MCAS is not a rare disease.

Myth: MCAS is a rare disease.
It is estimated that 5-10% of the population has MCAS(1)!

There are 327 million people in the US, thus 16 to 33 million of those people have MCAS. In order for a disease to be considered rare, it needs to affect less than 200,000 Americans. You can see that the MCAS population is substantially beyond that mark.

The misconception that MCAS is a rare disease may exist because mastocytosis, a related disease to MCAS, is rare. The misconception also exists because, according to what we hear from the MCAS community, MCAS is under diagnosed. When test results come back in normal range many doctors conclude that the patient does not have MCAS, however, we now know that mediator testing is not conclusive and is not as reliable as was once thought.

We will discuss why this is, within this slide-show, however, you can also Click Here to learn more.
MCAS symptoms are not universally experienced amongst all MCAS patients.

Myth: MCAS is symptomatically straightforward.
What MCAS patients have in common, universally, is that they are experiencing chronic Mast Cell (MC) activation. That is to say, their MCs are easily stimulated and are releasing mediators more frequently than a healthy person’s MCs would be. The hallmark, primary symptoms of MCAS, are not experienced by all MCAS patients. These include recurrent anaphylaxis, throat tightening, syncope, pruritis, hives, flushing, tingling mouth or skin, malaise, nausea, vomiting and diarrhea(2,3,4,5). There are certainly more symptoms associated with this disease, that are also not experienced universally and that still need to be verified through research.

There could be an argument made that aside from degranulation, multi-system inflammation is the only symptom that all, or at least the large majority of MCAS patients share. Dr. Hamilton states: “Mast Cell Activation Syndrome might be the underlying cause of unexplained symptoms when several organ systems are involved, such as the gastrointestinal tract and the skin”(6). Dr. Lawrence Afrin has also stated that the MCAS patient often has inflammation presenting in multiple systems(7).
The etiology of MCAS varies. There are several different types of biological and environmental circumstances to consider.

Myth: ALL MCAS is caused by ______!!
We often come across the opinion (brought forth by MCAS patients) that there is a singular root to all MCAS, however, there is no evidence to support this. There are many types of circumstances which can result in the activation of this disease. **We encourage the MCAS community to be aware that there still needs to be research done in order to confirm or deny many of suspected causes of MCAS.** (Please read our [Q&A Page](#) for more information on this topic).

Here are some noticeable trends suggesting root causes of MCAS:

- Extreme taxation of the body caused by factors such as physical or emotional trauma, other diseases, stress, allergies and or inflammation.
- A severe IgE event (i.e. allergic reaction).
- Lyme disease, Epstein Barr and other viruses.
- Gastrointestinal issues.
- Exposure to mold, synthetic chemicals or heavy metals.
- Inherited gene mutations.
- Gene mutations and inherited gene predispositions.
Persons with MCAS can go into anaphylaxis induced from IgE antigens but also from IgG antigens.

Myth: Severe MCAS allergic reactions are only caused by IgE antigens.
There are many receptors on the MC, aside from the IgE, which respond to many kinds of stimulus, and which are responsible for the degranulation of some or all of the 50-200 types of mediators held within.

IgE allergy stimulus and receptor is most studied and is noted for its role in anaphylaxis, but the IgG stimulus and receptor is also linked to anaphylaxis! An IgG receptor on the MC, specifically FcγRIIA, can set off the polymorphism c.7421871A>G, and this can induce anaphylaxis. As doctor Heather Caslin explains an IgG antigen can cause a response similar to that of IgE from the MC:

“Mast cells can be activated by IgG immune complexes binding pro-inflammatory FcγRI, FcγRIIA, or FcγRIII, which are variably expressed on mouse and human mast cells. These receptors induce a signaling cascade resembling IgE–FcεRI activation that elicits cytokine secretion, arachidonic acid metabolism, and degranulation.”
This knowledge supports the phenomena that many of us are all too familiar with: that one can experience the symptoms of MC activation, even anaphylaxis, induced from non-IgE stimulus: allergy tests show normal results yet exposure to the very same substances that a patient was tested on, results in a debilitat-ing and or fierce reaction.

