Myth #1:
Patients with shellfish allergy are at high risk of allergic reaction to contrast dye

The antigen (allergen) in shellfish is tropomyosin, not iodine

Tropomyosin is a muscle protein that triggers an IgE mediated (immediate hypersensitivity) reaction in patients with food allergy to shellfish

Contrast triggers a non-IgE mediated reaction, sometimes called "anaphylactoid", or "pseudoanaphylaxis," which causes direct mast cell degranulation

Clinical Pearl
ALL atopic patients are at slightly higher risk of reactions to contrast

What about Gadolinium?

Named after J. Gadolin, 18th c French chemist
Atomic number 64
Silvery white metal
Used in magnets, as a recording medium for compact discs, and in nuclear power industry

Gadolinium

As an IV contrast agent it enhances images in MRI and MRA
Excreted almost exclusively by the kidney

What is the incidence of allergic reactions?

Gadolinium

Gadopentetate dimeglumine (687,255)
Gadodiamide (74,275)
Gadoteridol (64,005)

Range of incidence of non-allergic reactions 0.015 - 0.267%


Mild allergic reactions: 0.016 - 0.017%
Moderate allergic reactions: 0.004 - 0.017%
Severe allergic reactions: 0.001 - 0.007%

De Ritter analysis of 30,000 patients receiving IV injection of 0.1 mmol/kg gadoterate meglumine or gadopentetate dimeglumine for an MRI exam:

3 reports of moderate or severe reactions

Cochran analysis of trends in adverse events after administration of contrast media

19 adverse events after 28,340 administrations of gadolinium (0.06%)  

June 2006

FDA reported a possible connection between high dose gadolinium use in renal failure patients and potential risk for nephrogenic systemic fibrosis/nephrogenic fibrosing dermopathy during MRA.  
25 cases in Denmark  
5 cases in Austria

Update - December 2006

Approximately 200 cases worldwide  
Cause and effect not yet established, but there is concern about high dose use of gadolinium in MRA (up to 3 times higher than in MRI).

Clinical Pearls

- Severe allergic reactions after gadolinium administration are extremely rare, but do exist; changing brands has been associated with improved tolerance - is it meaningful?  
- Use particular caution in patients with renal failure or with use of high doses  
- The FDA recommends consideration of early hemodialysis in renal failure patients (not evidence based)

www.fda.gov/cder/drug/advisory/gadolinium_agents.htm

Recommendations for patients with contrast allergy:

Avoid contrast, if possible  
Use contrast with lower osmolality

Consider premedication for patients who have a history of:

- Multiple food allergies  
- Multiple drug allergies  
- History of previous reactions to contrast
One regimen for premedication:

Prednisone 40 mg, 13, 7, and 1 hour prior to contrast
Diphenhydramine, 50 mg IM or po 1 hour prior to contrast
Emergency care on hand (including epinephrine) for management of anaphylaxis

JCAAI.org *Practice Parameters *Anaphylaxis Guidelines

Myth #2:

Bee sting anaphylaxis is best treated with prayer (and maybe an epinephrine injection)

Hymenoptera Reactions

About 4-5 people per 1000 will have a systemic reaction when stung by Hymenoptera. There are 40-100 deaths annually in the US due to systemic reactions. Better recognition, prevention and treatment are needed.

Systemic allergic reactions

- mild, diffuse itching
- hives
- angioedema
- abdominal pain or menstrual cramps
- asthma or upper airway edema
- cardiovascular collapse
- reactions closer to the face and throat

Local reactions are not usually "allergic" reactions, and are not predictive of the development of systemic reactions

Hymenoptera

- Honey Bee
  - Apis mellifera
- Yellowjacket
  - Vespula germanica
- Paper Wasp
  - Polistes dominulus
- Bumble Bee
  - Bombus pascuorum
- Bald-faced Hornet
  - Dolichovespula maculata
- Hornet
  - Vespa crabro

