



# Enfermedades Infecciosas y Microbiología Clínica

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## Editorial

### Vaccination coverage for people living with HIV: a key intervention that should be improved



### Cobertura vacunal en personas que viven con el VIH: una intervención clave que debe ser mejorada

The high efficacy of current antiretroviral therapy (ART), along with its simplicity and mostly good tolerability, allow to achieve and maintain plasma HIV-RNA suppression and to improve immune alterations in a high proportion of people living with HIV (PLWH). Subsequently, the morbidity and mortality of PLWH receiving ART has dramatically decreased.<sup>1</sup> However, vaccination remains a key healthcare intervention for PLWH due the higher risk of several preventable infections in this population. Invasive pneumococcal disease is significantly more frequent in PLWH compared with HIV-negative population, even in those with CD4 cell count above 200/ $\mu$ L,<sup>2</sup> as well as meningococcal disease,<sup>3</sup> and higher mortality related with Influenza infection has been reported in PLWH.<sup>4</sup> Other infections share transmission route with HIV, such as hepatitis B virus (HBV) and human papillomavirus (HPV), or are associated with high-risk behavior, such as hepatitis A virus (HAV), meningococcal infection or Monkeypox virus (MPXV).<sup>5,6</sup> In addition, HBV and HPV are associated with higher risk and more rapid progression to significant liver disease (cirrhosis, hepatocellular carcinoma) and cervical and anal cancer, respectively, in PLWH compared to general population.<sup>7,8</sup> PLWH has been disproportionately affected in some infection outbreaks such as HAV or MPXV and vaccines play an essential role to face these outbreaks.

It is also important to note that the population of PLWH over 50 years of age is growing. A study from the ATHENA Cohort in Netherlands predicted that PLWH with 50 years of age or older will rise from 28% in 2010 to 73% in 2030.<sup>9</sup> Thus, an increasing number of PLWH should also receive vaccine recommendations for older general population.

Other key group are PLWH who were born in other countries and may have had incomplete systematic vaccinations. In 2020 the 33.9% of the individuals newly diagnosed with HIV in Spain, came from other countries.<sup>10</sup> In these cases, it is important to evaluate the serostatus of vaccine-preventable infections (including those generally given in childhood), to establish catch-up campaigns and to offer vaccinations when they are indicated. In addition, Yellow Fever vaccination should be discussed when PLWH are from

endemic countries, or intend to travel to tropical areas, and are not severely immunosuppressed.

Despite the multiple potential benefits of vaccination in PLWH several concerns might remain among patients and clinicians regarding the efficacy and safety of vaccines in PLWH.

Actually, the serologic response to some vaccines is expected to be poorer in PLWH, especially in those individuals with low CD4 cell counts. These deficits are related both T cell and B cell impairment which may reduce the magnitude and durability of the antibodies response. However, immunogenicity can be improved by using adjuvants, conjugated vaccines<sup>11</sup>, or modified vaccination schemes, such as 4 doses of 40 micrograms instead of 3 doses of 20 micrograms for HBV vaccine or booster doses for other vaccines in cases of lower antibody titers after standard vaccination scheme. The serologic response to 23-valent polysaccharide pneumococcal vaccine (PPV) can be lower and decrease more rapidly in PLWH<sup>12</sup> and for this reason a sequential pneumococcal vaccine is recommended to increase its immunogenicity. Nevertheless, a retrospective study showed that although 23-valent PPV failed to prevent invasive pneumococcal disease (IPD) in a proportion of PLWH, prior vaccination was associated lower illness severity and lower mortality related to IPD.<sup>13</sup>

On the other hand, the safety profile of vaccines is generally similar in PLWH and HIV-negative population, except for live attenuated vaccines (i.e. chickenpox vaccine) which are contraindicated in those individuals with a CD4 count lower than 200 cells/ $\mu$ L because of the potential risk of post-vaccine complications in immunosuppressed individuals. Although live vaccines contain a weakened form of the microorganism, secondary mutations might restore the natural virulence and cause symptomatic disease.

Regarding the potential effect of vaccines to cause immune disorders in PLWH, it has been observed transient plasma HIV RNA increases after vaccination and small and transient reductions of CD4 count. In PLWH on ART, viral load “blips” can be observed after vaccinations but no long-term negative effects on HIV RNA, CD4 count, or disease progression is expected.<sup>14</sup>

Therefore, it is clearly demonstrated that the potential benefits of vaccines overcome their risks and weaknesses in the majority of PLWH. However, vaccination coverage remains an important challenge to achieve immunization in PLWH.

