While it makes sense to regularly monitor the temperatures and symptoms of hospital workers with exposure to Ebola, no additional measures are really either necessary or useful. Not only is a policy of mandatory quarantine impractical, it also serves as a disincentive for the very healthcare workers who are needed to care for these sick patients in a manner that will improve their chances of survival while containing the epidemic. In conclusion, mandatory quarantine of asymptomatic healthcare workers who have had exposure to patients infected with Ebola virus simply does not compute.

ACKNOWLEDGMENTS

Financial support: No financial support was provided relevant to this article.

Potential conflicts of interest: Both authors report no conflicts of interest relevant to this article.

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Infect. Control Hosp. Epidemiol. 2015;36(9):1118–1119

 0899-823X/2015/3609-0025. DOI: 10.1017/ice.2015.155

REFERENCES

1. Gonsalves G, Staley P. Panic paranoia, and public health—The AIDS epidemic's lessons for Ebola. *N Engl J Med* 2014;371: 2348–2349.
2. Drazen JM, Kanapathipillai R, Campion EW, et al. Ebola and quarantine. *N Engl J Med* 2014;371:2029–2030.

Short- and Long-Term Effects of a Challenge Dose of Hepatitis B Vaccine in Individuals With and Without Residual Anti-HBs

To the Editor—In the recent article "Response to challenge dose among young adults vaccinated for hepatitis B as infants: importance of detectable residual antibody to hepatitis B surface antigen,"[1] Spradling et al. raise important questions regarding (1) the considerable resources spent in settings such as occupational and student health clinics where individuals are tested for antibody to hepatitis B surface antigen (anti-HBs) many years after vaccination and (2) the need to identify persons who retain HB-induced immunity despite a decrease in anti-HB level to <10 mIU/mL. The authors report excellent response to a challenge dose among 16–19-year-olds with residual anti-HB levels (0.5–9.9 mIU/mL) but lower response in those without detectable antibodies (0 mIU/mL).[1] Our data, obtained from subjects vaccinated at school age with 2 different vaccines, also indicate the presence of immune memory in those with residual antibodies and in the great majority of those without detectable antibodies.

We conducted two 15-year-long follow-up clinical trials.[2] Subjects were vaccinated at 8–10 years of age with 3 doses (0, 1–2, and 6 months) of Engerix (10 μg; n = 1,129) or Recombivax (2.5 μg; n = 1,126). Subjects were tested for the presence of anti-HBs 1 month following the third dose and were randomly allocated to be retested 5, 10, or 15 years later. Nonresponders to the primary vaccination (anti-HBs <10 mIU/mL) received additional doses of vaccine and were excluded from the follow-up. Despite different vaccine dosage used and almost twice higher GMTs in Engerix group when compared to Recombivax (7,307 vs 3,800 mIU/ml), similar seroconversion (99.1%–99.7%) and seroprotection rates (98.9%–99.2%) were observed in the 2 study groups.[2] The great majority of followed subjects (99.1%–100%) showed the presence of immune memory defined as at least 10 mIU/mL and a 4-fold anti-HB titer increase 1 month following the challenge dose. Here, we present the response to a challenge dose in subjects with and without residual antibodies (0.5–9.9 or 0 mIU/mL) 5, 10, or 15 years after vaccination (Table 1), as well as the persistence of ≥10 mIU/mL anti-HB levels 1, 5, and 10 years following challenge-dose administration.[3,4]

The criterion for the presence of immune memory was met by 99.1% (226 of 228) and 94% (79 of 84) of subjects with and without residual anti-HB levels, respectively. Among subjects with an immune memory, anti-HB titers ≥10 mIU/mL were still persistent 1, 5, and 10 years after challenge in 91.3% (158 of 173), 77.3% (109 of 141), and 64.4% (38 of 59), respectively.[3,4]

Similar to the study by Spradling et al., our results indicate that virtually all those vaccinated with residual anti-HBs titers (0.5–9.9 mIU/mL) have an immune memory to the HBV surface antigen (HBsAg). However, in our study, a higher proportion of those without residual anti-HBs showed an immune memory compared to those in the aforementioned study (94% vs 82%). This difference might be related to the exclusion of nonresponders to primary vaccination (≈1%), to different age at the time of vaccination, to longer period between challenge dose administration and blood collection (4 weeks vs 2 weeks), to differences in assay performance characteristics at the low end of antibody detection, or to shorter follow-up before challenge in our studies (5–15 years vs 16–19 years). However, our results indicate no trend toward a lower proportion of subjects showing an immune memory with time since vaccination among those with and without residual anti-HBs (Table 1). The similar proportion of subjects

