
Human papilloma viruses: new challenges for infection prevention

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Summary

Human papilloma virus infections are one of the most common sexually transmitted diseases in humans. Certain types of HPV are known to cause cancer and HPV infection has gained attention as a major public health issue. It is now known that high-risk HPV is strongly resistant to a number of disinfectants including aldehyde-based high level disinfectants. These results are of major concern given that aldehyde based disinfectants are used to high-level disinfect endocavitary ultrasound probes and other semi-critical items. Infection preventionists need to be aware of these latest developments and to consider appropriate steps to mitigate transmission risk in the healthcare setting.

As the most prevalent cancer-causing infectious disease, human papilloma virus (HPV) infections continue to receive considerable attention in the public health setting.

HPV infections are caused by small non-enveloped DNA viruses that infect basal epithelial cells. It is in these cells that the virus replicates before being shed from mucous membranes or from skin. HPV virions are comprised of a circular double stranded DNA genome enclosed in a 55-60 nanometer protein capsid (Figure 1). The lack of a lipid coat means that HPVs are classified as non-enveloped viruses, meaning that they are generally hardier and are less susceptible to disinfectants.

Epidemiology

HPV infections are highly prevalent with approximately 79 million Americans currently infected and with the majority of males and females expected to contract an HPV infection in their lifetime.¹ Many of these infections are with low-risk types of HPV and while HPV

infection is very common, development of these infections into cancer occurs only at a low frequency.

Over 170 HPV types have been identified to date with only a subset of these showing a high propensity to cause cancer, enabling grouping of HPV types into high and low-risk categories.²

The major cancer causing types are HPV 16 and 18, which together are responsible for the majority of HPV induced cancers and can be considered especially high-risk. A further six types (HPV 45, 31, 33, 35, 52 and 58) are commonly associated with cancers globally, and together with HPV 16 and HPV 18, collectively form the group of 'high-risk' HPV types.³

In the US from 2004–2008, the CDC estimated that an average of approximately 26,000 new cancers attributable to HPV occurred each year, including 18,000 among females and 8,000 among males.⁴

Of the 18,000 cancers linked to HPV in women, over 11,000 are cases of cervical cancer and HPV is most widely recognized as the causative agent of this disease. HPV16 and HPV18 cause the majority of cervical cancers with other high-risk types contributing (Table 1).

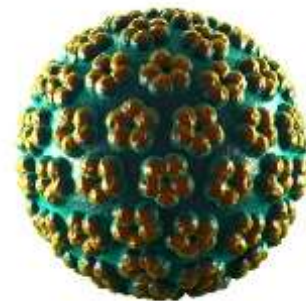


Figure 1. The capsids of HPV virions are assembled from repeating units of the L1 protein to create a 55-60 nanometer structure which houses a double stranded DNA genome. Source: stock image.

HPV is also associated with a number of other cancers including oropharyngeal and anogenital cancers. The incidence of each of these cancers types and the estimated number of cases caused by HPV are detailed in Table 2 and Table 3 below.

Table 1. Frequency of HPV types associated with cervical cancer. Data adapted from ⁵.

Type	% associated with HPV type	Cumulative total
HPV 16	54.6	54.6
HPV 18	15.8	70.4
HPV 33	4.4	74.8
HPV 45	3.7	78.5
HPV 31	3.5	82
HPV 58	3.4	85.4
Others*	14.6	100

*Further specific HPV types <3% each

Transmission of HPV

HPV is well understood to be transmitted via contact during sexual activity and is considered one of the most common sexually transmitted diseases. However there is also evidence to suggest that transmission may occur through non-sexual contact. Such routes of transmission might include auto-inoculation, fomite-mediated transmission via medical

devices and equipment or transmission via the environment.⁶

Naturally, such modes of transmission are of interest to the infection preventionist as they present an opportunity to limit HPV infection by adopting standards of practice which reduce transmission risk. While conclusive cases of transmission via a medical device or the environment have not yet been reported, there are a number of lines of evidence that support the risk of transmission in the clinical setting.

