Indian Academy of Pediatrics (IAP) Advisory Committee on Vaccines and Immunization Practices (ACVIP) Recommended Immunization Schedule (2018-19) and Update on Immunization for Children Aged 0 Through 18 Years

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Justification: There is a need to revise/review recommendations regarding existing vaccines in view of current developments in vaccinology. **Process:** Advisory Committee on Vaccines and Immunization Practices (ACVIP) of Indian Academy of Pediatrics (IAP) reviewed the new evidence, had two meetings, and representatives of few vaccine manufacturers also presented their data. The recommendations were finalized unanimously. **Objectives**: To revise and review the IAP recommendations for 2018-19 and issue recommendations on existing and certain new vaccines. **Recommendations**. The major changes in the IAP 2018-19 Immunization Timetable include administration of hepatitis B vaccine within 24 hours of age, acceptance of four doses of hepatitis B vaccine if a combination pentavalent or hexavalent vaccine is used, administration of DTwP or DTaP in the primary series, and complete replacement of oral polio vaccine (OPV) by injectable polio vaccine (IPV) as early as possible. In case IPV is not available or feasible, the child should be offered three doses of bivalent OPV. In such cases, the child should be advised to receive two fractional doses of IPV at a Government facility at 6 and 14 weeks or at least one dose of intramuscular IPV, either standalone or as a combination, at 14 weeks. The first dose of monovalent Rotavirus vaccine (RV1) can be administered at 6 weeks and the second at 10 weeks of age in a two-dose schedule. Any of the available rotavirus vaccine may be administered. Inactivated influenza vaccine (either trivalent or quadrivalent) is recommended annually to all children between 6 months to 5 years of age. Measles-containing vaccine (MMR/MR) should be administered after 9 months of age. Additional dose of MR vaccine may be administered during MR campaign for children 9 months to 15 years, irrespective of previous vaccination status. Single dose of Typhoid conjugate vaccine (TCV) is recommended from the age of 6 months and beyond, and can be administered with MMR vaccine if administered at 9 months. Four-dose schedule of anti-rabies vaccine for Post Exposure Prophylaxis as recommended by World Health Organization in 2018, is endorsed, and monoclonal rabies antibody can be administered as an alternative to Rabies immunoglobulin for post-exposure prophylaxis.

Keywords: *Guidelines, Immunity, Infections, Prevention, Vaccination.*

The Indian Academy of Pediatrics (IAP) Advisory Committee on Vaccines and Immunization Practices (ACVIP) has recently reviewed and updated the recommended immunization schedule for children aged 0 through 18 years based on recent evidence for the vaccines licensed in India. The process of preparing the new recommendations consisted of review of data and literature, consultative meetings twice (4th and 5th August 2018 at Mangalore, and 22nd and 23rd September 2018 at Chennai), taking the opinion of various National Experts and arriving at a consensus and drafting the recommendations while taking into consideration the existing National immunization schedule and policies of the government. All decisions were taken unanimously and voting was not required for any issue. The recommendations in brief along with supporting evidence from relevant literature are presented in this article. The detailed information will be presented later in IAP Guidebook on Immunization. While using these guidelines, pediatricians are free to use their discretion in a particular situation within the suggested framework.

The current IAP ACVIP recommendations for the 2018-19 IAP Immunization Timetable are presented in ***Table* I** and ***Fig.* 1**, and this also include some alterations from the earlier recommended schedule [1].

HEPATITIS B VACCINE

The burden of chronic hepatitis B virus infection is substantial as the coverage of the birth-dose (estimated as 39% globally) is still low. World Health Organization (WHO) Position paper 2017 states that hepatitis B vaccine (HBV) should be administered as a birth dose, preferably within 24 hours (timely birth dose) [2]. This dose may only be delayed if the mother is known to be hepatitis-B surface antigen (HBsAg) negative at the time of delivery. When the

TABLE I KEY UPDATES AND MAJOR CHANGES IN RECOMMENDATIONS FOR IAP IMMUNIZATION TIMETABLE, 2018-2019

Hepatitis B vaccine

- One dose of hepatitis B vaccine within 24 hours of birth.
- In case of use of a combination vaccines a total of four doses of hepatitis B vaccine are justified.

