

# Occupational opiate contact dermatitis

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doi:10.1111/cod.12666

**Key words:** allergic contact dermatitis; case report; codeine (CAS no. 76-57-3); cross-sensitization; ethylmorphine (CAS no. 76-58-4); morphine (CAS no. 57-27-2); naloxone (CAS no. 465-65-6); naltrexone (CAS no. 16590-41-3); occupational; opiate; thebaine (CAS no. 115-37-7).

Occupational sensitizations to opiate derivatives have been described by several authors over the past century (1). We describe 2 cases of employees working in the same pharmaceutical plant who developed contact dermatitis caused by opiates they handled.

## Case Reports

Two female laboratory workers aged 38 and 58 years were employed for 18 and 7 months, respectively, in a pharmaceutical company that manufactures several opiates. Both handled morphine and codeine. The first one also worked with dihydrocodeine, and the second one with naltrexone. Both developed papulovesicular contact dermatitis with an airborne pattern.

Patch tests were performed according to ICDRG criteria (2), with the products from the plant at different concentrations (0.01–5% or 10%) in pet. and aq., respectively. The products tested were morphine, codeine, thebaine, ethylmorphine, naloxone, and oxycodone. Prick and intradermal tests were also performed with synthetic products such as alfentanil, sufentanil, fentanyl, and tramadol.

All substances tested in water gave negative results (0.01–10%). Both cases showed positive patch test reactions to codeine 5% pet. (+), which was still positive on D9 for case 2, and ethylmorphine 1% and 10% pet. (+). Case 1 also showed positive patch test reactions to morphine [(+) for a 0.1% dilution and (++) for higher

concentrations], and case 2 showed a positive patch test reaction to naloxone 10% (+). No immediate or delayed reactions to synthetic opiates were observed in the 2 patients.

## Discussion

We describe 2 cases with work-related contact dermatitis related to handling natural opiates and opioids. Contact allergy was diagnosed with patch test dilutions in pet., whereas aq. preparations yielded negative results, which favours the use of pet. Our patients handled the same products, but showed different airborne sensitization profiles: Case 1 developed occupational sensitization to morphine and codeine she handled, and cross-reactivity to ethylmorphine. Case 2 was specifically sensitized to codeine she was handling, and showed cross-reactivity to ethylmorphine and naloxone. Codeine does indeed have a close chemical relationship with ethylmorphine, and other authors have already shown cross-reactivity between these compounds (3). The cross-reactivity with ethylmorphine observed in both patients is probably attributable to codeine rather than to morphine sensitization, as case 2 did not develop morphine sensitization, despite handling it. Interestingly, potential cross-reactivity between codeine or ethylmorphine and naloxone has not actually been shown, but only suggested in one study (4). Rodriguez et al. (5) described a female patient who was sensitized by the ingestion of codeine-containing products. She developed codeine sensitization and cross-reactivity to morphine without cross-sensitization to naloxone. Codeine and ethylmorphine have structural similarities (phenanthrene) with naloxone, but also with morphine and oxycodone. Cross-reactivity between the latter and naloxone has already been found in immunoassays; however, the patient did not react accordingly (6). Further studies are needed to examine cross-sensitization. Moreover, it is

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*Conflicts of interest:* The authors declare that there are no conflicts of interest.

*Source of Funding:* None declared.

crucial to establish that no other cross-reactivity exists, in particular with synthetic products used for general anesthesia, as shown for fentanyl (1). Fortunately, our patients did not show cross-sensitization to fentanyl, sufentanil, alfentanil, sufentanil, or tramadol, which can thus be used safely.

## Acknowledgements

We would like to sincerely thank the Sanofi factory for providing us the manufactured products.

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