A proposal to reduce the risk of transmission of human papilloma virus via transvaginal ultrasound

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The problem

Commonly used disinfectants glutaraldehyde and orthophthalaldehyde have negligible activity against human papilloma virus, and commercial ultrasound probe covers have high rates of leakage, so there is a potential for transmission of human papilloma virus by transvaginal ultrasound examination if these methods are used.

A solution

Disinfection of internal-use ultrasound probes with sonicated hydrogen peroxide (H_2O_2) and covering them with condoms during examinations will greatly reduce the potential for human papilloma virus transmission.

Three steps must be followed to prevent the transmission of infection via a contaminated transvaginal ultrasound probe: cleaning the probe after every use, high-level disinfection, and covering the probe with a single-use barrier during the examination. There may be critical flaws in at least 2 of these steps as they are currently practiced. First, 2 widely used disinfectants, glutaraldehyde and orthophthalaldehyde, have recently been found to be ineffective at neutralizing human papilloma virus type 16 and type 18. Second, commercial ultrasound probe covers have an unacceptable rate of leakage (8—81%) compared to condoms (0.9—2%). We recommend the use of a sonicated hydrogen peroxide disinfectant system rather than aldehyde-type disinfectants. We recommend that the probe be covered with a condom rather than a commercial probe cover during transvaginal ultrasound examination. Combined with probe cleaning, these 2 steps are estimated to result in an 800 million- to 250 billion-fold reduction in human papilloma virus viral load, which should translate to greatly enhanced patient safety.

Key words: disinfection, human papilloma virus, nosocomial infection, patient safety, sterilization, ultrasound safety, vaginal ultrasound

Introduction

The safety of transvaginal ultrasound depends critically on procedures to reduce the risk of transmission of microbes from patient to patient or from provider to patient. Guidelines from the American Institute of Ultrasound in Medicine[1] recommend 3 steps to reduce this risk: (1) the endovaginal probe must undergo a thorough cleaning after each use; (2) after cleaning, the probe must undergo high-level disinfection with an approved disinfectant; and (3) the probe must be covered by a single-use barrier during the examination.

Recent evidence suggests that there may be critical flaws in 2 of these steps as currently performed by many practices. Specifically, 2 widely used disinfectant solutions (glutaraldehyde and orthophthalaldehyde) appear to have virtually no virucidal activity against human papilloma virus types 16 and 18.[2,3] Furthermore, commercial ultrasound probe covers have reported leakage rates of 8—81%.[1] These 2 flaws combined may result in a high risk of human papilloma virus transmission if practices use glutaraldehyde or orthophthalaldehyde in combination with commercial probe covers.

Human papilloma virus is the most prevalent sexually transmitted infection in the United States, affecting more than 8 million reproductive-age women.[4,5] Human papilloma virus 16 and human papilloma virus 18 are responsible for about 70% of cervical cancers worldwide.[5,6] It has been known for years that this nonenveloped, capsid virus retains its infectivity for days or weeks on environmental surfaces, including medical equipment, and is highly resistant to low-level disinfection procedures.[7,8] But newer studies show that human papilloma virus is also resistant to glutaraldehyde and orthophthalaldehyde,[2,3] which are considered high-level disinfectants.

In this review, we aim to alert ultrasound providers about potential pitfalls in common disinfection and probe-covering practices and to suggest safer alternative practices. Although there have not been proven cases of iatrogenic human papilloma virus transmission via infected ultrasound probes,[9] isolated cases would be difficult or impossible to prove, even if iatrogenic transmission were suspected. Patient safety requires that we adopt the safest practices to prevent such infection before any cases occur. We must not wait for cases to be proven before we abandon suboptimal practices.

Step 1: cleaning

Cleaning is defined by a guideline from the Centers for Disease Control and Prevention[10] and quoted by the American Institute of Ultrasound in Medicine guidelines[1] as:

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> "… the removal of visible soil (eg, organic and inorganic material) from objects and surfaces and normally is accomplished manually or mechanically using water with detergents or enzymatic products. Thorough cleaning is essential before high-level disinfection and sterilization because inorganic and organic material that remains on the surfaces of instruments interfere with the effectiveness of these processes."