DTwP, DTaP and combination vaccines

- DTwP or DTaP can be offered in primary series.

Polio vaccines

- Ideally IPV should replace OPV as early as possible.
- Three doses of intramuscular IPV in primary series is the best option.
- Two doses of intramuscular IPV instead of three for primary series if started at 8 weeks, with an interval of 8 weeks between two doses is an alternative.
- In case IPV is not available or feasible, the child should be offered three doses of bOPV. In such cases, the child should be referred for two fractional doses of IPV at a Government facility at 6 and 14 weeks or at least one dose of intramuscular IPV, either standalone or as a combination vaccine, at 14 weeks of age.

Rotavirus vaccine

- In case of Rotavirus vaccine, RV1 can be used in 6, 10 weeks schedule.

Influenza vaccine

- Inactivated influenza vaccine (either trivalent or quadrivalent) is recommended routinely to all children below 5 years of age starting from 6 months of age annually (2-4 weeks before influenza season).

Measles-containing vaccines

- Measles-containing vaccine (MMR/MR) should be administered after 9 months of age.
- MR vaccine as part of the national campaign is to be administered irrespective of previous vaccination.

Typhoid vaccines

- Single dose of any of Typhoid conjugate vaccine (TCV 25 mg) is recommended from 6 months onwards and can be administered with MMR also.
- Booster dose of Typhoid conjugate vaccine not recommended in subsequent years.

Rabies vaccines

- ACVIP IAP endorses administration of a 4-dose schedule of Rabies vaccine recommended by WHO 2018 for Post-exposure prophylaxis.
- ACVIP also endorses administration of Rabies monoclonal antibody as an alternative to Rabies immunoglobulin for category-III bites.

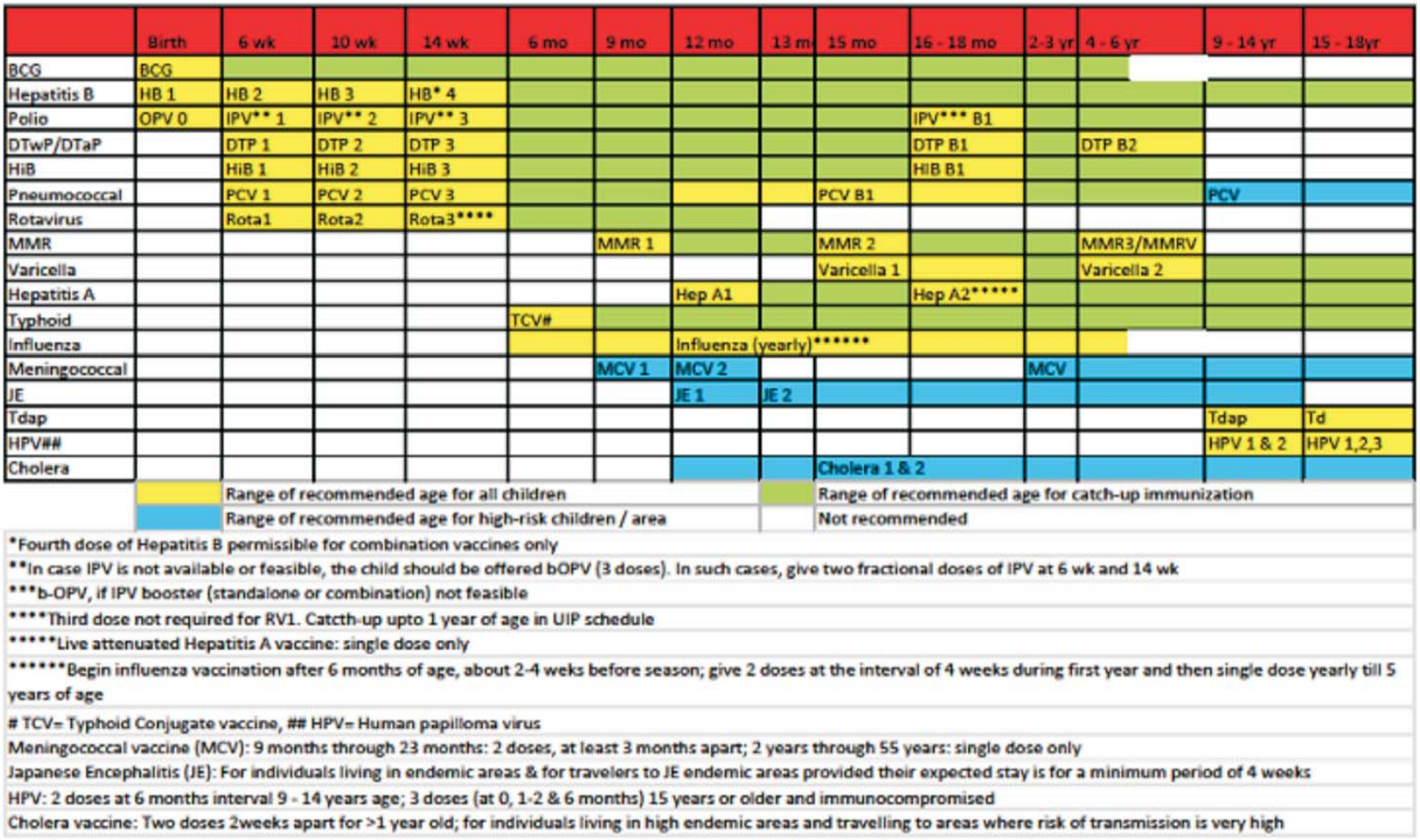
ACVIP: Advisory Committee on Vaccines and Immunization Practices; IAP: Indian Academy of Pediatrics; IPV: Injectable polio vaccine; OPV: Oral polio vaccine; bOPV: bivalent oral polio vaccine; MR: Measles-Rubella vaccine; MMR: Measles-Mumps-Rubella vaccine.

