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# The New York Times

Health

February 3, 2005

## *Chickenpox Vaccine Cuts Deaths but Raises Questions on Shingles*

By ANDREW POLLACK

The vaccine against chickenpox has sharply cut the death rate from the childhood disease, according to a study released yesterday.

But even as the vaccine protects children, questions are arising about whether its use will increase the incidence of a related disease, shingles, in adults.

The concern arises from a hypothesis, backed by some evidence, that exposure to children with chickenpox helps increase adults' immunity to shingles, which is caused by the same virus. With far fewer children contracting chickenpox because of the vaccine, that effect would vanish, and adults, who have by and large, not been vaccinated, would be at greater risk of shingles.

"We already know the impact the varicella vaccine has had on chickenpox," Dr. Marietta Vásquez, an assistant professor of pediatrics at Yale University School of Medicine, said as she used the medical term for the vaccine. "Now it's time to see what impact the varicella vaccine has had on shingles."

Dr. Vásquez, along with a Yale colleague, Dr. Eugene D. Shapiro, wrote a commentary in the current edition of *The New England Journal of Medicine* that hailed the effectiveness of the vaccine for chickenpox but urged more study of its effects on shingles.

The same journal includes the study that shows that deaths from chickenpox in the United States dropped to 66 a year from 1999 to 2001, from 145 a year in

1990 to 1994.

The vaccine was introduced in 1995. While not usually fatal, chickenpox can be deadly, particularly to infants or adults or to people sick with another illness.

The paper, written by researchers at the Centers for Disease Control and Prevention, was based on nationwide statistics culled from death certificates.

The new information could spur greater use of the vaccine, researchers said.

The vaccine has been somewhat controversial and is not routinely used overseas. In the United States the vaccination rate for children, although having risen to 85 percent, is still below that for some other vaccines, said Dr. Jane F. Seward, the chief of the viral vaccine preventable disease branch at the C.D.C. and a senior author of the paper on the mortality from chickenpox.

One concern in other countries is whether using the vaccine would increase the rate of shingles in adults. Shingles, evidenced by a rash, blisters and pain, can lead to nerve damage called post-herpetic neuralgia that can last for weeks or months and cause excruciating pain, even from the touch of a shirt against the skin.

Infectious disease modelers at the Health Protection Agency in Britain estimated that shingles might increase 30 percent to 50 percent from vaccination. The harm from that increase would outweigh the benefits of reducing chickenpox rates in children, the modelers said. They conceded that their conclusions rested on

assumptions about how much the rate of shingles would increase, which is not known.

Dr. Ann M. Arvin, a professor of pediatric infectious disease at Stanford, who has been a consultant to Merck, maker of the chickenpox vaccine, said, "We definitely need to pay attention to this question, but at this point it's a hypothetical question, I think."

Shingles, also called herpes zoster, is caused by reactivation in the body of the varicella-zoster virus, the cause of chickenpox. After people have chickenpox, the virus remains dormant, held in check by the body's immune system. But sometimes it becomes active again, particularly in elderly people or those with compromised immune systems.

There is already evidence that exposure to children with chickenpox helps act like a booster shot to the immune system, keeping shingles from occurring.

Mothers caring for children with chickenpox experience an increase in immunity against the virus, as shown by measurements of their blood. And a study by researchers at the London School of Hygiene and Tropical Medicine that compared 244 people with shingles with controls without the disease found that people who had the most contact with children had one-fifth the risk of shingles of those with the least exposure.

Whether shingles is increasing in the United States is not clear. Dr. Seward said the disease control center was conducting studies. One study, using records from the

Group Health Cooperative, a health system in Seattle, has not shown an increase, she said, adding that she could not discuss the study in detail because it is awaiting publication.

"We would say based on the best available data we have that we don't see any increase in herpes zoster," Dr. Seward said.

Kaiser Permanente, a big health maintenance organization, has experienced an increase in hospitalizations for shingles. It appears to be the result of an aging of the population, said Dr. Steven B. Black, director of the vaccine studies center at the organization.

One researcher said the incidence of shingles among unvaccinated children in the Antelope Valley outside Los Angeles was much higher than expected. The valley is one of two locations where the disease control center is closely monitoring the effects of the chickenpox vaccine. The researcher, Dr. Gary S. Goldman, whose degree is in computer science, was a data analyst on the project but said he quit in 2002 because his superiors were trying to suppress the findings on shingles. He managed to have his papers published in the journal *Vaccine* in 2003.

Scientists from the disease control centers sharply criticized Dr. Goldman's statistical methods and assumptions in a commentary also published in that journal. The center said it did not believe that shingles had increased.

People who receive the chickenpox vaccine are widely considered less likely to contract shingles. In several decades, when today's vaccinated children become elderly adults, the shingles rate is generally expected to decline, even if it increases between now and then.

But if using the vaccine does raise the risk of shingles, the manufacturer also has a solution. Merck has said it will apply in the first half of the year to the Food and Drug Administration for approval of a shingles vaccine for older adults.

The vaccine is a stronger version of the chickenpox vaccine. Merck and investigators expect results soon from trials in more than 38,000 people older than 60.

"We'll probably be able to handle an increase in zoster," said Dr. Michael N. Oxman of the University of California, San Diego, and the Veterans Affairs medical center there, who was lead investigator in the trial.