As far as IgG food sensitivity and anaphylaxis, there certainly needs to be more research done, but there is enough research to know that it is possible. Because of the FcγRIIA polymorphism IgG MC degranulation and the many thousands of people who are reporting anaphylaxis and or MCAS symptoms from food intolerance, we discourage the unfounded belief that IgG food sensitivity can not result MC symptoms and cannot cause anaphylaxis.
Persons with MCAS may experience hypersensitivity to food or their environment.

Myth: Hypersensitivity is not related to MCAS.
Thousands of persons with MCAS consistently report that their primary MCAS symptoms result directly after they are exposed to intolerances such as pollen, fragrances, synthetic chemicals and certain foods. This is why, part of the standard treatment for MCAS involves the removal of “triggers” from the patients diet, medications and environment(13, 14).

We often hear the stories of persons with MCAS hypersensitivity who live off very few foods, and in some cases, even have to go onto a feeding tube. Another common MCAS story is of those who are confined to their home, due to debilitating hypersensitivity. It is important to realize that hypersensitivity directly results in MCAS flares and symptoms. There may be other cells and pathologies involved in the presence of hypersensitivity, aside from MC activation, but here is what we do know: **MCAS appears to be directly correlated to hypersensitivity.** For many people, hypersensitivity is a key trait correlated with the progression and worsening of the disease.
Hypersensitivity reactions may correlate to IgE stimulus but may also correlate to IgG and other stimulus as well. That is to say, a person’s IgE tests show normal results for substances that directly result in hives, anaphylaxis and other primary MCAS symptoms.

It has been argued by a select few that hypersensitivity should not be considered a characteristic trait of MCAS. This is completely nonsensical.

With MCAS, the MCs themselves become chronically hypersensitive reacting to a large array of stimulus. There are many receptors on the MC which respond to many kinds of stimulus and those manifold receptors release many kinds of mediators that induce an array of effects upon the body. The world contains many substances, that when absorbed through the skin, through breathing or eating, may eventually translate to stimulus that can dock on MC receptors. The mechanics of hypersensitivity pathology are largely unknown, but we do know one of most notable traits of MCAS is chronic heightened sensitivity.
The degree of intolerance and which stimulus an MCAS patient is intolerant to, largely varies. As doctor Matthieu Picard states:

“A primary mast cell disorder should be suspected in any patient presenting... without an identifiable trigger or with multiple unrelated triggers”(14).

Here is a quote from Dr. Anne Maitland describing the sensitivity of the MCAS patient:

"Your body has to figure out what should stay and what should be kept out. At the forefront of this is the mast cell... If there is a perceived danger you are going to increase the presence [of mast cells]"(15).

Because of all of these factors, we passionately promote the awareness that hypersensitivities, including IgG food sensitivities and environmental intolerances, can directly result in the exacerbation of MCAS reactions and symptoms.

Click Here, to participate in our Hypersensitivity Research Study.
Mast Cells can be activated from external triggers that come into contact with the body but they can also be activated through events happening within the body.

Myth: All triggers are external.
The following are a few examples of internal stimulus.

**Exercise**
MC degranulation has been clinically observed after exercise which can result in all primary mast cell symptoms including asthma and anaphylaxis(17, 18, 19). Exercise induced anaphylaxis often happens when a person eats food in close proximity to exercise(20).

**Fatigue**
Fatigue is one of the most common symptoms among MCAS patients(21) and it results in part, from mediator release. There is a genetic factor to consider as well. As doctor Omdal has said “Although pain and psychological factors influence fatigue, there is an increasing understanding that there is a genetic basis, and that activation of the innate immune system is an essential generator of fatigue”(22). Thus, for some patients there appears to be a cyclical loop of MC activation resulting in fatigue, and that fatigue resulting in further MC activation.
**Stress**
Life stress can play a major role in the onset and progression of MC diseases (23). Several varieties of CRF (stress hormones) can bond to the CRF receptor on MCs and activate it (24).

**Comorbidities and Co-diseases**
Illnesses can escalate one another. (Please see our Q&A page for a list comorbidities that are commonly associated with MCAS.) One could argue that most diseases have the potential to influence MC activation within the MCAS patient, because of the direct role MCs play in all aspects of tissue repair as well as in fighting viral, parasitic and bacterial infections (25, 26).

