

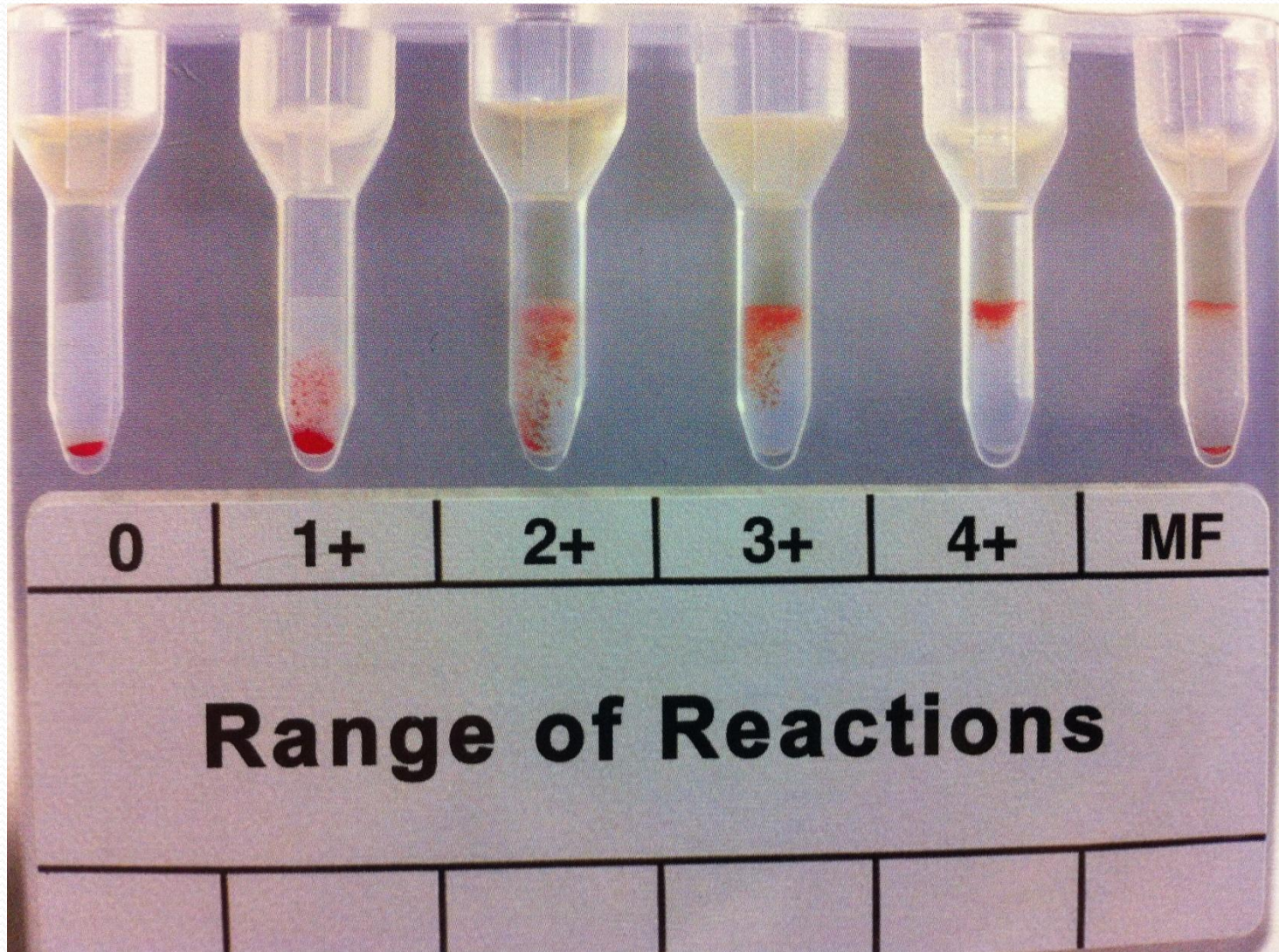
“D”Winding Rh Type

A Case Study Involving Weakening of D Antigen in
Malignancy

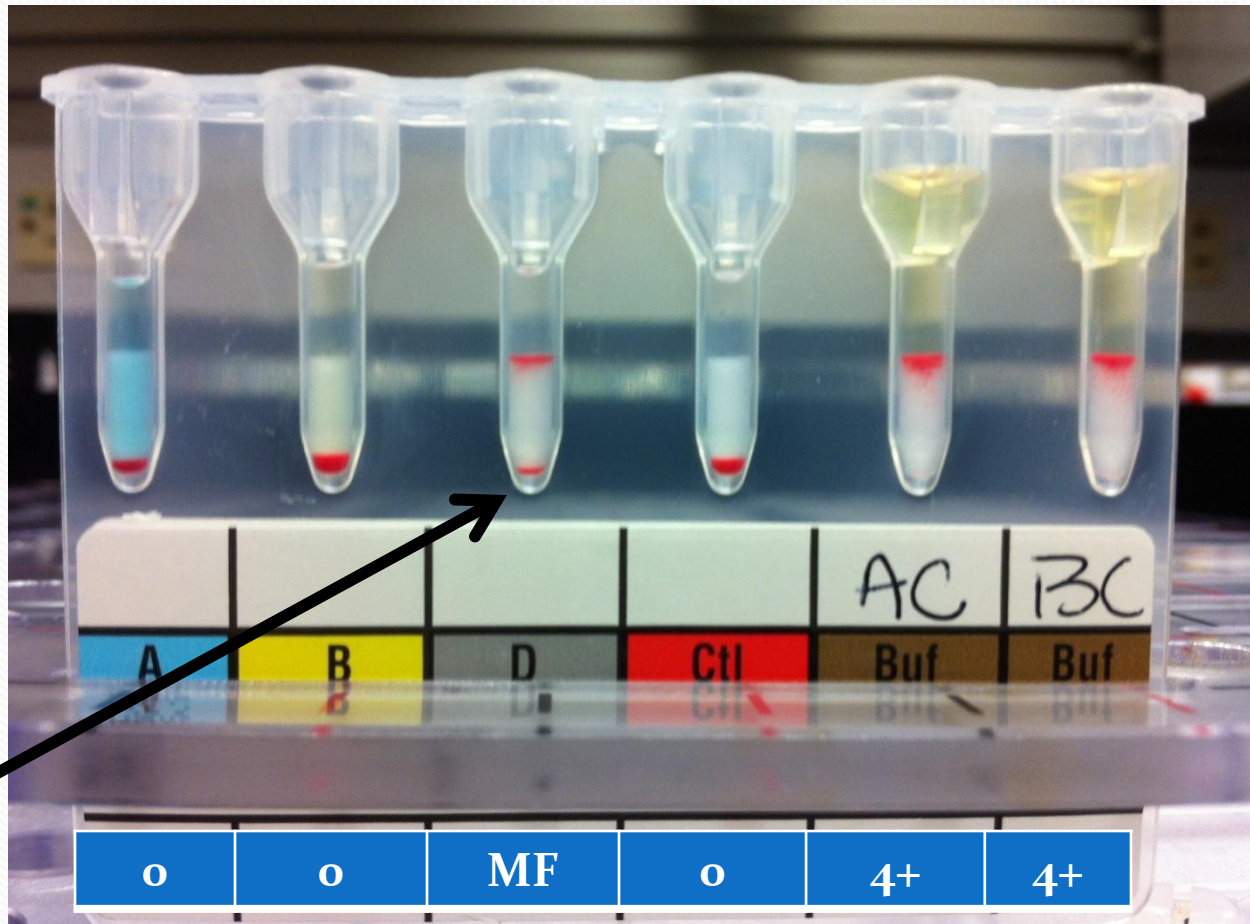
July 11, 2012

- Blood bank received an order to Type and Crossmatch 2 units for LL, an 82 year old female Oncology patient.
- Patient's Hemoglobin was 6.2 gm/dL
- Prior history check
 - O Positive and no alloantibodies detected
 - Last RBC transfusion at LMH on May 5, 2010
 - Received 27 units of RBCs between Dec 2006 and May of 2010