Images: cirrusimage.com, USDA, Wikipedia
**Major Hymenoptera Antigens**

<table>
<thead>
<tr>
<th>Species</th>
<th>Allergen</th>
<th>Common name</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Apis mellifera</em></td>
<td>Api m1</td>
<td>Phospholipase A1</td>
</tr>
<tr>
<td></td>
<td>Api m2</td>
<td>Hyaluronidase</td>
</tr>
<tr>
<td></td>
<td>Api m3</td>
<td>Acid phosphatase</td>
</tr>
<tr>
<td><em>Vespula vulgaris</em></td>
<td>Ves v1</td>
<td>Phospholipase A1</td>
</tr>
<tr>
<td></td>
<td>Ves v2</td>
<td>Hyaluronidase</td>
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<tr>
<td><em>Dolichovespula</em></td>
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<tr>
<td></td>
<td>Dol m2</td>
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<tr>
<td></td>
<td>Dol m5</td>
<td>Antigen 5</td>
</tr>
<tr>
<td><em>Polistes annularis</em></td>
<td>Pol a5</td>
<td>Antigen 5</td>
</tr>
</tbody>
</table>

**Cross-reactivity of antigens**

- Greater cross-reactivity among yellow jackets and hornets, although wasps also related (all called “vespids”)
- Degree of cross-reaction among the vespids is hyaluronidase > antigen 5 > phospholipase
- Minimal but known cross-reactivity between honey bees and vespids

**Hymenoptera Immunotherapy**

- UCSF - about 12 weeks of several injections, then decreasing to every 4th-8th week for up to 5 years
- “Ultra-rush” immunotherapy at some institutions
- Patients with decreased baseline FEV1 are at higher risk of systemic reactions

**Clinical Pearls**

- Hymenoptera anaphylaxis is highly treatable, and appropriate therapy can prevent death
- Patients with a history of systemic reactions should carry an epinephrine injection system, and know how to use it
- Patients with severe anaphylactic reactions: check serum tryptase to rule out mastocytosis
- Refer to AI for definitive diagnosis and treatment

**Practical preventive tips**

- Avoid wearing brightly colored clothes or strong perfumes
- Exert caution at outdoor events where food is present
- Remove nests from around the house
- When working outdoors, wear long pants, long sleeve shirts, shoes and gloves

**Hymenoptera Immunotherapy**

Venom immunotherapy reduces the risk of subsequent life-threatening reactions from about 60% to less than 2%.
Myth #3
Chronic urticaria/angioedema is usually caused by allergy

Clinical Pearl
If urticaria/angioedema is caused by allergy (IgE mediated), the trigger is usually evident

Urticaria and Angioedema

- “Chronic” is more than 6 weeks
- Various triggers cause release of mast cell granules, which contain histamine, tryptase, and many other substances. Basophils can also release mediators, with some differences from mast cells
- Superficial lesions cause urticaria; deeper lesions manifest as angioedema

30 - 50% of chronic urticaria/angioedema is due to newly recognized autoantibodies

- These patients make autoantibodies to:
  - IgE
  - Fc epsilon RI (cell receptor)
  - Fc epsilon RII (cell receptor)

- These autoantibodies likely bind to the surface of basophils and mast cells, resulting in signal transduction and degranulation


Mast cell degranulation

- Recognition of underlying autoimmunity will change the treatment approach for severe urticaria/angioedema that does not respond to antihistamine therapy.
Most patients with urticaria/angioedema respond well to long acting, non-sedating antihistamines (loratidine, cetirizine, fexofenadine).

There is a higher incidence of other autoimmunity (such as thyroid autoantibodies) in patients with chronic urticaria. In patients whose urticaria/angioedema persists, consider checking thyroid function and presence of autoantibodies.

**Clinical Pearls**

Can hereditary angioedema (HAE) be distinguished easily from acquired disease? HAE, an autosomal dominant disease, is NOT accompanied by urticaria. Tests of C1 esterase inhibitor quantity and function are therefore (generally) not indicated in patients with urticaria.

New onset of angioedema in an older person can be a hallmark of lymphoproliferative disease or other immune dysregulation.

**Additional references/websites**

- JCAAI.org: Practice Parameters
- AAAAI.org, ACAAI.org, FoodAllergy.org (FAAN)