The American Institute of Ultrasound in Medicine guidelines[1] recommend cleaning with quaternary ammonium sprays or wipes, running water, liquid soap, and/or a brush to clean crevices and angulations, although they do not specify a single preferred combination or order for these methods. The guidelines[1] estimate that cleaning results in a 99% reduction in microbial load on the surface of the transducer, but this may be optimistic.[7]

Step 2: high-level disinfection

The American Institute of Ultrasound in Medicine and the Centers for Disease Control and Prevention guidelines[1,10] describe several levels of disinfection and sterilization:

> "Disinfection describes a process that eliminates many or all pathogenic microorganisms, except bacterial spores.
>
> Low-level disinfection—destruction of most bacteria, some viruses, and some fungi. Low-level disinfection will not necessarily inactivate *Mycobacterium tuberculosis* or bacterial spores.
>
> Midlevel disinfection—inactivation of *Mycobacterium Tuberculosis*, bacteria, most viruses, most fungi, and some bacterial spores.
>
> High-level disinfection—destruction/removal of all microorganisms except bacterial spores.
>
> Sterilization describes a process that destroys or eliminates all forms of microbial life and is carried out in health care facilities by physical or chemical methods."

The American Institute of Ultrasound in Medicine guidelines[1] also specify the level of cleaning and/or disinfection required for different types of devices:

> Critical instruments: devices intended to penetrate skin or mucous membranes (eg, surgical instruments) require sterilization.
>
> Semicritical instruments: devices that come into contact with mucous membranes (eg, vaginal ultrasound probes) require high-level disinfection.
>
> Noncritical devices that come into contact with intact skin but not mucous membranes (eg, external ultrasound probes) require only cleaning.

The US Food and Drug and Drug Administration lists a variety of sterilants and high-level disinfectants.[11] Commercial ultrasound probe-cleaning systems using glutaraldehyde, orthophthalaldehyde, and H_2O_2 are marketed in the United States under various brand names.

Two recent studies investigated the efficacy of various high-level disinfectants against human papilloma virus 16 and human papilloma virus 18. In the first study, human papilloma virus 16 was mixed with several disinfectants and incubated for 45 minutes.[2] Only peracetic acid-silver and hypochlorite significantly inactivated human papilloma virus 16 (5.2 and 4.8 $\log_{10}$ reduction in viral load, respectively). Glutaraldehyde and orthophthalaldehyde were ineffective at various concentrations (<0.02 $\log_{10}$ reductions), as were ethanol, isopropanolol, and phenol. The 45 minute incubation time was much longer than the 12 minute soaking time recommended in commercial probe-cleaning systems using glutaraldehyde and orthophthalaldehyde.

In the second study,[3] a solution containing human papilloma virus 16 or human papilloma virus 18 was spread onto a carrier made of the type of plastic used to make utrasound probes. After air drying, the carriers were treated with a hypochlorite or an orthophthalaldehyde disinfection system (Cidex orthophthalaldehyde; Advanced Sterilization Products, Irvine, CA) or an sonicated H_2O_2 system (Trophon EPR; Nanosonics, Lane Cove, Australia) according to the manufacturer's instructions. The hypochlorite and sonicated H_2O_2 systems both showed strong virucidal activity (4.6−5.0 and 5.2−7.4 $\log_{10}$ reductions in viral load, respectively), but the orthophthalaldehyde system did not (0.4 and 0.5 $\log_{10}$ reductions of human papilloma virus 16 and human papilloma virus 18, respectively).

The Food and Drug and Drug Administration's listing of glutaraldehyde and orthophthalaldehyde as high-level disinfectants is based on extensive testing demonstrating that these agents are effective against a variety of microbes. To demonstrate disinfectant efficacy against nonenveloped viruses, the Food and Drug and Drug Administration requires testing against poliovirus. However, one cannot extrapolate to assume that disinfectants are effective against all viruses. As stated by Meyers et al,[2] "Presently, hospitals' and other health care institutes' use of disinfectants to inactivate human papilloma virus is based on what is used for other viruses or simply on what someone thinks should be effective."

At present, the only system for high-level ultrasound probe disinfection with specific, proven efficacy against human papilloma virus is the sonicated H_2O_2 system, which treats the probe with a mist of H_2O_2 nanodroplets.

We are aware of another H_2O_2 system that involves soaking the probe rather than treating with a mist. We have 2 reservations about H_2O_2 soaking. First, at present, we do not have empiric evidence that soaking is actually effective against human papilloma virus. Second, unlike the sonicated H_2O_2 system, the soaking system disinfects only the transducer head, not the probe handle. Disinfection of the handle has been advocated as an important step in reducing risk of infection transmission[12,13] because the handle is not covered by many probe covers and may

inadvertently contact the patient's vulva during a transvaginal examination.

