[SCIENCE]

House dust yields clue to asthma: roaches

Daniel Remick and his team got out of the lab to gather material for studying asthma in children and found that allergies to roaches are a major cause

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Asthma is the most common chronic disease of childhood, one that strikes the poor disproportionately.

Up to one-third of children living in inner-city public housing in the US have allergic asthma, in which a specific allergen sets off a cascade of events that cause characteristic inflammation, airway constriction and wheezing.

Now, using an experimental model that required leaving the pristine conditions of the laboratory for the messier ones of life, a team of scientists from the Boston University School of Medicine have discovered what that allergen is.

"For inner-city children," said the lead researcher, Daniel Remick, a professor of pathology, "the major cause of asthma is not dust mites, not dog dander, not outdoor air pollen. It's allergies to cockroaches."

Remick and his colleagues (then at the University of Michigan) published their first paper in 2002, after developing their model over several years. Their laboratory was in Detroit, where, as in many other cities, public housing suffered from pest infestation.

The team made home visits with an old-time data-collection instrument: the vacuum cleaner.

"We collected house dust — big dust bunnies — added water, let them mix overnight, and spun the junk out of them, until we had extract," said Remick, now 56.

The extract was filled with proteins from *Blattella germanica* — the common cockroach — whose exoskeletons and droppings become airborne after death. Back in the laboratory, mice were exposed to the dust bunny particles. After being injected, they were immunologically primed: Their cellular response systems went on alert.

When exposed to the same particles a second time by inhaling them, the systems on alert went to attack. Mice that had been breathing easily had difficulty exhaling, and their respiration slowed — a rodent equivalent to wheezing. They were having asthma attacks.

Analysis of their lungs showed that their airways were clogged with white blood cells, mostly of a type called eosinophils, that caused mucus secretion, tissue damage and changes in muscle contractibility. Mice in a control group, exposed to dust mites instead of cockroach protein, had none of the same respiratory or pathologic changes.

The team reproduced their results in several sites; different dust bunnies, same allergic reaction.

"We're pretty excited," Remick said in an interview, "because this is the first time someone has actually taken stuff from houses where kids have asthma."

Researchers not directly involved with the studies said they were excited, too. "It's a clever thing," said Lester Kobzik, a pathology professor at Harvard Medical School. "He's collected the nasty material people actually get allergic to.

"You can't call up your chemical supplier of scientific reagents and say, 'I would like 5 pounds [2.3kg] of exactly the same house dust,'" Kobzik continued. "Remick had a bucketload, so he could do several years' worth of experimentation and study it carefully."

Peter Ward, a professor of pathology at the University of Michigan Health Services, who recruited Remick into residency almost 25 years ago, called the work "probably the closest thing in animal models to simulating what one sees in human asthma."

Most laboratory asthma research still uses genetically created proteins to induce symptoms in mice; often, the proteins are taken from egg whites. This is scientifically pleasing, but less relevant to real life. Egg whites (which humans rarely grow allergic to) have little in common with the city dust children are more likely to cavort through and inhale.

Using the same mouse model, Remick is now studying the effects of various asthma treatments, including the anti-inflammatory drugs called tumor necrosis factor inhibitors, like Remicade and Enbrel. The drugs, already used for treating rheumatoid arthritis and inflammatory bowel disease, appear to derail a crucial immunologic compound that attracts eosinophils.

"Blocking tumor necrosis factor in a mouse model improves asthma," Remick said. "It's pretty slick."

And a more exotic strategy is also under investigation. A few years ago, when Remick's colleague Jiyoun Kim presented results of the mouse model at a professional conference in Korea, an audience member asked whether he had heard about standard Chinese herbal treatment.

He took herb samples back to the US, and in mice they proved to block eotaxin, the compound that sets off asthmatic reactions.

Chinese herbs carry the whiff and romance of an easy solution without the rigors of federal drug trials. But Remick warns that caution is in order.

"The power and trouble with Chinese herbal medicines," he said, "is that they have more than one active ingredient — they have dozens. We know they block eotaxin, but we don't know everything they block, or what actually makes things better."

Complicating the treatment is the disease; asthma has many mechanisms.

"There may be 50 different inflammatory processes going on," Remick said. "We're still in the process of precisely defining which part of the herbs block which part of the inflammatory response."

Still, hopeful parents, attracted by herbal treatments, have caused the researchers some anxious moments. "Yesterday," Remick said, "I was contacted by someone whose co-worker wanted to know whether she should use Chinese herbs to treat her daughter's asthma. I immediately replied that she shouldn't. It's not a question of Eastern versus Western medicine. Other drugs that treat asthma are better defined at this point. Herbs shouldn't be front-line.

Left: In Daniel Remick's study, mice had asthma attacks when exposed to a protein from roaches, whose exoskeletons and droppings become airborne after death.

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