The study was conducted in 5-11 year-old rural children in five districts in [earstwhile] Andhra Pradesh. HBV-vaccinated (born in 2003/2004, given 3 doses) and unvaccinated (born in 2001/2002) children were compared for HBV serology parameters. Anti-HBs was found in 53% of vaccinated and 18% of unvaccinated children – suggesting vaccine-induced immunity prevalence in only 35% of children. Part of the problem is waning immunity; the youngest (5-year-olds) had the highest anti-HBs prevalence, but even that was only 64%. These are not satisfactory results since HBV vaccine is highly immunogenic if scheduled properly. The relatively low immune response is corroborated by closely similar frequency of Anti-HBc (marker of HBV infection): 1.79% in unvaccinated and 1.05% in the vaccinated. The frequency of chronic infection (carrier state with HBsAg) was also equal (0.17% in unvaccinated and 0.15% in vaccinated).

HBV immunization ought to induce more than 95% seroconversion and significantly lower breakthrough infection frequency than in the unimmunized, and zero incidence of chronic infection. The results reported here call for immediate further investigations – on a much larger scale – to examine the influence of vaccination schedule in inducing optimum protection. If need be, we should design a more efficient schedule – in terms of the number of doses or the interval between the second and third dose. Getting less than optimum benefit for the investment is unfair to the people.

UIP is in urgent need of re-engineering, with in-built capacity to fulfil management principles : to measure and document optimum outcomes – immunological and epidemiological – commensurate with the massive investment.

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Utility of Hepatitis B Vaccination in India

Pediatrician's Perspective

RAJEEV KUMAR AND JACOB PULIYEL
Department of Pediatrics, St Stephens Hospital, Delhi, India.
puliyel@gmail.com

Global health interventions are being scrutinized more closely than previously. According to an article published recently, the Center for Global Development in Washington is looking for evidence in real-life field conditions to ascertain whether large-scale health interventions have actually led to lower numbers of cases or deaths, and whether these improvements are sufficient to justify the costs [1]. This issue of *Indian Pediatrics* includes a paper on limited evaluation of the effect of inclusion of hepatitis B (HB) vaccine in childhood immunization program in India [2]. The authors carried out a serological survey of children aged 5 to 11 years in rural Andhra Pradesh; 2674 of those surveyed had received HB immunization and 2350 had not received such immunization. Babies who get infected with the

hepatitis B virus (HBV) either develop antibodies to HBV [Anti-hepatititis B antibody to core antigen (AntiHBc) and Anti-hepatititis B antibody to surface antigen (AntiHBs)] and clear the organism from their system or else they become chronic carriers of hepatitis B antigen (HBsAg). Vaccination is meant to reduce the numbers who become chronic carriers. Three salient points emerge from their study:

1. Authors found that vaccination did not reduce hepatitis B carrier rate, which is the primary aim of the immunization program. The hepatitis B surface antigen positivity, which is an indicator of chronic HBV infection, was 0.15% among the vaccinated compared to 0.17% in those not vaccinated (*P*=0.855).

2. AntiHBc was present in 1.79% of the unvaccinated but also in 1.05% of the vaccinated. The absolute risk reduction (ARR) was 0.74%; 135 babies need to be vaccinated to prevent 1 child from getting infected with hepatitis B using this criterion. The authors note that this is a statistically significant reduction (Risk ratio 0.59, 95%CI 0.36-0.94). However, the clinical significance and utility of decreasing asymptomatic infection from 1.79% to 1.05% is questionable.

3. Vaccine-induced seroprotection (AntiHBs) is another useful surrogate of vaccine efficacy [3]. At 6 years of age, protective levels of anti-HBs antibody (10 mlU/mL) were present only in about 59% of those immunized. By 11 years, only 13% had protective levels. This is in stark contrast to reports from other countries where 95% of those vaccinated have protective levels and it drops to 92% at 40 years [4]. As also mentioned in this paper, few other studies have reported protective levels of 90% to 76% on follow up, 5 to 10 years later. The low antibody response in the present study correlates with low ARR against hepatitis described above.