HBsAg report of the mother is not known or reported incorrectly, or in case of infants born to HBsAg positive mothers, this dose becomes a very important safety net [3].

Four doses of hepatitis B vaccine may be administered for programmatic reasons (*e.g.*, 3 doses of hepatitis B-containing combination vaccine or monovalent HBV after a single monovalent dose at birth [2].

DIPTHERIA, TETANUS AND PERTUSSIS VACCINES (DTwP AND DTaP)

Long-term efficacy over 10 years has been observed to be superior with whole cell pertussis vaccine (wP) [4]. Recent outbreaks of pertussis in various developed countries have sparked a debate on the effectiveness of acellular pertussis (aP) vaccines. However, none of these countries are planning to revert back to whole-cell pertussis vaccines as that can result in an increase in the prevalence of the disease due to poor acceptance of a vaccine that is much more reactogenic [5]. Though the reasons for this resurgence are complex and vary from place to place, the lesser duration of protection and decreased impact on transmission of the disease by acellular pertussis vaccines appears to be crucial [6]. Waning of immunity has been reported with whole cell and acellular vaccines over a period of time. Current evidence suggests that the efficacy of both aP and wP vaccines in preventing pertussis in the first year is equivalent. After the first year, the immunity wanes more rapidly with the aP vaccines and the impact on transmission by aP vaccines is also inferior to wP vaccines [7-9]. WHO clearly mentions that countries currently using the wP vaccine in their national programs should continue



