



MYELOYDYSPLASTIC SYNDROMES

BY ELEANOR MAYFIELD



It began suddenly, with swelling in her hands and feet that quickly became extremely painful. Joan Banich, then 42, who all her life had avoided seeing doctors because of a pathological fear of blood and needles, couldn't avoid it any longer.

"It took five people to hold me down for the blood test," recalls Joan, of Campbell, California. The doctor took one look at the test results and referred her to a hematologist, who quickly diagnosed myelodysplastic syndrome (MDS).

Myelo-*what*? Like most newly diagnosed patients, Joan had never heard of MDS, a disorder in which bone marrow fails to make enough healthy blood cells. The American Cancer Society estimates that about 12,000 Americans are diagnosed with MDS every year. As a relatively young woman, Joan did not fit the profile of a typical MDS patient. The disease is rare in people under 60 and more common in men than in women.

MDS AND BLOOD: A QUICK PRIMER

Myelodysplastic is derived from Greek: *myelo* means "marrow," *dys* means "difficult" or "disordered" (as in dysfunctional and dyslexic), and *plastic* means "capable of being formed or molded." *Syndrome*, also from Greek, means "a group of symptoms that occur together and characterize a disease." Because there are multiple types of MDS, many doctors refer to the condition in the plural: "myelodysplastic syndromes."

The bone marrow (the soft tissue inside bones) is a factory for making blood cells. Whole blood contains three types of cells:

- *Red cells* contain hemoglobin, a protein that keeps the body supplied with oxygen.
- *White cells* form a key part of the body's immune system, its defense against infection.
- *Platelets* help the blood to clot.

A blood cell's life span ranges from about nine days for platelets to about four months for red cells. Healthy bone marrow is always making new blood cells to replace the old ones. When it doesn't, immature cells called *blasts* may build up in the marrow but fail to develop

into mature blood cells. In healthy bone marrow, fewer than 5 percent of the blood cells are blasts. MDS is diagnosed when 5 to 20 percent of the blood cells in the bone marrow are blasts and counts of at least one type of blood cell are below normal, or when fewer than 5 percent of the blood cells are blasts but the cells appear abnormal.

MDS AND LEUKEMIA

When blasts constitute at least 20 percent of the blood cells in the bone marrow, the diagnosis changes from MDS to leukemia.

“MDS is really a precursor disease to leukemia, although in many patients it never progresses to leukemia,” explains David Steensma, MD, a hematologist-oncologist at Dana-Farber Cancer Institute in Boston.

Some doctors debate whether MDS is cancer, adds Dr. Steensma. “MDS differs from cancer in that it does not spread to other organs and it may remain stable for many years without treatment—behavior more typical of a pre-cancerous condition than a cancer.” Both the World Health Organization and the National Cancer Institute, however, recognize MDS as a form of blood cancer.

BLOOD TRANSFUSIONS

In 2003, when Joan was diagnosed with MDS, no drugs had yet been approved in the United States to treat it. The standard treatment was transfusions of healthy blood cells to replace those not being made in the patient’s bone marrow.

“I would get a transfusion every three to six weeks,” she recalls. To minimize the disruption of their family life—she and her husband, Dave Keller, have a daughter, Atley,

Like most newly diagnosed patients, Joan had never heard of MDS, a disorder in which bone marrow fails to make enough healthy blood cells.

who was then 10—she arranged to get her transfusions at night. “I would go to the hospital overnight, after Atley was in bed, and be home for breakfast,” she says.

The first drug approved to treat MDS became available in 2004; two others soon followed (see sidebar). Joan’s doctors tried two of the new agents, to little apparent effect at first. She continued to need blood transfusions. “Then, after I stopped taking [the drugs], I went for more than two and a half years without needing transfusions or having to be hospitalized for complications,” she says.

BONE MARROW TRANSPLANT

In December 2010 tests revealed that Joan’s red blood cell count was extremely low, and a biopsy showed scar tissue in her bone marrow. This was bad news. “My doctors said I should have a bone marrow transplant within six months,” she recounts.

A bone marrow transplant replaces the patient’s unhealthy



Joan Banich

TIPS FOR NEW PATIENTS

For patients facing a new diagnosis of MDS, Joan offers the following tips.

- “You can have a more normal life than you might expect. What’s normal changes, but you learn to live with it.”
- Do your research, but be aware that information found on the Internet may be misleading or inaccurate. Learn to identify and use reputable websites.
- Ask for and keep copies of medical records, prescriptions, and lab test results.
- Take a notebook and a list of questions with you on doctor visits.
- Be an active partner in your care.
- Join the MDS community at cancerconnect.com/groups/leukemia-aml-or-mds/

TREATMENT OPTIONS FOR MDS: IT'S COMPLICATED

"It can be a challenge to decide on the best initial treatment" for a patient newly diagnosed with MDS, says David Steensma, MD, a hematologist-oncologist at Dana-Farber Cancer Institute in Boston. The following are just some of the factors that doctors must consider when selecting a treatment option.

- **Subtype.** Depending on the classification system used, MDS has five or seven subtypes, identified by blood and bone marrow findings.
- **Genetic abnormalities.** More than 20 genetic abnormalities have been identified so far in patients with MDS, and many more are likely still unidentified. Most of these abnormalities occur randomly: people don't inherit them from their parents or pass them on to their children. MDS very

rarely runs in families. Some genetic changes confer a higher risk that MDS will progress to leukemia, while others don't have any effect on progression.

- **Number of blast cells.** A higher proportion of blasts in the bone marrow at diagnosis (e.g., more than 10 percent) indicates a higher risk of progression to leukemia.
- **Number of low blood counts.** A patient with only one low blood count probably has a better outlook than one with low counts of all three types of blood cells (red cells, white cells, and platelets), says Dr. Steensma.
- **Age and general health.** Doctors might propose a different treatment strategy for a young, otherwise healthy patient than for an older patient with other chronic health problems in addition to MDS.

