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Vaccine-induced immunity in early life

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Fifty-eight percent of the nearly 8 million deaths in children under the age of 5 years in 2010 were due to infectious diseases [1]. The majority could have been prevented by known, simple, affordable and low cost interventions, including infant immunization [1]. The Expanded Program on Immunization (EPI) and complementing national immunization programs undoubtedly represent major triumphs of preventive medicine and public health [2,3], resulting in a reduction from 12 million deaths in 1990 to 7.6 million in 2010 [1]. However, in 2010, approximately 3 million children under 5 years of age still died of infectious diseases that could have been prevented with currently available vaccines [3]. To avert these deaths, infant immunization needs to become more common and complete. This, in turn, requires vaccines that are more effective in the very young, easy to administer, and acceptable as well as affordable on a population basis [2].

Over the last decade much has been learned about the immune responses to vaccines administered early in life. Key progress in this field is reviewed by leading experts for this Special Edition. For example, Ota and colleagues highlight how the complex interaction of biological, socio-economic and ethical issues can influence immune responses to vaccines administered in the first year of life. In their review of animal models for neonatal diseases in humans, Levast and colleagues outline the many advantages and disadvantages of each. Levy et al. then discuss the role of innate immune ontogeny in modulating responses to adjuvants contained in already licensed as well as new infant vaccines. Schillie and Murphy focus on Hepatitis B, and suggest that high levels of protection can be achieved by vaccinating full-term newborns. Similarly, Mateen and colleagues conclude that a birth dose of the oral (live) polio vaccine is still the most effective approach for most countries in the world, but that inactivated poliovirus vaccine also leads to high seroconversion rates in newborns. Van den Biggelaar and Pomat present evidence that neonatal vaccination with bacterial conjugate vaccines appear safe, without induction of immune tolerance. Lastly,

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Gans reviews efficacy and barriers to more widespread application of live viral vaccines in early life.

In toto, the body of evidence reviewed here strongly supports the notion that early life vaccination in general, and neonatal vaccination in particular, can offer substantial protection from otherwise deadly or crippling infectious pathogens. Newborn vaccination is therefore not only feasible but also desirable. However, the reviews in this Special Edition also highlight significant gaps in our understanding that prevent widespread implementation of neonatal vaccination. For example:

- There is a need for delineation of immune development in early life in regions with high-infectious related morbidity and mortality, to identify the most optimal approach to vaccine mediated protection in these vulnerable populations.
- The long-term protective effect of vaccination at birth, compared with vaccination later in infancy, is not known.
- There is insufficient data to introduce alternate vaccines or alternate schedules for most vaccines; this prevents simplification of vaccine formulations and schedules.
- It remains unclear whether neonatal administration of safe, non-tolerogenic bacterial conjugate vaccines would result in induction of earlier protection.
- A lack of validated biomarkers of vaccine-induced protection, as well as the biological mechanisms through which these immune determinants act.
- Lack of vaccine safety studies for neonatal vaccines.

Because infants represent the major target population for immunization around the world [4], these knowledge gaps contribute to the millions of infectious deaths in children under 5 years of age. As summarized here, closing these gaps represent a scientifically feasible quest. This is not merely of academic interest but has the potential to save the lives of millions of newborns and infants every year. In short, given the moral and ethical imperative, optimizing neonatal vaccination should be on the forefront of the agenda for vaccinologists as well as funding agencies.

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