

BOOK REVIEWS

**THE CUTTER INCIDENT:
HOW AMERICA'S FIRST POLIO VACCINE
LED TO THE GROWING VACCINE CRISIS**

By Paul A. Offit. 238 pp., illustrated. New Haven, Conn., Yale University Press, 2005. \$27.50. ISBN 0-300-10864-8.

“LIABILITY WITHOUT FAULT” WAS THE VERDICT in a 1958 lawsuit in the aftermath of the paralysis of children in the United States who had received a licensed polio vaccine manufactured by Cutter Laboratories. In *The Cutter Incident*, Paul Offit lays out the meaning of this verdict: that pharmaceutical companies are liable for damage without negligence, even if they make a product according to industry standards using the best science available.

Offit makes the convincing argument that this verdict has figured largely in the decision by many U.S. manufacturers not to develop or produce vaccines. He also provides a comprehensive history of the development, production, and wide use of the inactivated polio vaccine in the United States during the 1950s. By including in this clearly written book historical information about polio epidemics in North America and the paralysis of Franklin Delano Roosevelt, a description of the three types of virus that cause polio, and an explanation of the Salk theory of inactivation of the polio virus, Offit sets the stage for his discussion of the tragic events that led to, and the unfolding of, what is now known as the Cutter incident.

Offit also suggests other factors that may have influenced the course of vaccine development. These include the high cost of vaccine development and of compliance with the regulations of the Food and Drug Administration for biologic preparations and the relatively lower cost of the development of and compliance for drugs, which also have a larger and more sustained market. Add to this mix the low price of vaccines — with governments as the dominant purchasers for public health programs — and the litigation in the wake of the mass vaccination of U.S. residents against swine influenza in the mid-1970s, and

there are even more factors with the potential to discourage vaccine manufacturers in the United States.

The verdict of nearly half a century ago has repercussions today for diseases that can be prevented with the use of vaccines. The development of the inactivated polio vaccine and global access to the live attenuated polio vaccine have brought the world to the verge of the eradication of polio. It is estimated that fewer than 2000 children were paralyzed by this disease in 2005, whereas when eradication efforts against polio began in 1988, an estimated 1000 children were becoming paralyzed each day. The World Health Organization's technical advisory groups on polio eradication have predicted that polio transmission worldwide could be interrupted in 2006. After the wild poliovirus is eradicated, there will still be a continued risk of paralytic polio from polioviruses in vaccines as long as the current live attenuated vaccines continue to be used — a fact that complicates the issue of polio eradication. Not enough funding or research and development has been invested to have resulted in a more stable live attenuated polio vaccine. In addition, Offit's book offers one explanation of why manufacturers may have shied away from developing such a vaccine.

At the same time, it is no surprise that until the recent advent of funding from the Bill and Melinda Gates Foundation and other philanthropic organizations, less than 10 percent of the financial resources for global health research were used to address health problems in developing countries. Yet AIDS, tuberculosis, and malaria, along with diarrheal diseases and respiratory infections in children, account for approximately 90 percent of deaths from infectious diseases in those countries. Nor is it surprising that manufacturers have not made large investments in up-to-date technology for the production of seasonal influenza vaccines. Such production still involves the time-consuming growth of viruses in chicken eggs with embryos and a gap of at least six months before marketing and subsequent use — a delay that is risky because another influenza pandemic could occur within that pe-

riod. Infectious diseases remain a primary cause of human suffering and death around the world. As Offit so clearly outlines in *The Cutter Incident*, solutions must be found to the predicaments that contribute to the lack of vaccines against many of these diseases.

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**THE GRAND CHALLENGE
FOR THE FUTURE: VACCINES
FOR POVERTY-RELATED DISEASES
FROM BENCH TO FIELD**

(Birkhäuser Advances in Infectious Diseases.) Edited
by Stefan H.E. Kaufmann and Paul-Henri Lambert.
290 pp. Basel, Switzerland, Birkhäuser Verlag, 2005. \$119.
ISBN 3-7643-7175-7.

VACCINES HAVE BEEN ONE OF THE GREAT success stories in preventive medicine. Smallpox has been eradicated, polio has been eliminated from much of the world, and measles — which once killed several million children annually — has been markedly reduced. However, the burden of infectious diseases, particularly those that affect persons in the developing world, remains unacceptably high. In the cases of some infectious diseases, delivery of vaccines to target populations in developing countries has been suboptimal. In other cases, such as invasive pneumococcal disease, vaccines exist but have not yet made their way into immunization programs in developing countries. Finally, the resources needed to develop vaccines for the prevention of diseases that do not affect persons in the industrialized world have been insufficient.

The Grand Challenge for the Future focuses on vaccines and vaccination programs for the developing world. Most vaccinology books concentrate on specific vaccines against specific diseases. That is not the focus of this book, which instead brings together micro and macro views of the development of vaccines and issues involving the implementation of vaccination. The first three chapters describe the underpinnings of the development and use of vaccines. These include methods used to assess the economic and societal value of vaccines, an industry perspective on

the hurdles faced, and potential interventions the industrialized world could undertake to facilitate vaccination. Local manufacture is one means of reducing the cost of existing and new vaccines for developing countries, but there are multiple obstacles to overcome. One chapter of the book discusses ways of resolving these problems.

The three chapters of the “Bench” section of the book have relevance to both the developing world and the developed world. Among the topics addressed are new techniques to develop vaccines. For example, computer analysis of an organism’s genome can be used to predict potential protective antigens. Adjuvants may enhance immunogenicity and reduce the quantities of vaccine antigens needed. Overcoming immunologic immaturity may be critically important; inducing an immune response at the earliest possible age would be crucial for the prevention of many diseases in developing countries, because exposure is common in early infancy, and vaccine-delivery programs tend to focus on the first year of life.

The chapter on regulatory issues lays out many of the steps that must be addressed in gaining approval for a vaccine. However, there is inadequate coverage of the special regulatory problems that are faced in developing countries, which often lack the resources to test and license vaccines. Clinical trials of vaccines in developing countries are complicated because critical research infrastructure may be lacking. Major ethical issues often arise when a vaccine that was developed in industrialized countries first is clinically tested in the populations of developing countries. *The Grand Challenge for the Future* offers suggestions for overcoming these hurdles. No discussion of vaccines is complete without consideration of vaccine safety, and this book offers a comprehensive discussion of safety evaluations and the development of safety monitoring systems.

After the development of vaccines comes their incorporation into routine immunization programs. Despite adequate financing of vaccines for many countries, vaccine-administration programs fail to reach target populations. Investments in health care delivery systems are essential if vaccines for the developing world are to achieve their optimal effect.

This book could have been improved by greater discussion of the implementation of immunization programs. Nevertheless, it is an excellent