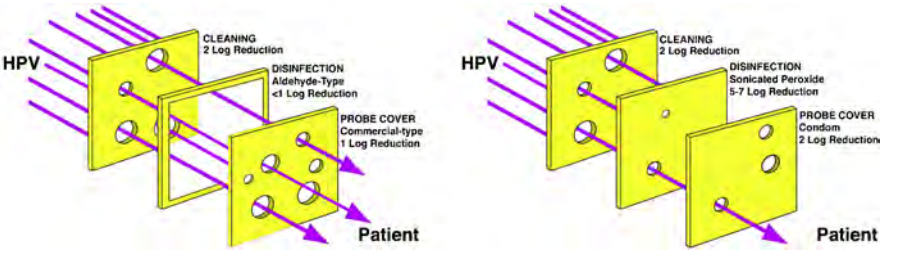
A disadvantage of the sonicated H_2O_2 system is its cost. The device currently costs several thousand dollars, and the consumables cost a few dollars per use. These costs may be offset by cost savings in other areas. The cycle time per probe is less than glutaraldehyde or orthophthalaldehyde soaking systems, which may result in improved patient flow. Also, the sonicated H_2O_2 system can be used at the point of care, so probes do not need to be sent off-site for centralized processing, which may reduce the number of probes needed by a practice. Also, personnel using the sonicated H_2O_2 system do not have to don protective gear as they do with toxic or volatile organic solvents like glutaraldehyde and orthophthalaldehyde. But even without these offsetting factors, the cost for the sonicated H_2O_2 system seems reasonable in our opinion, given its clear advantage in patient safety.

Step 3: barriers

The American Institute of Ultrasound in Medicine[1] guidelines state, "All internal probes should be covered with a single-use barrier." The guidelines cite evidence of unacceptably high leakage rates of commercial probe covers (8-81%).[14-16] The guidelines note that condoms are manufactured to a 6-fold enhanced acceptable quality level, the same as surgical gloves, and have leakage rates of 0.9-2%.[17-19]

Although the American Institute of Ultrasound in Medicine guidelines[1] stop short of a clear directive that condoms should be used during transvaginal ultrasound rather than commercial probe covers, condoms are clearly the safer alternative. We see no reason for anyone to use commercial probe covers for this purpose. Any difference in cost between condoms and probe covers is negligible. Nonlubricated, nonmedicated condoms are recommended[1] and are readily available through a number of suppliers. For latex-allergic patients, nonlubricated, nonlatex condoms may be used; if these are unavailable, a nonlatex surgical glove may be used (not an examination glove, which is manufactured to a lower acceptable quality level).

FIGURE
Swiss cheese models



Swiss cheese models illustrate that the risk of human papilloma virus (HPV) transmission depends on the combined effectiveness of three layers of protection. Aldehyde-type disinfectants and commercial probe covers (left panel) do not provide as much protection as sonicated peroxide disinfectant and condoms (right panel).

Combs. HPV on ultrasound probes. Am J Obstet Gynecol 2016.

Have women been harmed?

A recent systematic review[9] reported a pooled prevalence of 1.0% (range, 0-10%) for common genital tract viruses (human papilloma virus, herpes simplex virus, cytomegalovirus) after transvaginal ultrasound. However, the mere presence of virus does not prove a causal linkage. Thus, we do not know how many cases, if any, of human papilloma virus may have been transmitted by transvaginal ultrasound.

There have been a few well-documented outbreaks of *bacterial* infection transmitted by endocavitary ultrasound examinations, and these were generally attributed to suboptimal disinfection procedures, mainly the use of low-level disinfection for probes that required high-level disinfection.[9]

Layers of protection

One framework for conceptualizing patient safety is the Swiss cheese model by Reason,[20] which we have adapted in the Figure. In this model, the health care system attempts to insert layers of protection between a potential hazard (human papilloma virus) and the patient. None of the layers is perfect; rather, each of them has a finite failure rate, represented in the Figure by holes that appear like the holes in a slice of Swiss cheese. If all the layers fail, the hazard will reach the patient.

In this framework, our choices to optimize patient safety are to insert more layers or to make the existing ones better. In this case, we do not know of any new layers to insert. Thus, to optimize patient safety, we must pick the most effective protections (ie, we should use sonicated H_2O_2 rather than glutaraldehyde or orthophthalaldehyde and use condoms rather than commercial probe covers).