**Physical Trauma**
As stated, when MCs are healthy, they play a key role in the healing of tissue damage and wounds (25). However, when a MC activation disorder is present, the damage itself can activate MCs with inappropriate mediator release (27, 28).
Many people who have MCAS, **never** go into anaphylaxis.

Myth: All patients with a severe form of MCAS, go into anaphylaxis. If they do not, they have a less severe form of the disease.
There are three types of MC activation/degranulation: transgranulation, explosive or anaphylactic degranulation (AND) and piecemeal degranulation (PMD).

With transgranulation MCs actually insert granules into neighboring cells (29). Here is an excerpt wherein Dr. Flores describes the remaining two types:

“Anaphylactic degranulation (AND) after IgE-mediated activation is characterized by a rapid swelling and fusion of MC granules as well as abrupt mediators release. Piecemeal degranulation (PMD) is a slow and selective secretion of distinct granule mediators by vesicles shuttling from the granule compartment to the plasma membrane, and it is associated with several chronic diseases (30)”

Some who have MCAS, only undergo piecemeal degranulation and therefore experience MCAS symptoms while never going into anaphylaxis. That being said, PMD can still cause debilitating symptoms, that have a tremendous impact on quality of life.
Persons with MCAS can experience MC activation, and even go into anaphylaxis, without producing elevated tryptase levels.

Myth: Tryptase is the best way to measure MCAS.
There is one mediator of which the most focus is placed: tryptase. There is a grouping of researchers, scientists and doctors who acknowledge that tryptase is typically lower in patients with MCAS as opposed to Systemic Mastocytosis (SM). However, there is also a grouping of persons who are still placing tremendous weight on this mediator. **This unfounded emphasis on tryptase is one of the biggest obstacles that the MCAS patient faces.**

Tryptase is the correct lens of which to see the degree of suffering within some MCAS and SM patients but this absolutely does not transfer to being able to accurately assess the entire MCAS patient population. It must have been a revelation at first to be able to trace this mediator but it’s initial value has not withstood the test of time. The continued focus on tryptase has become problematic to say the least.

**Tryptase is not always released, and when it is released, can not always be measured through testing, even by those suffering from severe reactions. This is why anaphylaxis is a clinical diagnosis.**
With food-induced anaphylaxis (FIA), total tryptase is not always elevated:

“At present, there is no laboratory test that reliably confirms cases of FIA [Food Induced Anaphylaxis].” (31). Dr. Antonella Cianferoni.

“The diagnosis of anaphylaxis is based on clinical history since no reliable biological marker is currently available to confirm the diagnosis” (32). Dr. Anna Sala-Cunill

“Over a 4-year period, 203 children had serum tryptase levels measured. Among these, 39 children (19.2%; 95% CI, 14.1%-25.4%) had elevated levels. Only severe reactions were associated with reaction levels of 11.4 μg/L or more... Importantly, tryptase was not raised in 36.3% of cases; furthermore, in 60.6% of these patients, no changes were observed in tryptase levels... Anaphylaxis was more severe and tryptase concentration higher when the causative agent was a drug compared to food” (33). Dr. Sarah De Schryver
If tryptase is **not** a “reliable biological marker” to determine FIA, then why is it determined that is it a reliable marker to measure MCAS? Many times food is what causes anaphylaxis in MCAS patients and MC activation is the culprit within both FIA and MCAS. **Why is there a double standard: diagnostic weight is not placed on tryptase when diagnosing FIA and other anaphylaxis, so why so is there so much focus on it when diagnosing MCAS?**

If you have normal numbers of mast cells, you may not have increased total tryptase upon testing:

> “The levels of the protrypases reflect the total number of mast cells within the body, but are not an indication of mast cell activation”(34). The Mayo Clinic

> “...local mast cell activation is not necessarily reflected in the circulation”(35). Dr. Lawrence B. Schwartz
“Tryptase released by mast cells at mucosal sites may not diffuse into the circulation as efficiently as that released near blood vessels, and mast cells at mucosal surfaces contain less tryptase than those in the skin and perivascular tissues” (36). Dr. Lawrence B. Schwartz