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In the present number of *Enfermedades Infecciosas y Microbiología Clínica*, Corma-Gómez and collaborators, analyze the HAV serologic status in a cohort of PLWH and the effectiveness of a vaccination strategy in those individuals identified as seronegative.<sup>15</sup> The first important and disturbing finding of this study is the high prevalence of HAV seronegative individuals, especially among those who acquired HIV by sexual transmission. This is relevant considering that HVA infection can be associated with certain sexual practices and the high impact of previous HVA outbreaks in HIV-positive men who have sex with men (MSM).<sup>5</sup> Second, the study shows a very poor response to the vaccination program and, subsequently, (after subsequently) a very low percentage of seroconversion. MSM are at higher risk for a number of vaccine-preventable infections such as HAV, HBV, HPV or meningococcal disease.<sup>16</sup> Therefore, vaccination should be recommended as a regular measure of primary care,<sup>17</sup> and screening should be discussed prior to vaccination according to previous exposures. MSM should be aware of the potential risks of contracting HAV infection through sexual activity as well as the possibility of receiving post-exposure prophylaxis along with their close contacts if they are not immunized.

Beyond the worrisome low immunization against HAV, this study alerts about the importance of testing vaccination status among PLWH. Unfortunately, this study is not an exception. Similar findings have been reported with different vaccines in different countries. The Centers for Diseases Control and Prevention in the United States published a comprehensive analysis on surveillance vaccination coverage among adult populations. Despite an increasing trend between 2010 and 2018, this study showed a low coverage of all recommended vaccines among different adult populations.<sup>18</sup>

Corma-Gómez and collaborators describe that at the end of the study period less than 60% of individuals referred to the vaccination delivery Unit had not yet received the first vaccine dose and only 35.8% had received a complete vaccination scheme. The study also highlights the importance of identifying barriers that difficult the access to vaccines and designing feasible and patient-centered vaccination strategies.<sup>15</sup>

Barriers to vaccination include patient-related issues, physician-related issues and structural issues.<sup>19</sup> Misinformation about vaccine recommendations and concerns about low efficacy and high toxicity might lead patients to refuse vaccines. Regarding the role of the physicians, it is important to review the serologic and vaccination status and offer vaccines according to recommendations. The HIV physician has a key role to improve vaccination coverage among PLWH. An accurate information about clinical indication, the expected benefits and safety should be provided. The serologic status (i.e. HAV, HBV, measles, rubella, parotiditis or chickenpox) as well as the indications of vaccines or booster doses (i.e. pneumococcal or meningococcal vaccines) should be included in medical records and must be reviewed at each medical visit.

Several structural barriers might difficult the access to vaccines or the completion of the full vaccination scheme. Vaccination requires additional visits, especially when more than one dose is needed. Moreover, the HIV care team and the vaccines provider team is not usually the same and a fluid communication and organization are key to achieve immunization goals. It is also essential to check the adherence to the vaccination visits, try to know the causes leading to lose doses and reschedule vaccination appointments to who missed visits. This is especially important for vaccines schemes including more than one dose and for the population groups at higher risk. In people needing more than one vaccine concomitant administration, if possible, reduce the number of visits. In summary, a good communication with patients and a good coordination between healthcare providers, as well as an active follow-up of people referred to vaccination are the cornerstones to guarantee

successful immunization outcomes. Well-coordinated strategies are also essential to face outbreaks, such as the current MPXV infections outbreak. Therefore, any contact with the healthcare system, must be an opportunity to upgrade the rates of vaccines administration among PLWH. In addition, non-immunized PLWH should be aware of the recommendations for receiving post-exposure prophylaxis or vaccine against HBV or MPXV.

Despite the wide knowledge about benefits for PLWH vaccination coverage percentages remain low in this population. This has implications at both individual and public health levels and health care professionals attending PLWH should join efforts to improve the situation. Studies like the one published in *Enfermedades Infecciosas y Microbiología Clínica* by Corma-Gómez and collaborators are important to raise awareness among health care professionals.

## Conflicts of interest

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Arkaitz Imaz<sup>a,\*</sup>, Cristina Masuet<sup>b</sup><sup>a</sup> Department of Infectious Disease, Bellvitge University Hospital, Bellvitge Biomedical Research Institute (IDIBELL), University of Barcelona, L'Hospitalet de Llobregat, Spain<sup>b</sup> Department of Preventive Medicine, Bellvitge University Hospital, Bellvitge Biomedical Research Institute (IDIBELL), University of Barcelona, L'Hospitalet de Llobregat, Spain

\* Corresponding author.

E-mail address: [aimaz@bellvitgehospital.cat](mailto:aimaz@bellvitgehospital.cat) (A. Imaz).