

Analysis of the scientific strength of published data on the resistance of HPV type 16 to clinical disinfectants (Myers J et al JAC 2014). [prepared by Dr. M. Alfa; Sept 20, 2016]

Issue:

The recent publication by Myers et al (2014) has raised concern that Human Papilloma virus (HPV) is resistant to some of the commonly used hand sanitizers and high level disinfectants (HLD). Myers et al (2014) evaluated the infectivity of HPV16 native virion as well as Quasivirion against; Ethanol (70%, 95%), Isopropanol (70%, 95%), Glutaraldehyde (2.4%, 3.4%), OPA (0.55%), phenol, PAA-silver (0.25%, 1.2%) and hypochlorite (0.525%). ***They reported that ethanol, glutaraldehyde and OPA had no ability to inactivate viral infectivity.*** The authors stated: “*Our data support the possibility of HPV fomite-related transmission, autoinoculation and nosocomial transmission even via instruments that were considered ‘sterile’.*” Furthermore, they suggested that new infection control practices are warranted.

Question:

Is this finding of resistance to commonly used disinfectants scientifically sound and should healthcare facilities modify their reprocessing protocols in response to this publication?

Expert Opinion:

Scientific validity of Meyer et al's study:

The viral preparations used in Meyer et al's study (2014) were incubated with each disinfectant/sanitizer (at the manufacturer's recommended concentration) for 45 mins at room temperature and then neutralizer was added to prevent further action of the disinfectant/sanitizer. The neutralized viral preps were rinsed to remove the neutralized disinfectant and then tested for infectivity. The methods used for this process are scientifically sound and were based on many years of research undertaken by Meyers since 1992 (Meyers et al 1992, Ryndock et al 2014). The method in the 2014 research study by Meyers et al (2014) references Buck et al (2004) and Conway et al (2009). In summary, the scientific research into HPV assembly and infectivity by Meyer's group has a long and scientifically solid history in their laboratory as well as other laboratories.

The Meyer et al's (2014) investigation uses “crude viral preparations” and not purified viral preparations. Purified virus is prepared by first homogenizing the virus growing in tissue culture (crude viral preparation) and then separating out the viral particles by passing the crude viral preparation through a density gradient column using centrifugation. I believe the use of crude viral preparations may partially explain the resistance observed by Meyer's et al (2014) to Glutaraldehyde, OPA and ethanol. Most other evaluations of the susceptibility of disinfectants/ sanitizers have utilized purified viruses. It has been well established that the efficacy of many disinfectants and sanitizers against microorganisms is detrimentally affected by the addition of organic material. So a key question regarding this study is whether the use of a “crude viral preparation” is an inappropriate way to test efficacy of disinfectants/sanitizers? It is my expert opinion that the use of crude viral preparations is totally appropriate for these types of investigations.

Human viruses such as HPV are obligate intracellular pathogens that can only replicate inside human cells. Medical devices are exposed to both free viral particles as well as human

secretions where the virus is inside human cells in the secretions (e.g. an intra-vaginal probe contacts virus in secretions and in human cells in the mucous membranes of the vagina). In addition the survival of human virus on inanimate objects is improved when in the presence of human secretions that protect the virus. As such it is very important to evaluate the efficacy of disinfectants/sanitizers in the presence of organic material – otherwise the killing ability of the agents being tested will be over estimated compared to the clinical setting where the virus is almost always in the presence of human cells and/or secretions. Indeed, Vickery et al's (2014) recent simulated-use evaluation to assess efficacy of a hydrogen peroxide nebulized mist for HLD of ICVPs followed ASTM methods and included an organic load as well as high microbial levels.

Guidelines recommendations:

The recent Canadian guideline (2011) to manufacturers regarding testing of disinfectants/sanitizers indicates:

“When a target surface to be disinfected has heavy soil deposits, a pre-cleaning step prior to the application of the product may be appropriate in order to achieve the tested efficacy level. In the absence of efficacy testing being conducted with the addition of an organic soil load, a pre-cleaning step should be indicated on the label.”

For simulated-use testing the Canadian guideline for disinfectant/sterilant testing (2014) does require a test soil and states: *“Applicants should ensure that the tests are performed on devices that are difficult to clean (e.g., those with small lumens, matt surfaces and hinges), that the most difficult areas for the disinfectant to penetrate and contact should be inoculated, and that the organic and inorganic challenge (i.e., soil load) that would be expected to be encountered and which is appropriate for the intended use of the device (e.g., blood or feces for endoscopes; blood or sputum for bronchoscopes) should be included..”*

Furthermore, the FDA Guidance document (2015) recommends: *“The manufacturer should select an artificial test soil, the composition of which accurately represents materials that the device would likely be exposed to during an actual clinical use, and would create the greatest (worst-case) challenge to the cleaning process.”*

In summary both Canadian and USA guidelines recommend the use of organic material to validate disinfectant efficacy.

What do guidelines recommend for other pathogens that may also be resistant to commonly used HLDs? A prime example is *Cryptosporidium* as it is resistant to chlorine and most other surface disinfectants used in healthcare. Despite this resistance the CDC Guideline for Disinfection and Sterilization (2008) states: *“Although most disinfectants are ineffective against C.parvum, current cleaning and disinfection practices appear satisfactory to prevent healthcare-associated transmission.”* This approach hinges on the efficacy of the cleaning practices in healthcare.

Clinical practice:

An effective pre-cleaning step prior to HLD is a critical necessity especially if the validation of HLD efficacy for non-enveloped viruses was done in the absence of an organic load. For ICVPs adequate cleaning is still required even if a sheath (or condom) is used as clinical studies have confirmed that virulent HPV strains can still contaminate the probe despite use of a sheath (Casalegno 2012, Leroy 2013, M'Zali 2014, CDC Guideline 2008). Furthermore, recent clinical

data on intra-cavitary vaginal probes indicates that the pre-cleaning is frequently sub-optimal as Sanz et al (2011) reported that ultrasound probes in the medicine, trauma, and pediatrics areas were found to be visibly clean 65%, 33%, and 70% of the time, respectively. These factors combined (i.e. sheaths not sufficient to preclude HPV contamination, poor cleaning of ICVPs) indicate that HPV in the presence of organic material is very probable and is a frequent “real life” occurrence.

Summary:

In summary it is my expert opinion that the Meyer’s et al (2014) study is scientifically valid and takes into consideration HPV in the presence of organic material. If healthcare facilities consistently have meticulous cleaning of ICVPs followed by disinfection with currently cleared HLDs then the risk of HPV transmission from contaminated ICVPs is likely very low. However, if cleaning of ICVPs is sporadic as reported by Sanz et al (2011) then the risk of HPV contamination of patient-ready ICVPs may be up to 1% (Leroy 2013).

It is my expert opinion that healthcare facilities offering ICVP procedures should urgently provide education regarding the risk of HPV transmission and provide adequate training to personnel reprocessing ICVPs. Furthermore, they should routinely audit reprocessing of these devices to ensure ongoing compliance with cleaning and HLD. Finally, the preferred disinfection technologies for ICVPs would be those with known efficacy against HPV (or other surrogate non-enveloped virus) in the presence of an organic load similar to the crude viral preparation that was used by Meyer et al (2014).

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