“[There is a] lack of published validation that the suggested diagnostic tryptase calculation [for MCAS] reliably distinguishes ordinary baseline fluctuation of tryptase from fluctuation induced by aberrant MC activation…while still quite useful as an initial laboratory screen for MC neoplasia in mastocytosis – is a relatively poor indicator of MC activation, and old precepts that MC disease is unlikely when the serum tryptase level is normal can no longer stand” (37). Dr. Lawrence B. Afrin

“Tryptase is a biomarker related to the severity of anaphylaxis. However, since its concentration remains unaltered in a considerable number of
patients during acute anaphylaxis, there is a need for more reliable diagnostic biological tests” (38). Dr. Anna Sala-Cunill

The assumption that MCAS patients with normal tryptase range cannot go into anaphylaxis, is simply unfounded and incorrect. Tryptase levels do not always correlate to the severity of anaphylaxis or the severity of other MCAS symptoms.

The category of MCA (Mast Cell Activation), a category known as less severe than MCAS, is unethical because the degree of illness within the MCAS patient, can not be measured by their tryptase level, and the level of their tryptase is exactly how some doctors are issuing that diagnosis.

If you are a doctor, please do not place diagnostic weight on the tryptase test. If you are a patient or family member of a patient, please politely relay the inefficiency of tryptase testing to your doctor.
There is not a single mediator test of which 50% of the MCAS patient population can meet with elevated results.

Myth: If tryptase comes back in normal range, then one of the other mediator tests will definitely be able to show the presence of MCAS.
Dr. Lawrence Afrin did a study that illuminated the inconsistencies in mediator test results among MCAS patients. He discovered that there is not a single mediator test, of which, even 50% of the MCAS patient population can meet with elevated results (39).

If a patient can have anaphylaxis without presence of elevated tryptase, then it is possible that an MCAS patient can go into anaphylaxis without producing other mediator rise, as detectable by any of these current tests? The answer is yes. Just because some persons with MC disease do show elevated levels on some of the mediator tests does NOT make testing with elevated levels universal among those with MC disease.

Consider that studies focusing on MC disease have progressed using only the patient population that is positive on mediator testing. (They use patients who test with elevated mediator levels as starting criteria to be in the study, which is
great for understanding that subset of MC patients with that particular characteristic of degranulation, but not MC patients as a whole.)

The focus on mediator testing has created a perpetual cycle of exclusion in testing, diagnosis and treatment, of which “non-elevated mediator” patients (according to the current tests) cannot break into. It is possible for a person with MCAS to test within normal range on ALL of these mediator tests and STILL HAVE MC disease/degranulation, including more severe forms.

Normal test results, despite MC activation can happen due to several different Problems and Factors.

This leaves as far as we have witnessed, a very large percentage of MC patients medically unrepresented and under treated. One of the primary goals of this non-profit, is to raise funds that will be used to develop more accurate and or different, diagnostic testing for MCAS.
Persons with MCAS may not exhibit hives, welting or angioedema, even during anaphylaxis.

Myth: If there aren’t any skin symptoms, it’s not MCAS.
Cutaneous symptoms (most commonly urticaria or ‘hives’) are absent in some anaphylactic reactions. It is also possible to have anaphylaxis without breathing difficulties, though not common.

The Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium(40) determined that Anaphylaxis is highly likely when any ONE of the following 3 criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula

AND AT LEAST ONE OF THE FOLLOWING

a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)

b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
   a. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
   b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
   c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)
   d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

3. Reduced BP after exposure to known allergen for that patient (minutes to several hours):
   a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP
   b. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline
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REFERENCES


   "Systemic mast cell activation disease (MCAD, prevalence 5–10%) is a multifactorial, polygenic disease with multisystemic symptoms that is characterized by an unregulated increased release of mast cell mediators and an accumulation of activated mast cells potentially in all organs and tissues."