Gel Technology Reactions



LL's ABO/Rh by gel testing



Mixed field D Reaction

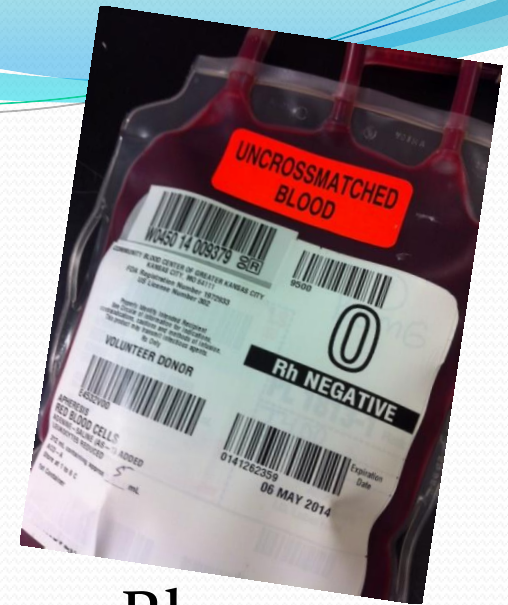
What's with that?



Trouble Shooting Mixed Field Reactions

- Recent Transfusions
- Transplantation
- Fetomaternal Hemorrhage
- Twin or dispermic chimerism

Recent Transfusions



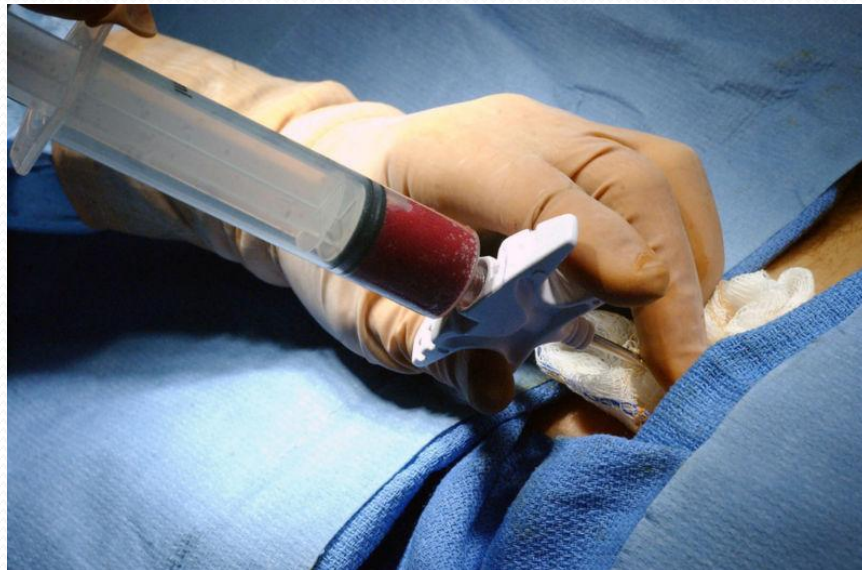
- Is this an O Negative patient who was given Rh Positive red blood cells in an emergency situation?

OR

- Is this an O Positive patient who has been given O Negative red blood cells?

Transplantation

- Has this patient had a bone marrow or stem cell transplant??
- Is the patient's Rh type changing to that of her donor?



Fetomaternal Hemorrhage

- Is this an OB patient who has experienced a large fetomaternal hemorrhage and her Rh type is mixed field due to contamination with baby's blood?



