Novartis Oncology

No Disease Too Small Fact Sheet

What Is Systemic Mastocytosis (SM)?

- **Systemic mastocytosis (SM)** is a group of rare blood diseases, where too many abnormal mast cells, which are specialized immune cells, grow and accumulate in the body.[1,2]
  - Organs affected by mast cell build-up may include the skin, liver, spleen, bone marrow, and organs of the gastrointestinal tract.[1,3]
- Mast cells are produced in the bone marrow and found in connective tissues all over the body. They release multiple chemical mediators, such as histamine, tryptase, heparin, and other inflammatory substances. These mediators are released as part of allergic and inflammatory reactions.[4,5]
  - In healthy people, mast cells help protect the body from infection and defend it from other harmful substances.[2]
  - The accumulation of abnormal mast cells seen in SM leads to the release of higher levels of mast cell mediators and generalized inflammation in the body, causing a range of symptoms. These can include flushing of the skin, headaches, digestive problems, extreme allergic reactions, bone pain, and fatigue.[2,3]
- Very serious cases of SM can lead to organ damage or even organ failure.[3]
- Early identification of the disease by a health care provider can be critical as there are several different subtypes of SM and each varies in severity and life expectancy.[3,6,7,8] It is important for patients to work closely with a health care provider to develop a treatment plan.

What Is *No Disease Too Small*?

Systemic mastocytosis (SM) affects between

1 in 20,000 and 1 in 40,000

people worldwide[1]

No Disease Too Small offers guidance for patients, their loved ones, and physicians as they search for answers about symptoms and the disease. The program also provides tools to support the SM community and drive broader awareness of the complexities of this disease. Visit **www.NoDiseaseTooSmall.com** for more information.

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Do I Have SM?

You may have SM if you have a history of persisting symptoms that remain undiagnosed or misdiagnosed, including itching, abdominal pain, anemia, nausea, diarrhea, vomiting, and anaphylaxis, a severe allergic reaction. A confirmed diagnosis of SM can only be verified by a bone marrow biopsy and a blood test.[3,9]

SM is a difficult disease to identify because its symptoms can be confused with those related to other diseases that health care professionals see more regularly.[10] Many people are not accurately diagnosed for 2 to 10 years after they first see symptoms.[6]

People with SM are frequently underdiagnosed or misdiagnosed with other conditions, such as irritable bowel syndrome or malabsorption syndrome.[8] Also, those diagnosed with a blood cancer such as leukemia could also have a mast cell disorder.[11]

Before they are correctly diagnosed, people with SM are likely to be referred to several different health care professionals, including dermatologists, allergists, hematologists, gastroenterologists, endocrinologists, internal medicine specialists, rheumatologists, cardiologists, and neurologists.[12]

SM can impact a person's mental health. People with SM are at risk for depression, anxiety, poor motivation, or increased stress.[13] Anyone experiencing mental health problems should seek support and counseling from a health care professional.

If the presence of SM is suspected, talk to a health care provider about SM testing early to confirm a diagnosis. Treatment may be needed once a diagnosis is confirmed, and a comprehensive care plan with follow-up may ease the emotional impact of living with the disease.

Testing for SM

If SM is suspected, patients should talk to a health care provider about tests that may help identify the disease.[3] As SM is an extremely rare disease, physicians may not be familiar with testing or diagnosing it.[1,6] Diagnosis can only be confirmed by the following tests:

- **Blood tests**, which identify abnormalities in the blood, help physicians diagnose SM.
  - **Blood serum tryptase test:** Serum tryptase is an enzyme, or chemical, released by mast cells.[4] Testing for elevated serum tryptase can help diagnose the disease, because a person who has SM is likely to have significantly higher levels of this enzyme.[3]
  - **Other blood tests to evaluate organ damage:**
    - ***Blood serum albumin test:*** *A serum albumin test is a blood test that measures the amount of albumin in the patient's blood. Low levels of albumin are often associated with inflammation in the liver, kidney disease, and malnutrition.*[14]
    - ***Alkaline phosphatase (ALP) test:*** *This test measures the amount of ALP enzyme in the bloodstream. If ALP levels are elevated, it indicates a problem with the liver or bones.*[15]
    - ***Hemoglobin test:*** *Anemia, a condition in which the blood has fewer red blood cells than normal, can be a sign of SM.*[3,16] *A hemoglobin test is used to check for anemia.*[17]
    - ***Complete Blood Count (CBC):*** *Low blood platelet count (thrombocytopenia) and high white blood cell count (leukocytosis) can be signs of advanced forms of SM.*[3,18] *CBC tests measure many different parts of the blood, including the overall number of white blood cells and platelets.*[17]
  - **Genetic mutation testing:** Learning if a genetic mutation is present can help physicians diagnose SM.[3] A mutation is a change in a gene's structure.[3] Mutations in a gene known as KIT mutation often cause uncontrolled growth of mast cells.[19] KIT D816V is the most common KIT mutation, occurring in approximately 9 out of 10 SM patients, which makes it a key tool for diagnosis.[3,20]
- **CT scanning and other imaging:** Infiltration of abdominal organs and lymph nodes can best be seen by a variety of CT and other scans.[21]
- **Biopsies:** Procedures performed using a biopsy needle to extract samples of the organ for evaluation.[22] They are vital in diagnosing SM.[3]
  - **Bone marrow biopsy[21]:** To confirm the overproduction of mast cells in bone marrow or other organs, a physician can test a patient's bone marrow to see if it contains too many mast cells. This test can also give information about the SM subtype.[3]

