Tristel™

SCIENCE

A BRIEF OVERVIEW ON HUMAN PAPILLOMAVIRUS:

BIOLOGY, DEVICES AND DECONTAMINATION

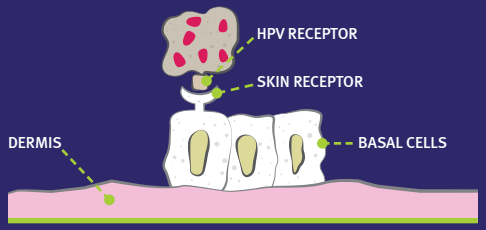

FIGURE 1. Binding of HPV to receptor on basal cell of the squamous epithelium.

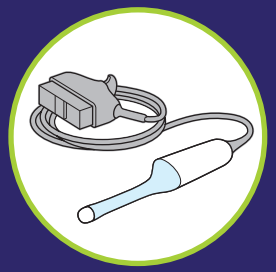

FIGURE 2. Endocavity ultrasound probe

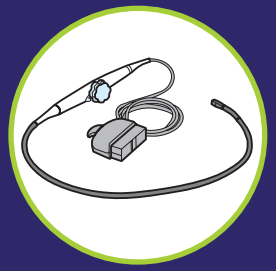

FIGURE 3. Transoesophageal echocardiography probe

FIGURE 4. Nasendoscope

The Human Papillomavirus (HPV) is a non-enveloped, Deoxyribonucleic Acid (DNA) virus.

OVERVIEW

More than 100 types of HPV have been identified[1] which include low-risk and high-risk types. Fifteen types are classed as high-risk (HR). HR-HPV types can lead to cancer of the cervix, anus, penis, vagina, vulva and oropharynx. Among these, HPV type 16 and HPV type 18 are by far the most prevalent in cancers, accounting for approximately 70% of cervical cancers, with other HR-HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82) accounting for the rest[2].

HPV type 16 accounts for approximately 95% of HPV-positive oropharyngeal cancers[4].

Medical devices including endocavity ultrasound probes and endoscopes are used daily to examine and diagnose areas of the body in which HPV may be present. Consequently, there is a risk of HPV transmission to these devices and subsequent iatrogenic infection to both patient and medical staff.

HPV LIFE CYCLE

HPV initiates host cell infection in the basal cell layer of the epithelium and cells in the epidermis (skin cells). Receptors on the HPV surface bind to receptors on the surface of basal cells allowing the virus to invade the cell and replicate as the cell undergoes division. This causes genetic mutations in the host cell which eventually may lead to cancer[3].

ULTRASOUND PROBES AND ENDOSCOPES

Endocavity ultrasound probes, such as transvaginal and transrectal probes, are used to examine areas including the vagina, cervix, uterus and prostate. These examinations may cause micro abrasions of the genital mucosa favouring HPV infection.

Parts of the device at risk of contamination include the insertion shaft (which enters the patient) and the handle of the device. The cord and plug, which may be handled by the operator, are also at risk, as gross blood and microbial contamination on the cord and plug of ultrasound devices have been reported in studies[4,5].

International guidelines recommend the use of a sheath or condom during procedure to minimise contamination[6,7], however, perforations and leakage of these covers have been discovered post use[8].

HPV DNA contamination on endocavity ultrasound probes pre and post disinfection is highlighted in the literature[9,10,11], as well as HPV contamination on fomites in the healthcare environment including examination lamps, bed control panels and examination beds[12].

Transoesophageal echocardiography utilises an ultrasound probe to provide images of the heart and surrounding blood vessels. During procedure, the device is inserted through the mouth into the throat and oesophagus. HPV DNA has been found within the saliva of patients[13] and the majority of tumour specimens analysed from carcinomas of the head and neck[14,15,16,17]. It is therefore possible that exposure of this device into areas of the head and neck in which HPV is known to reside can lead to a risk of transmission.

Endoscopes used as a diagnostic tool to examine the pharynx and larynx of a patient (such as nasendoscopes, see **Figure 4**), are also similarly at risk to contamination by HPV during procedure.

DEVICE CLASSIFICATIONS AND DISINFECTANTS RECOMMENDED BY HEALTH AUTHORITIES

Across the world, health authority guidelines provide recommendations to healthcare institutions on procedures that must be followed for the disinfection of medical devices. These processes vary depending on the level of risk the device holds, which is based on the area(s) of the body in which the device touches (**Table 1**).

To achieve the specific level of disinfection required, specific disinfectant types are also recommended by Regulatory Authorities (**Table 2**).

