Vaccine against Tuberculosis April 2007

The current TB vaccine is outdated and not very effective

The current TB vaccine, Bacille Calmette-Guérin (BCG) was developed early in the 20th century and is routinely given to infants in much of the world. BCG appears to reduce the risk of serious childhood forms of TB, such as TB meningitis, but protection against pulmonary TB is a controversial subject with numerous studies providing conflicting results. Despite being one of the most widely used children's vaccines, BCG has had no apparent impact on reversing the growing global TB pandemic. The need for a more effective TB vaccine has grown more urgent as the TB pandemic has evolved. TB is now the biggest killer of people with HIV/AIDS, accounting for approximately one third of AIDS deaths worldwide. Multi-drug resistant (MDR) TB and extremely drug resistant (XDR) TB are on the rise. They are more difficult and expensive to treat than drug-susceptible TB, with much lower success rates, and they threaten to undermine TB control efforts.

A New Vaccine: Critical to Controlling TB

Vaccines have made enormous contributions to the control of infectious diseases. Through vaccination, smallpox has been wiped out and polio nearly eliminated. Vaccines also hold great potential for better TB control. It is estimated that the introduction between 2014 and 2018 of a new, more effective TB vaccine that is widely adopted would reduce TB incidence in Africa and South-East Asia by over 20% during the first ten years of use and up to 40% by 2050.[1] Vaccines in combination with better drugs and diagnostics could achieve much better global control of the TB pandemic in the next 15-20 years and eliminate the problem by 2050, preventing millions of deaths in the process. Without a better TB vaccine, control of this deadly disease will be extremely difficult.

Recent advances in tuberculosis research and vaccine delivery systems have brought the goal of a new TB vaccine within reach. The elucidation of the genome sequence of *M. tuberculosis (Mtb)*, a greater understanding of protective immune responses, the introduction of modern manufacturing technologies and the development of new vaccine delivery systems have significantly strengthened efforts to develop new TB vaccines.

Today, the field is moving toward a combined prime-boost TB vaccine strategy in which BCG or an improved recombinant BCG vaccine (rBCG), the prime, will be given to infants, followed by a booster inoculation with a different vaccine. Adolescents and adults previously primed with BCG as children will be given a booster inoculation. Prime-boost regimens of this sort have proven to be powerful inducers of immune responses in humans.

A Global Development Priority Requiring a Global Commitment

Developing a new TB vaccine is a priority of the *Global Plan to Stop TB 2006-2015*, which sets out a bold course of treatment and new tools development to reverse the course of TB, halve TB deaths over the next ten years, and eliminate TB as a global public health problem by 2050. Broadly effective TB vaccines could have a large impact on Millennium Development Goal (MDG) #4 – *reduce child mortality,* as a 100,000 children die of TB each year, and MDG # 6 – *halting the spread of AIDS, Malaria, and other diseases.* Studies modelling the ten-year economic benefits of a vaccine that is 75% effective have estimated annual worldwide savings in medical costs in excess of US $25 billion.[2]

[1] Stop TB Partnership and World Health Organization. *Global Plan to Stop TB 2006 – 2015*. Geneva, World Health Organization, 2006.

[2] Bishai DM, Mercer D. Modeling the economic benefits of better TB vaccines. Dept Pop Fam Health Sci, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, USA

Ensuring TB vaccine development and access: what is needed?

Despite its potential to dramatically reduce and even eliminate TB, there is still a tremendous need for resources to develop better TB vaccines. The Stop TB Partnership estimates that current resources fall $1.5 billion short of what is needed for vaccine development. Some priority areas include:

Research and Development - Investment in all areas of research and development are critical to the successful development of a new, more effective TB vaccine. Basic research to understand the biology of the TB bacillus and human immunologic responses will greatly aid the development of drugs, diagnostics and vaccines. Translational research to ensure that early-stage discoveries are advanced through development to licensure is also critical to the realization of new products.

Clinical Trials – Large gaps exist in both funding and capacity for clinical trials and studies to field-test new technologies, the most cost-intensive phase of development. Prerequisites to vaccine trials include baseline epidemiological information, development of community interaction programs, development of protocols that comply with legal and ethical requirements, coordination with national regulatory authorities, local proficiency in immunological assays and diagnostic procedures, and infrastructure for vaccine delivery. Evaluation of vaccine candidates requires a series of clinical trials of increasing size, complexity and cost to progressively evaluate safety, immunogenicity and efficacy.

Preparation for the introduction and adoption of new tools – Public health advocates will need to work with governments in high-burden countries, international organizations and the WHO to prepare for the introduction and adoption of new TB tools. Public policies should be adopted that guarantee that all people who need TB vaccines, drugs and diagnostics will have access to them.

The Role of Product Development Partnerships (PDPs)

Product Development Partnerships (PDPs) are non-profit organizations that build partnerships between the public, private, academic, and philanthropic sectors to drive the development of new products for underserved markets. In the global health arena, PDPs are accelerating the development and testing of new technologies that fight TB, AIDS, malaria, and a wide range of other neglected diseases. In addition to product development, PDPs will also help ensure that all people in need have ready access to simple, affordable and effective technologies. The UK Department for International Development is a major supporter of PDPs, and is encouraging other donor governments to increase their commitments.

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For more information on Aeras's work visit http://www.aeras.org.