the attack rate and severity have been low compared to non-immunised children. It has been also noticed that the low titre vaccine administered at less than 12 months of age has poor immunogenicity. Hence, it may be ideal to consider vaccination in children older than 12-14 years of age if not infected by then. Seroprevalence of Hepatitis A has been reported to be 50 per cent of those less than three years and 80 per cent of those less than eight years of age. Children from a high socioeconomic group and hygienic families are likely not to be exposed to infection. Hepatitis A is a benign disease in childhood but assumes severity in adolescents and young adults. Like the varicella vaccine, immunity induced by the Hepatitis A vaccine is expected to last for 15-20 years, after which adolescents are likely to be susceptible if exposed to natural infection. It is best to consider administration of this vaccine in children over 12 years of age if not naturally infected.

To summarise, the varicella and Hepatitis A vaccines should be reserved for older children if they are not already infected by then. The typhoid vaccine must be administered to all susceptible children and adults. The HiB vaccine is ideal for children less than two years old.

References:
1. Thyagarajan SP, Jayaram S, Mohanvalli B: Prevalence of HBV in general population of India in Hepatitis B in India (Ed) SK Sarin, AK Singhal, CBS publishers and distributors 1996 p 9

Epidemiology and ethics in the Hepatitis B vaccine

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The current claims of Hepatitis B virus (HBV) carrier rate in India are highly exaggerated, unscientific and misleading. A series of errors is being made in estimating the burden of HBV disease and its significance. These errors must be corrected, and we must scientifically assess the burden of morbidity, mortality and consequent loss of life-years due to HBV in India. Finally, we must also discuss the various options for a HBV vaccination strategy in India on the basis of cost effectiveness and logistical feasibility. We are unaware of any such exercise by the Indian Association of Paediatrics before its strong recommendation of universal immunisation of Indian children against HBV.

Frightening figures

Most doctors seem convinced about the overwhelming danger of HBV infection in India. Based on frightening figures put forth by experts who claim that the carrier rate in India is 4.7 per cent with an estimated carrier population of 42.5 million (1). These widely-quoted estimates, based on the results of 19 studies, suffer from three types of errors.

First, the studies are all one-time cross-sectional studies of prevalence of HBsAg positivity. Positivity is different from a carrier state — the persistence of infection for six months or more (2).

Second, many of these studies are based on data from blood bank donors, including professional blood donors who are known to have a higher prevalence of HBV infection. One study reports on dental professionals, another high risk group. These groups cannot be used to estimate prevalence in the general population.

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Finally, the average prevalence of 4.7 percent has been arrived at not as a weighted average but by calculating the simple average of the numbers in the individual studies.

A more accurate estimate of the carrier rate — a carrier being someone who has tested positive for HBsAg in two tests six or more months apart — using the same data in the 19 studies, and after excluding the professional blood donors and dental personnel and those studies in which the numbers tested are not mentioned (and taking into account the positive predictive value of the test being used currently) works out to 1.42%, with a carrier pool of 12.75 million (3).

It is also important to note that, contrary to the current assertions (4), not all HBsAg positives are highly infectious. The prevalence of highly infectious carriers (“HBe positives”) is much lower than the estimate of 24.43 per cent of HBsAg positives or approximately 10 million (1). We arrive at the much lower figure of 3.26 million highly infectious carriers (3).

Is it a public health problem?

Some people have argued that HBV is a major public health problem. “Liver disease due to HBV infection is considered to be the fourth or fifth most important cause of mortality in the most productive period of life, 15-45 years (4). Approximately 25 per cent of carriers are expected to die of chronic sequelae of the infection — cirrhosis and primary hepatocellular carcinoma (5). In fact, the danger of chronic infection and chronic sequelae from HBV infection is much less than that. Recent observations suggest that the true rate of chronic infection is as low as one per cent in normal, immunocompetent young adults (6), not five per cent to 10 per cent. Even among these carriers, about two per cent clear the virus every year.

We do not have adequate data on prevalence of HBsAg positivity in

References:
1. Thyagarajan SP, Jayaram S, Mohanvalli B: Prevalence of HBV in general population of India in Hepatitis B in India (Ed) SK Sarin, AK Singhal, CBS publishers and distributors 1996 p 9
India, on the carrier rate in different age groups and on the prevalence of acute and chronic HBV diseases and their sequelae in these age groups, to estimate the number of life years lost due to HBV compared to other (especially vaccine preventable) diseases in India. While we do not attempt this here, a range of studies suggests that the overall burden of disease is much lower than it is made out to be (3). Before recommending Universal Immunisation of Hepatitis-B vaccine, it is necessary to estimate on the basis of available data (Western or Indian), the life years lost per lakh of population due to Hepatitis B. This will form the basis for estimating the cost-efficacy of this vaccine.

