

**FAST FACTS AND CONCEPTS #175
OPIOID ALLERGIC REACTIONS**

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Background Patient reports of opioid “allergies” are common, most often due to symptoms of nausea, vomiting, itching, hypotension, or constipation. This *Fast Fact* will review signs, symptoms, and management options of opioid allergies and pseudo-allergies.

Pathophysiology Allergies can be defined as an *exaggerated immune reaction to an antigen*. There are different types of allergic, or hypersensitivity, reactions (immediate, cytotoxic, immune complex, or delayed), but the common feature is that all such reactions are *mediated by the immune system*. In contrast, the vast majority of opioid side effects are not immune related. Opioid side effects can be divided into three categories: those that have no element of an immune reaction, those that mimic an immune reaction, and those that are immune mediated.

Side effects with no immune mechanism: these include nausea/vomiting, constipation sedation, delirium, respiratory depression, and urinary retention.

Side effects that mimic immune reactions: common signs/symptoms include mild itching, urticaria, bronchospasm, or hypotension. **Note:** if all these occur soon after an opioid dose, and the patient appears acutely ill, this may represent an anaphylactoid reaction (see below). For most patients, these symptoms are mild and self-limited. The etiology most commonly involves direct mast cell degranulation with histamine release, unrelated to a true immune-mediated reaction. Such reactions to opioids are usually idiosyncratic and may or may not recur with re-challenge of the same opioid; they are not a contraindication to continued opioid use, since an alternative opioid may be well tolerated. Hypotension can also occur due to arterial and venous vasodilation, thus, hypotension is more common in a volume depleted patient. Opioids can also have negative inotropic effects and induce a vagally-mediated bradycardia leading to hypotension – again, not a true allergic reaction.

Immune mediated reactions:

- **Allergic dermatitis** in response to opioids has been described. It is characterized as erythroderma, scarlatina, eczema, or exudative vesicular eruptions; these may represent a Type IV (delayed) hypersensitivity reaction. Patients can undergo diagnostic patch testing for confirmation.
- **Anaphylaxis/Anaphylactoid Reactions.** Anaphylaxis is a systemic IgE mediated reaction resulting in the immediate release of potent mediators; anaphylactoid reactions are clinically the same, but not IgE mediated. Early symptoms include nasal congestion, flushing, pruritus, angioedema; if the process worsens, patients can develop nausea, diarrhea, urinary urgency, bronchospasm, hypotension, and death. Opioids can lead to an anaphylactoid reaction, but such events are very rare.

Management True allergic reactions appear to be rare. If you suspect an immune-mediated skin rash you should consult a dermatologist or allergist to establish a definitive diagnosis and determine the need for desensitization or appropriate alternatives. Anaphylactoid reactions require emergent management with epinephrine and histamine blockers. For milder histamine-related symptoms, common practice is to rotate to an opioid in a different pharmacologic class (see below) along with use of anti-histamines or steroids. Anecdotal reports suggest that methadone and fentanyl cause fewer instances of itching.

Opioid Class	Drugs
Phenanthrenes	morphine; codeine; hydrocodone; oxycodone; oxymorphone; hydromorphone; levorphanol.

Phenylpiperadines	fentanyl; meperidine; sufentanil; remifentanyl
Diphenylheptanes	methadone; propoxyphene

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