"Vaccine Research, Availability … and Reality"

Précis of the March 15, 2001 USMI Executive Forum

Washington, D.C. - Vaccines, one of the most effective public health measures devised by man, are now seriously threatened themselves. Some of the concern stems from waning societal understanding of vaccines, while at the same time manufacturing firms face challenging economic and regulatory issues that have already restricted or eliminated the availability of influenza, tetanus-diphtheria and other vaccines. Some vaccines, such as those developed for adenoviruses and plague, are now lost. A potentially serious problem presents itself throughout the vaccine environment. If government and the private sector cannot effectively deal with the vaccine-related problems, we will suffer grave consequences should a naturally occurring epidemic threaten our country or a bio terrorist release an agent into a crowded public place.

Out of concern that the nation's vaccine manufacturing capacity is severely threatened, the *U.S. Medicine Institute for Health Studies* and the Defense Department's Global Emerging Infections Surveillance and Response System (*DoD-GEIS*) convened a forum in Washington, D.C. to bring together top officials from government, industry and the public health sector. Moderated by George K. Anderson, MD, MPH,• the March 15, 2001 meeting gathered experts from around the nation to assess factors affecting vaccine research, production, and distribution. A specific focus of the meeting was special use and limited market vaccines; those products often termed "orphan vaccines." Many of these vaccines are of great importance to prevent human outbreaks of anthrax, plague, hemorrhagic fevers, and even smallpox, should that ever reappear. The following summary represents the issues and opinions emerging from the forum entitled: "Vaccine Research, Availability … and Reality."

The first question addressed by the group was unfortunately never fully answered, and is perhaps the most significant issue coming out of the forum. Who is responsible for ensuring we have vaccines when we need them? *Although a number of public and private sector organizations play important roles, there is no single authority overseeing vaccine development, manufacture, and distribution in the United States or globally. This has prevented focused, coordinated action to resolve a critical situation now before us.*

The Challenge in Vaccine Manufacturing

Vaccines, manufactured by increasingly fewer companies, are not pharmaceuticals. These products generally do not offer the attractive profit margins expected from corporate research investments. Although the science may be compelling, companies are understandably slow to develop and manufacture vaccines in light of expensive development costs, lengthy regulatory clearances and significant liability exposure.

A further challenge comes as industry restricts the use of limited and costly biotechnology facilities and personnel devoted to vaccine research and production in order to dedicate adequate resources to other high-profit, pharmaceutical activities. This is occurring at a time when industry must deal with increasingly stringent regulatory

conditions for vaccine testing, licensure and production, which require an even greater commitment of resources. This situation, added to "just in time" business practices means the U.S. may have no surge capacity when a special need arises. In such situations, individuals needing vital vaccines may simply not be able to get them. These factors were likely involved in the recent delay in availability of the 2000 - 2001 influenza vaccines and the current shortage of tetanus-diphtheria vaccine.

All aspects of the vaccine story require renewed high level attention and a new infusion of resources. Significant concerns exist for all vaccine related activities, to include disease surveillance; immunization needs assessment; next generation vaccine research, development, and production; and stockpiling and distribution. Improving this situation depends first on identifying responsibility for national vaccine programs and properly coordinating activities with adequate funding.

Predicted advances in genetics and biotechnology will allow future products to simultaneously provide immunity to a broad spectrum of diseases. Until then however, disease surveillance, vaccine research, and immunization programs must be orchestrated disease-by-disease in almost every case. Historically, this approach has worked, but at a slow pace. Smallpox was eradicated in this manner as a naturally occurring disease, just as researchers hope to soon eliminate polio from the earth. By following a strategic plan of action, immunization has been effective in preventing many childhood diseases like measles, mumps, rubella, and chickenpox.

Unfortunately, many effective products are no longer available on the disease-by-disease list of vaccines. The complicated problems involved with manufacturing and stockpiling have resulted in the inability to employ vaccines used to prevent adenovirus infections, plague, Rift Valley fever, Korean hemorrhagic fever, Argentine hemorrhagic fever, and chickungunya. While most of these diseases are rare in the United States, vaccines are essential to individuals traveling in areas where risk of their infection is high. In today's global economy - and particularly with deployed military, Foreign Service and humanitarian personnel, - vaccines to prevent biological scourges and potential bio terrorism agents are essential.

Immunization Issues

Influenza vaccines are representative of the complexity of the vaccine story. Because influenza may be caused by several different viral types, with each changing characteristics over time, the annual formulation of an influenza vaccine is based on predictions of which viruses are most likely to be active during the next influenza season. Forecasting prevalent influenza viruses is based on an understanding of disease occurrence and spread patterns gained from information reporting from around the world. An important lesson is that improvement in global surveillance capability - especially in less developed nations, - needs high priority.

Military immunization requirements represent a special case. Preventing disease is fundamental to the medical support of military operations. The history of warfare

demonstrates that naturally occurring diseases can cause greater numbers of casualties than enemy weapons. Military members deploying to distant locations must be protected to the greatest extent possible from disease threats present there, as well as from the potential of rogue state or terrorist attacks using anthrax, plague or some other agent to decimate troops and support personnel.

The recent loss of manufacturing sources for adenovirus and plague vaccines, compounded with problems in anthrax vaccine production and tetanus-diphtheria vaccine supply, show that the Department of Defense vaccine programs are in urgent need of attention.

Vaccine Safety

The positive preventive value of vaccines has been generally understood and defended by medical professionals for decades. Their wide use has been a tremendous public health boon and contributed to the virtual elimination of some of the most dreaded diseases in history. However, when a problem suggests vaccines contribute in any negative way, communication about the problem is often intense and dramatic. Vaccines increasingly elicit emotional, high level reaction from the public due to their ubiquitous use. Regardless of the preventive health value of these products, anti-vaccine sentiment may be growing that could have an adverse impact on public opinion. The forum participants concluded that medical professionals should become more forthright in dealing with anti-vaccine sentiment, using readily available studies and data.

Conclusion

In leveraging scientific progress to improve health status, a broader understanding of the challenges facing vaccine availability is needed. To keep pace, new investment in vaccine research must be made. If incentives for private industry to invest are not sufficient, help from the federal government may well be necessary. This could include the possibility of government owned or funded production facilities for those products with markets so limited that industry cannot afford to address them.

Vaccines made it possible for mothers in the 20th century to expect their children to reach adulthood, and for society to progress without threat of massive deaths from epidemics. We need to continue investments toward more secure individual and public health in the 21st century and not lose ground gained over the past century. In government, we must develop a high level coordinated approach to vaccine research, production and availability or we risk a serious crisis in the not distant future.