Immunisation strategies
Supporters of universal immunisation quote the US decision to switch from selective, high-risk vaccination to universal immunisation. However, there is a vast difference between the predominant mode of transmission and age distribution of acquisition of HBV infection in developing and in developed countries. Most HBV infections in the developed world occur among adults, primarily through sexual transmission (2), whereas perinatal infection is the most important mode of HBV perpetuation in developing countries (6).

For these reasons, we should consider the option of selective immunisation of newborns of HBsAg positive mothers or of all pregnant women. Logistically this is feasible, because unlike the high risk groups in the US, this vulnerable group in India (newborns/infants) is visited by the health services. People are succumbing out of plain fear. We would appreciate if doctors could enlighten us about Hepatitis B. Is it truly more dangerous than AIDS? And is the public panic justified? Do we really need one more vaccine?

Lastly, in allocating resources to the vaccination programme, its expense, efficacy and contribution to the prevention of diseases in India must be placed in the context of other health programmes in India. For example, the cost of vaccines of all six vaccine-preventable diseases in the Expanded Programme of Immunisation was Rs 17 per child in 1992 (7), which may have increased to Rs 30. Even at a subsidised Rs 100 per child, the vaccine costs alone of vaccinating just newborns against HBV would be Rs 2,500 million per year. Extending the programme to the 0-4 or 5-14 age groups could send costs to Rs 12,730 million annually. To put these figures in context, this year’s budget for malaria is Rs 2,240 million and TB is Rs 1,050 million (8).

We also need an estimate of the programme’s cost efficacy. The cost efficacy of different immunisation strategies depends on the cost per life year saved from immunisation, and cost per unit reduction in the infectious pool. Can we afford to introduce a vaccination strategy with a cost efficacy of say Rs 15,000 per life year saved when our per capita annual income is around Rs 10,000?

Need for debate
This call for better studies on prevalence and burden of disease, for estimates of cost efficacy and for a strategy towards new vaccines is becoming particularly important as newer vaccines come into the Indian market each year, and pressures are exerted to include these vaccines in the national health programmes.

References:


**DISCUSSION**


**Additional reading:**


6. Lodha Rakesh, Jain Yogesh: Need for universal Hepatitis B immunisation in India: A review of literature. (under publication)

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**Ethical issues considered in Tamil Nadu Leprosy Vaccine Trial**

**MD Gupte, DK Sampath**

For more than eight years, we have been involved in a massive field-based comparative leprosy vaccine trial in Tamil Nadu, covering some 300,000 people. The study is supported by the Indian Council of Medical Research. The trial was launched in January 1991, and the study protocol was approved shortly before the publication of International Guidelines for Epidemiological Studies. This paper will discuss various ethical issues raised by these international guidelines in the context of the trial.

A number of candidate anti-leprosy vaccines became available during the 1980s. After an in-depth technical review of these candidate vaccines, it was considered essential to compare them in a single study (1). The three vaccine preparations being tested are *M. leprae* + BCG, ICRC and Mw. The two control preparations are BCG and a placebo.

Before the vaccination exercise, the entire population of the selected geographical area was enumerated and screened for its eligibility for inclusion in the trial. Vaccination was completed in two and a half years, after which the population was kept under surveillance and examined periodically for the occurrence of leprosy. All documents regarding consent, feedback, post-vaccination complications and surveillance have been stored for future reference.

An ethical review of such research must address a number of questions. These questions are discussed below.

Was the Phase III trial of efficacy preceded by a Phase II trial for safety? Before the large-scale vaccine trial was launched, Phase II trials of all the candidate vaccines, with a maximum of 300 volunteers, were conducted after obtaining permission from the Drugs Controller of India. The Phase II trials provided essential information on the vaccines’ short-term toxicity and possibly efficacy through proxy measures.

**Was the study protocol respect the principles of autonomy, beneficence and justice?**

The three basic principles of clinical and epidemiological research — autonomy, beneficence and justice — have been described in various international statements and guidelines. The first principle also provides protection to people with impaired or diminished autonomy. In the leprosy vaccine trial, information about the nature of the study was made available by oral presentations in the local language to groups of people in the villages taken up for study, and efforts were made to motivate individuals to participate, without compromising the voluntary nature of the programme.

Regarding the principle of beneficence, patients detected with leprosy were given prompt treatment. And as for the question of justice, random allocation of individuals to the five arms of the trial ensured equal distribution of risks and benefits among...