   See Table IV

   https://www.clinicaltherapeutics.com/article/S0149-2918(13)00171-9/fulltext


   See Table 2

   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5341697/

See Table 3

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3069946/


"Mild to moderate symptoms may include one or more of the following:
Hives (reddish, swollen, itchy areas on the skin)
Eczema flare (a persistent dry, itchy rash)
Redness of the skin, particularly around the mouth or eyes
Itchy mouth or ear canal
Nausea or vomiting
Diarrhea
Stomach pain
Nasal congestion or a runny nose
Sneezing
Slight, dry cough
Odd taste in mouth

Severe symptoms may include one or more of the following:
Swelling of the lips, tongue, and/or throat that blocks breathing
Trouble swallowing
Shortness of breath or wheezing
Turning blue
Drop in blood pressure (feeling faint, confused, weak, passing out)
Loss of consciousness
Chest pain
A weak or “thready” pulse
Sense of “impending doom”"
6) Matthew J. Hamilton, MD, Jason L. Hornick, MD, PhD, Cem Akin, MD, PhD, Mariana C. Castells, MD, PhD, and Norton J. Greenberger, MD. "Mast cell activation syndrome: A newly recognized disorder with systemic clinical manifestations." 2011.

"MC activation syndrome might be the underlying cause of unexplained symptoms when several organ systems are involved, such as the gastrointestinal tract and the skin."

https://www.jacionline.org/article/S0091-6749(11)00675-0/pdf


"Given that the essence of Mast Cell Activation Syndrome is chronic... multi-system illness, of a generally, though not necessarily, inflammatory, plus-minus allergic theme, given that broad statement, is it possible that some portions of the population bearing these and... many other chronic inflammatory illnesses, is it possible that MCAS might be, MCAS especially, with wide array of mutations that are at the root of various forms of Mast Cell Activation Syndrome, is it possible that the various forms of Mast Cell Activation Syndrome might be at the roots, of some portions of the populations with all of these and many other diseases? This is a question. It needs to be addressed with appropriate research"

https://www.youtube.com/watch?v=82dmZhCBuBo 51 minutes into video

See Figure 1 for a list of Non IgE receptors.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5932183/


"However, IgE is not the only component to stimulate these cells to degranulate, while mast cell activation can also result in differential release of mediators. There is a plethora of stimuli, such as IgG, complement components, TLR ligands, neuropeptides, cytokines, chemokines and other inflammatory products, that can directly trigger mast cell degranulation, cause selective release of mediators, and stimulate proliferation, differentiation and/or migration."


See Table 1 for a list of mediators.


See Table 4 for IgG anaphylaxis description.

"Permits alternative splicing of the C1* exon resulting in expression of “hyperactive” FcγRIIA3. Risk factor for IVIg anaphylaxis"

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6433993/


“Mast cells can be activated by IgG immune complexes binding pro-inflammatory FcγRI, FcγRIIA, or FcγRIII, which are variably expressed on mouse and human mast cells. These receptors induce a signaling cascade resembling IgE–FcεRI activation that elicits cytokine secretion, arachidonic acid metabolism, and degranulation"

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5932183/

13) Afrin, Lawrence B.(2016). "Never Bet against Occam: Mast Cell Activation Disease and the Modern Epidemics of Chronic Illness and Medical Complexity." SistersMedia, LLC.

"Triggers are bad. Duh. Therefore you can take this as 'Step 1' in the therapeutic plan for any MCAS patient is to indentification and avoidance of triggers, such as possible. Also, if possible, densensitization therapy (if available for identifiable but unavoidable triggers)..." Pg. 222
"Whenever possible, try to change only one thing in the MCAS patient's regimen at a time. Maybe that's trying a new medication, or trying a new dose, schedule or formulation of an old medication. Maybe it's trying a new food or soap or detergent. Maybe it's trying new clothes (which may be pretreated with some modern miracle textile chemical which might provoke a mast cell reaction).” Pg. 218

"Whenever a stabilized MCAS patient destabilizes, the first thing to do --and the second, third, fourth, and fifth things to do --is carefully review the events of the few days to few weeks prior to the destabilization to try to identify what changed" Pg. 220


"Identification and avoidance of relevant triggers of mast cell activation in a particular patient is of prime importance for symptom control."

https://www.clinicaltherapeutics.com/article/S0149-2918(13)00171-9/fulltext


"A primary mast cell disorder should be suspected in any patient presenting with a systemic reaction to hymenoptera stings or episodes of mast cell activation either without an identifiable trigger or with
multiple unrelated triggers, especially if associated with hypotension and if urticaria or angioedema is absent."

