

Hepatitis E Vaccine Trial in the Royal Nepal Army

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The article entitled "Hepatitis E in the Royal Nepal Army and the Kathmandu Valley, by Brig Gen Dr. K. B. Shrestha, in the MJSBH Vol. III, clearly elucidated the human economic, social and military toll of the Hepatitis E virusⁱ. This virus is transmitted through fecally contaminated food or more usually water. Due to its disabling onset and its prolonged convalescent period, it causes substantial morbidity. UP to 3% of hepatitis E cases dieⁱⁱ and mortality is especially high in pregnant women, where it reaches 20-30% in some studiesⁱⁱⁱ. In India it is estimated that there are about 5 million cases of hepatitis E each year^{iv}. Rates of disease in the Kathmandu Valley, is about 20/1000 person-years. Treatment and absence from work results in an estimated economic loss of approximately one third of the average family annual resources. With 32 healthy days lost for each case, totalling up to 768,000 days per year, the economic loss to the Kathmandu Valley is approximately NRps 90 million a year^v.

Jaundice due to hepatitis E causes economic and manpower difficulties to the Royal Nepalese Army. Studies over the past 10 years indicate an annual attack rate in the Army of 1-2%, with an average hospital stay of 15 days (1-92 days), with an average absence from duty, expanded by convalescent leave of 6.8 weeks (2-14 weeks). In the year from July 1997 to June 1998, the estimated monetary loss due to hepatitis E to the Royal Nepal Army, comprised of hospital costs, duty time lost and replacement of function came to over NRs 3 million^{vi}.

There is no specific treatment for hepatitis E. Treatment is symptomatic, composed of bedrest, which results in slow recovery and eventual return to normal activity. Currently, there are no specific preventive measures. Immune serum globulin is not protective. For this enterically transmitted virus the only way to prevent the transmission is through improvement of personal hygiene, socio-economic conditions and general sanitation. However, a candidate recombinant HEV vaccine has been developed by the U.S. national Institutes of Health (NIH).^{vii} This candidate vaccine has successfully completed safety and immunogenicity trials which meet Nepali and international scientific and ethical standards. These included challenge trials in rhesus monkeys which showed that the candidate virus was able to prevent hepatitis E in vaccinated animals^{viii}. Human safety and immunogenicity trials in 88 American volunteers followed by 44 Nepali volunteers showed the candidate vaccine to be safe and immunogenic^{ix}. Volunteers in both countries have been followed for up to two and a half years with no medical sequelae reported.

Now there is an ongoing randomized, double blind, placebo controlled vaccine trial, of the candidate recombinant hepatitis E vaccine, being undertaken in the Royal Nepal Army by the Shree Birendra Royal Nepalese Army Hospital in association with the Walter Reed Army Institute of Research's subsidiary, the Armed Forces Research Institute of the Medical Sciences (AFRIMS). This vaccine trial meets all Nepali and international scientific and ethical standards and is being monitored on a regular basis by the Nepal Health Research Council and American and European ethical oversight groups. The Command Structure of the Royal Nepalese Army, including the Chief of Army Staff, who is one of the volunteers, are fully supporting this trial.

Three vaccinations are planned over a six month period. Volunteers will be followed for the occurrence of hepatitis for a two year period. Of the 5263 volunteers screened for antibody to hepatitis E virus, 3113 were susceptible and therefore eligible to enroll in the study. Two thousand consenting volunteers have been enrolled and have received either 0 micrograms (placebo) or 20 micrograms of hepatitis E recombinant protein (the active vaccine). Thus, half of the volunteers received the hepatitis E protein and the other half did not. The vaccinations are given according to a coded randomized list in a double blind manner. That means that neither the volunteer nor the vaccinators know which does of the HEV protein the volunteer received. The code will be broken, only when there are sufficient cases of hepatitis E to ascertain whether the 20 microgram does was successful in preventing jaundice.

If vaccine efficacy is demonstrated in this pivotal vaccine trial performed in Nepal where the disease is prevalent, we expect the vaccine to be licensed and manufactured for international use, to become available at a reasonable price in Nepal and other countries. The Royal Nepal Army will be among the first organizations to get the hepatitis E vaccine when it becomes available.

This is the first vaccine trial of its kind performed in a South Asian country. The success of this vaccine study will be a tribute to the Royal Nepal Army and the Nepalese people. It will open a path for future collaborations between Nepal and external agencies in defining preventive strategies to promote the health of the Nepalese people. This will also enable the Royal Nepal Army and the Nepalese people to be recognized by the international medical community.

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