- It is known that HPV is resistant to desiccation and can remain infectious when exposed to a typical dry room environment for a number of days.⁶
- HPV DNA has been detected on the fingers of individuals with an active infection, demonstrating that infected patients can carry the virus on their hands and act as a source of infectious virions.^{7,8}
- Finally, there is evidence that HPV can be transmitted via touch, as low-risk HPV infection by self-inoculation has been

Table 2. Incidence of cancers commonly associated with HPV in males in the United States 2004-2008. Adapted from ⁴

	Avg annual cases	% attributable to HPV	Avg annual cases attributable to HPV
Penile SCC	1,046	36%	377
Anal SCC	1,678	93%	1,561
Oropharyngeal SCC	9,356	63%	5,894

SCC=squamous cell carcinoma; HPV=human papillomavirus.

Table 3. Incidence of cancers commonly associated with HPV in females in the United States 2004-2008. Adapted from ⁴

	Avg annual cases	% attributable to HPV	Avg annual cases attributable to HPV
Cervical carcinoma	11,967	96%	11,488
Vulvar SCC	3,136	51%	1,599
Vaginal SCC	729	64%	467
Anal SCC	3,089	93%	2,873
Oropharyngeal SCC	2,370	63%	1,493

SCC=squamous cell carcinoma; HPV=human papillomavirus.

documented in children in cases where no signs of sexual abuse can explain the transmission of genital warts.⁹

HPV and medical devices.

HPV associated cancers tend to occur either on mucosal membranes or cutaneous genital regions. Reusable medical devices such as ultrasound probes and endoscopes that are utilized in endocavitary procedures frequently come into contact with these body sites (Figure 2). These complex medical devices cannot be steam sterilized due to their sensitivity to heat. Instead these devices should undergo a minimum of high level disinfection according to CDC guidelines.¹⁰

A number of studies have investigated the presence of HPV DNA on transvaginal ultrasound probes after routine use. One study showed that 3% of probes were contaminated with DNA from high-risk HPV types (16, 31, 53, 58) following transvaginal ultrasound.¹¹ Another study showed that 7.5% of randomly sampled transvaginal probes were contaminated with HPV DNA and that 21% of transvaginal probes were contaminated with HPV DNA following routine procedures where patients were known HPV carriers.¹²



Figure 2. Transvaginal ultrasound probes are reusable medical devices that should be high level disinfected at a minimum between patients according to CDC guidelines.¹⁰ A number of studies have reported the presence of HPV DNA on transvaginal ultrasound probes after routine use.¹¹⁻¹³ Source: stock image.

A further study found that 7% of transvaginal ultrasound probes were contaminated by free HPV virions after low level disinfection with quaternary ammonium compound wipes.¹³ These samples were treated with an exonuclease, which destroys all unprotected DNA. HPV DNA that is protected inside capsids remains and can be detected by PCR.

While there is clear evidence to suggest that HPV can contaminate ultrasound equipment, it seems likely that other medical instrumentation used in these body sites might also be contaminated with HPV. Special consideration needs to be given to how these devices are disinfected between patients.

Efficacy of disinfectants against HPV.

The first study to look at the efficacy of disinfectants against native HPV was published in 2014. Prior to this, the efficacy of disinfectants against HPV had not been tested due to the lack of a suitable method for producing sufficient quantities of native HPV virions.

This method was developed by researchers in the laboratories of Prof Craig Meyers at Penn State University and Prof Richard Robison at Brigham Young University and was the first to enable testing of the susceptibility of HPV16 to disinfectants. In their 2014 publication, these authors presented the first efficacy testing of 11 widely used disinfectants versus high risk HPV16 (Figure 3). The efficacy tests were conducted in suspension at room temperature with a contact time of 45 minutes. Infectivity was measured by detection of the spliced E1^{E4} transcript in recipient cells.

