Abstracts

Does prophylaxis with isoniazid have an effect on the incidence of TB in children with HIV?

Research from South Africa, published in the *British Medical Journal* recently, suggests that isoniazid prophylaxis has an early survival benefit and reduces the incidence of TB in children with HIV.

Heather Zar and colleagues looked at the effect of isoniazid prophylaxis on mortality and incidence of TB among children with HIV. They studied children aged more than 8 weeks, who were attending Red Cross Children's Hospital or Tygerberg Children's Hospital. The study started in January 2003. The placebo arm of the study was ended on 17 May 2004 on the recommendation of the data safety monitoring board (DSMB) on the basis of interim results.

TB and HIV are dual pandemics in children in sub-Saharan Africa. TB accelerates the course of HIV, is an important cause of acute and chronic pneumonia in African children with HIV and is responsible for a major proportion of mortality. Infection with *Mycobacterium tuberculosis* confirmed by culture has been found in about 8% of children with HIV admitted to hospital for pneumonia in areas with a high prevalence of TB and HIV. In a postmortem study of Zambian children who died from respiratory disease *M. tuberculosis* was found in 18% of children with HIV; in children older than 12 months with HIV, TB was second to pyogenic pneumonia as a cause of death.

Prevention of TB in children with HIV through prophylaxis with isoniazid may be effective in reducing mortality in areas with a high prevalence of TB. In studies of adults with HIV, prophylaxis with isoniazid significantly reduced the incidence of TB and produced a favourable trend in mortality in those with a positive result on a tuberculin skin test. The effect of such prophylaxis in children, however, is unknown.

Children were given either isoniazid or placebo, given with co-trimoxazole either daily or 3 times a week. Data on 263 children were available when the DSMB recommended discontinuing the placebo arm; 132 (50%) were taking isoniazid. Median follow-up was 5.7 months. Mortality was lower in the isoniazid group than in the placebo group. The reduction in mortality was similar in children on 3 times a week or daily isoniazid. The incidence of TB was lower in the isoniazid group (5 cases) than in the placebo group (13 cases). All cases of TB confirmed by culture were in children in the placebo group.

The conclusion was that prophylaxis with isoniazid has early survival benefits and reduces the incidence of TB in children with HIV. This makes it an effective public health measure that can be used to reduce mortality in HIV-positive children in areas of high TB prevalence.

Zar H, *et al. BMJ* 2007; 334: 136.

Another vaccine success story

In 2002, the UN General Assembly Special Session on Children adopted a goal to reduce deaths due to measles by half by the end of 2005, compared with 1999 estimates. The authors of this paper in *The Lancet* describe efforts and progress made towards this goal.

Before the advent, and widespread use, of the measles vaccine in 1963, measles was the single most lethal infectious agent. In the early 1960s there were as many as 135 million cases of measles and over 6 million measles-related deaths annually, more than 50% as a result of either primary viral pneumonia or complicating bacterial pneumonia.

Routine measles vaccination was introduced in most developing countries as part of the Expanded Programme on Immunization and this had a major effect on global measles mortality. By 1987, the World Health Organization (WHO) estimated that the number of deaths from measles worldwide had been reduced to 1.9 million.

Global measles vaccination activities can be characterised into 3 broad phases. The first phase involved the introduction of routine vaccination against measles in almost every country in the world through the Expanded Programme on Immunization, beginning in 1974, and the UNICEF-led initiative for Universal Childhood Immunization by 1990. In this phase the recommendation was for one dose of measles vaccine to be administered at or shortly after 9 months of age to at least 80% of children in every country. During the second phase from 1990 to 1999, routine measles vaccination levelled off in the 70 - 80% coverage range and many industrialised countries introduced a second routine dose, usually at or around the time of school entry, to protect children who did not respond to the first dose. Also during this period, the Pan American Health Organization (PAHO) implemented a strategy that included a second opportunity for measles immunisation for all children to stop endemic measles transmission in the Americas.

The third phase began around 2000 with the realisation that despite the availability of a safe, effective, and relatively inexpensive measles vaccine for over 40 years, measles remained a leading cause of childhood mortality, especially for children living in developing countries. To address this problem, WHO and UNICEF began to target 45 priority countries, together accounting for more than 90% of estimated global measles deaths, to implement a comprehensive strategy for accelerated and sustained reduction in mortality due to measles. The strategy emphasised the PAHO approach to provide all children with a second opportunity for measles immunisation. At present 47 countries are targeted for measles mortality reduction, because Yemen and Timor Leste have been added to the list of priority countries.

Between 1999 and 2005, mortality related to measles was reduced by 60%. The largest percentage reduction in estimated measles mortality during this period was in the western Pacific region (81%), followed by Africa (75%) and the eastern Mediterranean region (62%). Africa achieved the largest total reduction, contributing 72% of the global reduction in measles mortality. Nearly 7.5 million deaths from measles were prevented through immunisation between 1999 and 2005, with supplemental immunisation activities and improved routine immunisation accounting for 2.3 million of these prevented deaths.

Achievement of the 2005 global measles mortality reduction goal is evidence of what can be accomplished for child survival in countries with high childhood mortality when safe, cost-effective, and affordable interventions are backed by country-level political commitment and an effective international partnership.

Wolfson LJ, *et al. Lancet* 2007; 369: 191-200.

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