Twin or Dispermic Chimerism

- In dispermic chimeras, two eggs that have been fertilized by two sperm fuse together.
- Dispermic chimeras demonstrate a dual-cell population in disparate body tissues derived from different germ layers
- Chimerism in humans is a rare phenomenon usually identified at the time of blood group determination when mixed field agglutination on the cell typing is noted.



Investigation of LL's Rh type



- Oncology physician was called
- Patient had not been transfused at another facility
- Patient had not received a bone marrow or stem cell transplant
- Patient was 82 - fetomaternal hemorrhage ruled out
- Patient had previously demonstrated 4+ reactions with anti-D reagent

Investigation Continued

- Did this specimen belong to LL or another patient?
- Did the specimen somehow get contaminated ?
 - Redrawn specimen from LL demonstrated the same mixed field reaction
- If the reason for mixed field D reaction cannot be resolved, what type of blood do we give LL?
 - Crossmatched 2 units of O Negative



Article Reviews

- Red blood cell antigen changes in malignancy: case report and review

J.L. Winters and D. S. Howard

<http://www.redcross.org/cgi-bin/pubs/171sm.pdf>

- Loss of red cell A, B, and H antigen is frequent in myeloid malignancies

Tina Bianco, Belinda J. Farmer, Robert E. Sage, and Alexander Dobrovic

<http://bloodjournal.hematologylibrary.org/content/97/11/3633.full.html>



Changes in RBC Antigens with Malignancy

- Loss or diminished expression of RBC antigens have been reported to occur in a number of malignancies, both hematologic and solid
- For hematopoietic diseases, the loss predominantly results from a mutation within a stem cell that affects antigen production
- Some antigens reported to be altered by malignancy include, ABO, Rh, Lewis, Ii, MNSs, LW, Colton, Cromer, Cartwright, Dombrock, JMH, & Tn

Loss or Weakening of the D Antigen



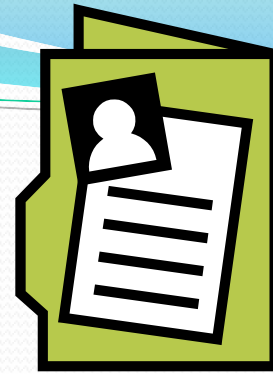
- Is the second most commonly reported change in blood group antigens after ABO
- Loss or weakening of other Rh system antigens including C and E have been reported. Frequently, this has occurred with concurrent loss or weakening of D.
- Patients present either with complete loss of selected Rh antigens or with development of a mixed population of antigen-positive and antigen-negative cells
- Thought to be a disruption or mutation of the RHD gene

Reported Cases



- In 3 reported cases of loss of the D antigen, chromosomal abnormalities involving either the entire chromosome 1²⁶ or the short arm of chromosome 1^{20,23} were seen on cytogenetic analysis
 - Chromosomal abnormalities are thought to be responsible for the loss of antigen expression through deletion or disruption of the RHD gene
- Another case involved sequencing of the RHD gene that revealed a single base pair deletion of the gene.

More Findings



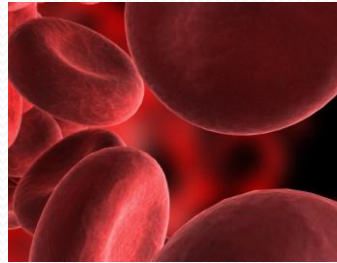
- One reported case was associated with development of anti-D. This patient suffered from myeloid metaplasia.
- Lost expression of the D antigen at age 37; had been typed as D+ at age 33
- Twenty years later, he was still found to be D- but had developed anti D as well as anti-C

And yet another case



- 48 year old Caucasian woman diagnosed with CML was being evaluated for a stem cell transplant
- Her twin sister was to be the donor and molecular studies revealed them to be identical twins
- ABO and Rh typing of the patient was A Negative while her sister typed as A Positive
- Additional testing was performed with new specimens and confirmed the previous ABO and Rh typings
- History obtained revealed the patient had been typed as Rh Positive at the birth of her child and also at four whole blood donations