HEALTH AUTHORITY GUIDELINE/REFERENCE	EXAMPLES OF STERILANTS RECOMMENDED/CONTA CT TIME/ RE-USE PERIOD (IF STATED)	EXAMPLES OF HIGH-LEVEL DISINFECTANTS RECOMMENDED/CONTACT TIME/ RE-USE PERIOD (IF STATED)	EXAMPLES OF LOW-LEVEL DISINFECTANTS
French Infection Control Society (SF2H) - specific to endocavity ultrasound disinfection – published March 2019	Not Included	Chlorine dioxide wipes or foam/30 seconds/single use, systematic between each patient	Not provided, as the minimum requirement is full conformity to ILD criteria : EN 16615, Mycobacteria EN 14563, etc.
		Semi-Automated disinfection	
Ear Nose and Throat United Kingdom (ENT UK)	Autoclaving (i.e. heat)	Chlorine dioxide wipes/ 30 seconds/single use. Automated disinfection	Not provided
United States Food and Drug Administration (FDA)	2.4% glutaraldehyde/ 10 hours/ 14 days	0.55% Ortho-phthalaldehyde (OPA)/ 12 min/14 days	Not provided
	3.4% glutaraldehyde/ 10 hours/28 days	2.4% glutaraldehyde/ 45 min/14 days	
	3% peracetic acid/ 2 hours/5 days	3.4% glutaraldehyde/ 20 min/28 days	
Asia Pacific Society of Infection Control (APSIC)	>2% glutaraldehyde/10 hours	>2% glutaraldehyde/ 20-90 min	Quaternary ammonium compounds
	7.5% hydrogen peroxide/6 hours	7.5% hydrogen peroxide/ 30 min	Phenols
	0.2% peracetic acid/12 mins	0.55% Ortho-phthalaldehyde (OPA) / 5 min	Diluted sodium hypochlorite
Australasian College for Infection Prevention and Control (ACIPC) and *Australian Society for Ultrasound in Medicine* (ASUM)	Not included	States to use a government approved disinfectant of either: liquid HLD, automated disinfection, light based (UV) disinfection or high-grade disinfection wipes	States to use a government approved disinfectant

TABLE 2. Examples of health authority guideline recommendations across the world for sterilisation, high-level disinfection and low-level disinfection.

Endocavity probes and endoscopes touch mucous membranes and therefore according to their classification as semi-critical devices, require high-level disinfection after use.

DISADVANTAGES OF DISINFECTANT RECOMMENDATIONS TO DATE

As noted above, devices touching mucous membranes require high-level disinfection. High-level disinfectants are described as agents that destroy all microorganisms, (excluding high amounts of bacterial spores)[20]. It is therefore expected that HPV, a small, non-enveloped virus would be destroyed by sterilization or high-level disinfection, as it is listed as a microbe of lesser resistance to disinfection than bacterial spores (**Figure 5**).

CATEGORY	DEVICE APPLICATION	EXAMPLES OF DEVICES	LEVEL OF DISINFECTION REQUIRED
CRITICAL	Contact with the bloodstream or sterile tissues	Surgical instruments (e.g. scalpels)	Sterilisation – destroys all forms of microbiological life
SEMI-CRITICAL	Contact with intact mucous membranes or non-intact skin	Endoscopes, endocavity ultrasound probes	High-level disinfection – destroys all microorganisms excluding high amounts of bacterial spores
NON-CRITICAL	Contact with intact skin	Stethoscopes, blood pressure cuffs	Intermediate-level disinfection – destroys Mycobacteria, most viruses, most fungi and bacteria OR Low-level disinfection – destroys most bacteria, some viruses and some fungi

TABLE 1. Classification of medical devices and the corresponding disinfection level required[18]

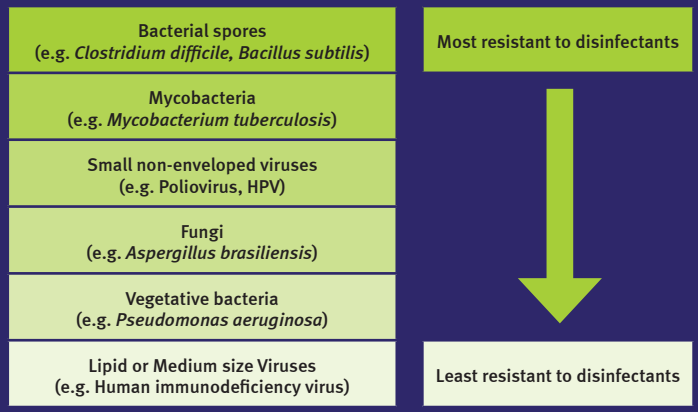

FIGURE 5. Descending hierarchy of resistance of microorganisms to Disinfectants[20]

Recent research has been performed on a variety sterilants, high-level disinfectants and low-level disinfectants, including those recommended by authorities. In testing performed by Meyers et al., (2014), HPV type 16 was assessed in-vitro, which prior to this study had not been performed using disinfectants due to the stringent life cycle requirements of the virus.

