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## Commentary

## HPV Vaccination in Males: Another Step Forward



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Using a clinical trial, Foresta and co-workers showed that the use of prophylactic vaccination against human papillomaviruses (HPV) in patients with HPV semen infection is effective in reducing virus clearance time (Foresta et al., 2015). By using randomized controlled trial, they demonstrated in 179 infertile patients from a cohort of 619 that HPV prophylactic vaccination is able to reduce the multiple infections and decrease prevalence of HPV semen infection at 12 months (Foresta et al., 2015). On the basis of these findings, they suggested that all patients attending assisted reproduction techniques centers with HPV semen infection may benefit by the union of both specific counseling and available prophylactic vaccination. The results of this trial highlight two important aspects to discuss: 1) the high prevalence of HPV infection in males and the impact of HPV on semen quality and 2) the role of male prophylactic vaccination against HPV. The prevalence of HPV in males ranges from 1.3 to 72.9%, but the majority of studies conducted so far have been performed on specific male populations, such as homosexuals or HIV-infected (Repp et al., 2012). Recently, Bartoletti and coworkers reported a 27% prevalence of HPV in asymptomatic men, highlighting that the HPV infection is often asymptomatic and it allows a greater infection diffusion (Bartoletti et al., 2014). On the other hand, a growing number of clinical trials reported a higher prevalence of HPV infection in semen from infertile patients (Garolla et al., 2013; Cai et al., 2014). In this sense the HPV infection represents an emergent problem for the management of couples eligible for assisted reproduction techniques, too (Foresta et al., 2015). In other words, men not only play a key role in the transmission of HPV to women, but they are, probably, one of the targets of HPV viruses. Therefore, little is known about the natural history of HPV infections in men. Extensive knowledge of the natural history of HPV is an absolute requirement when prevention strategies, such as vaccination programs, are designed and implemented. For that reason, this is the time to re-think the role of

HPV infection in males. Several authors reported that the spontaneous time of infection clearance of HPV is usually short, even if the consensus among researchers is lacking about this issue (Giuliano et al., 2011). Giuliano reported that the mean time-to infection clearance (i.e., the time necessary to determine a complete regression in at least 50% of infected subjects) has been estimated to be 5.9 months, while the complete clearance of HPV-DNA in at least 75% of infected subjects has been estimated to occur within 12 months, independently of the HPV genotype considered (Giuliano et al., 2011). These findings, however, should be viewed in the light of the biological samples collected from patients. On the one hand, Giuliano and co-workers evaluated the HPV-DNA presence by using swabs obtained from the coronal sulcus, glans penis, penile shaft, and scrotum (Giuliano et al., 2011). Moreover, they did not evaluate the HPV-DNA on the semen. On the other hand, Foresta evaluated the HPV DNA on the semen samples. Semen represents a sampling site of high diagnostic value not only for the assessment of HPV infection in asymptomatic males (Laprise et al., 2014), but also for the evaluation of the mean time-to infection clearance. Moreover, semen sample analysis for HPV in males shows sufficiently accurate due to higher compliance of patients to sampling procedure, as reported by Kyo et al. (Kyo et al., 1994). Finally, the role of male prophylactic vaccination against HPV in the management and control of HPV infection diffusion. The main disparity in vaccination rate between males and female is due to the lack of data in the assessment of cost-effectiveness of HPV vaccine use in males (Cifu and Davis, 2014). Vaccination in males could reduce both the prevalence of cervical cancers and the evidence of HPV-related cancers/genital warts. This aspect has been demonstrated by several randomized control trials with the quadrivalent HPV vaccine that demonstrate robust antibody responses and high efficacy against genital warts anal precancers in men (Stanley, 2014). However gender-neutral vaccination has been recommended in the USA, Canada, Austria, and Australia. Careful cost effective modeling has preceded these decisions showing that when the burden of disease in men is included in the models then, depending upon coverage, vaccine price, and other factors male vaccination can become cost effective (Stanley, 2014). Even if the cost-effective analysis is essential in order to diffuse the vaccination in males, the Foresta's study increases our knowledge in the direction of male vaccination program worldwide approval. As future developments we must consider: 1) evaluating the best biological sample to use in order to evaluate the mean time-to infection clearance in males, 2) evaluating the role of prophylactic vaccination against HPV in males to maintain healthy male fertility. Finally, the key messages to take into account are: 1) humoral immunity has a major role in healing

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from HPV infection; 2) patients positive to HPV semen infection and eligible for assisted reproduction techniques may benefit by the union of both specific counseling and available prophylactic vaccination.

### Disclosure

I declare no competing interests.

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