Surprisingly, only 2 of the 11 disinfectants tested were effective against HPV16 within the 45 minute contact time, based on a >4 log₁₀ reduction in infectivity as required by regulatory agencies for a virucidal claim.¹⁴

Of most concern with these results is the fact that the aldehyde-based high level disinfectants glutaraldehyde (GTA) and *ortho*-phthalaldehyde (OPA) were ineffective against HPV16.

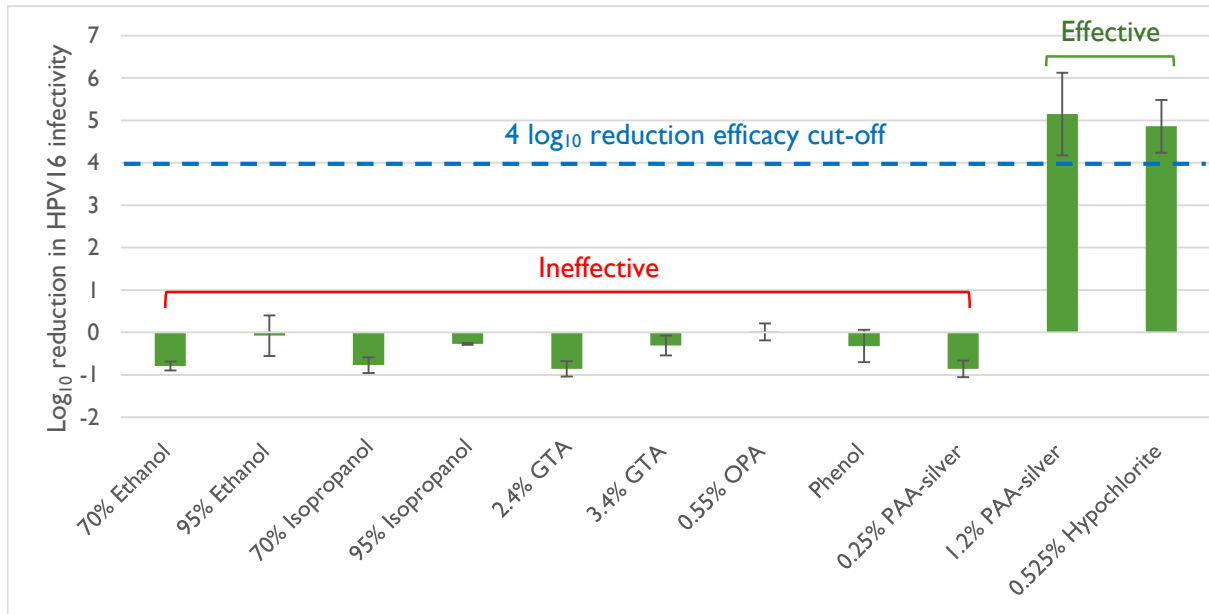


Figure 3. Efficacy of 11 disinfectants against high-risk HPV 16 virions. Disinfectants were tested in suspension tests at room temperature with a 45 minute contacted time. Infectivity is expressed versus input by measuring the expression of the spliced E1^{E4} transcript which is expressed following viral integration into recipient cells. Adapted from¹⁵

The authors also tested GTA and OPA with extended contact times up to 24 hours but still showed <1 log₁₀ reduction in infectivity.

The study showed that high concentrations of hypochlorite and peracetic acid (PAA) with silver were effective within the contact time. Hypochlorite is useful as a general disinfectant for environmental surfaces but is not approved as a high-level disinfectant and is not suitable for disinfecting ultrasound probes or endoscopes. PAA is a high-level disinfectant used in endoscope reprocessing however the specific formulation used in this paper is not readily available.

HPV and the future

In order to protect patients against the risk of HPV cross contamination, it is important that high level disinfectants, specifically tested and proven effective against high risk HPV types, are identified and adopted into clinical practice.

Disclosures

Dr Burdach is a consultant to Nanosonics Ltd. The statements in this article represent the views of the author.

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