https://www.clinicaltherapeutics.com/article/S0149-2918(13)00171-9/fulltext


"We have embodied, inherited responses to injuries. To recognize and respond to injury. What has happened with industrialization is that we have so dramatically changed our environment. All of us have a tendency to focus on what we have a lot of control on, meaning what we eat but here is the thing... you maybe eat three or four times a day. You might drink a little bit more than that. You breathe eighteen times per minute. And your skin is constantly exposed to the environment. So your body has to has to figure out what should stay and what should be kept out. At the forefront of this is the mast cell... If there is a perceived danger you are going to increase the presence [of mast cells]"

https://www.youtube.com/watch?v=LddITjni4G0


"When patients with exercise-related anaphylaxis were subjected to exercise challenge while they were wearing a plastic occlusive suit, they developed mild, partial attacks and demonstrated a rise in serum histamine. 2 To directly assess the role of tissue mast cells in the exerciseinduced anaphylactic reaction, skin biopsy specimens were obtained before and after exercise challenge from five subjects with EIA, and the structural state of the mast cells was assessed by TEM."

"Exercise-induced anaphylaxis is an uncommon disorder in which anaphylaxis occurs in response to physical exertion. Food-dependent exercise-induced anaphylaxis is a disorder with similar symptoms, although symptoms develop only if exercise takes place within a few hours of eating and, in most cases, only if a specific food is eaten."


"Co-factors can either trigger the elicitation of a severe allergic reaction or affect its severity. Among such co-factors are physical activity, the intake of certain drugs, and psychological stress."


"The ingestion of specific foods, including seafood, tree nuts, and wheat, or a nonspecific meal consisting of multiple food components shortly before or after physical exertion, is sometimes, but not always, the principal precipitant of EIA."

"Demographics, comorbidities, symptoms, family histories, physical examination and laboratory findings were reviewed in 298 retrospective and 115 prospective patients with MCAS."

"Gastroesophageal reflux, fatigue and dermatographism were the most common comorbidity, symptom and examination finding."


"Although pain and psychological factors influence fatigue, there is an increasing understanding that there is a genetic basis, and that activation of the innate immune system is an essential generator of fatigue."


"MCs play a critical role in host defense and are among the earliest immune cell responders to environmental, immunologic, and infectious stressors [2, 50]. To perform that role, MCs express a myriad of receptors to sense and integrate stress cues from the microenvironment and, in turn, elicit a quick and powerful immune response via degranulation. Stress is known to modulate MC degranulation and exacerbate MC-associated disorders."

"Life stress is a major risk factor in the onset and exacerbation of mast cell–associated diseases."


"Psychological stress is a significant risk factor in a number of inflammatory and allergic diseases. We have previously demonstrated that CRF1 receptors expressed on mast cells (MCs) can potentiate psychological stress-induced MC degranulation intestinal permeability, and IgE-mediated anaphylaxis."

"Contrasting effects of CRF2 were observed with de novo synthesized mediator release as IL-4, IL-6, MCP-1 and prostaglandin D2 release were reduced (by ~40–50%) in CRF2−/−BMMCs following stimulation with IgE-antigen, LPS and IL-33. In summary, these data show that CRF2 signaling inhibits MC degranulation and associated pathophysiology induced by acute psychological stress and IgE-mediated anaphylaxis, while enhancing the release of de novo synthesized mediators."

https://www.jimmunol.org/content/200/1_Supplement/105.5

"With the aid of a wide array of newly formed or preformed mediators released by degranulation, the activated mast cell controls the key events of the healing phases: triggering and modulation of the inflammatory stage, proliferation of connective cellular elements and final remodeling of the newly formed connective tissue matrix. The importance of the mast cell in regulating healing processes is also demonstrated by the fact that a surplus or deficit of degranulated biological mediators causes impaired repair, with the formation of exuberant granulation tissue (e.g. keloids and hypertrophic scars), delayed closure (dehiscence) and chronicity of the inflammatory stage."


"Mast cell mediator release during parasitic infection promotes immune cell recruitment and regulation of gastrointestinal permeability. Moreover, the microenvironment generated in response to mast cell mediators produces favorable conditions for the expulsion of the parasite and containment of a chronic infection"

"Similar to DCs, mast cells are among the first cells of the immune system to interact with antigens, toxins, and pathogens."

