprin, etc.)</p> <p>1 <input type="checkbox"/> No                  2 <input type="checkbox"/> Yes                  3 <input type="checkbox"/> Not sure</p>	<p>□□ days per month</p>	<p>□□ number of pills</p>	<p>□□ years</p>
<p>What was your main reason for using this? _____</p>			

## Acknowledgements

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**U of Minnesota**

**Michelle Roesler  
 Colleen Geary Carter  
 Cindy Blair, Ph.D.  
 Arlene Wellemeyer  
 Betsy Hirsch, Ph.D.  
 Erica Warlick, M.D.  
 Adina Cioc, M.D.**

**MCSS**

**Sally Bushouse, Ph.D.  
 John Soler, MPH**

**All of the participating  
 hospitals and clinics**

**Mayo Clinic**

**Jim Cerhan, M.D., Ph.D.  
 Phuong Nguyen, M.D., Ph.D.  
 Mark Litzow, M.D.**