

Chiron flu flap suggests vaccine industry needs shot in the arm

Scientists are calling for changes to vaccine development after the surprise announcement that Chiron will be unable to deliver half the US flu vaccine supply. The severe shortage also suggests the government is unprepared to deal with an infectious pandemic.

Vaccines are an unprofitable venue for drug companies: the annual flu jab normally sells for \$7–10, compared with \$3,500 for a year's supply of Viagra. As a result, the US has only two major flu vaccine suppliers: California-based Chiron, whose manufacturing license was suspended because of sterility concerns, and French company Aventis Pasteur. "In 1955, 36 companies made vaccines. Now there are 4 or 5," says Paul Offit, chief of infectious diseases at Children's Hospital of Philadelphia.

Vaccine prices are low in part because the government buys a large percentage of vaccines and can command low prices. But another reason is that society doesn't value these preventative medicines, says Charles Helms, chair of the National Vaccine Advisory Committee. Although people are clamoring for vaccine now, there is normally little public demand, Helms says.

In press conferences following the Chiron announcement, Julie Gerberding, director of the US Centers for Disease Control and Prevention (CDC), said that the government needs to develop long-term solutions for recurring vaccine problems. But neither the CDC nor the US Department of Health and Human Services (HHS) responded to questions about details of those plans. A 2003 Institute of Medicine report on financing vaccines recommended federal subsidies to encourage manufacturers to invest in vaccine production.

One significant obstacle in vaccine production is the lengthy and expensive manufacturing process, which makes it difficult to ramp up production in response to shortages. The traditional method uses eggs to grow the necessary viral proteins, but researchers hope to develop faster methods. "We should develop vaccines we can produce and save throughout the year, and put more effort into new research, such as the live vaccine," says Helms.

In late September, the US National Institutes of Health awarded a \$9.5 million grant to a Canadian firm to develop a flu vaccine based on cell culture. The HHS also announced \$232

million in new biodefense contracts to develop vaccines for smallpox, plague and tularemia.

Despite these measures, the flu crisis raises concerns over how the nation would cope with other infectious emergencies, such as a bird flu that could easily spread between people.

Experts worry that a concurrent outbreak of human influenza and bird flu could create a more a virulent strain. If someone is infected with two virus strains, "gene segments from each virus can mix and match," says Richard Webby, an infectious disease expert at St. Jude Children's Research Hospital in Tennessee.

If segments of the highly pathogenic bird flu H5N1—which is rarely passed between humans—were to mix with the human virus, it could create a new strain that is easily transmitted between people. "We're not sure it's possible, but it's a definite worry," Webby says.

Tim Uyeki, a medical epidemiologist at the CDC, says the current flu vaccine shortage has no immediate impact in the US on risk of H5N1 because that virus is not part of the human vaccine. "But [reassortment of flu viruses] is a very concerning theoretical risk," he says.

Emily Singer, Boston

Genetics may aggravate India's growing AIDS problem

The genetic makeup of Indians favors a fast and easy spread of AIDS, Indian scientists have cautioned their government. The presence of certain genetic variants also suggests that an AIDS vaccine developed elsewhere may not be effective in India, they say.

The researchers examined genes for components of the immune system—including the major histocompatibility complex (MHC), chemokines and cytokines—in HIV-positive and control groups in India. The results suggest that Indians are more likely to carry genetic variants that favor faster progression to AIDS, says lead researcher Narinder Mehra, an immunologist at the All India Institute of Medical Sciences (AIIMS) in New Delhi.

A variant of the chemokine coreceptor CCR5, known to protect against HIV infection and found in less than 15% of white people, is absent among Indians, Mehra adds.

Mehra and his colleagues' results are based on their study of 400 Indians. Another study by Akhil Banerjee at India's National Institute of Immunology found one person with the protective CCR5 variant in a group of 145. Further analysis of the CCR5 promoter by the AIIMS researchers suggests that a haplotype associated with fast



Doubly damned: Scientists say Indians' genes may accelerate the course of AIDS.

progression to AIDS is frequent in the Indian gene pool and those linked with slow progression are less common.

The results could have grave implications for India. According to Richard Feachem, director of the Geneva-based Global Fund to Fight AIDS, Tuberculosis and Malaria, India has surpassed South Africa as the nation with the most cases of HIV/AIDS.

Mehra's team has also noted several new genetic variants in the immune system among Indians. The presence of different alleles might mean that Indians present a different side of HIV to the immune system, says Mehra, and render an AIDS vaccine made for the Western world ineffective.

The Indian health ministry, together with the International AIDS Vaccine Initiative, is planning to test an AIDS vaccine in India. The ministry has declined to comment on the AIIMS researchers' findings.

Mehra's argument is true for a vaccine based on small proteins, notes Bruce Walker, professor of medicine at Harvard Medical School. "But if one is making a vector that expresses a larger protein such as gag, this is much less an issue," Walker says. Still, it is important to know what the immune response is targeting in the clade C virus prevalent in India and in the context of local alleles, he says. "Lots to learn, but I don't think we have reason to say that the current vaccines will not be useful in India."

Some researchers note that many factors—such as age, other infections and socioeconomic factors—can affect disease progression. But Simon Mallal, who runs the Centre for Clinical Immunology and Biomedical Statistics at the Royal Perth Hospital in Australia, says an individual's genetics play a significant role in HIV disease susceptibility and progression. "Understanding the genetics will undoubtedly help us develop effective vaccines," he says.

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