Food allergy: Analyzing fatal reactions

It's common knowledge that for people allergic to bee venom, a simple sting can bring death. Less well appreciated—both among physicians and the public—is that food allergies can also kill, and they appear to be on the rise. Indeed, they may now claim more lives than insect stings among children and adolescents, according to data from a new study.

In reviewing the course of life-threatening reactions to food in 13 children, six of whom died, the researchers turned up several surprises, including signs of an increased risk of severe reactions in food-allergy sufferers with asthma.

Their findings also strongly suggest that all food-induced reactions involving respiratory symptoms, such as trouble breathing, deserve respect — *and* a visit to the hospital, says study coauthor Hugh A. Sampson of Johns Hopkins University in Baltimore. In three to four hours, reactions that initially appeared mild to moderate can turn deadly, his team reports in the Aug. 6 NEW ENGLAND JOURNAL OF MEDICINE.

Allergists tend to expect that in cases where reactions will prove severe, symptoms will progress rapidly, probably within 30 minutes of allergen ingestion. But Sampson notes that three of the children who died had recovered from early symptoms for an hour or two before suddenly entering a catastrophic phase.

The protracted nature of some reactions also surprised his team. One young girl, Sampson notes, "spent three weeks on a ventilator with all the major suppressor drugs before she came through."

One thing common to all children in the study was asthma, a disease that can have allergic underpinnings. This "provocative" finding certainly hints that asthma "may be a risk factor for death from food allergy," says Marshall Plaut, asthma and allergy branch chief at the National Institute of Allergy and Infectious Diseases in Bethesda, Md.

Plaut was also surprised to learn that concentrations of the enzyme tryptase were not elevated in the blood samples taken from two of the children with food allergies (one of whom died). Tryptase elevations typically characterize severe reactions to other allergens, such as bee venom. Tryptase is a marker for the activity of mast cells—one of the two cell types generally considered responsible for triggering the many symptoms associated with allergy. Plaut says that the normal tryptase levels seen here "make you wonder if we understand why these patients die" — if there isn't something other than mast cells at work.

Somewhat to his surprise, Sampson notes that among the cases he reviewed, epinephrine — the primary drug for reversing allergic symptoms — did not prevent severe food reactions. However, he says, it "did buy patients time to reach a medical center." Indeed, no child who received early treatment with epinephrine died.

John W. Yunginger of the Mayo Clinic in Rochester, Minn., sees a major message there: Physicians should prescribe and train families of allergic patients in the use of kits containing epinephrine. Wesley Burks, a food-allergy researcher at Arkansas Children's Hospital in Little Rock, agrees but adds that "it's very atypical for a practicing physician to do that."

Finally, the study's authors note that none of the children knowingly ate foods containing items to which they were allergic. That's not surprising, Yunginger says, since food labels currently mask several problem items. For instance, he notes that "reflavored" peanuts are sometimes labeled "artificial walnuts" because they look and taste like walnuts. Not only is that label "totally uninformative," he says, "but it also could pose a lethal risk to certain people." Three of the six deaths in this study resulted from allergies to peanuts.

Nor are labels the only problem. Last year, Sampson's team discovered why children with milk allergies occasionally react severely to certain "nondairy" foods: The researchers found name-brand products heavily contaminated with milk protein. *—J. Raloff*

Treatment for premature labor reevaluated

The drug ritodrine, widely used to prevent premature delivery, does not work in many cases, according to a large-scale study reported by Canadian researchers in the July 30 NEW ENGLAND JOURNAL OF MEDICINE.

Experts call for reduction of ritodrine treatments in light of potentially serious maternal side effects. "These results should greatly influence the treatment of preterm labor all over the world," concludes an editorial in the same journal by Kenneth J. Leveno and F. Gary Cunningham, obstetricians at the University of Texas Southwestern Medical Center at Dallas.

Given to an estimated 100,000 U.S. women each year, ritodrine relaxes the muscles of the uterus and thus may temporarily halt preterm labor, says Leveno. The first randomized clinical trials of this drug took place in the early 1970s, but it was not approved for use in the United States until 1980. Developed for obstetrical use, ritodrine is the only drug specifically approved for treatment of preterm labor by the Food and Drug Administration.

But controversy has long surrounded its use, says Leveno, who believes the new findings confirm that ritodrine has few long-term benefits. In the largest ritodrine test yet conducted, researchers at six Canadian hospitals studied 708 women in danger of delivering their babies prematurely and followed 246 of their infants for 18 months. Each mother received randomly assigned treatment with either ritodrine or a placebo. Infants' gestational ages at the initiation of the study ranged from 20 to 35 weeks.

While ritodrine lowered the proportion of women who delivered within 24 to 48 hours after administration, it had no significant beneficial effects on the overall rates of premature delivery, low birthweight, or infant mortality, the team reports. In addition, mothers given ritodrine showed an increase in serious side effects such as chest pain, irregular heart rhythms, and fluid-filled lungs.

Although none of the women in the Canadian study died, some maternal deaths have been associated with ritodrine use, according to Leveno and Cunningham. The Dallas obstetricians call for FDA to "reappraise the vanishingly small neonatal benefits in light of the substantial maternal risks of ritodrine."

The drug may often be given unnecessarily, since "most of the women who threaten to deliver prematurely do not," Leveno adds. "The Canadian study shows very clearly that not giving any medicine does not mean that the patient delivers prematurely."

Although ritodrine "shouldn't be used in the majority of cases where we do use it, there is still a place for it," contends study coauthor Sidney B. Effer, an obstetrician at the University of British Columbia in Vancouver.

Effer emphasizes that ritodrine can help to delay delivery until patients can be transferred to a hospital with a neonatal intensive care facility. In addition, the study indicates that for a crucial time in pregnancy — between 24 and 27 weeks, while the infant's lungs are developing — ritodrine may achieve a 7.2 percent decline in infant mortality. Effer and his coworkers conclude that ritodrine may be beneficial if used before a gestational age of 28 weeks or in conjunction with drug therapies designed to stimulate the growth of the baby's lungs.

While this study highlights the need for new treatments, "there is still a lot of hope" for today's premature babies, says Leveno, who notes that overall infant mortality in the study was less than 6.5 percent for both the ritodrine and the placebo groups.

The FDA plans an open advisory committee meeting on Oct. 20 to reassess the maternal risks and neonatal benefits of ritodrine and other uterine-relaxing agents. *— K. Hoppe*