	Birth	6 wk	10 wk	14 wk	6 mo	9 mo	12 mo	13 m	15 mo	16 - 18 mo	2-3 yr	4 - 6 yr	9 - 14 yr	15 - 18yr
BCG	BCG													
Hepatitis B	HB 1	HB 2	HB 3	HB* 4										
Polio	OPV 0	IPV** 1	IPV** 2	IPV** 3						IPV*** B1				
DTwP/DTaP		DTP 1	DTP 2	DTP 3						DTP B1		DTP B2		
HiB		HiB 1	HiB 2	HiB 3						HIB B1				
Pneumococcal		PCV 1	PCV 2	PCV 3					PCV B1				PCV	
Rotavirus		Rota1	Rota2	Rota3****										
MMR						MMR 1			MMR 2			MMR3/MMRV		
Varicella									Varicella 1			Varicella 2		
Hepatitis A							Hep A1			Hep A2*****				
Typhoid					TCV#									
Influenza							Influenza (yearly)******							
Meningococcal						MCV 1	MCV 2				MCV			
JE							JE 1	JE 2						
Tdap													Tdap	Td
HPV##													HPV 1 & 2	HPV 1,2,3
Cholera									Cholera 1 & 2					

Range of recommended age for all children

Range of recommended age for high-risk children / area

Range of recommended age for catch-up immunization

Not recommended

*Fourth dose of Hepatitis B permissible for combination vaccines only

**In case IPV is not available or feasible, the child should be offered bOPV (3 doses). In such cases, give two fractional doses of IPV at 6 wk and 14 wk

***b-OPV, if IPV booster (standalone or combination) not feasible

****Third dose not required for RV1. Catcth-up upto 1 year of age in UIP schedule

*****Live attenuated Hepatitis A vaccine: single dose only

******Begin influenza vaccination after 6 months of age, about 2-4 weks before season; give 2 doses at the interval of 4 weeks during first year and then single dose yearly till 5 years of age

TCV= Typhoid Conjugate vaccine, ## HPV= Human papilloma virus

Meningococcal vaccine (MCV): 9 months through 23 months: 2 doses, at least 3 months apart; 2 years through 55 years: single dose only

Japanese Encephalitis (JE): For individuals living in endemic areas & for travelers to JE endemic areas provided their expected stay is for a minimum period of 4 weeks

HPV: 2 doses at 6 months interval 9 - 14 years age; 3 doses (at 0, 1-2 & 6 months) 15 years or older and immunocompromised

Cholera vaccine: Two doses 2weeks apart for >1 year old; for individuals living in high endemic areas and travelling to areas where risk of transmission is very high

FIG. 1 *IAP-ACVIP Recommended immunization schedule for children aged 0-18 years (2018-19).*

the same for the primary series [10,11], while those using the aP vaccine should continue the same and consider additional boosters and strategies like immunization of mothers in case of pertussis resurgence [10]. The duration of protection for both the aP and wP vaccines after the three primary doses and a booster dose at least after a year varies from 6-12 years [11]. A German study reported acellular pertussis vaccine being quite efficacious (88.7%) (95% CI, 76.6% to 94.6%) [12].

Number of Components

In a couple of systematic reviews, it was concluded that multi-component acellular pertussis vaccines are more efficacious than the single- or two-component vaccines [13,14]. However, effectiveness studies of long-term usage of two-component acellular pertussis vaccines in Sweden [15] and Japan [16], and the mono-component vaccine in Denmark showed high effectiveness in prevention of pertussis. Thus the higher efficacy for the multi-component vaccine as demonstrated in the trials should be cautiously interpreted, and at present the evidence is insufficient to conclude categorically that the effectiveness of the aP vaccines is related to the number of components alone [10].

IAP ACVIP Recommendation on Pertussis-containing Vaccines

The primary series should be completed with three doses of either wP or aP vaccines, irrespective of the number of components. wP vaccine is definitely superior to aP vaccine in terms of immunogenicity and duration of protection but more reactogenic. In view of parental anxiety and concerns for its reactogenicity, aP vaccine can also be administered even in the primary series. The primary aim is to increase the vaccination coverage with either of the vaccines.

