

Occupational allergic contact dermatitis caused by morphine

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Natural alkaloids extracted from *Papaver somniferum* have long been known to cause allergic contact dermatitis, but the number of reported cases remains small. Herein, we describe a case of airborne occupational allergic contact dermatitis caused by morphine, with cross-reactions to chemically related congeners.

Case Report

In February 2009, a 30-year-old atopic female researcher working for a generic drug manufacturer was exposed to the powder of atorvastatin, quetiapine, and morphine. Within a few days, she developed a severe papulovesicular, oozy airborne contact dermatitis involving her face, neck, and the upper part of her anterior chest. The eyelids were markedly swollen, but the most severely affected areas were the retro-auricular areas, the nape of the neck, and the chin and lower lip. Her hands and arms remained uninvolved, because she always worked with gloves and gowns. The lesions slowly cleared with topical corticosteroids and withdrawal from work. One month later, she was reassigned to clerical duties outside of the laboratory, and initially did well. However, she sustained a relapse of her dermatitis after handling a binder that was brought to her from the laboratory. She was then sent home on workers' compensation, and will eventually be re-trained.

Patch testing was performed in two separate sessions according to the International Contact Dermatitis Research Group criteria. In October 2009, the patient was first tested with the North American Contact Dermatitis baseline series (AllergEAZE™, SmartPractice®, Calgary, Canada) applied on Finn Chambers® (SmartPractice®,

Phoenix, AZ, USA), as well as with 18 medicaments and inert ingredients from the workplace, applied on IQ Ultra® chambers (Chemotechnique Diagnostics AB, Vellinge, Sweden) (Table 1). A single reaction, to morphine 1% pet., was detected on both D2 and D4 (Table 1).

A second patch testing session was carried out in March 2010, to characterize the patient's sensitization to opioid analgesics better, and to determine what substances she should avoid. We used four different narcotics supplied by the hospital pharmacy, namely codeine, hydromorphone, meperidine (pethidine), and fentanyl. The patient showed positive reactions to codeine and hydromorphone, but did not react to meperidine or fentanyl (Table 1).

Discussion

Cutaneous sensitization resulting from topical application or systemic administration of opium and its derivatives

Table 1. Patch tests results

	D2	D4
First session		
NACDG Standard Series	—	—
Atorvastatin, crystalline, 5% pet.	—	—
Atorvastatin, crystalline, 1% pet.	—	—
Atorvastatin, crystalline, 0.1% pet.	—	—
Atorvastatin, amorphous, 5% pet.	—	—
Atorvastatin, amorphous, 1% pet.	—	—
Atorvastatin, amorphous, 0.1% pet.	—	—
Quetiapine 10% pet.	—	—
Quetiapine 1% pet.	—	—
Morphine 1% pet.	2+	3+
Second session		
Codeine 1% aq.	2+	3+
Codeine 3% aq.	2+	3+
Hydromorphone 1% aq.	—	2+
Meperidine 5% aq.	—	—
Fentanyl 0.005% aq.	—	—

NACDG, North American Contact Dermatitis Group.

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has been reported as early as 1882, according to Touraine's extensive review (1). The first half of the 20th century saw the publication of a certain number of cases of occupational dermatitis caused by opioids (2–4). Additional reports have since followed (5–8). Affected workers have included nurses or other health personnel who handle the drugs, or factory employees engaged in their preparation. Most of these workers have been exposed to the drugs in powder form, and have developed an airborne pattern of contact dermatitis. In their description of 9 cases that occurred in a morphine factory, Dore et al. stated that the eruption began on the eyelids, and then affected the nape of the neck and the sub-mental area, and later the arms and hands (4). This pattern exactly describes the sequence of events in our patient.

The natural phenanthrene alkaloids derived from opium include morphine, codeine (3-methylmorphine), and thebaine. Semi-synthetic derivatives such as heroin (diacetylmorphine) and hydromorphone share a similar chemical structure with morphine (Fig. 1). Not surprisingly, many patients sensitized to one compound exhibit cross-reaction to one or more of the other phenanthrene opioids (2, 3, 5–13). Among 8 nurses sensitized to heroin, 6 also reacted to morphine and 4 to codeine (8). The concentrations and vehicles used vary from one publication to another, 1% in aqueous or alcoholic solutions being most common. When serial dilutions were used, positive reactions were sometimes seen down to dilutions of 0.001% for codeine (9) or 0.00001% for morphine (2).

The fully synthetic opioid meperidine, a phenylpiperidine, and its congeners fentanyl, anileridine, alphaprodine and diphenoxylate are structurally different from the natural phenanthrene opioids (Fig. 1). Not surprisingly, no cross-reaction is seen between the two groups of analgesics (6, 8, 10).

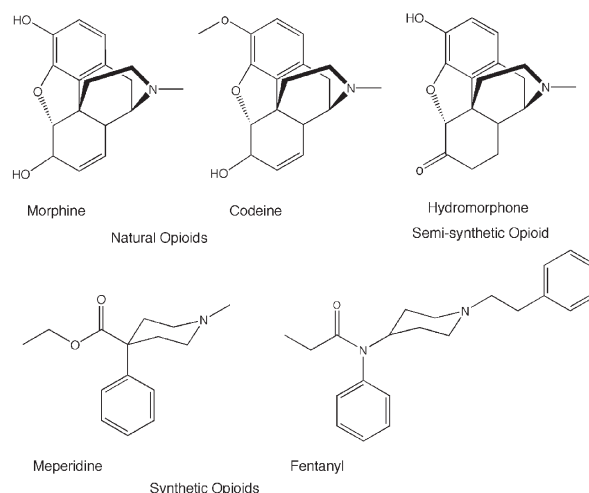


Fig. 1. Chemical structures of the tested natural, semi-synthetic and synthetic opioids.

Many patients who had positive patch test reactions to opioids presented with a drug eruption and were therefore sensitized through systemic administration (9–17). However, systemic administration after sensitization by topical exposure can also trigger systemic allergic dermatitis with generalized eruptions (2, 3). Given that such patients may need opioid analgesics after trauma as well as dental or other surgical procedures, it is important to test them with different drugs in order to determine which one they can safely use.

A recent publication describes allergic contact dermatitis caused by apomorphine (18). This dopaminergic agonist used as an emetic and in the treatment of Parkinson's disease is produced by degradation of morphine by strong acids. It is devoid of analgesic properties, but its chemical structure retains much of the configuration of its parent compound. It would be interesting to determine whether it cross-reacts with morphine-derived opioids.

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