

Prescribing opioids safely in patients with an opiate allergy

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True immunologic opioid allergy is rare. Most patients are actually reporting a known adverse effect of the drug, or a pseudoallergy. Pseudoallergic drug reactions mimic true immunologic reactions, but they are not immune-mediated. Such reactions have been coined *nonimmune hypersensitivity reactions* (or anaphylactoid reactions). The most common adverse effects of opiates are drowsiness and GI upset (nausea, vomiting, constipation) and should be noted on the patient record as such. Proper documentation allows clinicians to choose a better alternative without the concern for cross-allergy with other opioids.

Nonimmune hypersensitivity reactions to opioids are very common and occur much more frequently than immunologic (IgE-mediated) reactions. Unfortunately, distinguishing between the two clinically may be difficult. Pseudoallergic reactions result when direct stimulation of mast cells leads to release of mediators, such as histamine. Itching is a common symptom; flushing, hives, sweating, and mild hypotension may also occur. The most common offenders in pseudoallergic reactions are the low-potency opiates (meperidine [Demerol, generics], codeine, and morphine).

For prevention and treatment of nonimmune hypersensitivity reactions, first, determine if the patient truly requires an opiate. Try scheduled acetaminophen or an NSAID if no contraindications exist. If a narcotic is required, give the lowest possible dose because histamine release is a dose-dependent effect. Another option is to prescribe a high-potency opioid, which is less likely to cause histamine release. The following agents are listed in order of increasing potency: meperidine, codeine, morphine, hydrocodone, oxycodone (Oxecta, OxyContin, Roxicodone, generics), hydromorphone (Dilaudid, Exalgo, generics), fentanyl (Duragesic, generics).¹ Finally, concurrent administration of an antihistamine (such as diphenhydramine [Benadryl, generics]) may be effective.

To determine what opioids may be safely prescribed in a patient with a documented allergy, a detailed description of the reaction is crucial. A true allergic reaction may include severe hypotension or cardiovascular collapse; angioedema or swelling of the lips, tongue, face, or mouth; bronchospasm or respiratory distress; or cutaneous reactions other than hives, flushing, or itching (such as rash or erythema multiforme). In a patient reporting any of these symptoms, care should be taken to avoid the offending agent, and the patient should be asked what opioids he or she has taken safely in the past.

Knowledge of opioid metabolism is also helpful in differentiating a true allergy from a pseudoallergy and avoiding agents that may result in cross-reactivity. For example, codeine is metabolized to morphine and hydrocodone is metabolized to hydromorphone. Therefore, codeine should be avoided in patients with a morphine allergy. Alternatively, patients who report an allergy to hydromorphone but can tolerate hydrocodone are unlikely to have a true IgE-mediated allergy.

If a patient with a history of opiate anaphylaxis requires a narcotic analgesic and has never been challenged with an alternative opioid, the safest option is to consult an immunologist or choose a drug from a different structural class (**Table 1**). The patient must be monitored closely for anaphylaxis. Because true opiate allergy is so rare, there is not enough information to accurately

assess the risk of cross-allergy between the different structural classes. Patients can be allergic to more than one structural group and may exhibit cross-reactivity between classes.

TABLE 1. Opioid agents by structural class

Structural class	Agents	
Diphenylheptanes	• Methadone (Dolophine, Methadose, generics)	• Propoxyphene (withdrawn from US market)
Phenanthrenes	• Buprenorphine • Butorphanol (Stadol, generics) • Codeine • Hydrocodone • Hydromorphone	• Levorphanol • Morphine • Nalbuphine • Oxycodone • Oxymorphone (Opana, generics)
Phenylpiperidines	• Fentanyl • Meperidine	• Remifentanyl (Ultiva) • Sufentanyl (Sufenta, generic)

If you cannot clearly determine whether a patient has experienced an immune-mediated allergic reaction versus a nonimmune hypersensitivity reaction, take into consideration the severity of the reaction, extent of systemic involvement, previous exposure, and timing of the symptoms in relation to drug administration. [JAAPA](#)

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REFERENCE

1. Analgesic options for patients with allergic-type opioid reactions. *Pharmacist's Letter/Prescriber's Letter*. 2006; 22(220201).

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