## Is Post-Surgery Codeine a Risk for Kids?

hildren are often prescribed codeine for pain relief after surgery to remove their tonsils or adenoids to treat sleep apnea, a condition in which breathing problems make it hard for them to sleep soundly.

However, some children may be at risk of developing serious side effects, or even dying, after being given codeine in amounts that are within the recommended dose range.

The Food and Drug Administration (FDA) has reviewed recent reports in medical literature of three deaths and one life-threatening case in children who took codeine for pain relief after surgery to remove their tonsils or adenoids to treat sleep apnea. The agency is warning the public that this danger exists for some children whose livers convert codeine to morphine in higher than normal amounts.

FDA wants parents and caregivers to be aware of the warning signs that could indicate their child is having trouble breathing because of this higher morphine level.

The agency is trying to determine if there have been other cases of accidental overdose or death in children taking codeine, and if there have been incidents like this when children have taken codeine after other kinds of surgical procedures, says Bob Rappaport, M.D., director of the Division of Anesthesia, Analgesia and Addiction Products (DAAAP) in FDA's Center for Drug Evaluation and Research.

## The Problem

Codeine is an opioid pain reliever—a narcotic medication—used to treat mild to moderate pain. It is also used to reduce coughing, usually in combination with other medications. Codeine is available by prescription either alone or in combination with acetaminophen or aspirin, and in some cough and cold medications.

Codeine is converted to morphine in the liver by an enzyme. Some people have genetic variations that make this enzyme over-active, causing codeine to be converted to morphine faster and more completely



than in other people. These "ultra-rapid metabolizers" are more likely to have higher than normal amounts of morphine in their blood after taking codeine. High levels of morphine can result in breathing difficulty, which may be fatal.

From one to seven in every 100 people are "ultra-rapid metabolizers," but they are more common among some ethnic groups. Twenty-nine percent of North African and Ethiopian populations are "ultra-rapid metabolizers," with about 6 percent of African American, Caucasian and Greek populations also affected.

The only way to know if someone is an ultra-rapid metabolizer is to do a genetic test. There are FDA-cleared tests to check for ultra-rapid metabolism.

The cases occurred in children who showed evidence of being ultra-rapid metabolizers. The children ranged in age from 2 to 5 years old. All of the children received doses of codeine that were within the typical dose range, meaning that they were not given extra amounts of the medication.

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In these cases, the signs of morphine overdose developed within one to two days after the children started taking codeine.

## Signs of Trouble

FDA warns that when prescribed to treat pain after surgery, codeine should not be given on a schedule, but only when the child needs relief from pain. Children should never receive more than six doses in a day.

Parents and caregivers should watch their children closely after surgery, and after they have returned home, for signs of a morphine overdose.

There are a number of symptoms to watch for, says Rappaport. If your child shows these signs, stop giving the codeine and seek medical attention immediately by taking your child to the emergency room or calling 911:

 Unusual sleepiness, such as being difficult to wake up

- Disorientation or confusion
- Labored or noisy breathing, such as breathing shallowly with a "sighing" pattern of breathing or deep breaths separated by abnormally long pauses
- Blueness on the lips or around the mouth

"The most important thing is that caregivers should tell the 911 operator or emergency department staff that their child has been taking codeine and is having breathing problems," Rappaport says.

Talk to your child's health care professional if you have any questions or concerns about codeine. Health care professionals are being advised by FDA to prescribe the lowest effective dose for the shortest period of time when prescribing drugs that contain codeine.

If your child experiences any side

effects from codeine, report them to the FDA MedWatch program.

FDA will update consumers about this issue when more information is available.

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