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Commentary

New approaches for infective HPV detection, quantification and inactivation: Preventing accidental virus transmission in medical settings

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A group of 13–15 mucosal human papillomavirus (HPV) types, including HPV-16 and HPV-18, are type 1 carcinogens and classified as high-oncogenic risk HPV types (hrHPV) due to their association with almost the totality of cervical cancer cases. Besides, they are the causative agents of a significant proportion of vulvar, vaginal, anal, penile and oropharynx carcinomas. Low-oncogenic risk types (lrHPV), including HPV-6 and HPV-11, are associated with genital warts with low tendency to malignant progression. Overall, mucosal HPV types impose a heavy burden on human populations. Every year, hrHPV are responsible for 630,000 new malignancies, notably cervical cancer (530,000 cases), corresponding to 4.5% of all human cancers worldwide [1]. Besides, hrHPV types cause millions of low- and high-grade cervical intraepithelial neoplasia (CIN) cases annually. Moreover, lrHPV are the etiological factor of over thirty-million genital warts cases [2]. An important fraction of CIN and all genital warts constitute productive lesions shedding new infective HPV particles as free virions or in epithelial squames. Besides, many productive HPV infections occur without any clinical manifestation but release infective viral particles.

The main route of mucosal HPV transmission is through close sexual contact. However, HPV are resistant to desiccation and other physical stresses and maintain their infectivity in the environment for days. Detection of HPV DNA in surfaces in different backgrounds raise the concern of indirect transmission of mucosal HPV through contaminated fomites [3,4]. This is particularly true in nosocomial/health care settings were the use of different instruments (transvaginal ultrasound probes, colposcopes, endoscopes, speculums, etc.) entering different body cavities may constitute vehicles of HPV transmission. In this context, the use of sanitizing agents, including high-level disinfectants (HLDs), with proved virucide potential is of critical importance to hamper virus spread warranting the safety of patients, physicians and health care personnel.

For many years, testing the virucide efficacy of different compounds on HPV inactivation was impossible due to our inability to produce high titer HPV virions in culture systems and test their infectivity. During the last decade, this problem was overcome and now several laboratories have the expertise to produce infective HPV particles of the most relevant HPV types. Together with advances in animal models to address papillomavirus (PVs) infection/pathogenesis, these tools allow the direct comparison of HLDs efficacy to inactivate different PV types.

In two articles of *EBioMedicine*, the authors presented a very detailed and controlled set of experiments to determine the efficacy of ortho-phthalaldehyde (OPA), hypoclorite and hydrogen peroxide in inactivating PVs particles from experimental models, including quasivirions, xenografts, raft cultures and *Mus musculus* PV type 1 (MmuPV1) induced-lesions in mice. Besides, they included the analysis of HPVs virions retrieved from recurrent respiratory papillomas, anal warts and cervical lesions from patients with hrHPV [5,6].

The study by Ozbun and colleagues described a precise workflow to determine the efficacy of disinfectants against HPV virions that may remain on surfaces [5]. This is important to prevent the transmission of different HPV types by fomites in nosocomial/health care settings. The data presented in this work for HPV-11, HPV-16 and HPV-31 can be extended to other HPV types warranting the reduction of accidental HPV transmission by correct virus inactivation.

The work by Egawa and colleagues established a clear correlation between viral titers obtained *in vitro* and the pathogenic potential *in vivo*, and presented a detailed analysis of inactivation of PVs particles by the HDLs mentioned above, confirming the efficacy of these compounds [6]. They also presented interesting results showing that OPA-glycine, but not OPA-lysine, was also able to inhibit PVs infectivity *in vitro* and this correlated with the capacity of the former to interact with virus particles. Besides, they performed an interesting comparative study of the duration of the viability and infective potential of free MmuPV1 particles and those contained in exfoliating cells.

Previous studies from another group indicated that certain HLDs, including OPA, were ineffective in preventing HPV inactivation from medical instruments putting both patients and healthcare personnel at risk [7,8]. These studies were of great importance due to their originality and for generating the first experimental results and draw the attention to this important question. The pair of studies published in *EBioMedicine* extend and refine the reported findings. In fact, they show some opposing results using a broader range of HPV types, virus sources, new quantifying methods and a comprehensive set of technical approaches. The comparison made between the different protocols used for viral

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particles purification are critical to determine the real amount of infective viral particles in a sample. The results presented are relevant since they likely reproduce, in a more precise and controlled fashion, the process of contamination of fomites used during clinical examinations. Therefore, they will help to set effective protocols for disinfection and consequent reduction of accidental HPV transmission.

Contributors

Dr Enrique Boccardo wrote this commentary

Declaration of Interests

Dr Boccardo has nothing to disclose.

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