

TREATMENT OF MAST CELL DISEASES depends both on the specific diagnosis and the presenting symptoms. For indolent (benign) disease, treatment is directed at controlling the symptoms by trigger avoidance and medication. Typical medication used for these symptoms include: H1 antihistamines such as hydroxyzine, doxepin, diphenhydramine, loratadine, fexofenadine, or cetirizine; H2 antihistamines such as ranitidine, cimetidine, and famotidine; Mast cell stabilizers such as cromolyn sodium or ketotifen; Leukotriene inhibitors such as montelukast, zileuton or zafirlukast; Aspirin therapy (under direct supervision of your physician only!); Epinephrine is used for anaphylaxis; Steroids are reserved for extreme conditions when a patient cannot be stabilized any other way. For advanced variants of mastocytosis with indications of a large mast cell burden, involvement of multiple cell lineages and/or findings which indicate organ damage, more powerful treatment including cytoreductive agents (chemotherapy) may be prescribed. Options may include interferon alpha/beta, imatinib (only if KIT D816V negative), cladribine, midostaurin and other drugs now in clinical trials.

Prognosis depends on the type of mast cell disease and age of onset. Please visit <https://tmsforacure.org/prognosis> for more specific information about prognosis.

Emergency treatment for anaphylaxis requires epinephrine. Patients with a mast cell disease should carry two self-injectable epinephrine units at all times. Units must be protected from heat and light. Patients on beta blockers may require glucagon along with epinephrine (please check with your physician). Patients should also have access to bottled water and doses of their other essential medication. In addition, patients should wear medical identification jewelry and carry their medical history with relevant information including: • Physician names and contact information • Medications by indication including dosing • Allergies, intolerances, and triggers • Emergency contact information • A copy of this brochure • Emergency Response Plan signed by their physician.

Please go to https://tmsforacure.org/wp-content/uploads/2019-TMS-ER_Response_Plan.pdf.

Other considerations: Accommodations may be required in the school and work environment for patients affected by mast cell diseases. In the school setting, both a 504 and IEP may be required to meet both the medical and educational needs of the child/teen. Many adults and children affected by mast cell disorders may require disability support.

AS A RESULT OF GIFTS FROM OUR GENEROUS DONORS... TMS MEMBERSHIP IS NOW FREE!

However, donations to support our mission of mast cell disease research, education, support and advocacy are always welcome! Please help us keep our membership free by donating now! www.tmsforacure.org/donate-to-tms

BENEFITS INCLUDE:

Online newsletter sent by email to members, patient care coordination and active support of our mission. To join: www.tmsforacure.org/membership

The Mastocytosis Society, Inc. (TMS) is a 501(c)(3) nonprofit organization dedicated to supporting patients affected by mast cell diseases as well as their families, caregivers, and physicians through research, education and advocacy. We are a patient, volunteer-led organization guided by an expert Medical Advisory Board. TMS welcomes mast cell disease patients of all ages. Anyone affected by, or interested in learning about, mast cell diseases is encouraged to join. TMS sponsors online and regional support groups as well as periodic joint patient and physician conferences, including CMEs when available. All proceeds from donations and fundraisers are used to support our TMS mission. There are also many volunteer opportunities. To learn more visit www.tmsforacure.org. Thank you for your interest in TMS!

For further information, contact info@tmsforacure.org.

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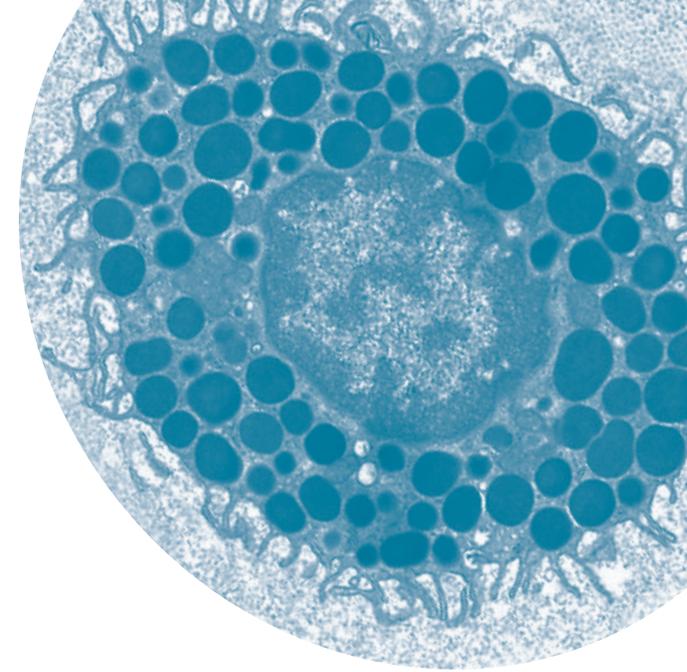
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MAST CELL DISEASES:

Mastocytosis and Mast Cell Activation Syndromes

An informational brochure for patients, caregivers and families



Mastocytosis and Mast Cell Activation Syndromes

OVERVIEW

Mast Cell Diseases are a group of rare diseases, including **mastocytosis** and its variants, and **mast cell activation syndromes (MCAS)**. In mastocytosis there is an excess of mast cells, abnormal in both shape and function, in various body organs and tissues. In mast cell activation syndromes the number and shape of mast cells in the tissues may appear normal. However, in both mastocytosis and MCAS, mast cells may be easily triggered to activate, releasing their mediator contents. These mediators, which include histamine, tryptase, heparin, prostaglandins and leukotrienes, among others, are responsible for many symptoms seen in patients with mast cell diseases. Children are primarily affected by cutaneous forms of mastocytosis, although rarely, systemic disease may be seen. Mast cell sarcoma is a very rare form of mastocytosis that can affect any age group.

