Systemic mastocytosis (SM) is a group of rare blood diseases where too many abnormal mast cells, which are specialized immune cells, collect in more than one body tissue. Mast cells can accumulate in the skin and internal organs, including the liver, spleen, bone marrow, and tissues of the gastrointestinal tract.¹,²,³

Mastocytosis is a rare disease where the body makes abnormal mast cells that accumulate in various organ systems²,⁴

A “mast” cell is a type of white blood cell in the immune system²
- Mast cells help heal wounds and protect the body from infection. Mast cells also are specialized to release multiple chemical mediators, including histamine, tryptase, heparin, and others, which can contribute to inflammatory and allergic reactions and other clinical symptoms.⁵,⁶

“Cytosis” is a suffix that means an increase in the number of cells⁷

There are two types of mastocytosis: systemic and cutaneous²

*Cutaneous mastocytosis is more common in children, and is outside the scope of this document¹*

In SM, the accumulation of mast cells can affect both the skin and internal organs, resulting in systemic symptoms, and may cause organ damage¹,³

No Disease Too Small is a campaign that offers information and guidance for patients and their loved ones as they search for answers about systemic mastocytosis and its symptoms. An educated patient and physician can work together as partners throughout the diagnosis and treatment journey.

A guide to systemic mastocytosis (SM)

What is the clinical definition of mastocytosis?

Mastocytosis is a rare disease where the body makes abnormal mast cells that accumulate in various organ systems²,⁴
How common is SM?

- SM is very rare, and people who have SM may have difficulty finding support.
- Around the world, SM affects between 1 in 20,000 and 1 in 40,000 people.
- The median age at SM diagnosis in adults is 55 years.
- SM is not usually linked to family history; the risk of getting SM is greater if there is a change in a particular gene.
- Blood tests that measure levels of tryptase, as well as bone marrow tests, are necessary to diagnose SM.

Why is SM so difficult to diagnose?

SM is underdiagnosed for several reasons:

- Symptoms may initially be minor and progress over time.
- Symptoms frequently seen in SM are often the same as those seen in many other illnesses, often leading to incorrect diagnosis.
- Physicians are not accustomed to seeing the disease. Patients may cycle between many different physicians and specialists before receiving a correct diagnosis.

An accurate SM diagnosis can take 2 to 10 years.

What impact does SM have on the body?

- There are different kinds of SM, and some are more serious than others. Very serious cases can lead to organ damage or even organ failure.
- When the body produces too many mast cells, the increased number of chemical mediators released can result in symptoms, including, but not limited to, flushing, itching, nausea, diarrhea, low blood pressure, and anaphylaxis.
- The organs SM affects are usually the bone marrow, skin, liver, spleen, lymph nodes, and those of the gastrointestinal tract.
- Symptoms may depend on which organ is being affected:
  - Bone involvement can result in bone pain.
  - Nausea, vomiting, abdominal pain, and diarrhea are seen when cells in the gastrointestinal (GI) tract are affected.
  - When mast cells begin to accumulate in body tissues, the lymph nodes, liver, and spleen may swell.
  - When the skin is affected, symptoms including severe itching and flushing, which can be triggered by temperature changes, fever, exercise, and friction.
- Physicians should work to develop a treatment plan best suited to manage patients’ symptoms related to mast cell growth and accumulation.
What are the symptoms of SM?

**SM symptoms can vary significantly from one person to another**

If the following symptoms are present, the patient should talk to a health care provider:

- Skin rash
- Itching or pruritus
- Flushing of the skin
- Anemia
- Swelling in liver, spleen, or lymph nodes
- Headache
- Fatigue
- Osteoporosis
- Bone pain
- Digestive problems such as stomach pain, diarrhea, malabsorption, weight loss, nausea, or vomiting
- Extreme allergic reactions called anaphylaxis that can occur, for example, after a bee or insect sting that can cause swelling of the face, tongue, or eyes, trouble breathing, or dizziness
- Extreme reactions to heat, cold, or other physical triggers

**Misdiagnoses of other diseases**

People with SM are often diagnosed with other, more common illnesses because they have the same symptoms as SM, including:

- Irritable bowel syndrome
- Malabsorption syndrome
- Urticaria
- Carcinoid syndrome
- VIPoma
- Zollinger-Ellison syndrome
- Leukemia
- Other myeloproliferative disorders

If a patient has been diagnosed with chronic myelomonocytic leukemia (CMMML), myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPN), acute myeloid leukemia (AML), myeloproliferative disorder (MPD), non-Hodgkin’s lymphoma (NHL), or hypereosinophilic syndrome (HES) and the above symptoms are present, the individual could also have a mast cell disorder.