POLIO VACCINES

The elimination of circulating wild poliovirus from our country and the decline worldwide in the number of cases is the proof of efficacy of Oral polio vaccine (OPV). At the beginning of 2013, 126 countries using OPV exclusively, decided to introduce Injectable polio vaccine (IPV), at least one dose, in their National Immunization Schedule. This was part of WHO's Endgame Plan to withdraw type-2 polio virus and prepare for 'the switch' from trivalent OPV (tOPV) to bivalent OPV (bOPV) in April 2016 [17,18]. However, IPV introduction in these countries has increased the global IPV demand, to over 200 million in 2016 from 80 million in 2013 [17,18]. The attempt to meet the global requirements for IPV by rapidly increasing the IPV production has led to multiple challenges, resulting in a shortage worldwide. Intradermal IPV administration with fractional doses of IPV (fIPV) (0.1 mL or one-fifth of a full dose) offers potential cost reduction and allows immunization of a larger number of persons with a given vaccine supply [19]. Two fractional doses administered *via* the intradermal (ID) route offer higher immunogenicity compared to one full intramuscular (IM) dose of IPV [20-23]. As a result, a two-dose fIPV schedule has been strongly recommended to countries that are endemic and the those with high risk of importation of wild polio virus [24].

Private medical practitioners have irregular and inadequate access to standalone IPV, and are thus compelled to administer combination vaccines, and thus are not able to follow the Indian government schedule, which consists of fIPV and standalone IPV. It is not feasible for pediatricians in private settings to refer all children to government facilities for the same. In addition, the recent controversy of the contamination of OPV with type-2 Poliovirus has resulted in the awareness of vaccine-derived paralytic poliomyelitis (VDPP) amongst public. In this background, there is a need to recommend a regimen containing IPV as combination vaccine in the private settings.

IAP ACVIP Recommendations

- Birth dose of OPV is a must.
- Extra doses of OPV on all Supplementary immunization activities should continue.
- No child should leave the health facility without polio immunization (IPV or OPV), if indicated by the schedule.
- bOPV should be continued in place of IPV, only if IPV is not feasible, with a minimum of 3 doses at 6,10,14 weeks of age.
- Minimum age of administration of IPV is 6 weeks with the best option being 3 doses of IM IPV in 6-10-14 weeks schedule. This can be as a combination vaccine, in view of non-availability of standalone IM IPV.
- Two doses of IM IPV, instead of 3 doses can be administered provided the primary series is started at 8 weeks with the minimum interval between them being 8 weeks.
- In case IPV is not available or feasible, the child should be offered 3 doses of bOPV in a 6-10-14 weeks schedule. In such cases, the child should be advised to receive two fractional doses of IPV at a Government facility at 6 and 14 weeks of age or at least one dose of IM IPV either standalone or as a part of combination vaccine at 14 weeks.

ROTAVIRUS VACCINES

A review of studies from 38 populations found that all

rotavirus gastroenteritis events (RVGE) occurred in 1%, 3%, 6%, 8%, 10%, 22% and 32% children by age 6, 9, 13, 15, 17, 26 and 32 weeks, respectively. Mortality was mostly related to RVGE events occurring before 32 weeks of age [25]. The highest risk of mortality was noted in the children having earliest exposure to rotavirus, living in poor rural households, and having lowest level of vaccine coverage [26]. It is ideal if immunization schedule is completed early in developing countries where natural infection might occur early [27].

Infants in developing countries may be at risk of developing RVGE at an earlier age than those in developed countries. They also tend to have a higher risk of mortality coupled with the risk of lower vaccine coverage. No observational study has compared different ages at first dose. A schedule of two doses at 10 and 14 weeks may result in incomplete course of vaccination, especially in developing countries because of restriction of upper age limit for rotavirus vaccine administration. Such children would remain immunologically susceptible to get rotavirus infection. Early administration of the first dose of rotavirus vaccine as soon as possible after 6 weeks of age has been recommended by WHO recently [27]. Administration of RV1 or RV5 vaccine at 6 weeks has also been recommended and approved even in developed countries [28].