SYMPTOMS may include: anaphylaxis, flushing, skin lesions/rashes, including maculopapular cutaneous mastocytosis (MPCM), chest pain, nausea, vomiting, diarrhea, abdominal pain, bloating, gastroesophageal reflux disease (GERD), fainting, blood pressure changes, itching, bone pain, osteoporosis, fatigue, weakness, anxiety/depression and cognitive difficulties. The symptoms of mast cell diseases are highly variable and may have an unpredictable onset, which may cause havoc and significant disability in the lives of patients. Mast cell diseases, including the skin rashes associated with them, are NOT CONTAGIOUS. These diseases may affect patients of all ages from newborn to adult. In pediatric and adult cutaneous disease, systemic symptoms may arise due to mediator release from skin lesions. These systemic symptoms by themselves are not an indication of true systemic involvement.

TRIGGERS FOR PATIENTS WITH MAST CELL DISEASES

are highly individualized. The most common triggers include: heat, cold, temperature change, exercise, fatigue, friction, vibration, pressure, sunlight, perfumes, odors, insect and other venoms, certain foods, alcohol, anesthetics, viral/bacterial/fungal infections, and stress of all kinds (environmental, physical and emotional). Some patients may experience reactions to certain medications, including but not limited to opiates, antibiotics, and NSAIDs. Use with caution.

While there is no cure for most cases of systemic mastocytosis, certain cases of aggressive disease are currently being treated in clinical trials with stem-cell transplants.

For more current information about anesthesia and perioperative management of a patient with mast cell diseases, please visit www.tmsforacure.org/perioperative-management.

DIAGNOSTIC CRITERIA FOR MASTOCYTOSIS

was established in 2001. Cutaneous mastocytosis is divided into maculopapular cutaneous mastocytosis (MPCM) [including urticaria pigmentosa (UP) and telangiectasia macularis eruptiva perstans (TMEP), the latter of which is no longer identified as a separate diagnosis], diffuse cutaneous mastocytosis (DCM), and cutaneous mastocytoma. Systemic disease is divided into indolent (benign) systemic mastocytosis (ISM), with a sub variant of bone marrow mastocytosis (BMM); smoldering systemic mastocytosis (SSM); systemic mastocytosis with an associated hematologic neoplasm (SM-AHN); aggressive systemic mastocytosis (ASM); and mast cell leukemia (MCL). In order to diagnose systemic mastocytosis, a patient must fulfill one major criterion and at least one minor criterion. Alternately, a diagnosis may be made if a patient fulfills three minor criteria.

Major criterion:

Multifocal compact tissue infiltration by mast cells, >15/cluster, in an organ other than skin

Minor criteria:

1. Abnormal morphology of mast cells (spindling, immature forms, abnormal nuclei, hypogranulated cytoplasm)
2. Atypical immunophenotype of mast cells, with expression of CD2 and/or CD25
3. Presence of KIT mutation (D816V or other exon 17 mutation)
4. Persistently elevated serum tryptase > 20 ng/ml

The gold standard for diagnosis is an iliac crest bone marrow biopsy and aspirate. This includes flow cytometry and immunohistochemistry testing for normal and abnormal mast cells (CD117, tryptase, CD25). Common additional tests may include periodic serum tryptase levels, 24-hour or spot urine collections for histamine metabolites and prostaglandins (mediator levels at baseline and within 60 minutes of an activation event or anaphylaxis), CBC with differential, serum chemistries, bone scan, bone density test, and skin biopsy.

For more information on cutaneous mastocytosis variants, please visit <https://tmsforacure.org/overview/cutaneous-mastocytosis-variants>.

For more information on systemic mastocytosis variants, including the use of B- and C- findings for diagnosis of more advanced variants (SSM, SM-AHN, ASM, and MCL), please visit <https://tmsforacure.org/overview/systemic-mastocytosis-variants-including-b-c-findings>.

For information on mast cell sarcoma, please visit <https://tmsforacure.org/overview/mast-cell-sarcoma>.

PROPOSED CONSENSUS CRITERIA FOR DIAGNOSING MAST CELL ACTIVATION SYNDROME

requires fulfillment of three co-criterion:

1. The patient exhibits symptoms involving two or more organ systems in parallel, which recur, or are chronic, are found not to be caused by any other condition or disorder other than mast cell activation, and require treatment or therapy.
2. Documentation is obtained showing that mast cells are directly involved in the symptomatology. An increase in the serum level of tryptase (drawn one to two hours after an event), at least 20% above baseline plus 2 ng/ml, indicates that a mast cell activation event has occurred. When serum tryptase evaluation is not available or when the tryptase level does not rise sufficiently to meet the required increase for the co-criterion, other mediator tests, such as urinary n-methyl histamine, prostaglandin-D2, or its metabolite, 11 β -prostaglandin-F2 α , could suffice. All three mediators are frequently measured in one 24-hour or spot urine collection.
3. A response to anti-mediator or therapy must be demonstrated.

For more information on mast cell activation syndrome variants, please visit <https://tmsforacure.org/overview/mast-cell-activation-syndrome-variants>.