- These antigen changes have been reported to mirror the course of the disease



- When a patient enters remission, their original Rh phenotype returns, whereas antigen negative cells reappear during relapse

D⁺

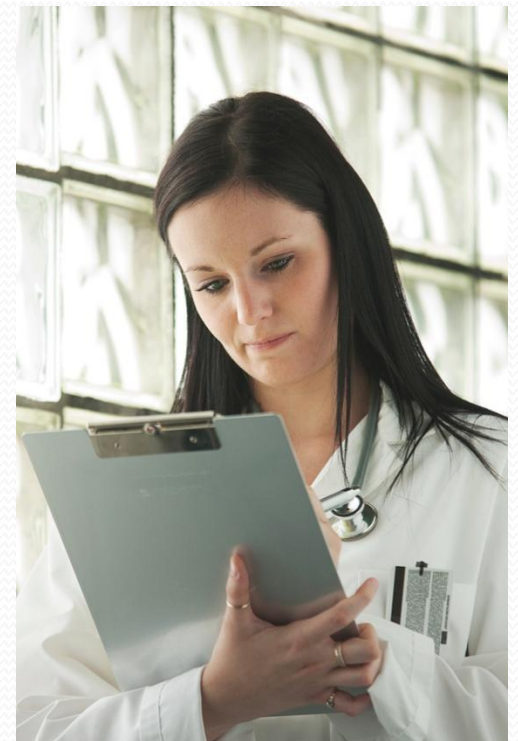
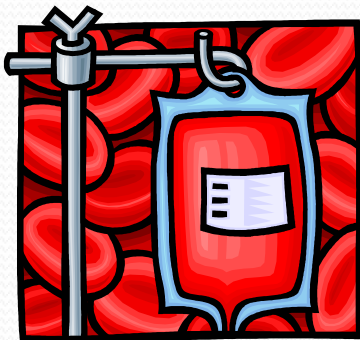


D⁻

Patient LL's Diagnosis

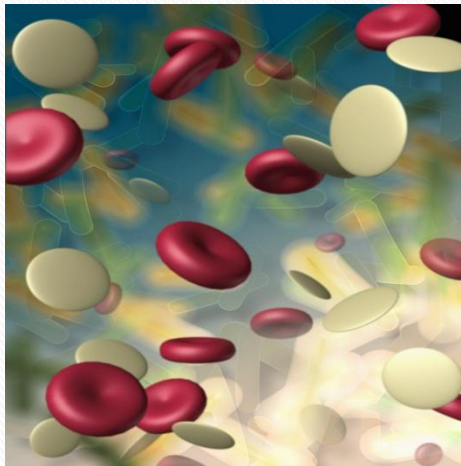
Myelodysplastic Syndrome (MDS) w/thrombocytosis

- Initial transfusion in December of 2006
 - Hemoglobin was 7.6
 - Platelets were 1,368,000



Myelodysplastic Syndromes (MDSs)