Two randomized controlled trials reported data on severe rotavirus gastroenteritis with up to one year follow-up, and directly compared children who received the first dose of RV1 at age 6 weeks *vs* 10 to 11 weeks. No statistically significant difference in efficacy was found between these two schedules [29]. The South Africa and Malawi RV1 trial [30] reported similar efficacy of vaccination schedules beginning at 6 weeks or 10 to 11 weeks against severe RVGE during the second year follow-up using only the Malawi cohort. Indirect comparisons based on stratification of RV1 and RV5 trials using different schedules showed no impact on mortality for different ages at first dose.

Considering these factors, ACVIP recommends RV1 in a schedule of 6 and 10 weeks. The recommendations for the schedule of other vaccines remain the same.

Currently the following live oral rotavirus vaccines are available in India: (*i*) Human monovalent live vaccine (RV1); (*ii*) Human bovine pentavalent live vaccine (RV5); (*iii*) Indian neonatal rotavirus live vaccine, 116 E; (*iv*) Bovine Rotavirus Vaccine – Pentavalent (BRV-PV). BRV-PV is a recently introduced pentavalent rotavirus vaccine that contains serotypes G1, G2, G3, G4, and G9 obtained from Bovine (UK) X Human Rotavirus Reassortant strains. It is a thermostable vaccine and can be stored below 24 ^{0}C till the duration of the shelf life of 30 months. This vaccine remains stable for 36 months at temperature below 25 ^{0}C, for 18 months between 37 ^{0}C and 40 ^{0}C, and a short-term exposure at 55 ^{0}C [31].

IAP ACVIP Recommendation on Rotavirus Vaccines

Any of the available rotavirus vaccines may be routinely administered as per the manufacturer's recommendations. All the available vaccines have been demonstrated to be safe and immunogenic.

- Minimum age: 6 weeks for all available brands
- Only two doses of RV-1 are recommended at 6 and 10 weeks
- If any dose in series was RV-5 or RV-116E or vaccine product is unknown for any dose in the series, a total of three doses of RV vaccine should be administered.

Recommendations on the age limit for the first dose and the last dose (16 and 32 weeks) should continue in spite of recommendation for increase in the age limit as per recent NIP guidelines.

TYPHOID VACCINE

Considering the continuation of significant burden of typhoid fever, widespread prevalence of antibiotic-resistant strains of *S. typhi* and availability of favorable evidence on the efficacy, effectiveness, immunogenicity, safety, and cost-effectiveness of typhoid vaccines, WHO recommends use of typhoid vaccines in national programs for the control of typhoid fever [32,33]. Typhoid conjugate vaccine (TCV) is preferred at all ages as it has improved immunological properties, can be used in younger children, and is expected to provide longer duration of protection. A meta-analysis summarized that typhoid cases across the age groups; 14% to 29% in <5 years, 30% to 44% in 5-9 years and 28% to 52% in 10-14 years [34]. It has been observed that more than one-fourth of all cases occur in children aged below 4 years, with approximately 30% of cases in children aged below 2 years, and 10% in children aged below 1 year [35]. Based on this, WHO has recommended TCV for infants and children from 6 months of age as a 0.5 mL single dose [36], and the same is endorsed by ACVIP.

Booster Doses/Revaccination

The need for revaccination with TCV is currently unclear [36]. The protection with TCV may last for up to 5 years after the administration of one dose, and natural boosting may occur in endemic areas [37]. The evidence concerning the need for booster vaccination is lacking currently. Until more data is generated or available, the ACVIP recommends only a single dose of TCV from 6 months onwards. If a child has received Typhoid polysachharide vaccine, it is

recommended to offer one dose of TCV at least 4 weeks following the receipt of polysaccharide vaccine.

Currently, three products of TCV are licensed in India. Two of them contain 25 µg of purified Vi PS of *S. typhi*, and one of them containing 5 µg purified Vi PS of *S. typhi*. The WHO position paper in 2018 has remarked that the body of evidence for the 5 µg vaccine is very limited.

