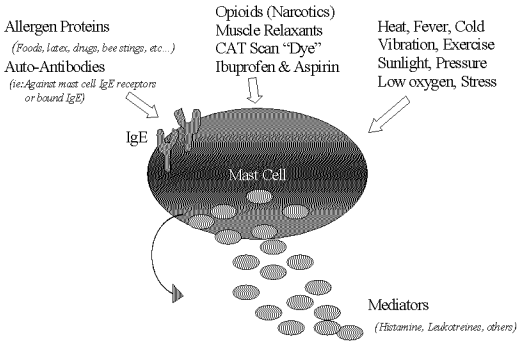
What Are Hives?

Hives are caused by leakage of plasma rich fluid out of your blood vessels & into the skin. Your vessels dilate & leak due to histamine. Histamine is contained in the storage granules within Mast Cells in the skin. Histamine is spilled into the skin when Mast Cells are triggered by various stimuli (as seen in the figure below). Heat, cold, allergens, medications, etc., can cause histamine release. (The figure on the other side of this sheet shows the whole process). When histamine is released in the top layer of the skin you get hives (urticaria); when in the lower skin, you get swelling (angioedema). Hives are usually short-lived (<24 hrs) per individual lesion.

Mast Cells: The Central Players in Hives



What Causes Hives?

Patients often think hives are due to some hidden allergy. Being an allergist, I wish that were true. However, if you've had hives for over 6 weeks, they are almost never due to allergies. Indeed, 95% of the time NO clear cause is ever found – even in large research based university allergy clinics. Many of these cases are now thought due to "auto-antibodies" (self –antibodies) that inappropriately stick to your own Mast Cell receptors and trigger the Mast Cell to spill it's histamine. These auto-antibodies have been found in specialized laboratories, but tests for their presence are not currently commercially available.

If a food were triggering your hives – it should become obvious by the 6-week mark and the hives only occur within 1 hour after eating that food again.

If "air-allergens" (dust, pollen, mold, animal dander) were the cause – you should also have severe hay fever, itchy eyes, asthma…during your "hive flare up," as these allergens in the air would get onto & into the pink mucus membranes of tthose organs first, before penetrating the thicker skin & causing hives there.

Allergy & Asthma

of the Black Hills

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Board Certified Allergist & Immunologist

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Hives (Urticaria) & Swelling (Angioedema)

Allergy & Asthma

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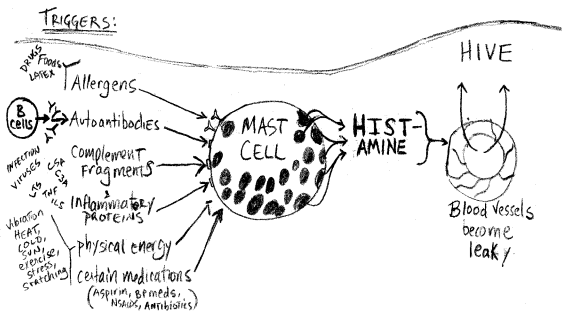
HIVES: FAST FACTS

- About 20% of the population will get hives.
- 0.1% of the population has hives at any given time (ie: 1 in 1000 suffer right now).
- Acute hives are often due to allergens & medications *(especially foods, antibiotics, aspirin/pain relievers, latex, stings)* or viral infections.
- Chronic hives (lasting >6 weeks) are rarely due to allergens, but often "auto-immune."

URITICARIA (HIVES)
TREATMENT APPROACHES



Treating Hives: Setting *up Roadblocks*

Regardless of what causes the mast cell to release its histamine, leukotrienes & other mediators *(ie: allergens, auto-antibody against mast cell IgE receptors, etc....),* the standard treatment is to "block" these mediators so that they don't reach the tiny blood vessels in the skin & cause leaking of plasma proteins & fluids there.

Anti-histamines block histamine – by binding to two types of histamine receptors found on the blood vessel walls.

Leukotriene inhibitors block leukotrienes (more delayed mediators in hives than histamine) – by binding LT receptors.

Immune-suppressants block the immune system's B-cells from making more allergic IgE antibodies & quiet down the entire "hive circuit" as illustrated above. May work on other cells as well & generally need long term monitoring for safe use.

Immunol Allergy Clin North Am. 2004 May;24(2):163-81, v.

thedinics.com

Autoimmune urticaria.

PubMed National Library of Medicine National Institutes of Health www.pubmed.gov

Grattan CE.

A growing body of evidence shows that at least 40% of patients with unexplained (idiopathic) chronic urticaria have clinically relevant functional autoantibodies to the high-affinity IgE receptor on basophils and mast cells. The term "autoimmune urticaria" is used for this subgroup of patients presenting with continuous ordinary urticaria. This article reviews the evidence for the autoimmune hypothesis and other nonantibody serum histamine-releasing factors in the etiopathogenesis of urticaria; defines autoimmune urticaria; looks at how autoimmune urticaria fits into existing classifications of urticaria; proposes diagnostic criteria that may be useful to the clinician; and reviews the management implications for patients with this subset of chronic disease.