REASONS FOR LOW VACCINE EFFICACY

The authors point out that the low antiHBc positivity rate among the unvaccinated indicates HBV transmission was low in the area, and it may be the reason they failed to find a reduction in hepatitis B carrier rate among the vaccinated. One-third of unvaccinated had developed antiHBsAg by 6 years of age which suggests that transmission of HB virus was not low in the area. It is comparable to world literature, that without vaccination, a third of the population get infected and the vast majority clear the infection [5]. The findings of the present study support the contention that Hepatitis B is widespread but it is a benign disease in India, possibly because of characteristics of the circulating virus strain and the genetic makeup of the population [6].

Viewing the same data of 33% antiHBs positivity among the unvaccinated, the authors speculate that these rural people may be getting Hepatitis B immunization surreptitiously, without entering it in their records. This seems a bit far-fetched and it seems more plausible that asymptomatic infection among the unvaccinated resulted in antiHBs positivity.

OTHER ISSUES

Two other factors must also be mentioned here when considering impact of Hepatitis B immunization in real-life conditions in the field:

a) The vaccine administered to babies in this study was a stand-alone Hepatitis B vaccine. It is known that this vaccine provokes a better antibody response than the combination Pentavalent vaccine, that is being administered currently. The efficacy with Pentavalent vaccine is likely to be even less than that reported in this paper [7].

b) The other factor that will impact outcomes in the field is the uptake of immunization. According to information obtained under the Right to Information Act, states with good surveillance systems like Goa and Kerala are reporting one death as adverse events following immunization (AEFI) per 4000 to 12000 babies immunized with the hepatitis B containing Pentavalent vaccine [8,9]. The District Level Household Survey in Tamil Nadu in 2012-13 has noted a decline in immunization coverage across districts which were considered to be well-performing in 2007-08 [10]. The number of fully immunized children has fallen in Tamil Nadu by as much as 25%. Adverse impact of the polio eradication campaign and social resistance in some states such as Tamil Nadu and Kerala due to reports of AEFI deaths following Pentavalent vaccine are being considered as possible explanations for this phenomenon [11]. Low uptake of vaccine will further erode the benefits.

If the findings of this study are replicated in other areas, it should prompt a re-evaluation of the need for this vaccine in the immunization program of the country.

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Time to Target Rubella Elimination

SAKSHI SACHDEVA AND PIYUSH GUPTA
From the Department of Pediatrics, University College of Medical Sciences, Delhi, India.
prof.piyush.gupta@gmail.com

Rubella, a viral infection caused by a RNA virus of family Togaviridae is a transient self-limiting exanthematous febrile illness of childhood and adolescence. Transplacental infection of fetus during the first trimester of pregnancy results in a constellation of congenital anomalies called as Congenital Rubella Syndrome (CRS). The affected fetus may be born with mental, visual, auditory, and systemic handicap with resultant lifelong morbidity and loss of function [1]. Though the exact burden of CRS in India is not known, it is one of the most important causes of preventable blindness and deafness in the country [2]. CRS is entirely preventable by ensuring vaccination of pre-pubertal girls with rubella containing vaccine (RCV). Unfortunately, till date India did not have a national policy on rubella vaccination, and rubella virus continued to circulate unabated in the country.

In this issue of *Indian Pediatrics*, Madhanraj, *et al.* [3] report an outbreak of rubella in the Union Territory of Chandigarh. This study is important in face of a virtually non-existent surveillance system for rubella in the country. According to WHO, till 2012 Africa and South East Asian Regions had yet to establish rubella control, prevention or elimination goals [4]. India has a significant pool of susceptible adolescents, pregnant and non-pregnant females [2,5-7]; this single outbreak portrays just the tip of the iceberg as majority of cases go unreported owing to absence of a surveillance system. Another reported outbreak is from Himachal Pradesh in 2006-07, in which 11-20 yr age group had the highest attack rate [8]. Outbreak of rubella is defined as two or more confirmed cases which are temporally related (with onset of rash in cases occurring between 12 and 46 hours after exposure), and epidemiologically or virologically linked or both [9]. A total of 3219 laboratory confirmed and epidemiologically-linked rubella cases were reported from the countries of SEA Region in 2013. There were a total of 189 outbreaks of exanthematous illness and a total of 2717 laboratory and epidemiology linked confirmed cases of rubella were reported from these outbreaks [10].