IAP ACVIP Recommendation on Typhoid Vaccines

Primary schedule

- A single dose of TCV 25 µg is recommended from the age of 6 months onwards routinely.
- An interval of at least 4 weeks is not mandatory between TCV and measles-containing vaccine when it is offered at age of 9 months or beyond.
- For a child who has received only Typhoid polysaccharide vaccine, a single dose of TCV is recommended at least 4 weeks following the receipt of polysaccharide vaccine. Routine booster for TCV at 2 years is not recommended as of now.

MEASLES, MUMPS AND RUBELLA (MMR/MR) VACCINES

Standalone measles vaccine is now not available for regular use. Measles-containing vaccine (MMR/MR) should be administered after 9 months of age (270 days). MR (Measles-Rubella) vaccine is currently not available in the private sector. Hence in view of morbidity following mumps infection, it has been recommended that MMR is administered instead of MR at 9 months, 15 months, and 4-6 years [38], or as two doses at 12 to 15 months of age with the second dose between 4 to 6 years of age. [39]. Additional dose of MR vaccine during MR campaign for children 9 months to 15 years, irrespective of previous vaccination status is to be administered, keeping in mind the need to support national programs.

INFLUENZA VACCINE

A meta-analysis and systematic review evaluating studies published between 1995 to 2010 estimated that children under 5 years of age had 90 million (95% CI 49-162 million) new influenza episodes, 20 million (95% CI 13-32 million) cases of acute lower respiratory infections (ALRI) where influenza was associated, and 1 million (95% CI 1-2 million) cases of severe ALRI (associated with influenza). This resulted in 28,000-111,500 deaths attributed to influenza, with 99% of them from developing countries [40]. Another study estimated that globally 160,000-450,000 children below 5 years of age die in hospitals each year due to all-cause ALRI [41].

A systematic literature review described that during the peak rainy season, influenza accounted for 20-42% of monthly acute medical illness hospitalizations in India [42]. This suggests that influenza is a substantial contributor to severe respiratory illness and hospitalization. The findings from the studies also show that influenza circulation and influenza-associated hospitalization are major public health concerns in India. There is poor uptake of the influenza vaccine in India. IAP position paper on influenza in 2013 stated the while it may not be practical to recommend routine influenza vaccination to everyone in India, the vaccination for high-risk groups such as the elderly, children below 5 years, medical practitioners and pregnant women should be seriously considered [43]. Influenza incidence in children below 5 years of age from developing countries is three times higher than those from developed countries, with a 15-fold higher case-fatality [41].

Health utilization surveys conducted in two rural sites (Ballabgarh, Haryana and Vadu, Maharashtra) in 2010-2012 reported adjusted all-age incidence rates of influenza-associated hospitalization as 3.8-5.4 per 10,000 in Ballabgarh and 20.3-51.6 per 10,000 in Vadu [44]. The age-specific influenza-associated hospitalization rates varied from year to year. In 2010, these rates were highest among persons aged <1 year, in 2011 among patients >59 years of age, and in 2012 in children 1-4 years in Ballabhgarh. Whereas in Vadu, in 2010, these rates were highest among persons aged 1-4 years, in 2011 in children <1 year, and in 2012 in children 5-14 years. Influenza viruses were found throughout the year and the peaks coincided with peaks in rain fall at both the sites.

The Influenza Serotype-B is reported almost round the year in India. A multi-site influenza study in India found that 27.8% isolates were Influenza A (H1N1) virus, 29.8% were type A (H3N2), and 42.3% isolates were type B [45]. A global influenza study found that during seasons, out of all influenza B isolates, Victoria and Yamagata lineages predominated or co-circulated (>20% of total detections), and this accounted for 64% and 36% of seasons respectively. The vaccine virus mismatch was found in 25% of the seasons [46].

With the available data, there is enough reason to believe that the magnitude of the problem is much higher in developing countries (including India) *vis-a-vis* developed countries. India lies within the northern hemisphere. Some parts of the country experience a distinct tropical environment because of its location close to the equator. These areas have a southern hemisphere seasonality with almost round-the-year circulation of influenza viruses peaking during monsoon. Northern parts of India experience another peak during winters similar to northern

hemisphere pattern. There is continuous influenza activity across the nation, with seasonal peaks during monsoon and winter, and an ever increasing number of influenza-like illnesses affecting a large number of children who can transmit the disease to their peers and adult counterparts.