The American Institute of Ultrasound in Medicine guidelines[1] state, "All cleaning, disinfection, and sterilization represent a statistical reduction in the number of microbes present on a surface rather than their complete elimination."

The Table quantitates this by estimating the reduction in viral load for each step. We used the following estimates: for cleaning, 99% reduction is assumed[1] (2 $\log_{10}$ reduction); for disinfection with glutaraldehyde or orthophthalaldehyde, reduction of 0−0.5 $\log_{10}$ is taken from the studies cited[2,3]; for disinfection with sonicated H_2O_2, reduction of 5.2−7.4 $\log_{10}$ is taken from the study cited[3]; for commercial probe covers, a leakage rate of 8−81%[1] corresponds to a 0.1−1.1 $\log_{10}$ reduction; for condoms, a leakage rate of 0.9−2%[1] corresponds to a 1.7−2.0 $\log_{10}$ reduction.

The total reduction in viral load for all 3 steps in sequence (cleaning, disinfection, covering) is obtained by adding the log reductions, the mathematical equivalent of multiplying the

TABLE

Reduction of human papilloma virus viral load by method of disinfection and type of probe covering

Variable	GTA or OPA plus commercial cover	GTA or OPA plus condom	Sonicated peroxide plus comercial cover	Sonicated peroxide plus condom
Reduction in viral load from cleaning (log_{10})	2	2	2	2
Reduction in viral load from disinfectant (log_{10})	0–0.5	0–0.5	5.2–7.4	5.2–7.4
Reduction in viral load from cover (log_{10})	0.1–1.1	1.7–2.0	0.1–1.1	1.7–2.0
Combined reduction in viral load (log_{10})	2.1–3.6	3.7–4.5	7.3–10.5	8.9–11.4
Combined reduction in viral load (log_{10})	130–4000	5000–32,000	20 million to 32 billion	800 million to 250 billion

GTA, glutaraldehyde; *OPA*, orthophthalaldehyde.

Combs. HPV on ultrasound probes. Am J Obstet Gynecol 2016.

natural numbers. To convert to a fold reduction, the antilog of the total log reduction is taken. By these estimates, the combination of sonicated H_2O_2 plus condom results in an 800 million- to 250 billion-fold reduction in the human papilloma virus load, which is at least 200,000-fold better than the combination of glutaraldehyde or orthophthalaldehyde plus acommercial probe cover.

Call to action: recommendations for safest practice

Based on currently available information, we have 3 recommendations for providers of transvaginal ultrasound:

1. A condom should be used to cover the probe during transvaginal ultrasound examination. Commercial probe covers should not be used. If the patient has latex allergy, a nonlatex surgical glove may be used to cover the probe.
2. Sonicated H_2O_2 should be used to disinfect the probe and handle after every transvaginal ultrasound examination. At present, only the Trophon system (Nanosonics) has demonstrated efficacy specifically against human papilloma virus, but this may change if new data become available.
3. All the recommendations in the American Institute of Ultrasound in Medicine guidelines[1] should be followed regarding cleaning, disinfection, covering, and handling of internal-use ultrasound probes. Our recommendations are more directive regarding 2 specific issues but are not intended to supplant the American Institute of Ultrasound in Medicine guidelines in any other way.

Finally, we recommend that the Food and Drug Administration consider adding neutralization of human papilloma virus to its standards for high-level disinfectants. Human papilloma virus is much more prevalent than poliovirus and causes significant disease in anal, genital, and oropharyngeal sites in which endocavitary ultrasound is commonly performed.

On March 4, 2016, the United States Food and Drug Administration granted a clearance to Sheathing Technologies (Morgan Hill, California), a manufacturer of polyurethane commercial ultrasound probe covers, allowing the words "viral barrier" to be added to the product labelling. The clearance was based on the manufacturer's bench tests showing that the material was impervious to Minute Mouse Virus which is 20 nm in diameter. It is assumed that the material should be impervious to any virus larger than 20 nm, including human papilloma virus which is about 55 nm in diameter. Thus, this brand of probe cover would appear to be a reasonable alternative to latex-free condoms for use in transvaginal ultrasound. We are not aware of any other brand of probe cover that has the labelling "viral barrier." Further details are available at: http://www.accessdata.fda.gov/cdrh_docs/pdf15/K153212.pdf (accessed April 18, 2016). ■

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