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) SKSarin, AKSinghal, CBS publishers and distributors 1996 p 9

2. John JT, Cherian T, Raghupathi P: Haemophilus Influenza disease in children in India- a hospital perspective *Pediatric Infectious Disease Journal* 1998, 17:S169-S171

3. IBIS group: Invasive Haemophilus influenza disease in India – a preliminary report of prospective multihospital surveillance *Pediatric Infectious.Disease. Journal*. 1998,17:S172-S175

4. Venkatraman AR, John TJ: Epidemiology of varicella in staff and students of a hospital in tropics *International Journal of Epidemiology* 1984, 13: 502-505

5. Dhavan PS, Shah SS, Alavares J.F: Seroprevalence of Hepatitis A virus in Mumbai *Indian Journal of Gastroenterology* 1998, 17(1): 16-18

Epidemiology and ethics in the Hepatitis B vaccine

Anant Phadke, Ashok Kale

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 errrors 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.

Anant Phadke, *CEHAT, 2/10, Swanand, Aapli Sahakari Society, 481, Parvatidarshan, Pune 411 009.*
Ashok Kale, *D-17, Taljai Greens Cooperative Housing Society, Dhankawadi, Pune 411 043.*

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 be 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

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 anyway, for immunisation work.

In the context of other health programmes

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:

1. S.P.Thyagarajan, S.Jayaram, B. Mohanvalli. Prevalence of HBV in the general population of India, in *Hepatitis B*

More dangerous than AIDS? H elp !

We reproduce below a handbill that has been widely distributed in Saligao and other parts of (Goa). Villagers are in a panic because this "... silent killer is MORE DANGEROUS than AIDS". A nine-year-old boy from Lourdes Convent in Saligao came home and demanded Rs. 90 from his parents for the injection. "If I do not take it, I will die...." the stricken boy told them.

Parents do not know where to turn. Do they believe this international organisation called 'Lions Club' and cough up these large sums of money? Or do they wait for this silent, but deadlier-than-AIDS-killer to strike because they do not have Rs. 900 to buy the vaccine for a family of six?

There has been no awareness programme from the government's directorate of 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?

The way this sudden campaign is let loose on the Goan public is very suspicious. Where is the vaccine coming from? Which are the pharmaceutical multinationals involved? Who are the distributors and agents who going to rake in these easy percentages? Is Lions Club justified in spreading panic to achieve what should normally be a very laudable health campaign?

Muriel and Mario, *Opposite St. Anne's Chapel, Saligao. Goa 403511. India. Tel.: 278276. E-mail: elinks@goal.dot.net.in*

POSTER

BEWARE OF HEPATITIS-B *The Silent Killer Is *More Dangerous Than AIDS**

Immunise yourself and your family against this dreaded disease.

(This announcement is followed by a list of dates and venues for immunisation days at municipal halls, Lions Club centres, church grounds and community recreational halls.)

The vaccine is given at a subsidised rate: Children below 10 years - Rs. 90/- per dose. Above 10 years - Rs 180/- per dose. We use disposable syringes only. Courtesy: Humanitarian Project of Lions Club of Margao - South and Lions Club of Chicalim, Bogmalo, Quepem, Panjim and Candolim. For details and advance registration contact: Project Manager Ln. Peter A Fernandes. Dalima Fast Food Corner, Below Miranda Hospital, Margao - Goa. Ph.: 720770 and Dr. Peter Fernandes, Camp Medical Officer, Res: H. No. 120, Behind Bank of India, Sanvordem. Ph: 651820.

in India (Ed.) S.K.Sarin, A.K.Singhal, CBS Publishers and distributors, 1996, p.9.

2. *Public Health and Preventive Medicine*, Maxcy-Rosenau-Last, 13th edition, 1992, p. 134.

3. Phadke A and Kale A: Some critical issues in the epidemiology of HBV in India (under publication)

4. B.N.Tandon. *Dimensions and issues of HBV control in India*, in Sarin-Singhal (Ed.) op.cit, p.1.

5.Kant Lalit, Hall Andrew. Epidemiology of childhood Hepatitis-B in India: vaccination related issues. *Indian Journal of Paediatrics* 1995, 62: 0635.

6. Harrisons *Principles of Medicine*. 1998 p. 1689

7. Phadke Anant, Fernandes Audrey, Sharda L., Mane Pratibha and Jesani Amar: *A study of supply and use of pharmaceuticals in Satara District*. Foundation for Research in Community Health, 1995, Page 11.

8. Economic Intelligence Service, CMIE, Public Finance, May 1998, p. 8.

Additional reading:

1. Textbook of Preventive and Social Medicine, K.Park, 15th edition 1997.

2. Alward WLM, Mcmohan B.J., Hall D.B. et.al.: The long-term serological course of asymptomatic Hepatitis B Virus carriers and the development of primary hepatacellular carcinoma. *Journal of Infectious Diseases*. 1985:15:605, table 1.

3. Gupta I., Sehgal R. et al.: Vertical transmission of Hepatitis B in North India. *Journal of Hygiene, Epidemiology, Microbiology and Immunology*, 36, 1992, No.3, P.265, table 1.

4. Elavia A.J. and Bankar D.D. :Prevalence of Hepatitis B surface antigen and its subtypes in high risk group subjects and voluntary blood donors in Bombay. *Indian Journal of Medical Research* 1991 September [A]93 280-285.

5. Agarwal R., Naik S.R.: Cost efficacy evaluation of inclusion of Hepatitis-B vaccine in expanded programme of immunization, in Sarin S.K., Singhal A.K.op.cit, P.206 to 216.

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

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 study protocol submitted for independent ethical review?

An independent ethical review was conducted by a committee conversant with local cultural norms and chaired by a retired judge of the Madras High Court. The committee included experts in leprosy, internal medicine and clinical pharmacology, an advocate and a representative of the community. The committee's report was sent to a national advisory committee consisting of epidemiologists, leprosy experts and policy makers. The ethical committee was involved in collecting feedback from volunteers post-vaccination and by periodic review and field visits. It continues to be involved in monitoring the trial.

MD Gupte, *Director, National Institute of Epidemiology (ICMR), P.O. Box 2577, Mayor V R R Road, Chetpet, Chennai, 600 031.*
DK Sampath, *member, Ethical Committee, NIE, Visiting Professor, National Law School of India University, Bangalore.*

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.

Does 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