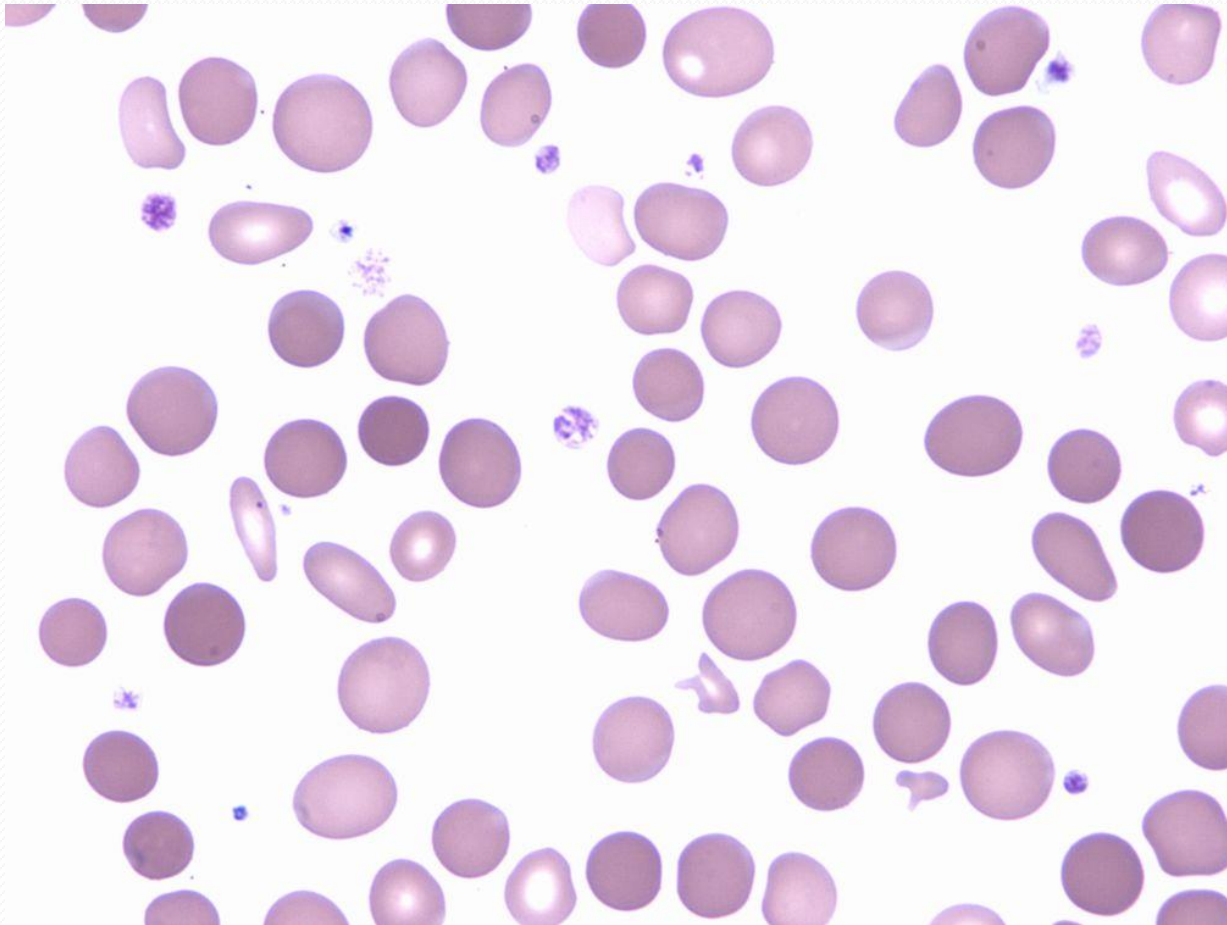
- MDSs are a group of acquired hematologic disorders characterized by progressive cytopenias in the peripheral blood. All are a result of proliferation of abnormal stem cells.
- The mutated stem cell produces a pathologic clone of cells that expands in size at the expense of normal cell production.

