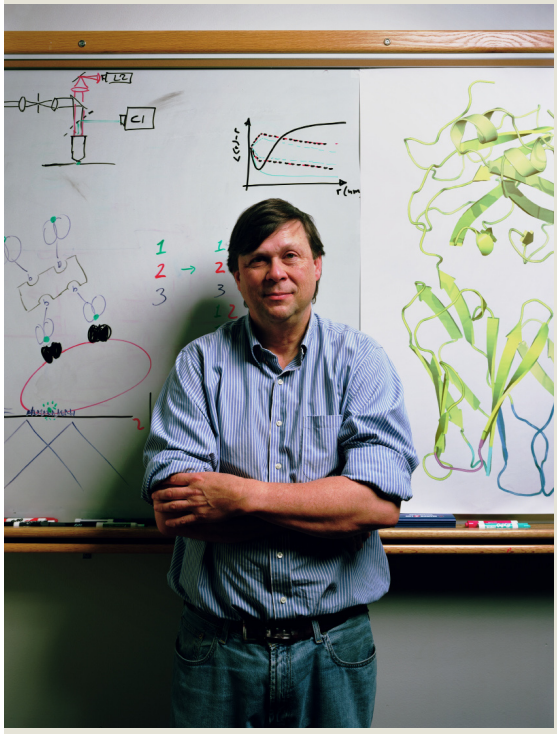
grow up

Can vaccines built for kids work in older immune systems too? Probably, with a little retooling.

ONE STRAIGHTFORWARD TACTIC IS THE "MULTIPLY AND CONQUER" METHOD. Simply upping the chicken pox vaccine's dose yields a product that's effective against shingles — the adult disease caused by reactivation of the same virus. And initial studies suggest that administering influenza vaccine at four times the normal dose raises flu-virus-specific antibody levels appreciably in older people. Boosting the payoff by boosting the payload? Maybe it's that simple — although, as Stanford vaccine gurus are quick to point out, bigger doses can also mean much more expensive vaccines and, where manufacturing bottlenecks are an issue, shortages. • An alternative strategy would focus on adjuvants: substances added to vaccines that improve the overall immune response. The only adjuvant now approved in the United States is alum, included in a variety of vaccines because it increases antibody levels. Another adjuvant called MF59, developed in the 1990s, was specifically designed to boost elderly people's immune responses to the flu vaccine. It's a part of vaccines licensed in Europe, but not here. • Or there's an indirect route to protecting seniors: boosting herd immunity. Viruses or bacteria typically spread from person to person through relatively close contact. If the pathogens can't get a foothold because most of the population has been immunized, transmission is slowed or foiled altogether. • This suggests that a great way to protect seniors is to immunize kids. From 1962 through 1987, most Japanese schoolchildren were vaccinated against influenza, says Corry Dekker, MD, professor of pediatric infectious diseases at Stanford. "During that mandatory period when the Japanese were immunizing all schoolchildren with influenza vaccine, the rate of excess deaths from seasonal influenza in adults, even in the elderly, dropped significantly. When they stopped immunizing the schoolchildren, that rate went up again."



Mark Davis is developing a way to give your immune system a checkup.

Herd immunity applies to pneumococcus, too. The licensing, in 2000, of a new pneumococcal vaccine tailored to infants' immature systems not only reduced infantile disease but, strikingly, was followed within three years by a greater than 40 percent reduction in hospitalizations of adults over age 65 for invasive pneumococcal disease, according to a 2005 study led by University of Minnesota professor Marshall McBean, MD, and published in *Vaccine*.

Knowledge is power

Optimizing vaccines for older immune systems will be easier when scientists understand what causes the decline. A Stanford flu-vaccine study now under way aims to do just that, by analyzing differences between older and younger people's immune responses to the influenza vaccine, as well as between older vaccinees who contract flu and those who don't.

A long-term goal of the study is to characterize the healthy immune system, says Mark Davis, PhD, director of the Stanford Institute for Immunity, Transplantation and Infection, who's collaborating with Dekker on the project. "The immune system is one of the last major health systems in the body that doesn't have benchmarks of normal functioning," says Davis. "I'd like to broaden that to the whole population, and make an immunological checkup as common as a cholesterol test. We're going to try to define, at the molecular and cellular levels, what a normal response looks like."

Even with such an understanding, coming up with a new vaccine or even optimizing an existing one can take years, or decades. Eleven years elapsed between the licensing of the chicken pox vaccine and approval of the shingles vaccine, which simply contains more of the same component. One of Stanford's most experienced vaccine researchers, senior associate dean for research Harry Greenberg, MD, points out that the first published findings on a modified version of the influenza vaccine he worked on, approved in 2003, were made in 1967.

In 1959 and 1960, microbiology and immunology professor Stanley Falkow, PhD, worked at the U.S. Army's Walter Reed Hospital. "People there thought that in five years they'd have really good vaccines against typhoid, cholera and dysentery," he recalls. "They're still working on it."