In view of influenza activity round the year with seasonal peaks, high morbidity and mortality in high-risk groups, including children below 5 years, paucity of facilities for laboratory diagnosis, high transmission rate, substantial socioeconomic burden, limitations of oseltamivir, availability of moderately efficacious vaccine, it would be justifiable to use Influenza vaccine routinely in the high-risk group of children below age of 5 years.

Vaccine Strains

FDA recommended the following combinations for 2018-19 influenza vaccines.

- Trivalent vaccines-to have (*i*) an A/Michigan/45/2015 (H1N1)pdm09-like virus, (*ii*) an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus; and (*iii*) a B/Colorado/06/2017-like virus (Victoria lineage).
- Quadrivalent vaccines to contain the above three, and a B/Phuket/3073/2013-like virus (Yamagata lineage) [47].

IAP ACVIP Recommendations

ACVIP recommends that quadrivalent/trivalent inactivated influenza vaccine should be routinely offered annually to all children between 6 months to 5 years of age. The latest available influenza vaccine can be administered after 6 months of age, 2-4 weeks prior to the influenza season: two doses at the interval of one month in the first year, and one dose annually before the influenza season up to 5 years of age.

RABIES VACCINE

Recent data indicate that duration and number of doses for post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) regimens can be shortened. ACVIP endorses the new schedule suggested by WHO in 2018 [48].

Pre-exposure prophylaxis (Pre-EP) is recommended in the following two situations.

- Children exposed to pets in home.
- Children identified to have a higher risk of being bitten by dogs.

WHO recommends a "1-site vaccine administration on days 0 and 7 for intramuscular administration" [48].

For post-exposure prophylaxis, recently the WHO [48] has recommended a new 4-dose schedule of either of the following: (*i*) 1-site intramuscular administration of vaccine on days 0, 3, 7 and between day 14-28, or (*ii*) 2-sites intramuscular administration on days 0 and 1-site on days 7, 21 (intramuscular).

Rabies Human Monoclonal Antibody (RHMAB)

Access to Rabies immunoglobulin (RIG) is limited resulting in high rabies mortality. RHMAB is a completely human IgG1 monoclonal antibody that binds to the ectodomain of the G glycoprotein produced by recombinant technology. It has been demonstrated to neutralize 25 different isolates of wild-type or street isolates of rabies virus. A recent study found that it is not inferior to Human rabies immunoglobulin (HRIG) in producing rabies virus neutralizing antibody in 200 subjects with WHO category-III suspected rabies exposures. The study subjects received either RMHAB or HRIG (1:1 ratio) in wounds, and intramuscularly wherever necessary, on day-0. All these patients also received five doses of rabies vaccine intramuscularly on 0, 3, 7, 14 and 28 days [49].

This newly introduced monoclonal antibody has emerged as a safe and potent alternative to rabies immunoglobulin. The WHO position paper on Rabies in 2018 has also suggested encouragement of use of this product, if available, instead of RIG. The comparative advantages include easy availability, standardized production quality, possibly greater effectiveness, no requirement of animals in its production, and less adverse events.

In view of the irregular availability and high cost of Rabies immunoglobin (RIG), ACVIP endorses the use of RHMAB as an alternative to RIG – human or equine – along with rabies vaccines in all category-III bites. RHMAB is licensed in India (as Rabisheild, Serum Institute of India; 40 IU/mL) since 2017. The recommended dose is 3.33 IU/kg body weight, preferably at the time of the first vaccine dose. However, this may also be administered up to the 7th day after the first dose of vaccine is given. If the calculated dose is insufficient (to infiltrate all the wounds), it should be diluted in sterile normal saline to get a volume that is enough to be infiltrated around all the wounds.

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ANNEXURE I IAP ADVISORY COMMITTEE ON VACCINES AND IMMUNIZATION PRACTICES, 2018-19

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