FIRST-LINE MEDICATIONS *(Generally very safe for the long-term; Minimal monitoring required)*

1) Antihistamines - Type I *(ie: Zyrtec, Allegra, Clarinex, Claritin, Benadryl, Hydroxyzine, Cyproheptadine, etc.)*

The best single agent for hives. The skin is loaded with histamine receptors (85% are Type I (H1), 15% are Type II (H2)) – so these agents block most of them. Newer ones last 24 hours & have little or no sedation. Sometimes the sedation of the older agents is used to "take the edge off of the itch." If using the older types: please don't drive if you are sedated!

2) Antihistamines - Type II *(ie: Zantac, Ranitidine, Tagamet, Cimetidine, Pepsid, Famotidine)*

They Type I antihistamines block most of the skin's histamine receptors, but since 15% of the receptors are of a different shape (ie: the H2 receptors), sometimes adding a Type II (or H2) type antihistamine provides additional benefit. Most of the H2 receptors are found in the stomach & stimulate acid production – so you will recognize these as H2 blockers as "antacid medications," now available over the counter. They are generally very safe & don't generally cause any sedation.

3) Leukotriene Inhibitors *(ie: Singulair, Accolate)*

Although blocking histamine is usually the most important treatment for hives, sometimes blocking leukotrienes is also helpful – adding a little extra improvement more than with antihistamines alone. Often, only a small subset of people with hives (ie: those with long-lasting hives) see improvement. These medications are very safe, but somewhat expensive for the small amount of extra benefit they usually provide.

4) Tricyclics *(ie: Doxepin, Sinequan, Trazodone, Desyrel, Amitriptyline, Nortriptyline)*

These medications were originally made to treat depression. However, doctors learned that they are very strong histamine receptor blockers. For example, Doxepin blocks histamine type I (H1) receptors 775 times more tightly than does Benadryl! Further, Doxepin also blocks H2 type receptors. We usually use them in lower doses than for depression & usually at bedtime because they are often very sedating.

Oral Steroids *(ie: Prednisone, Prelone, Medrol)*

This is the "nuclear bomb" of medicines. Very powerful at reducing inflammation. If needed, we try to limit its use to short periods (ie: 7-14 days) because long term use can cause many other problems (osteoporosis, cataracts, obesity, muscle wasting, and other undesirable effects). Not a good long term solution for hives.

SECOND-LINE MEDICATIONS *(When standard "first-line" medications fail; Need to monitor)*

1) Cyclosporine *(Neoral, Sandimmune)*

Originally use to prevent transplant rejection by "suppressing" one's own white blood cells so they wouldn't attack the "foreign" donor's organ. Effective in chronic "auto-immune" hives *(ie: the body's own white cells making anti-body that sticks to it's own Mast Cells).* Blood pressure & kidney blood test monitoring.

2) Plaquenil *(Hydroxychloroquine)*

An anti-malarial agent now used for lupus & other rheumatic diseases. Good for sun sensitive hives/swelling. Eye exams.

3) Dapsone (Avlosulfon)

An older anti-leprosy antibiotic found to have anti-inflammatory effects often helpful for chronic urticaria, urticarial vasculitis & dermatitis herpetiformis. Anemia labs.

4) Sulfasalazine *(Azulfadine)*

"Immune-suppressant" often used for inflammatory bowel, rheumatoid arthritis or skin disorders to suppress white cells called neutrophils (seen especially in deep pressure related hives). Liver tests and blood counts need close monitoring.

5) Colchicine

A anti-swelling gout medication. Blood count monitoring.

6) Imuran *(Azathioprine)* & Methotrexate *(Mexate)*

"Immune-suppressing" drugs like cyclosporine. Slow down the body's inflammatory response (in hives – ie: against itself). CBC & chemistry test monitoring is necessary.

7) NSAIDS *(Indocin, Ibuprofen, Naproxen, Celebrex)*

Can make some people's hives better & some worse.

8) Oral Beta-Agonists *(Albuterol, Terbutaline)*

Asthma drugs. Works on mast cell β-receptors to "stabilize" the membrane so it is not so prone to "spill" its histamine. Can act as a stimulant like caffeine (i.e.: cause tremor).

9) Anti-Virals *(Valtrex, Acyclovir)*

Although used to suppress cold sores, chickenpox, shingles, and herpes…they also have anti-inflammatory properties.

10) Hormones *(Lupron, Progestins, Androgens, Thyroid)*

When hives are "timed" to menstrual cycle stages estrogen/progesterone manipulation with BCP type meds may help. Male androgens may help a swelling condition caused by a lack of a blood enzyme (C1 Esterase Inhibitor). Slight Thyroid Hormone "over-replacement" may help those with chronic hives who also are found to have auto-antibodies against their own thyroid gland.