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AUTHORS' REPLY

The Advisory committee for vaccines and immunization practices (ACVIP) recommendations of 2018-19 are a mix of best practices for individual children, and for community use, based on published studies, World Health Organization (WHO) recommendations, and National immunization program.

Author cites the Centre for Disease Control (CDC), USA recommendation that the fourth dose of Hepatitis B vaccine should not be administered before 24 weeks whereas WHO recommends birth dose (using monovalent vaccine) to all infants followed by 2 or 3 additional doses (monovalent or combined vaccines) to complete the primary series with minimum 4 weeks' interval between doses [1]. CDC recommends primary vaccination at 2,4,6 months whereas WHO recommends primary vaccination at 6,10,14 weeks and the ACVIP recommends the latter. Indian studies using different schedules as 0,6,14 weeks and 0,1,2 months [2] and 6,10,14 weeks [3,4] have also reported adequate immunogenicity. All the 3-dose hepatitis schedules protect from the disease for as long as 15-20 years. Even if protective antibody titers decline with time, long-term protection relies on immunological memory that allows a protective anamnestic response after exposure to Hepatitis-B virus.

The effectiveness of licensed acellular pertussis (aP) and whole cell pertussis (wP) vaccines in preventing disease is similar in the first year of life [5], and hence the committee accorded near equal status to both types of the vaccines [6]. Clinical phase III studies in India demonstrated that the aP containing vaccines elicit a robust immune response in Indian children following a primary immunization schedule at 6, 10 and 14 weeks of age [7,8].

In view of limited manufacturing capacity for IPV, WHO has supported fractional IPV (fIPV) use and hence government has adopted the same. ACVIP recommends administration of full dose of IPV at 6,10,14 weeks as preferred option, and when this is not feasible the fIPV at 6 and 14 weeks along with bOPV at 6,10,14 weeks.

Reasons for introduction of influenza vaccine have been clearly detailed in the ACVIP recommendations [9].

As Measles-Rubella (MR) vaccine has been introduced in the national immunization schedule and in MR campaign, the same was mentioned. ACVIP supports the national MR campaign. We have not changed the earlier recommendations at all on Measles Mumps Rubella (MMR) vaccine.

Regarding TCV, the committee has brought down the age for the vaccination based on adequate immunogenicity data from earlier studies. The recommendation from 6 months onwards is to suit the convenience and avoid overcrowding of vaccinations around 9 months. The need for second dose of TCV has not been convincingly established though most studies indicate that a single dose might provide adequate antibody titres for up to 5 years. Until hard data is generated or available, we have endorsed the WHO recommendation of a single dose as of now. Antibody titres have been reported to be sufficient for 30 months after one dose and enough data is not there as of now to justify a booster at 2 years. It should be noted that no international scientific body has endorsed booster doses.

Infants in developing countries are at risk of developing rotavirus gastroenteritis at an earlier age than those in developed countries. Hence, it is ideal if immunization schedule is completed early. A recent meta-analysis [10] showed that 6,10 weeks' schedule for rotavirus 1 (RV1) is immunologically inferior to 10,14 weeks' schedule. However, the authors mentioned that the correlates of protection of anti-rotavirus IgA levels are not known and "the association between vaccine schedule and immunogenicity does not provide evidence of a difference in disease protection" [9]. The upper age limit of 12 months follows the same in National immunization schedule which recommends beginning of RV immunization up to 1 year of age. This age limit is for catch-up immunization.

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Capillary β-hydroxybutyrate in Diabetic Ketoacidosis

Kurup, *et al*. [1] recently published their study assessing the validity of capillary β-hydroxybutyrate (BOHB) for diagnosis and monitoring of ketonemia in pediatric diabetic ketoacidosis (DKA). However, I would like authors to clarify certain issues, which may help readers better interpret the study.

Lesser cost and availability of real-time results (avoiding treatment delays while awaiting laboratory results) are the potential advantages associated with the use of capillary BOHB in clinical practice. While the authors have reported cost-effectiveness of capillary measurement, it would be worthwhile mentioning the mean time taken for availability of serum BOHB result once the sample had been sent to the laboratory. This is important because the monitoring for BOHB was repeated initially at every two hours in the study, and a lag period close to or more than this time interval would probably indicate the futility of serum BOHB measurement.

It has also been reported in the study that the bias increased at values above 5 mmol/L, and results of capillary BOHB above this threshold should be interpretated with caution. Could the authors comment on total number of observations (>5 mmol/l) for which the bias was estimated?

Finally, in the discussion, authors propose that capillary BOHB may obviate the need for blood gas analysis in pediatric DKA. However, one should be cognizant of the fact that blood BOHB serves as a surrogate for high anion gap metabolic acidosis, and not normal anion gap acidosis. Hyperchloremic metabolic acidosis (HCMA) may develop during treatment of DKA due to urinary loss of bicarbonate precursors as ketones and administration of excessive chloride in form of intravenous fluids [2]. Such patients may fail to show recovery of serum pH and bicarbonate despite resolution of ketoacidosis. In a retrospective analysis of 59 pediatric DKA admissions, Mrozik, *et al.* [3] reported that the difference in time period between recovery of bicarbonate and closure of anion gap was >6 hours in one-fourth of cases. Clearly, BOHB measurement may help to reduce the frequency of blood gas analysis, but it would be largely ineffective in detecting HCMA, a potential cause of persistent metabolic acidosis in patients with DKA.

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