

FluMist Reshapes The Fight Against Flu

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Many children, as well as adults, cringe at getting an annual flu shot. But now, with the development of FluMist®, there is a needle-free, highly beneficial alternative to getting a shot in the arm.

FluMist, which has been available in the United States since 2003, is a trailblazer in the annals of flu prevention. The research behind its innovation spanned seven presidencies, but for millions of people nationwide, the nasal spray vaccine, which has its origins in research at the University of Michigan, was well worth the wait.

While many viruses can make people moderately ill, true influenza can cause serious illness. The Centers for Disease Control and Prevention point out that each year more than 200,000 people are hospitalized with flu complications and about 36,000 people die from the flu.

Since the flu virus mutates and changes quickly, prevention is an ever-challenging issue. FluMist has demonstrated protection against both matched and drifted strains of the flu. “That alone makes this product vastly different,”

explains James Young, Ph.D., president of research and development at MedImmune, the company that manufactures the vaccine.

Flu shots have been around since World War II, but it wasn't until 2003, when FluMist® first became available, that the world had an alternative. That's when the Food and Drug Administration (FDA) approved the new nasal spray vaccine for healthy people between the ages of five and 49 who are not pregnant.

Recently, the FDA approved FluMist for children between the ages of two and five years. MedImmune also has developed a new refrigerated version of the vaccine, which was first available in the 2007/2008 flu season.

Freezer storage is no longer needed as it was during the first four flu seasons the nasal spray was on the market.

Young says, "It was more difficult to transport it to schools or other sites, but now, because it's available as a refrigerated product, we anticipate that it will have higher usage."

For those who wonder why the vaccine was developed as a nasal spray, Hunein "John" Maassab, FluMist's inventor and professor of epidemiology at the University of Michigan, has the answer. The vaccine, which contains three live (weakened) flu viruses, stimulates the body's immune system to develop protective antibodies. Maassab says, "The viruses, which are attenuated, cold-adapted, and temperature sensitive, can grow in the nose but not in the lower respiratory system and in the lungs where the body's temperature is warmer."

Maassab further explains that the cold-adapted live vaccine has shown to be highly successful in warding off the flu. "As the virus mutates, it becomes temperature-sensitive," he says. "The weakened virus used in FluMist®, which does not cause the flu, will not grow well at higher temperatures in the lungs."

Since flu is transmitted from one person to another as an airborne pathogen, the nose is a logical place to stop the virus where it enters the body. Maassab adds, "By squirting the vaccine in the nose it induces a more complete, broader immune response."

University-Business Collaboration

In 1955, Maassab, a public health graduate student, was in the audience at the University of Michigan, Ann Arbor, when Dr. Thomas Francis, Jr., Dr. Jonas Salk's teacher and mentor, announced that the polio vaccine developed by Salk was safe and effective. Maassab, who was born in Damascus, Syria, in 1926, was young enough to have heard about the accounts of the pandemic flu of 1918, designated the Spanish Flu. The devastating outbreak was responsible for the deaths of more than 20 million people throughout the world.

Maassab's interest in developing a vaccine for the nasal passages became his life's work. By 1960, he had isolated the "A" Ann Arbor influenza virus, which he used to create the cold-adapted live influenza virus. Over the next 20 years, he worked with scientists at the Laboratory of Infectious Diseases in the National Institute of Allergy and Infectious Diseases in Bethesda, Md. refining the cold-adapted virus.

In the late-1970s and early 1980s the National Institutes of Health funded clinical trials to test the efficacy of the new vaccine. In 1995, the University of Michigan licensed the vaccine technology to Aviron, a biopharmaceutical company.

Partnering with Aviron and later MedImmune, after its purchase of Aviron, researchers at the University of Michigan provided information from earlier research studies and materials from the University of Michigan School of Public Health laboratories to assist with the commercialization efforts. By 1997, the vaccine was proven effective in a major study in children at 10 centers throughout the United States.

In 2003, the FDA approved FluMist as a nasal spray commercially available through MedImmune Vaccines, Inc., a wholly owned subsidiary of MedImmune, Inc. Dr. Maassab's dream, to develop an effective flu vaccine without the need for needle injection, was becoming a reality due to his pioneering efforts and the collaboration among Aviron, MedImmune and the University of Michigan.

First Line of Defense

Since preschoolers and school-age children are often considered the vectors in transmitting the flu, one important strategy in reducing its spread is to vaccinate this age group.

Robert Belshe, M.D., professor of medicine and pediatrics at Saint Louis University School of Medicine in St. Louis, was the lead investigator on the pivotal pediatric FluMist trial. This trial was key to the recent expanded approval of FluMist for use in children as young as two years. The doubleblind study included approximately 8,500 children between six months and five years of age in 16 countries at 249 sites. The study was conducted between 2004 and 2005 and published in 2007.

"It was the biggest influenza vaccine trial ever done with children," Belshe comments.

For the 2006-2007 influenza season, MedImmune made about 3 million doses of FluMist. Now, with the approval for FluMist use with children as young as two, Young says, "We intend to make approximately 4.5 million doses this year."

MedImmune has invested about \$2 billion in FluMist since commercializing the technology. Young points out, "Based on current data, there may be an increased cost savings to communities who vaccinate more people. Fewer parents may need to stay home from work, and fewer children may have to stay home from school."

By some estimates, over 1.5 million work days are lost in a single year due to the flu. Research published in December 2006 in the *New England Journal of Medicine* showed that school-based influenza vaccination programs using FluMist may represent an effective and feasible strategy to help lessen the impact of seasonal influenza on households and communities.

In this study, researchers found that households with children who attended schools with influenza vaccination programs reported missing approximately two fewer school days per 100 school days during the flu season (4.34 vs. 6.63 days) than households with students in schools without programs. While not statistically significant, there was a trend toward adults missing fewer workdays due to being ill or staying home to care for a sick child.

“*As more pediatricians choose FluMist during the flu season, there is the potential for an even greater effect on fighting the flu.*”

Belshe sees new applications for the technology ahead. Instead of going to the flu clinic or medical clinic to receive FluMist, he envisions vaccination centers where people congregate.

Although FluMist is not right for everyone and proper screening is necessary, Belshe says, "There may come a day when you'll see the vaccine available at kiosks at shopping malls. FluMist has changed the world of public health. It's easy to give — no special skills are needed to administer the nasal spray, and children and parents love it."

And there is nothing like it in the U.S. marketplace. That fact alone is remarkable, but when coupled with the astonishing talent, vision and scientific strides that took 40 years of research to bring FluMist® to market, it could be called a medical marvel. The collaborative work between university research and industry has opened the door to a brand new way of helping protect people from debilitating flu.

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