TABLE 1. Response Rate to a Challenge Dose of Hepatitis B Vaccine in Subjects with Residual (0.5–9.9 mIU/mL) or No Anti-HB (0 mIU/mL) 5, 10, or 15 Years after First Vaccination

	% Positive Response (≥4-fold and ≥10 mIU/mL) to a Challenge Dose by Time Since First Vaccination, % (n/N)								
	5 y		10 y		15 y		Total		
Before Challenge Dose	Engerix	Recombivax	Engerix	Recombivax	Engerix	Recombivax	Engerix	Recombivax	Total Engerix & Recombivax
Anti-HB 0 mIU/mL	81 (13/16)	93 (13/14)	100 (12/12)	100 (18/18)	100 (1/1)	96 (22/23)	90 (26/29)	96 (53/55)	94 (79/84)
Anti-HB 0.5–9.9 mIU/mL	100 (22/22)	100 (38/38)	100 (31/31)	100 (27/27)	96 (50/52)	100 (58/58)	98 (103/105)	100 (123/123)	99.1 (226/228)

NOTE. Anti-HB, antibody to hepatitis B surface antigen.

with an anti-HB titer ≥10 mIU/mL 15 years post-primary vaccination (68.2%) and 10 years post challenge (64.4%) brings into question the long-term utility of a booster dose. Additionally, the loss of antibodies or immune memory (measured as presence of anti-HBs) does not necessarily mean that the individual is not protected against clinical or chronic infection.[5] Recent data suggest the presence of cellular immunity in vaccinated individuals without residual anti-HBs.[6,7] Although the role of cellular immunity is not well understood, epidemiological data show that individuals not infected at the time of vaccination almost never develop acute clinical or chronic hepatitis B.[5,8]

In conclusion, our results and those from Spradling et al. suggest that there is no need for boosters in vaccinated individuals with residual anti-HB antibodies.

ACKNOWLEDGMENTS

Financial support: The two clinical trials were financially supported by GlaxoSmithKline and Quebec Ministry of Health and Social Services.

Financial support for the present analysis: None

Potential conflicts of interest: VG, NB, and GDS have received research grants from GlaxoSmithKline and Quebec Ministry of Health and Social Services; GDS has received travel reimbursement from GlaxoSmithKline; DM reports no financial conflicts.

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Infect. Control Hosp. Epidemiol. 2015;36(9):1119–1120
 0899-823X/2015/3609-0026. DOI: 10.1017/ice.2015.147

REFERENCES

1. Spradling PR, Kamili S, Xing J, Drobeniuc J, Hu DJ, Middleman AB. Response to challenge dose among young adults vaccinated for hepatitis B as infants: importance of detectable residual antibody to hepatitis B surface antigen. *Infect Control Hosp Epidemiol* 2015;36:529–533.
2. Duval B, Boulianne N, De Serres G, et al. Comparative immunogenicity under field conditions of two recombinant hepatitis B vaccines in 8–10-year-old children. *Vaccine* 2000;18:1467–1472.
3. Gilca V, De Serres G, Boulianne N, et al. Long-term persistence of immunity after vaccination of pre-adolescents with low doses of a recombinant hepatitis B vaccine. *Hum Vaccin Immunother* 2013;9:1685–1690.
4. Gilca V, De Serres G, Boulianne N, et al. Antibody persistence and the effect of a booster dose given 5, 10 or 15 years after vaccinating preadolescents with a recombinant hepatitis B vaccine. *Vaccine* 2013;31:448–451.
5. Fitzsimons D, Hendrickx G, Vorsters A, Van Damme P. Hepatitis B vaccination: a completed schedule enough to control HBV lifelong?: Milan, Italy, 17–18 November 2011. *Vaccine* 2013;31:584–590.
6. Zaffina S, Marcellini V, Santoro AP, et al. Repeated vaccinations do not improve specific immune defenses against Hepatitis B in non-responder health care workers. *Vaccine* 2014;32:6902–6910.
7. Carollo M, Palazzo R, Bianco M, et al. Hepatitis B specific T cell immunity induced by primary vaccination persists independently of the protective serum antibody level. *Vaccine* 2013;31:506–513.
8. Poorolajal J, Mahmoodi M, Majdzadeh R, Nasseri-Moghaddam S, Haghdoost A, Fotouhi A. Long-term protection provided by hepatitis B vaccine and need for booster dose: a meta-analysis. *Vaccine* 2010;28:623–631.