Pneumococcal vaccine offers protection to HIV-infected African adults in clinical trial

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A clinical trial of a vaccine against a major cause of pneumonia and meningitis has shown that it can prevent three out of four cases of re-infection in HIV-infected adults in Africa.

The trials, conducted in Malawi and funded by the Wellcome Trust, studied the efficacy of a vaccine against infection with the *Streptococcus pneumoniae* bacteria. These bacteria are a primary cause of pneumonia and when they invade the blood stream and brain - so called invasive pneumococcal disease (IPD) - they cause the serious and often fatal illnesses of septicaemia and meningitis. In HIV-infected adults, particularly in sub-Saharan Africa, the risk of developing IPD increases between thirty and a hundred-fold.

The pneumococcal polysaccharide vaccine (PPV), which is currently used to protect adults in the UK and US, has been shown to have limited efficacy in HIV-infected adults and is not recommended in Africa.

Polysaccharide vaccines consist of long chains of sugar molecules isolated from the infectious agent (in this case, the pneumococcal bacteria). To enhance the vaccine's ability to elicit protective immunity, the sugar molecules can be bound to a 'carrier' protein which magnifies the immune response to the antigen - such vaccines are known as conjugate vaccines.

Researchers at the Malawi-Liverpool-Wellcome Trust Clinical Research Programme, University of Malawi College of Medicine in Blantyre, Malawi, tested the efficacy of Prevnar, a pneumococcal conjugate vaccine (PCV) developed by pharmaceutical company Wyeth, in a double-blind randomized placebo-controlled clinical efficacy trial. The results are published today in the New England Journal of Medicine.

The trial, led by Dr Neil French, formerly at the Liverpool school of Tropical Medicine, tested the vaccine on almost five hundred predominantly HIV-infected adults who recovered from IPD after being admitted to the Queen Elizabeth Central Hospital in Blantyre. They found that the vaccine prevented 74% of recurrent cases of IPD in patients with underlying HIV infection.

"This is the first trial to use a conjugate pneumococcal vaccine in an adult group and find clinical benefits," explains Dr French, who is now based at the London school of Hygiene and Tropical Medicine.

Of particular note was the fact that the vaccine prevented disease even when given to patients with CD4 counts of below 200 cells per cubic millimetre of blood. CD4 cells are an essential part of the immune system, but are targeted and destroyed by HIV. An HIV-infected person with a CD4 count below 200 is considered to have AIDS. This is the first time a conjugate vaccine has been effective at generating a protective response at low CD4 counts.

"The vaccine's efficacy at low CD4 counts is remarkable," says Dr French. "The general view on the use of any vaccines in HIV is that low CD4 counts make the vaccine useless. We've shown that conjugate technology overcomes the profound immune deficiency at these low counts. This gives hope for the possible use of conjugate technology in other vaccines targeting important HIV associated bacterial infections, most notably non-typhoidal *Salmonella*."

Dr French believes the study suggests that the conjugate pneumococcal vaccine may be applicable for use in other adults groups at risk of IPD.

"Since it works in patients with HIV infection, then by extension, it is likely to work in other adult groups, including the elderly and other at risk groups," he says. "This is an important finding to

support the further development and use of conjugate vaccines for adults in general."

However, according to Dr French, the cost of the conjugate vaccines (around US$40 per dose) means that financing mechanisms akin to those available for paediatric vaccines through GAVI (Global Access to Vaccines Initiative) or other forms of subsidy will be needed to make these vaccines widely available to adults within Africa.

More information: French, N et al. A trial of 7-valent Pneumococcal Conjugate Vaccine in HIV-infected Adults. NEJM; 3 March 2010.

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