

#### **LETTER**

# Long-term persistence of immunity after hepatitis B vaccination: A fact, not a fancy

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#### **ABSTRACT**

On the basis of an article previously published in the journal regarding immune persistence after hepatitis B vaccination in infancy, I discuss why this persistence is a fact and not a fancy. Immune memory after a primary vaccination series has been widely demonstrated by prompt response to booster doses and the proliferation of T cells secreting IFN $\gamma$ . In a large cohort of medical students, 79% of subjects were positive for anti-HBs antibodies, and only 1.9% of the subjects had serological evidence of past hepatitis B infection. To prevent severe diseases, such as hepatitis B, it is very important that the majority of the population is vaccinated, especially those employed in health care, as vaccination is the most effective weapon to hepatitis B, which is still widespread worldwide.

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The commentary by Lao on immune persistence after hepatitis B vaccination in infancy<sup>1</sup> and, in particular, the conclusions derived regarding vaccine persistence and the loss of anamnestic response are inconsistent with the literature on these issues.<sup>2</sup>

The persistence of immune memory has been well-supported in the literature by both the demonstration that a booster dose is generally sufficient to induce a robust response<sup>3</sup> and the ability of T cells to proliferate and secrete IFNy.4

The introduction of the mandatory vaccination against hepatitis B virus (HBV) at 3 months of age and in adolescence in Italy in 1991 has led to 2 significant results: 1) a dramatic decrease in the incidence of the disease<sup>5</sup> overall and, most importantly, 2) in the most vulnerable age group (15–24 years).

In a large cohort of medical school students,<sup>3</sup> we demonstrated that after an average of 10.8 y since the administration of the primary series (3 doses) during adolescence, 87.6% of the students showed protective antibody levels, and of those who were apparently unprotected, an immunocoverage rate of 94.6% was achieved after a booster dose.

The disappearance of circulating antibodies is a problem that affects the surveillance of vaccination coverage among the subjects exposed to biological risk in hospital settings. A recent study demonstrated that after 18-years follow-up, the waning of apparently protective antibody levels depended on the age at vaccination; for subjects vaccinated at 3 months of age, there was a large percentage (47.2%) of subjects in whom there was no detectable anti-HBs, while this proportion was lower those vaccinated after the first year of life (17.0%). On the other hand, after a booster dose, both groups reached a 97.8% immunocoverage rate, further demonstrating the persistence of immune memory.

A criticism could be that these data were collected in a low endemicity country, being that the populations with the highest

prevalence rates of HBV reside in sub-Saharan Africa and East Asia rather than in Eastern Europe. This is a further reason to make vaccination mandatory.

In a large cohort (health surveillance data collected over the course of more than 10 y for 6945 medical school students i.e. medicine and surgery, dentistry, and health professions) with a wide range of ages (18-68 years), we discovered that 133 of these students (1.9%) had serological evidence of past HBV infection. The majority (111, 1.6%) of the students were anti-HBc antibody positive, while 21 (0.3%) students were HBsAg carriers, and only 1 (0.014%) student was a HBeAg carrier. Approximately one third of these subjects (Table 1) were vaccinated (by history or documented). The four subjects who were HBsAg carriers and had documented vaccination were vaccinated during adolescence, not at birth, and were presumably not delivered by HBsAg carrier mothers. We have no convincing evidence to explain these data except for the possibility of prior silent infection or vaccine failure.

A history of disease was reported by one HBsAg positive carrier student and 3 anti-HBc positive students. This is a further evidence that the disease frequently occurs without clinical signs, again highlighting the potential risks that may result from an illness so elusive.2

The rate of anti-HBs positivity was 79.0%, excluding a cohort of students in which 50.4% was born in 1992 or later, which had a lower rate (63.4%) of positivity for reasons that have been previously published.

Several foreign students attending our university were included in the study population, including 458 subjects who were predominantly from Eastern Europe (212, 46.3%), Africa (104, 22.7%, 89.4% of whom were from sub-Saharan regions) or Asia (65, 14.2%, 12.3% of whom were from East Asia, 24.6% of whom were from the Indian subcontinent, and 63.1% of whom were from the Middle East). The rate of anti-HBc



Table 1. Vaccination status of students with previous infection.

	No.	Ignored <sup>a</sup>	Anamnestic, no vaccination <sup>b</sup>	Anamnestic, vaccination <sup>c</sup>	Documented, no vaccination <sup>d</sup>	Documented, vaccination <sup>e</sup>
anti-HBc +	111	28	33	22	10	18
HBsAg +	21	4	7	4	2	4
HBeAg +	1	0	0	1	0	0

<sup>&</sup>lt;sup>a</sup>Subjects who do not remember if they were vaccinated.

positivity was 15.7% (in Italian students 0.6%), and 3.7% were antigen carriers (in Italian students 0.05%).

In conclusion, the duration of the immunity induced by HBV vaccination is a fact not a fancy, and the vaccine is likely associated with long-life immune memory. The major problem associated with vaccination is compliance, and, especially in countries in which opponents to vaccinations are very aggressive, it is important that HBV vaccination become mandatory, as was demonstrated by a previous comparison of vaccine compliance between compelled and not compelled students. Prevention (vaccination) and protection (personal protective equipment) are the weapons that allow us to fight the risk associated with HBV infection, which is still widespread worldwide.

## Disclosure of potential conflicts of interest

The author declares no conflict of interest.

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<sup>&</sup>lt;sup>b</sup>Subjects without a vaccination booklet but who reported no history of vaccination.

<sup>&</sup>lt;sup>c</sup>Subjects without a vaccination booklet but who reported a history of vaccination.

<sup>&</sup>lt;sup>d</sup>Subjects submitting a vaccination booklet in which it is certified that the vaccine was not administered.

<sup>&</sup>lt;sup>e</sup>Subjects submitting a vaccination booklet in which it is certified that the vaccine was administered.