TB trial highlights challenges with introducing new vaccine into childhood immunization schedule

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A new vaccine to combat tuberculosis is less effective at stimulating an immune response when administered to Gambian infants in combination with the routine immunisation schedule, according to clinical trial results published today in *Science Translational Medicine*.

The findings may have important implications for designing the most effective immunisation schedules for children, and also for the design of future clinical trials of the new vaccine.

Standard childhood vaccinations are routinely given as part of a schedule known as the Expanded Program on Immunisation, EPI, which helps to improve vaccine coverage in the population by reducing the number of visits to the clinic required. The schedule includes vaccines for diphtheria, tetanus and whooping cough, as well as the current vaccine for TB, Bacille Calmette-Guérin (BCG). The aim is to vaccinate children in early infancy, in order to protect them from disease as early as possible.

With 1.8 million people per year killed by TB and more than two billion people worldwide infected with the bacteria that causes the disease, it is clear that BCG offers limited protection and there is an urgent need for more effective vaccines against TB.

MVA85A is a vaccine designed to be given after BCG to boost the

body's immune response and improve protection against TB. Originally developed by Dr Helen McShane at the University of Oxford with funding from the Wellcome Trust and the Medical Research Council (MRC), it has already been shown to be safe and capable of eliciting powerful immune responses in clinical trials in adults in the UK, Gambia and South Africa. This is the first trial to evaluate safety of the vaccine in infants.

The purpose of the study was to assess whether MVA85A can stimulate immune responses against the tuberculosis bacteria in infants and whether it could feasibly be given at the same time as other childhood vaccines as part of the EPI.

The randomised trial, funded by the Wellcome Trust, the MRC and the European Commission, involved 214 healthy, 4-month-old infants, who had already received BCG at birth. Children were given either EPI alone, MVA85A alone, or MVA85A in conjunction with EPI.

Overall, MVA85A was deemed to be safe, well tolerated and induced a strong immune response. Importantly, the responses to the standard EPI vaccines were not affected by giving MVA85A at the same time. However, the immune response to MVA85A was lower in infants who received it in conjunction with EPI vaccines compared with those that received the new vaccine alone.

Dr McShane, a Wellcome Trust Senior Clinical Research Fellow at the University of Oxford, explains: "It's reassuring to see that MVA85A does not affect immunity to the other vaccines that are included in the EPI and important to see that it is safe in infants. This study will help us determine the best way to integrate MVA85A into routine infant immunisation schedules in future."

Dr Martin Ota, who led the study at the Medical Research Council

(MRC) Unit in The Gambia, welcomes the results: "These important results highlight that we have a real opportunity to make sure that children are protected in the future against tuberculosis by introducing effective and well-timed immunisation programmes. This can only be achieved with robust information gathered from well-conducted clinical trials such as this."

"We don't yet know how the immune response we generate with MVA85A relates to protection from TB and we are currently conducting an efficacy trial of a higher dose of the vaccine in South African BCG-vaccinated infants to assess this. The results of this trial will be available in 2012," added Dr McShane.

The South African efficacy trial of MVA85A is supported by a Wellcome Trust Strategic Translation Award. Supporting research to combat infectious disease is one of the Wellcome Trust's strategic goals.

Dr Ted Bianco, Director of Technology Transfer at the Wellcome Trust, commented: "The EPI has been enormously important in protecting successive generations of children from preventable infections for over twenty years. But a limitation of the programme is that not all vaccines can be easily accommodated within a universal vaccination schedule. It is one of the great challenges in public health to resolve this conundrum so that the fruits of today's vaccine research can be delivered to where they are needed with the efficiency that underpins the success of the EPI."

More information: M. Ota et al. Immunogenicity of the Tuberculosis Vaccine MVA85A is reduced by coadministration with EPI vaccines in a randomised controlled trial in Gambian infants. *Science Translational Medicine*, 2011.

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