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4230976/

"While MCs initially promote healing, they can be detrimental if they are chronically stimulated or if too many MCs become activated at the same time."

"Detrimental effects can occur, and this is often dependent on inappropriate cellular activation during the varied phases of tissue repair."

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4115062/


"The risk of systemic reactions during general anesthesia can be reduced by assessing risk on an individual basis (previous reaction to a drug or reaction during surgery) and by avoiding specific trigger factors (patient temperature changes, infusion of cold solution, tissue trauma, friction, and other mechanical factors)."

http://www.jiaci.org/summary/vol24-issue5-num1145


"Due to their paracrine nature, mast cells can modulate events in their microenvironment through explosive degranulation, piecemeal degranulation, or "transgranulation" as they insert granules into neighboring cells".

"Anaphylactic degranulation (AND) after IgE-mediated activation is characterized by a rapid swelling and fusion of MC granules as well as abrupt mediators release. Piecemeal degranulation (PMD) is a slow and selective secretion of distinct granule mediators by vesicles shuttling from the granule compartment to the plasma membrane, and it is associated with several chronic diseases.”


"At present, there is no laboratory test that reliably confirms cases of FIA."

"The diagnosis of anaphylaxis is based on clinical history since no reliable biological marker is currently available to confirm the diagnosis."

https://www.karger.com/Article/Abstract/339749


"Over a 4-year period, 203 children had serum tryptase levels measured. Among these, 39 children (19.2%; 95% CI, 14.1%-25.4%) had elevated levels. Only severe reactions were associated with reaction levels of 11.4μg/L or more."


"The levels of the protypases reflect the total number of mass cells within the body, but are not an indication of mast cell activation."

https://www.mayocliniclabs.com/test-catalog/Clinical+and+Interpretive/32283?
fbclid=IwAR1BFdyKhGlX1hGBLGKZoUhRTeDXRIwxQMO5nONsHzhTfVuXskzWqCyls8M

"In 62 subjects with ongoing allergic rhinitis, tryptase levels were no different in serum than for 19 normal controls, indicating that local mast cell activation is not necessarily reflected in the circulation."


36) Schwartz, Lawrence B. (2012). “Laboratory tests to support the clinical diagnosis of anaphylaxis”

"Tryptase released by mast cells at mucosal sites may not diffuse into the circulation as efficiently as that released near blood vessels, and mast cells at mucosal surfaces contain less tryptase than those in the skin and perivascular tissues"

http://freeuptodate.scientificjournals4all.com/contents/mobipreview.htm?39/54/40809


“We disfavored the Valent et al. criteria [32] for several reasons discussed previously in the literature [e.g., 33] including (1) nonrecognition of many of the symptoms of MC activation, (2) lack of published validation that the suggested diagnostic tryptase calculation reliably distinguishes ordinary baseline fluctuation of tryptase from fluctuation induced by aberrant MC activation, (3) practical difficulties in providing/obtaining a specimen for serum total tryptase shortly after exacerbation of symptoms, and (4) practical difficulties in finding – in such a heterogeneous disease – effective treatment prior to diagnosis."
"Furthermore, our present study adds to evidence mounting in the last decade that the serum tryptase level – while still quite useful as an initial laboratory screen for MC neoplasia in mastocytosis – is a relatively poor indicator of MC activation, and old precepts that MC disease is unlikely when the serum tryptase level is normal can no longer stand".

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5341697/


"Tryptase is a biomarker related to the severity of anaphylaxis. However, since its concentration remains unaltered in a considerable number of patients during acute anaphylaxis, there is a need for more reliable diagnostic biological tests"

https://www.karger.com/Article/Abstract/339749


See Table 3

http://www.bloodjournal.org/content/128/22/3683?ssChecked=true&fbclid=IwAR3oqURGRFt4i8Xg42eHhclNpT0bf9kHoRTcAtxhzeWlbqeWwTxsMNfx9Q
40) Sampson, Hugh A. et al. "Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium." Journal of Allergy and Clinical Immunology, Volume 117, Issue 2, 391 - 397

See Table 1