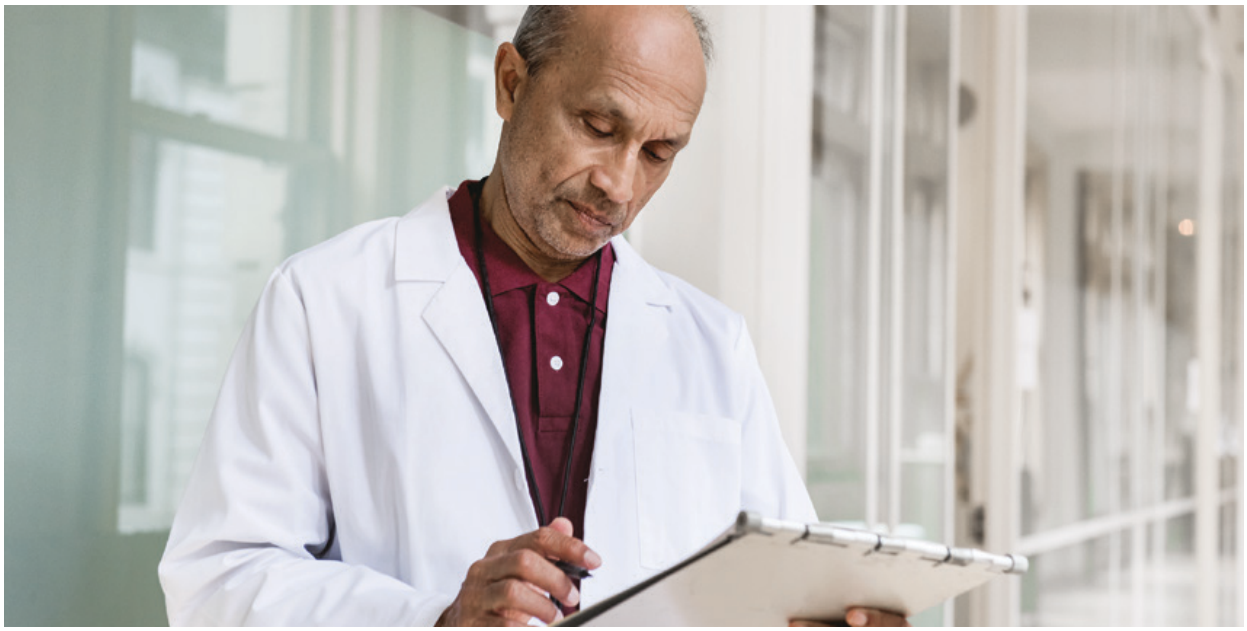
A Closer Look at the Five Types of SM[7]

Type of SM	Description	Percentage of SM Cases
Indolent SM (ISM)	ISM is the most common and mild form of SM.[3] Symptoms may include itching skin, fainting, headaches, vomiting, and diarrhea.[2,3] Those with ISM have a low risk of progression to a more advanced form.[5]	~60–70%
Smoldering SM (SSM)	SSM usually is characterized by an accumulation of mast cells in the bone marrow. Patients with SSM may have a higher likelihood of progressing to an advanced disease category.[5]	
SM with an associated hematologic neoplasm (SM-AHN)	SM-AHN is a form of SM with the presence of an additional blood disorder, often myeloproliferative disorders or a myelodysplastic syndrome.[5]	~20-30%
Aggressive SM (ASM)	ASM is a severe form of SM associated with widespread infiltration of mast cells in various organs leading to organ damage or failure.[3]	~5-10%
Mast cell leukemia (MCL)	MCL is a rare and serious form of SM, characterized by a much higher circulation of mast cells in the bone marrow and peripheral blood. Prognosis is typically poor with a short survival time.[5]	~1%

SM-AHN, ASM, and MCL are all defined as advanced SM and have lower survival rates compared to ISM and SSM.[8,18]

For more information and resources, visit *No Disease Too Small* **(www.NoDiseaseTooSmall.com)**.
The Mastocytosis Society* may be another source of information for you: **www.tmsforacure.org**.

*The Mastocytosis Society is a not-for-profit group, independent from Novartis. Novartis has no financial interest in this organization, but has provided occasional funding support. Novartis is not responsible for the organization's information or actions.



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