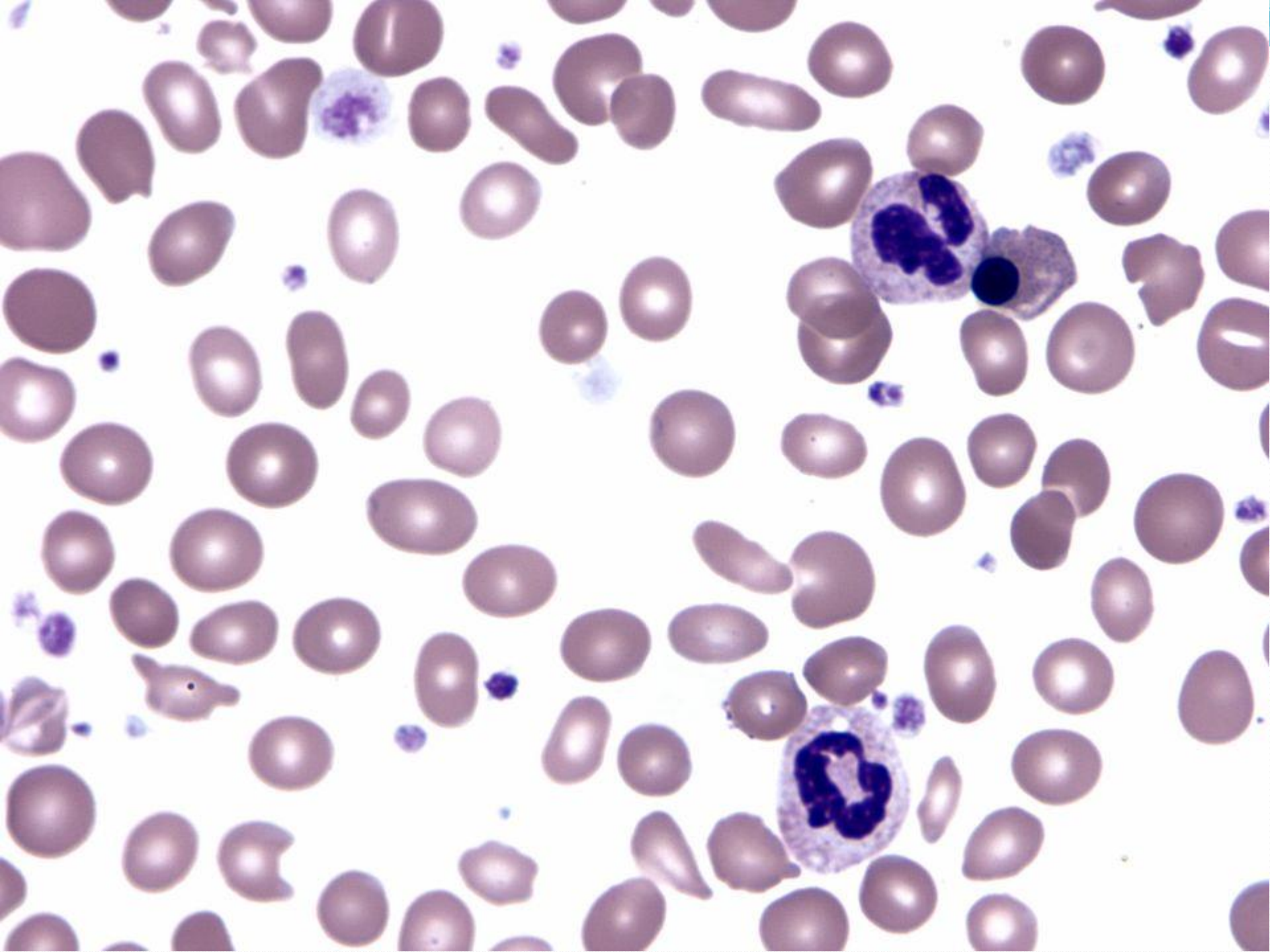


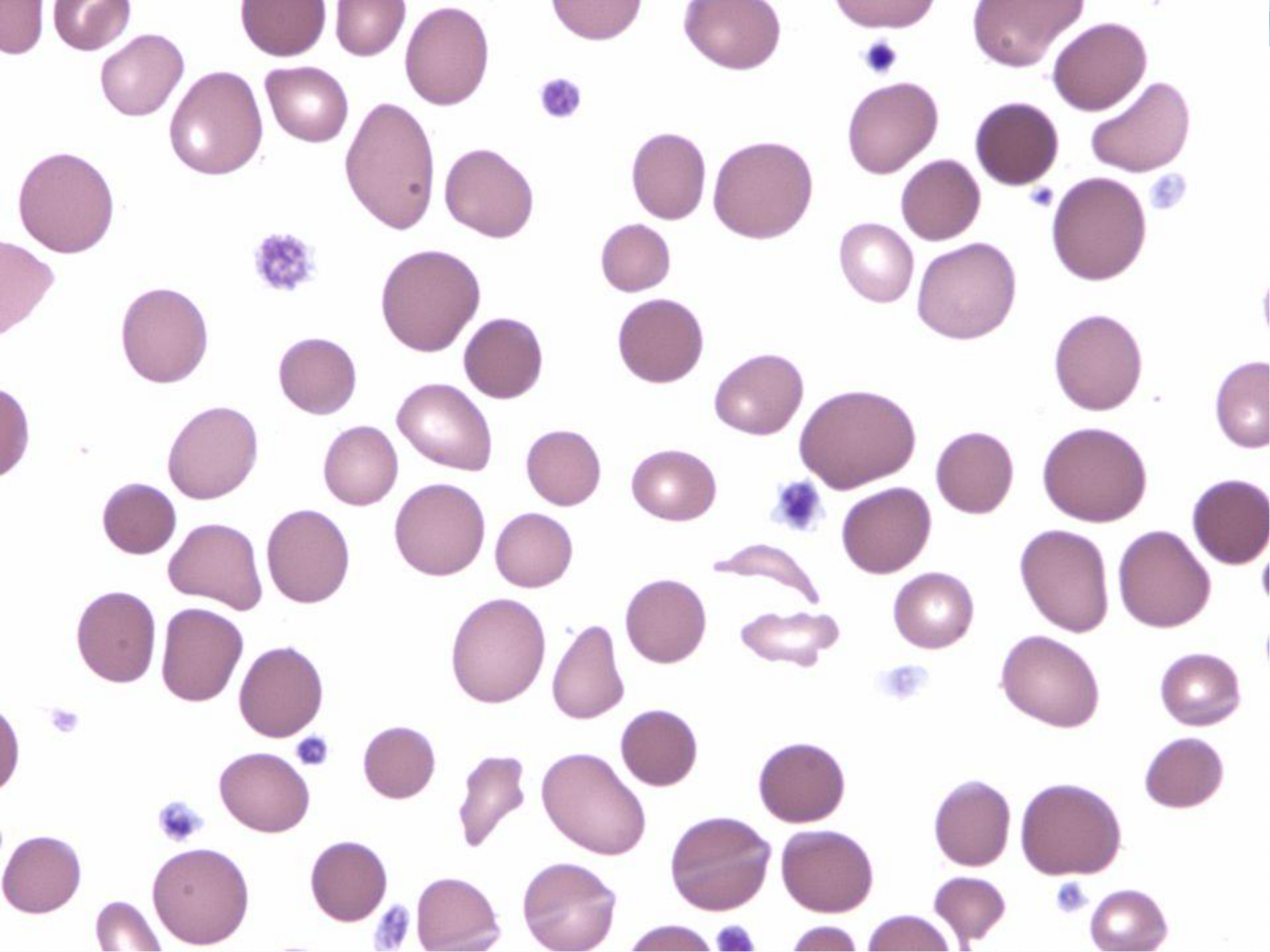
MDS Findings

- Blood cells fail to mature normally
- Cells that are produced may not function normally
- The marrow eventually becomes filled with the immature cells and there is not room for the normal cells and in this case caused anemia
- May evolve into acute leukemia
- Median age at diagnosis is 70 (LL was 76)

Peripheral Blood Smear in MDS







Patient LL

- First mixed field reaction in July 2012
Initially gave 2 O Neg RBCs and again with next transfusion
Later discussed with Medical Director again and decided to give O Positive going forward since patient was not of child bearing age
- D reaction continued to be mixed field until April of 2013 when 4+ reaction returned
- In October of 2013, mixed field reactions once again appeared and continue currently
- Has received 31 O Positive units since initial discovery of MF reactions and has not developed anti-D

