

## Global Hib vaccination: reasons to cheer and fear



Conjugate *Haemophilus influenzae* type b (Hib) vaccination is one of the major global health achievements of the past three or four decades. *H influenzae* type b is a key cause of disease and death in unvaccinated populations, and that burden falls most severely on young children. Those of us at medical schools in developed countries in the late 1980s learned about *H influenzae* type b disease but rarely saw it in practice, such was the effectiveness of the conjugate vaccine introduced in those settings in the 1990s. At that time the disease's principal impact was to be seen in low-income countries, which would not use the vaccine for years.

More than 90% of countries now routinely provide conjugate Hib vaccine to their children, a proportion that was achieved through an impressive global public health push. However, the world is divided on the dosing schedule used: the vast majority of developed countries give a booster dose at age 12–23 months, whereas most low-income countries do not. WHO policy is a three-dose primary series in infancy with no booster, and vaccine funding for low-income countries follows this recommendation. For health agencies and experts in the field, the question of whether low-income countries should have a booster dose is one that is not going away.

Therefore, the report in *The Lancet Global Health* by Laura Hammitt and colleagues,<sup>1</sup> who have assessed Hib vaccine effectiveness, nasopharyngeal carriage, and population immunity in Kenya, is important. The investigators report that the introduction in 2001 of routine conjugate Hib vaccination with a three-dose primary series without a booster resulted in a major and sustained reduction in invasive Hib disease in the Kilifi district of Kenya over 13 years. This adds to earlier evidence of sustained long-term control of disease with the same schedule in The Gambia, the first country in Africa to introduce the vaccine in 1997.<sup>2</sup>

So why should we worry that the vaccine will stop working, or stop working so well, without a booster? There are both empirical and theoretical reasons to worry. Good long-term control has not occurred in all countries that have started with a three-dose primary series alone. The UK introduced Hib vaccine in 1993 and was one of the few developed countries not to schedule a booster dose from the outset. Control was excellent

initially<sup>3</sup> and *H influenzae* type b carriage in the upper respiratory tract was eliminated,<sup>4</sup> but after several years a resurgence of disease prompted the introduction of a booster dose in 2003, which was associated with a return to good control.<sup>3</sup> This resurgence in disease was concerning, and Ireland seemed to have a similar experience to the UK.<sup>5</sup>

Another, theoretical, reason to worry is that immunity of vaccinated children to *H influenzae* type b infection could wane over the years (by contrast with earlier generations whose immunity was based on exposure to the pathogen itself). In this state of lowered immunity, this vaccinated group might form a new reservoir of Hib carriage and disease (typically mild disease) and expose young children to greater risk of disease, typically severe. This kind of dynamic contributes to resurgences in another disease, pertussis. Clearly, a booster dose might help to avert this. Mexico introduced a booster in 2007 in the face of evidence of waning immunity in children.<sup>6</sup>

The evidence from Kenya for sustained immunity in older children and the absence of a *H influenzae* type b reservoir in that group partly allays concerns about waning immunity with long-term use of Hib vaccine, but not completely. Different contexts have varying factors at play, and the Hib vaccine has not been in use in enough low-income countries for long enough to be sure that no pitfalls await. Indeed, Mackenzie and colleagues<sup>7</sup> reported a resurgence of disease in The Gambia beyond 14 years of vaccine use.

So what can be done? It is tempting to recommend a unified global policy of a booster dose and be done with it. This solution will not suffice though because of constrained budgets, competing priorities, complicated logistics, and, crucially, a lack of evidence for its necessity. But doing nothing is not an option. Countries must first be vigilant with disease surveillance—they will not know if they have a problem unless disease burden is measured, a principle that clearly applies not just to *H influenzae* type b disease. Second, the dynamics of *H influenzae* type b control and resurgence must be better understood in varying contexts to avoid countries being caught unprepared by resurgent disease. The world has enough challenges without letting this disease get a second hold on countries that have already taken actions against it.

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I declare no competing interests.

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