# About Myelofibrosis

**Myelofibrosis is a rare but serious cancer of the bone marrow that disrupts the body's normal production of blood cells.[1]**

As the cancer progresses, bone marrow is gradually replaced with fibrous scar tissue, limiting the marrow's ability to produce red blood cells.[1] This defect can lead to a severe lack of red blood cells known as anemia, as well as weakness, fatigue and swelling of the spleen and liver, among other symptoms.[2]

**Myelofibrosis is a myeloproliferative neoplasm (MPN), a group of blood cancers that derive from blood-forming stem cells.**[2,3] Along with myelofibrosis, two other blood cancers – essential thrombocythemia and polycythemia vera – are categorized as MPNs. Myelofibrosis is considered primary if the patient has no prior history of another MPN. A small portion of people with myelofibrosis developed the condition as a complication of essential thrombocythemia or polycythemia vera. If myelofibrosis is developed after these MPNs, it is known as secondary myelofibrosis.[4]

**In the U.S., between 16,000 and 18,500 people are living with myelofibrosis[5], and 1.5 of every 100,000 people – are diagnosed with myelofibrosis each year.**[4,6] The median age at diagnosis ranges from 60 years to 67 years.[7,8] Global estimates of prevalence and incidence vary widely.

## Risk Factors

- The cause of myelofibrosis remains unclear, but more than half of patients have a mutation in the Janus Kinase 2 (JAK2) gene.[4]
- About 20% of patients have mutations in the calreticulin (CALR) gene;[9] between 5% and 10% of myelofibrosis patients have a mutation in the myeloproliferative leukemia (MPL) gene, which also affects the JAK pathway.[4]
- Additional risk factors include:[1]
  - Age
  - History of thrombocythemia or polycythemia vera
  - Exposure to certain industrial chemicals or high radiation levels



## Symptoms and Diagnosis

- About one-third of patients with myelofibrosis in its very early stages may have no symptoms of the disease.[4]
- Signs and symptoms of myelofibrosis include:[1,3]
  - Feeling tired, weak or short of breath, stemming from anemia
  - Bruising or bleeding easily, related to low platelet counts
  - Unexpected weight loss or lowered appetite, due to enlarged spleen
  - Bone or joint pain
  - Night sweats
  - Itching
  - Mild fever
- Myelofibrosis is commonly associated with an enlarged spleen (called splenomegaly) that can cause pain or a feeling of fullness in the upper left portion of the stomach.[9] When the bone marrow cannot make enough normal blood cells, the spleen can begin to make them. This causes the spleen to enlarge. More than 85% of people with myelofibrosis have an enlarged spleen at diagnosis.[10]
- Some people with myelofibrosis remain symptom-free for years, while others progressively worsen.[1]
- There are two stages: pre-fibrotic/early primary myelofibrosis or overt primary myelofibrosis.[11]
- Criteria involved in the diagnosis of disease stage include whether the bone marrow contains abnormal platelet-forming cells, the degree of bone marrow fibrosis, whether a genetic mutation is present, the presence of anemia, high white blood cell count, a high lactate dehydrogenase (LDH) level, an enlarged spleen or presence of immature blood cells in the blood.[11]
- Testing in the diagnosis of myelofibrosis includes:[1,4]
  - Routine physical exam, a check of vital signs, lymph nodes, spleen and abdomen
  - Blood tests that measure levels of red blood cells, white blood cells and platelet counts
- To confirm a myelofibrosis diagnosis, a patient may undergo:[1,4]
  - Imaging tests to determine spleen size or identify changes in bone marrow
  - Bone marrow biopsy
  - Genetic tests to identify mutations

Bristol-Myers Squibb

## Prognosis[4]

- Prognosis varies by patient, according to certain factors. For myelofibrosis, there are multiple scoring systems used to assess the course of the disease.
- The International Prognostic Scoring System (IPSS) identifies five risk factors that help estimate approximate survival from time of diagnosis:
  1. Age – 65 years or older
  2. Anemia as shown by hemoglobin level less than 10 grams per deciliter
  3. Presence of symptoms that may include fever, night sweats or weight loss
  4. An elevated white blood cell count, known as leukocytosis
  5. At least 1% of immature blood cells in the bloodstream
- While the median survival for people with myelofibrosis is 3.5 years to 5.5 years, people younger than 55 and with good prognostic factors have a median survival of 11 years. According to the IPSS, patients without any of the adverse risk factors, outside of age, have a median survival of more than 10 years. If at least two of the IPSS adverse risk factors are present, the median survival time can be less than three years.

