BIOTECHNOLOGY Breakthroughs May Yield Magic Bullet Vaccines

New biotechnology-based efforts in vaccine research and development have made a "quantum leap" in the field, leaving classical—if successful—approaches of the past behind, according to a new book from the Pan American Health Organization (PAHO).

New technologies being applied in recent vaccine ventures include recombinant proteins, non-infectious particles, replicons, recombinant viral vectors, peptides, and nucleic acids—approaches that would have seemed the stuff of science fiction only a short time ago. This revolution promises better, more effective, and more clearly targeted vaccines, according to *Vaccines: Preventing Disease and Protecting Health*, just published by PAHO. Perhaps more remarkable, vaccines are now being developed to prevent, cure—perhaps even eradicate—chronic diseases such as certain cancers. Late-breaking, sophisticated delivery systems also enhance the therapeutic value of vaccines.

"It seems to me that there never has been a more auspicious time for the future of vaccine research, development, and application," writes D. A. Henderson, special advisor to the Center for Biosecurity, who spearheaded the successful world campaign to eradicate smallpox.

The new PAHO book provides an in-depth look at the past, present, and future of vaccines and immunization programs. It brings together the men and women at the vanguard of vaccine development to explore the latest approaches in vaccine types, vaccine targets, and vaccine-delivery systems.

Nearly a quarter-million women die each year from cervical cancer, most of them in the developing world. Two vaccine approaches—prophylactic and therapeutic—are currently being trialed against human papilloma virus, a precursor to gynecological cancer. Evidence from trials of prophylactic human papilloma vaccines based on a virus-like particle suggests they can prevent infection. Results of early-phase trials of several therapeutic vaccines also are encouraging. Many other vaccines will be put through clinical trials in the near term. These heartening results bring the hope of preventing cervical cancer to women around the world.

Infections with *Helicobacter pylori* produce gastritis and, in some infected persons, peptic ulcers and eventually gastric cancer. The current therapy for eradicating *H. pylori* involves the administration of antibiotics for several weeks. With this approach, *H. pylori* can become resistant to antibiotics. Moreover, antimicrobial eradication does not result in long-lasting immunity to the infection, leaving people that live in endemic regions at risk of reinfection. In the last decade, immunization efforts against *H. pylori* have advanced significantly. Several purified or recombinant candidate vaccine antigens have successfully prevented or cured chronic *H. pylori* infections in animals. Other promising options include the use of mucosal adjuvants as well as intranasal and rectal delivery systems that dramatically decrease the amount of antigen required compared to oral immunization. It is now possible to consider that vaccination may be used to prevent infection and to eradicate the infection or cure chronically infected persons. Finally, a systemic immunization may be an inexpensive and effective method to protect children and cure adults already chronically infected with *H. pylori*.

Advances in molecular biology and plant biotechnology have opened the door for the production of transgenic, plant-derived vaccines that offer tantalizing advantages: they can be delivered orally, they are heat-stable, the cost of manufacturing the active ingredient is low, and the manufacturing technology can be easily used in developing countries. Work has been done with the hepatitis B surface antigen, Norwalk virus capsid protein, a subunit of heat labile enterotoxin of *E. coli*, and cholera toxin. The next major milestone in developing "edible vaccines" will

be to conduct animal and human clinical trials to show their effectiveness in establishing protective immunity.

Molecular biology breakthroughs also have been responsible for the successful development of vaccine adjuvants—immune response boosters. Three adjuvant systems of the more than two-dozen being worked on at Glaxo-SmithKline deserve special mention. The first, and simplest, is being used in a series of vaccines currently in phase 2 and 3 clinical trials. The vaccines mainly target adolescents and focus on sexually transmitted infections, such as herpex simplex. The second is more powerful and is being used in vaccines against highly complex pathogens such as *Plasmodium falciparum*, HIV, and *Mycobacterium tuberculosis*. The third and most powerful is being used to develop therapeutic cancer vaccines.

In addition, *Vaccines: Preventing Disease and Protecting Health* discusses the historic role of vaccines in disease prevention and eradication; the threat of emerging and re-emerging diseases and the battle being waged against them; and discussions on the regulation and licensing of vaccines and the ethical and financial sustainability of vaccination programs. The book's editor, Dr. Ciro A. de Quadros, is currently director of international programs at the Albert B. Sabin Vaccine Institute, and was for several decades the architect of PAHO's highly successful immunization programs in the Americas.

The Pan American Health Organization (PAHO) is an international public health agency with 100years of experience working to improve health and living standards of the people of the Americas. It enjoys international recognition as part of the United Nations system, serving as the Regional Office for the Americas of the World Health Organization, and as the health organization of the Inter-American System.

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