

The Dark Side of Immunizations?

A controversial hypothesis suggests that vaccines may abet diabetes, asthma

By NATHAN SEPPA

As newborns, human babies can't do much more than sleep, eat, cry, and—well, you know.

Even their immune systems seem idle. That's why babies are usually 2 months old before they are given vaccinations—to ensure that they can muster an adequate immune response. However, some scientists now believe that the seeds of immune system problems, perhaps including asthma, may be sown in the early weeks of life and activated later by vaccination. Recent studies suggest that juvenile-onset diabetes, an autoimmune disease, may take root because a baby's immune system is asleep at the switch early on.

Although some scientists have suggested that an unknown genetic component may predispose particular people to getting diabetes, that theory wouldn't explain the increases observed over recent decades. The genetic makeup of people in countries such as Finland and England, where juvenile diabetes has become more prevalent in the past 30 years, hasn't changed much in that time.

There seem to be one or more hidden environmental factors at work. Researchers have suggested exposure to viruses in utero, infant milk consumption, poor hygiene, and even cesarean birth as possible causes. So far, nothing stands out.

Now, J. Barthelow Classen, a physician who heads Classen Immunotherapies in Baltimore, has begun investigating whether infant vaccinations may influence the incidence of diabetes. Vaccination schedules vary from country to country, and some parents refuse to let their children be vaccinated at all, thereby providing control groups. Cross-checks of vaccination data against diabetes registries have loosely linked various vaccinations and juvenile diabetes.

Even if a connection between vaccinations and immune system disorders were firmly established, few people would suggest halting vaccination programs: Only a small fraction of children develop autoimmune diseases, whereas millions of children evade disease via vaccination. Yet a clear link between vaccines and immune disorders could offer a valuable clue to



Some research suggests babies should be vaccinated at birth, not at 2 months.

researchers still searching for the cause of diabetes and asthma.

Classen suggests that a change in the timing of the vaccines—namely, adding one set at birth—might reduce the incidence of diabetes and still protect against viral diseases.

Viruses passed from mother to child at birth may inflame the insulin-producing islet cells of the pancreas, setting the stage for diabetes. Classen's hypothesis holds that vaccinations given at the age of a few months, while spurring immunity against disease, may also abet a lurking autoimmune challenge in some infants, allowing it eventually to develop into diabetes.

Meanwhile, a new study by researchers at the Wellington School of Medicine in New Zealand finds that unvaccinated New Zealand children report fewer cases of asthma than vaccinated children. Like diabetes, asthma is becoming more common and has no known cause.

There may also be a genetic predisposition to asthma, but don't blame the gene pool: The population mix isn't changing much in Australia, yet the number of asthma cases is rising there. Asthma researchers have puzzled over allergy-triggering agents in houses and schools, air pollution, the urban environment, secondary smoke, and low birth weights—without finding an answer. Whether vaccination will provide one remains to be seen.

Because vaccines are so efficient, and the case against them still sketchy, some scientists are skeptical. "It's a very intriguing hypothesis, but I don't think it's proven, by any means," says Patricia M. Graves, an epidemiologist at the University of Colorado Health Sciences Center in Denver.

Drawing a direct association between diabetes and vaccination "is pushing it," says Ronald E. LaPorte, an epidemiologist at the University of Pittsburgh. "It's very, very dangerous to say that immunizations cause autoimmune disease. It's right to publish [the data], but I don't think any conclusions can be made."

LaPorte and his colleagues keep a registry of diabetes in Allegheny County, Pa. The incidence of juvenile diabetes has risen sharply there in the last decade, even as vaccination schedules have remained static, he says.

Elsewhere, data hinting at a link don't focus on any single vaccine. New Zealand researchers report in the November *EPIDEMIOLGY* that a review of 1,265 people born in 1977 shows that 23 didn't get any early childhood vaccinations. Of these people, none suffered childhood asthma. Of the remaining 1,242, who received polio and diphtheria-tetanus-pertussis vaccinations, more than 23 percent later had asthmatic episodes.

Similarly, a 1994 survey of 446 British children with an average age of 8 showed that 91 received no vaccinations in early childhood. Of this group, only one got asthma. About 11 percent of the children who had been vaccinated with pertussis and other vaccines had asthma.

Juvenile diabetes numbers are rising in Finland. Between 1970 and 1976, Finnish children under age 4 had a 12 in 100,000 chance of developing diabetes within a year. Between 1990 and 1992, that rose to 29 cases in 100,000. Classen reviewed vaccination programs in 17 countries in the Oct. 22 *INFECTIOUS DISEASES IN CLINICAL PRACTICE*. He noted that between 1976 and 1990, Finland began giving children a bolstered pertussis vaccine and hemophilus influenza B vaccine.