## Treatment[1,4]

- The choice of therapy may be based on a patient's characteristics such as age, abnormal blood cell counts, disease progression and overall health, as well as each therapy's potential side effects.
- Patients may go without treatment if they don't show signs or symptoms of anemia, an enlarged spleen or other complications. These patients are monitored regularly for signs of disease progression.
- For those who require treatment, two primary goals are to reduce symptoms and improve blood counts. An additional goal is to reduce the chance of progression to acute myeloid leukemia.[9,11] There is currently no medicine that can cure myelofibrosis.
- Therapies used in treatment include:
  - JAK inhibitors aimed at blocking the dysfunctional JAK pathway
  - Blood transfusions, androgen therapy and other medicines to treat anemia
  - Chemotherapy, radiation therapy or targeted drug therapy to help alleviate an enlarged spleen
  - A splenectomy – surgical removal of the spleen – is an option if the spleen remains enlarged, causing a very low platelet count, severe anemia or high blood pressure in the area of the spleen and liver
- The only potentially curative treatment option is a stem cell transplant, which is typically only appropriate for a small subset of younger patients – less than 5% of all myelofibrosis patients – due to risks associated with the procedure.


1 Mayo Clinic. Myelofibrosis. Available at https://www.mayoclinic.org/diseases-conditions/myelofibrosis/symptoms-causes/syc-20355057. Accessed November 2019.

2 OncoLink. All About Myelofibrosis. Available at https://www.oncolink.org/cancers/leukemia/myelofibrosis/all-about-myelofibrosis. Accessed November 2019.

3 MPN Research Foundation. An Overview of MPNs. Available at http://www.mpnresearchfoundation.org/Understanding-MPNs. Accessed November 2019.

4 Leukemia & Lymphoma Society. Myelofibrosis facts. Available at https://www.lls.org/sites/default/files/file_assets/FS14_Myelofibrosis_Fact%20Sheet_Final9.12.pdf Accessed November 2019.

5 Voices of MPN. About Myelofibrosis. Available at https://www.voicesofmpn.com/myelofibrosis-information.aspx. Accessed November 2019.

6 Mesa RA, Silverstein MN, Jacobsen SJ, et al. Population-based incidence and survival figures in essential thrombocythemia and agnogenic myeloid metaplasia: an Olmsted County Study, 1976-1995. *Am J Hematol.* 1999;61:10-15.

7 Abdel-Wahab O and Levine R. Primary myelofibrosis: Updates on Definition, Pathogenesis and Treatment. *Annual Review of Medicine.* 2009;60:233-245.

8 Mesa R, Niblack J, Wadleigh M, et al. The burden of fatigue and quality of life in myeloproliferative disorders (MPDs). Cancer. 2007;109:68-76.

9 NORD. Primary Myelofibrosis. Available at https://rarediseases.org/rare-diseases/primary-myelofibrosis/. Accessed November 2019.

10 Cervantes F, Dupriez B, Pereira A, et al. New prognostic scoring system for primary myelofibrosis based on a study of the International Working Group for Myelofibrosis Research and Treatment. *Blood.* 2009;113:2895-2901.

11 NCCN. NCCN Guidelines for Patients: 2018 Myeloproliferative Neoplasms. Available at https://www.nccn.org/patients/guidelines/mpn/files/assets/common/downloads/SurveyQuickGuide_waldenstroms.pdf. Accessed November 2019.