
Point of view / Point de vue

Reduced doses of hepatitis B vaccines: is it a good idea?

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Hepatitis B vaccines are not generic products and it cannot be assumed that all such vaccines can be used in reduced doses in order to save costs. Any use of vaccines in an unlicensed manner should only be performed in the context of a study that is approved by the national control authority and appropriate ethical review committees.

When asked how long a person's legs should be, Abraham Lincoln replied "Long enough to reach the ground". A similar answer is perhaps required to the question of how much antigen should be put into a dose of hepatitis B vaccine: enough to do the job. Clearly, the well-executed study carried out by Goh et al. and reported in the previous article demonstrates that 10 µg of plasma-derived Merck, Sharpe & Dohme hepatitis B vaccine (now no longer produced) is enough to do the job in healthy young people in Singapore (1). However, just as legs come in many varieties, so do hepatitis B vaccines, and we cannot assume that it is effective to use all hepatitis B vaccines in reduced doses to save costs.

Hepatitis B vaccines are not generic products: the optimal dose for each manufacturer's product is usually different and is determined using dose titration curves in studies that vary the dose, age, schedule and sometimes the number of dose. For example, doses of 1.5 µg, 2.5 µg, 3 µg, 5 µg and 10 µg of different vaccines are approved infant doses of hepatitis B vaccines in different countries. Some manufacturers try to build a "margin of safety" into their dose because the vaccine will be used under various conditions of storage and delivery and on humans of different sizes, ages, and immunocompetence. Other manufacturers market doses that may not allow for a reduction in dose. The performance of any vaccine

"in the field" is usually less than that in carefully performed studies where the vaccine is properly stored and delivered on schedule, and where the recipients are often healthy young adults or children screened for factors that may reduce the immunogenicity of the vaccine.

Most hepatitis B vaccines are highly immunogenic (>90% seroconversion in controlled trials) in individuals aged up to 40 years; however, in older subjects reduced seroconversion may be encountered, which is related to age, male sex, obesity, and smoking. Suboptimal vaccine storage, freezing, improper delivery, intradermal and gluteal injection routes, use of steroids, and occurrence of immunosuppressive diseases, kidney disease, dialysis, Down syndrome, *inter alia*, also decrease vaccine performance. Therefore, use of more antigen than the minimum amount determined in carefully controlled clinical studies makes sense.

Vaccine dosage is usually approved by a country's national control authority (NCA), as part of the licensing procedure for the product. Manufacturers must provide data to support their contention that the dose of vaccine they wish to sell is safe and effective. If the vaccine is used in a reduced dosage or in another way not approved by the NCA, problems can arise (in some countries medicolegal problems) should unforeseen consequences occur through the use of the vaccine in this way. A vaccine should be used in an unlicensed manner only in the context of a study (as was the case in the study by Goh et al. (1)) that has been approved by the NCA and appropriate ethical review committees.

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Résumé

Doses réduites de vaccin antihépatite B: est-ce une bonne idée?

Les vaccins antihépatite B ne sont pas des produits génériques et il n'est pas possible d'affirmer que tous peuvent être utilisés à doses réduites pour diminuer les coûts. Toute utilisation de vaccins sous une forme non homologuée ne peut

avoir lieu que dans le cadre d'une étude approuvée par l'autorité nationale de contrôle et par des comités d'éthique compétents.

Reference

1. **Goh KT et al.** Long-term immunogenicity and efficacy of a reduced dose of plasma-based hepatitis B vaccine in young adults. *Bulletin of the World Health Organization*, 1995, **73**(4): 523–527.