Vaccines in the 21st Century

Stanley A. Plotkin

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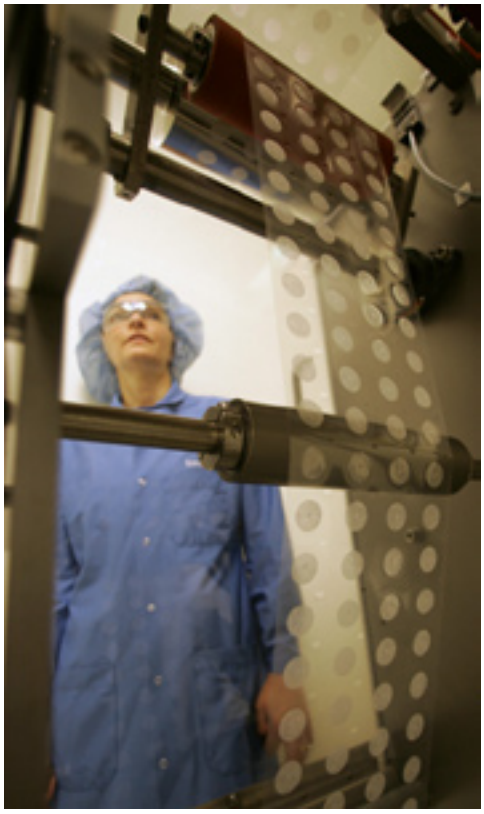
It has been often remarked that predicting the future is fraught with error, and that it is much easier to predict the past. Nevertheless, I believe certain tendencies in the field of vaccine development are likely to flourish in the near- and long-term future, and so I venture to make the following 10 predictions:

• The development of combined vaccines containing multiple valences will increase. Valence is the number of different antigens in a vaccine—a trivalent vaccine has three antigens, for example. An antigen is a chemical substance, usually a protein that stimulates the immune system to produce an antibody specific to the antigen. As the schedule for early childhood vaccination becomes more crowded with new vaccines, and as we deal with disease syndromes having multiple causes, it will be necessary to combine vaccines so that fewer injections are given. These combinations of vaccines will not be simple to develop, as the immunologic rules of interference among vaccines are not well described.



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The Iomai Corporation is developing needle-free vaccines and immune system stimulants targeting influenza and pandemic flu. The director of plant operations looks over an automated vaccine patch manufacturing machine at company headquarters in Gaithersburg, Maryland, near Washington, D.C.

• Although many vaccines are administered to infants under the age of one year, protection is slow to develop because of the immaturity of the immune system. In fact, immunity may fade later in childhood if no booster doses are given. The specific factors that contribute to the immaturity are just becoming known, and I anticipate that immunologic adjuvants—substances that enhance responses to vaccination—will come into use in infancy.

• Sexually transmitted diseases, respiratory diseases transmitted by crowding, infections that cause cancer later in life, and infections transmitted from mothers to their fetuses all require vaccination before adolescence begins. Thus, the age of 11 to 12 years will become a time for administration of many newly emerging vaccines to provide protection during early adult life.

• The elderly suffer a natural aging of the immune system, both with respect to antibody production and cellular responses to infection or vaccination. Here again, we are beginning to understand the defects that come with age, and correction of these defects should improve the efficacy of vaccines in an increasingly aged population.

• Two new strategies have become widespread for experimental vaccine development: injecting humans with DNA segments from pathogenic microorganisms that produce protective proteins after injection, and inserting genes from pathogens into harmless microorganisms that serve as carriers, or vectors, for production of immune responses. Although each strategy separately may generate useful vaccines, the combination of the two in a so-called "prime-boost sequence" provides synergy. Thus, there will be vaccinations consisting of

prime-boost regimens, particularly in those cases where antibodies are insufficient to give complete protection.

• Intramuscular or subcutaneous injections have served us well as the means to introduce vaccines into humans. However, there are limitations to the feasibility of numerous injections and theoretical reasons for preferring other routes of immunization. Thus, intranasal, aerosol, and oral routes of administration are being intensively explored for certain vaccines. Moreover, transcutaneous immunization using patches, microneedles, and other ingenious technologies to pass vaccines through the skin is promising.

• Malaria, tuberculosis, and HIV are major targets of vaccine development. Short-term protection against malaria has already been achieved, and I foresee the extension of protection by combining several malaria antigens in one vaccine, although I suspect that regular boosters will be necessary to maintain protection.

• Prospects for a vaccine that protects against adult tuberculosis are good. This will be based on the current BCG vaccine. The Bacillus Calmette-Guérin vaccine, developed at the Institut Pasteur in Lille, France, in the early 20th century, is effective in children but does not prevent the infection in adults. Insertion of genes that code for additional protective proteins should improve BCG.

• HIV has proven to be a difficult target for vaccination, but a vaccine that reduces the seriousness of infection and prolongs life, even while not preventing the disease completely, is likely to be the product of current clinical trials. The development of a vaccine that prevents infection entirely is less likely in the near future.

• Influenza remains a banal but deadly infection. Although the vaccines we have are very beneficial, better protection will be derived from the inclusion of more influenza proteins, adjuvants, and the combined use of live and killed vaccines. ■

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