When a diagnosis of SM is made, a patient may have visited other types of health care providers to find relief for their symptoms, including:

- Dermatologists
- Allergists
- Hematologists
- Gastroenterologists
- Endocrinologists
- Internal medicine specialists
- Rheumatologists
- Cardiologists
- Neurologists

How does SM impact someone’s everyday life?

Like many other long-term or chronic diseases, SM can dramatically affect a person’s daily quality of life.

**Living with a chronic illness, especially one so difficult to diagnose, can impact the mental health of the patient**

Some of the feelings a patient with SM may experience during diagnosis and treatment are:

- Increased stress
- Fear and/or anxiety
- Poor motivation
- Sadness and/or depression
- Isolation

If a patient with SM is experiencing physical or emotional health problems, he or she should talk with a health care professional. It is important to seek support and counseling to help cope with these feelings.
If a patient is concerned about SM, what should he or she do?

• An informed conversation with a physician is the first step. Patients with symptoms common in SM should not hesitate to ask questions about the disease.
• It is important to know about the different types of SM—there are five—and to ask specific questions about testing that can help a physician make an SM diagnosis, so treatment can begin.
• For a list of key questions to help both patients and health care providers, visit No Disease Too Small (www.NoDiseaseTooSmall.com).

The 5 types of Systemic Mastocytosis

SM is categorized into five subtypes, determined by the affected organs. They differ in severity, treatment approach, and life expectancy.

• **Indolent SM (ISM)** is the most common and mild type of SM. Symptoms may include itching skin, fainting, headaches, vomiting, or diarrhea. Those with ISM have a low risk of progression to a more advanced form.
  - **Prognosis:** Typically favorable

• **Smoldering SM (SSM)** is usually characterized by a high volume of mast cells in the bone marrow. Those with SSM may have a higher likelihood of progressing to an advanced disease category.
  - **Prognosis:** May indicate tendency to progress to a more advanced form

• **SM with an associated hematologic neoplasm (SM-AHN)** is a type of SM where the patient has an additional blood disorder, most often myeloproliferative disorders or a myelodysplastic syndrome.
  - **Prognosis:** Depends on associated hematological neoplasm

• **Aggressive SM (ASM)** is a severe type of SM. Mast cells will collect in different organs and can cause organ damage or failure.
  - **Prognosis:** Less favorable

• **Mast cell leukemia (MCL)** is a rare and serious type of SM. There are many more mast cells circulated in the bone marrow with MCL. The outcome with MCL is very poor.
  - **Prognosis:** Life expectancy may be limited

SM-AHN, ASM, and MCL are all defined as advanced SM and have lower survival rates compared to ISM and SSM.
Which tests can diagnose SM?

Because SM symptoms (such as a skin rash) are commonly found in other diseases, it can be difficult to diagnose. There are, however, several specific tests that can more precisely determine if SM is present:

- **Blood tests** are frequently used to diagnose SM.
  - **Blood serum tryptase test:** Serum tryptase is an enzyme, or chemical, produced by the mast cells. A person with SM is likely to have higher levels of tryptase in the bloodstream.
  - **Other blood tests to evaluate organ damage:**
    - **Blood serum albumin test:** A serum albumin test is a simple 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.
    - **Alkaline phosphatase (ALP) test:** The test measures the amount of ALP enzyme in the bloodstream. If ALP levels are elevated, it indicates a problem with the liver or bones.
    - **Hemoglobin test:** Anemia, a condition in which the blood has fewer red blood cells than normal, can be a sign of SM. A hemoglobin test is used to check for anemia.
    - **Complete blood count (CBC):** Low blood platelet count (thrombocytopenia) and high white blood cell count (leukocytosis) can be signs of SM. CBC tests measure many different parts of the blood, including the overall number of white blood cells and platelets.
  - **CT scanning and other imaging:** Infiltration of abdominal organs and lymph nodes can be seen best by a variety of CT and other scans.
  - **Biopsies**
    - **Bone marrow biopsy:** Mast cells form in the bone marrow. Physicians can test a patient’s bone marrow to see if it contains abnormal mast cells meeting specific criteria. In addition to determining the presence of SM, the test can help physicians understand which type of SM is present.

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.

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*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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