A successful vaccine that missed its target

The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis

By Paul A Offit

Yale University Press, 2005
256 pp., hardcover, $27.50
ISBN 0300108648

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In April of 1955, fearing the polio epidemic sweeping the US, Josephine Gottsdanker took her five-year-old daughter Anne to the pediatrician to receive Jonas Salk's new polio vaccine. Four days later, Anne developed headaches, nausea, muscle weakness and paralysis of both legs. She was one of the 40,000 children in California and Idaho who became ill after vaccination and one of the 200 who became permanently paralyzed. Ten children died. The adverse effects were quickly shown to be associated with vaccine lots that still contained live polio virus: lots manufactured by Cutter Laboratories. This was the beginning of 'the Cutter incident' and of the landmark Gottsdanker v. Cutter lawsuit that revolutionized popular and legal perceptions of vaccine safety and whose repercussions are still felt today. Lessons from the Cutter incident have considerably influenced present ways of testing and introducing new vaccines, and have even influenced the economic evaluation of vaccines.

Paul Offit does a superb job of maintaining the readers' attention as he describes 'the Cutter incident' using a thriller-style approach combined with an accurate dissection of what went wrong and of the short- and long-term consequences. He reviews the incident from multiple angles: he vividly evokes the panic caused by the polio epidemic, the perspective of the researchers and the relative impatience of funding partners to find a vaccine; he portrays the incipient status of the regulatory environment, the overwhelming pressure of the media, the lawyers' invasive approaches and the eventual jurors' dilemma.

In 1952, polio had affected 58,000 children in the US. Effective interventions were badly needed. When the results of one of the largest clinical trials ever organized, involving 1.6 million subjects and including 420,000 children, suggested that Jonas Salk's vaccine was safe and effective, the findings brought tremendous media coverage and had a large political impact. The vaccine—based on an inactivated polio virus—was manufactured and the trial conducted under the auspices of the National Foundation for Infantile Paralysis, using largely private funds.

Most manufacturers that were subsequently commissioned by governmental agencies to produce the Salk vaccine were well known. But the governmental requirements that were issued for production were far less stringent than those established by Salk and the National Foundation for Infantile Paralysis, leaving the door open to flexible interpretations by individual manufacturers. The black sheep proved to be Cutter Laboratories, but other manufacturers also had problems in avoiding live virus in some of their vaccine lots. At the time of the incident, regulatory agencies in charge of vaccine safety were still at an embryonic stage and certainly not in a position to ascertain the absence of live viruses in the inactivated polio vaccine. The importance of lot-to-lot consistency was not yet fully realized, and communication was limited between the different players.

In today's context, it is not surprising that what could go wrong did go wrong. Offit clearly explains the technical reasons accounting for the persistence of live virulent polio virus in the Cutter vaccine. He notes that several of the vaccine lots produced by Cutter were found by the company to be contaminated with live virus and were discarded. This obviously reflected serious lot-to-lot discrepancies and indicated major problems in the production line. It is still puzzling why this did not raise more awareness of a potential risk.

For those who are not familiar with the heavy regulatory environment that now surrounds vaccine development, production and licensing, Offit's book provides an insightful justification for the high standards of safety that are now required for prophylactic vaccines. Several of these products are given to more than 100 million healthy children, and the risk that such interventions could cause serious adverse effects is not acceptable.

Offit also discusses how the Cutter incident led to a revolution in the concept of compensation for vaccine-related adverse effects. The legal acceptance that vaccine producers may be declared "liable without fault" has had considerable repercussions on vaccine manufacture. As vaccines are usually given to a very large number of apparently healthy subjects, any coincidental pathological event that occurs within weeks after vaccination may occasionally be claimed to be vaccine related. This has opened a growing area of litigations often sustained by active advocacy from interested law firms. Litigations are now built not only on liability without fault but also liability without any scientific evidence of vaccine-related adverse effects. As Offit illustrates, the present corporate perception of litigation-related financial risks is negatively influencing investments in new vaccines that could have a considerable impact on public health.

Overall, Paul Offit's story of the Cutter incident and its long-term consequences helps readers understand why and how vaccine manufacture has moved from the dairy product–like status of the 1950s to the sophisticated biotechnology industry of today, and why the vaccine regulatory framework has become more stringent than for any other pharmaceutical product. Vaccines that used to be seen by parents as quasi-divine gifts that would protect their children from prevalent and dreadful diseases are now often considered government-driven mandatory injections to prevent diseases that are becoming quasi-invisible.

Could current fears of a potential influenza pandemic and the pressure to develop a vaccine create conditions that could lead to similar Cutter-like problems? As vaccine safety is now the primary concern of the vaccine industry, such adverse effects would have no chance of occurring in the present regulatory environment. But society may have to pay for many more years for the confidence gap resulting from some technical imperfections and deficient interpretation of safety data at the Cutter Laboratories five decades ago.

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