In Christchurch, New Zealand, juvenile diabetes, which averaged 11 cases per 100,000 between 1982 and 1987, rose to

18 per 100,000 in 1989 through 1991. This rise coincided with a hepatitis B vaccination campaign begun in 1988, says Classen.

Some of the higher rates of diabetes and asthma could stem from more accurate diagnoses, Classen acknowledges. Conversely, unvaccinated children may see a doctor less often than others and so report less asthma, the Wellington researchers say. In addition, some of the study samples are small, limiting the statistical strength of the findings.

Nonetheless, a Swedish study has led Classen to suggest that timing may play a role in vaccinations' effects. In 1973 and 1974, newborns in Sweden were given the vaccine for tuberculosis. That vaccine was stopped in 1975. The Swedes continued to give children other vaccines, but not at birth. The rates of juvenile diabetes rose after 1975.

The Swedish researchers found no direct correlations. Classen did, however. He notes that past laboratory findings make this question of timing intriguing. Pertussis and tuberculosis vaccinations at birth block some cases of diabetes in rodents, several studies show.

Further confounding the effects of vaccination are lingering uncertainties over whether childhood viruses initiate immune system problems or

build resistance to them.

Classen points to the virus that causes rubella, also called German measles, and to coxsackievirus, which causes a polio-like infection. When passed from mother to fetus, both viruses can attack the insulin-producing beta cells of the pancreas. Some of the amino acid sequences of these viruses resemble proteins made by beta cells. The viruses elicit an immune response that then spills over to the beta cells, says Joan T. Harmon, a biochemist at the National Institute of Diabetes and Digestive and Kidney Disorders in Bethesda, Md.

Classen suggests that this response may trigger an autoimmune disease and that vaccination at birth would therefore suppress such problems.

Immunization skews the activity of the immune system, says Howard L. Weiner, an immunologist at Harvard Medical School in Boston. "If a person has a tendency toward a disease at a certain age, a vaccine might . . . make [him or her] more susceptible later, when other challenges come along."

At the same time, vaccination limits children's contact with viruses in the environment.

Studies in animals indicate that an absence of contact with naturally occurring viruses actually increases the risk of diabetes, suggesting that exposure to viruses imparts some protection against

the disease, Harmon says. Research in humans has suggested that some childhood infections may prime a person's immune system to fend off asthma.

"It's logical that there might be some immune manipulation that happens in childhood that might have a positive or negative effect on these diseases," says Weiner.

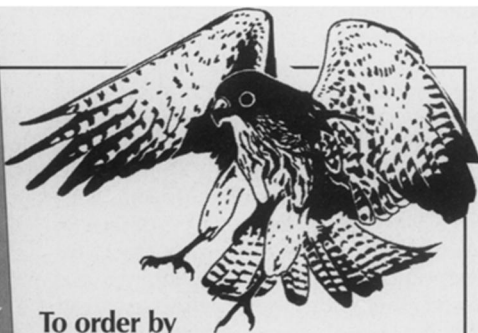
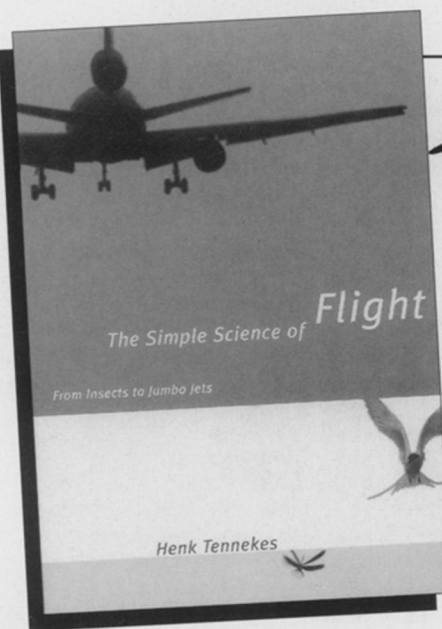
Classen says public health authorities may someday have to consider stopping some vaccination programs. "The benefit of vaccination is strong, but compared with some diseases, such as meningitis, the vaccination risk of diabetes may exceed the risk of an adverse reaction to the infection itself," he says. What's more, "diabetes may be a marker for other autoimmune diseases. While meningitis complications are bad, these other diseases are more common."

Classen, whose firm tests vaccines and develops immunization schedules, acknowledges that halting vaccinations is heresy in the biomedical community. As a first step, he is calling for a long-term study to determine whether the timing of vaccinations plays a role. Researchers would vaccinate some babies at birth, add another dose after a few weeks, then follow up with the normal course that begins at 2 months. They would then compare these infants with babies who received the traditional course of vaccinations throughout childhood. □

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