Vidaza® (azacitidine) became the first drug approved by the US Food and Drug Administration (FDA) to treat MDS in 2004. It was followed by Revlimid® (lenalidomide) in 2005 and Dacogen® (decitabine) in 2006.

None of these drugs is a cure for MDS, says Mikkael Sekeres, MD, a hematologist-oncologist at Cleveland Clinic's Taussig Cancer Center. Vidaza and Dacogen both slow the progression of MDS to leukemia and are most helpful for patients at high risk of that progression, he explains. In a 2009 study, MDS patients treated with Vidaza lived about nine months longer, on average, than patients not treated with Vidaza.¹

Revlimid is approved to treat a subset of MDS patients who have a genetic abnormality called the 5q deletion, in which a piece of chromosome 5 is missing in the patient's bone marrow cells. (Chromosomes are "packets" of DNA, the material that carries genes.)

Chemotherapy drugs and growth factors—drugs that stimulate the body to make more blood cells—may also be used to treat MDS, although they are not FDA-approved to do so.

The keys to improving MDS treatment in the future lie in combining drugs and in tailoring treatment to a patient's own genetic profile, says Dr. Sekeres.

"Trials are now under way to find out if we can improve treatment effectiveness by using more than one drug," he says. "The next frontier is to use genetic abnormalities to predict which drug or drug combination may be most effective for an individual."

Reference

1. Fenaux P, Mufti GJ, Hellstrom-Lindberg E, et al. Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: a randomised, open-label, Phase III study. *Lancet Oncology*. 2009;10(3):223-32.

blood-forming stem cells—the "parents" of red cells, white cells, and platelets—with healthy ones from a donor. Although it represents the only hope of curing MDS, the procedure carries many risks (see sidebar).

Joan was fortunate to quickly find a matching donor in the National

Marrow Donor Registry (see sidebar). She will celebrate the one-year anniversary of her transplant in June 2012. She takes medication to keep the donated blood cells from attacking her own cells, a common transplant complication. "All things considered, I'm doing well," she says. ❀



More at: [news.cancerconnect.com/
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myelodysplastic-
syndrome](http://news.cancerconnect.com/types-of-cancer/myelodysplastic-syndrome)



For 23-Year Survivor, Positive Attitude Is Key

"The doctors told me I had aplastic anemia and I had three months to three years to live."

It was 1989, and Norma Good's blood tests had just come back abnormal. She was 57.

That prognosis turned out to be a wee bit off: Norma celebrated her eightieth birthday in January 2012.

Norma says she owes her life to a clinical trial at the National Institutes of Health (NIH) in Bethesda, Maryland, that was investigating growth factors to stimulate blood cell production.

For three and a half years, she traveled to NIH from her home in Ohio for growth factor injections, while going to her local hospital every 10 days or so for blood transfusions. The first two growth factors the NIH doctors tried had no effect, but after three months on the third one, Neupogen® (filgrastim), Norma's blood counts began to inch back up to levels close to normal.

About 18 months after joining the NIH trial, Norma got a new diagnosis: MDS, with a genetic abnormality called the 5q deletion (meaning that a piece of chromosome 5 was missing in her bone marrow cells).

"My last blood transfusion was in September 1992," she says. "I haven't needed one since." She still gets her blood counts checked every three months, however.

An active volunteer with the Aplastic Anemia & MDS International Foundation, Norma frequently counsels newly diagnosed MDS patients. Nowadays, she says, because of quicker diagnosis and new medications, "most of the patients I talk with have never had to have a blood transfusion."

The secret to her long survival with this chronic illness, Norma says, is a positive attitude. "There will be a tomorrow as long as you have a strong desire for one. Medicine can only do part of it."

A MATCH FOR LIFE

A successful bone marrow transplant is currently the only cure for MDS, but it's a high-risk option.

"For about one-third of patients, a transplant is curative," says David Steensma, MD, a hematologist-oncologist at Dana-Farber Cancer Institute in Boston. "Another one-third of patients survive the transplant procedure, but the disease comes back. And, sadly, the remaining one-third of patients succumb to complications from the transplant."

Candidates for a transplant must be in excellent general health. "We've done transplants in patients as old as the midseventies if their health is otherwise excellent," says Dr. Steensma.

The next hurdle is finding a compatible donor. About three in 10 patients have a compatible donor in their family, usually a sibling. The other option is to seek a donor through the Be The Match Registry (formerly the National Marrow Donor Program registry).

The registry "can find a compatible donor for about 70 percent of patients who are of European descent," says Dr. Steensma. For people of other ethnicities, finding a match may be more difficult because of a shortage of minority donors.

Another barrier is that health insurance may not cover all of the costs associated with a transplant. Be The Match Foundation, in addition to maintaining the marrow donor registry, may be able to offer financial assistance (see "Resources" sidebar).

RESOURCES

Aplastic Anemia & MDS International Foundation

100 Park Avenue, Suite 108
Rockville, MD, 20850
(800) 747-2820

help@aamds.org • aamds.org

Be The Match Registry

National Marrow Donor Program

3001 Broadway Street NE, Suite 100
Minneapolis, MN 55413
(800) MARROW2 [627-7692]

patientinfo@nmdp.org • marrow.org

Leukemia & Lymphoma Society

1311 Mamaroneck Avenue, Suite 310
White Plains, NY 10605
(800) 955-4572

infocenter@lls.org • lls.org

CancerConnect.com

The leading provider of social network connecting cancer patients

cancerconnect.com/types-of-cancer/myelodysplastic-syndrome