HPV type 16 was exposed to a variety of disinfectants in liquid suspension, neutralised after the contact time and subsequently injected into HaCat (culture) cells. If the virus was still viable, HaCat cells would be infected. Results were recorded as a log reduction in the infectivity of the virus to the HaCat cells compared to viruses and their infectivity not treated with disinfectants (**Table 3**). A 4 $\log_{10}$ reduction (99.99%) was required to be termed virucidal[19].

Disinfectants highlighted in pink have been found to be ineffective against HPV type 16 and are those recommended by healthcare authorities as documented in **Table 2**. Furthermore, the contact time tested in this study exceeds the contact time stipulated by authorities for sterilization or disinfection to be achieved with these disinfectants.

THE SOLUTION

Testing with another oxidising chemical, not included in the above referenced study has been reported in the literature as efficacious against HPV (**Table 4**).

Data reported in **Table 3** and **4** suggest oxidising disinfectants including chlorine dioxide and hypochlorite are efficacious against HPV. Active ingredients including glutaraldehyde and ortho-phthalaldehyde demonstrate no efficacy.

The sole use of oxidising chemicals to disinfect medical devices exposed to HPV is a future intervention that may reduce the risk of HPV iatrogenic infection.

Implementation of changes in authority guidelines is slowly beginning to transpire as shown by the College of Physicians and Surgeons of British Columbia. The 'Reprocessing Requirements for Ultrasound Probes'[22] document published by this organisation dictates an oxidising-based high-level disinfectant should be used to reduce the risk of HPV transmission, for which chlorine dioxide is provided as an example.

The Tristel Trio Wipes System utilises the oxidising active ingredient of chlorine dioxide. This decontamination system is listed in many international guidelines as a suitable disinfectant for the reprocessing of endocavity ultrasound probes and endoscopes[8,9,23]. The use of such system is an option available to healthcare institutions for the decontamination of devices in which there is a risk of HPV transmission.

Disinfectant Tested	Disinfectant Category*	Disinfectant Mode of Action	Contact Time Tested	$\log_{10}$ Reduction
70% Ethanol	LLD for use on surfaces, reagent in laboratory testing and also for the disinfection of hands	Non-oxidising	45 minutes	No reduction
95% Ethanol				
70% Isopropanol				
95% Isopropanol				
Phenol	LLD	Non-oxidising	45 minutes	No reduction
2.4% Glutaraldehyde	Sterilant/HLD	Non-oxidising	45 minutes	No reduction
3.4% Glutaraldehyde	Sterilant/HLD	Non-oxidising	45 minutes	No reduction
		Non-oxidising	24 hours	No reduction
0.55% Ortho-phthalaldehyde	HLD	Non-oxidising	45 minutes	0.017
		Non-oxidising	24 hours	No reduction
0.25% Peroxyacetic acid (PAA) silver	Surface disinfectant that kills spores	Oxidising	45 minutes	No reduction
1.2% PAA silver	Surface disinfectant that kills spores	Oxidising	45 minutes	5.15
0.525% Hypochlorite (bleach)	Surface disinfectant that kills spores	Oxidising	45 minutes	4.862

TABLE 3. Disinfectants tested and their efficacy against HPV type 16. Pink rows show ineffective disinfectants and those recommended by authorities. *As stated by healthcare authorities or disinfectant manufacturer. Data in table adapted from Meyers et al., (2014).

Reference	Disinfectant/ System, Active Ingredient	Disinfectant Mode of Action	How HPV Efficacy was Assessed	$\log_{10}$ Reduction or Recovery
Ma et al., (2012)[20] and Ma et al., (2014)[21]	Tristel Trio Wipes System, chlorine dioxide	Oxidising	50 endocavity probes were swabbed after disinfection then analysed via polymerase chain reaction for the presence of HPV-DNA.	No HPV-DNA recovered

TABLE 4. Disinfectant system reported in the literature as efficacious against HPV.

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