Mediators

*Remember:
The degranulation of mast cells lead to their release.

- Tryptase
- Heparin
- Histamine

The three most studied (but there are more).

They can play a role in:	
regulating vascular stability	acute allergic reactions, including those seen in mast cell activation syndromes, such as headache, nausea, itching, flushing, gastric hypersecretion, nasal congestion, and wheezing
the dysfunction of endothelial cells	angioedema and pulmonary edema
Edema, hypovolemia, and shock	mucus hypersecretion
gastrointestinal symptoms	fatigue
confusion	sense of impending doom
coagulation abnormalities	bleeding

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Treatment of Mediator Induced Reactions

- Focused primarily on trigger avoidance and symptom control
- Two doses of **Self-Injectable Epinephrine** (e.g., EpiPen®/EpiPen Jr®) should be carried by all patients with a mast cell disorder at all times, even if they have not previously experienced anaphylaxis. Both the patient and family members/caregivers should be trained on administering epinephrine!

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Treatment of Mediator Effects

MEDIATOR	POSSIBLE EFFECTS	Basic Medications for Symptomatic Patients with Mast Cell Diseases
Histamine	Flushing, itching, diarrhea, hypotension	H1 antihistamines: help with itching, abdominal pain, flushing, headaches, brain fog H2 antihistamines: help with gastrointestinal symptoms and overall mast cell stability (all mast cell activation symptoms) Mast cell stabilizers: help with stomach and intestinal symptoms and brain fog Leukotriene inhibitors: help with respiratory symptoms and overall mast cell stability (all mast cell activation symptoms) Aspirin therapy (under direct supervision of a physician): if tolerated and if prostaglandins are elevated, helps with flushing, brain fog and bone pain
Leukotrienes	Shortness of breath	
Prostaglandins	Flushing, bone pain, brain fog, cramping	
Tryptase	Osteoporosis, skin lesions	
Interleukins	Fatigue, weight loss, enlarged lymph nodes	
Heparin	Osteoporosis, problems with clotting/bleeding	
Tumor Necrosis Factor-α	Fatigue, headaches, body aches	

Note: *The H1 and H2 antihistamines are necessary to stabilize receptors on the mast cell. Therefore, if additional medication is required for control of gastroesophageal reflux (GERD), a proton pump inhibitor may be added to this protocol, but it cannot replace the H2 antihistamine.*

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Example Medications Used to Treat MC Mediated Symptoms

Full lists provided at link

H1 antihistamines:	H2 antihistamines:	Mast cell stabilizers:	Leukotriene inhibitors:	Targeting prostaglandins:
• diphenhydramine • loratadine • cetirizine	• famotidine • cimetidine	• cromolyn sodium • ketotifen	• montelukast • zileuton • safirlukast	• aspirin