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Ophthalmic Technology Assessment

Disinfection of Tonometers

A Report by the American Academy of Ophthalmology

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Objective: To examine the efficacy of various disinfection methods for reusable tonometer prisms in eye care and to highlight how disinfectants can damage tonometer tips and cause subsequent patient harm.

Methods: Literature searches were conducted last in October 2016 in the PubMed and the Cochrane Library databases for original research investigations. Reviews, non-English language articles, nonophthalmology articles, surveys, and case reports were excluded.

Results: The searches initially yielded 64 unique citations. After exclusion criteria were applied, 10 laboratory studies remained for this review. Nine of the 10 studies used tonometer prisms and 1 used steel discs. The infectious agents covered in this assessment include adenovirus 8 and 19, herpes simplex virus (HSV) 1 and 2, human immunodeficiency virus 1, hepatitis C virus, enterovirus 70, and variant Creutzfeldt-Jakob disease. All 4 studies of adenovirus 8 concluded that after sodium hypochlorite (dilute bleach) disinfection, the virus was undetectable, but only 2 of the 4 studies found that 70% isopropyl alcohol (e.g., alcohol wipes or soaks) eradicated all viable virus. All 3 HSV studies concluded that both sodium hypochlorite and 70% isopropyl alcohol eliminated HSV. Ethanol, 70% isopropyl alcohol, dilute bleach, and mechanical cleaning all lack the ability to remove cellular debris completely, which is necessary to prevent prion transmission. Therefore, single-use tonometer tips or disposable tonometer covers should be considered when treating patients with suspected prion disease. Damage to tonometer prisms can be caused by sodium hypochlorite, 70% isopropyl alcohol, 3% hydrogen peroxide, ethyl alcohol, water immersion, ultraviolet light, and heat exposure. Disinfectants can cause tonometer tips to swell and crack by dissolving the glue that holds the hollow tip together. The tonometer tip cracks can irritate the cornea, harbor microbes, or allow disinfectants to enter the interior of the tonometer tip.

Conclusions: Sodium hypochlorite (dilute bleach) offers effective disinfection against adenovirus and HSV, the viruses commonly associated with nosocomial outbreaks in eye care. Tonometer prisms should be examined regularly for signs of damage. *Ophthalmology 2017;124:1867-1875 © 2017 by the American Academy of Ophthalmology*

The American Academy of Ophthalmology prepares Ophthalmic Technology Assessments to evaluate new and existing procedures, drugs, and diagnostic and screening tests. The goal of an Ophthalmic Technology Assessment is to review systematically the available research for clinical efficacy and safety. After review by members of the Ophthalmic Technology Assessment Committee, other Academy committees, relevant subspecialty societies, and legal counsel, assessments are submitted to the Academy's Board of Trustees for consideration as official Academy statements. The purpose of this assessment by the Ophthalmic Technology Assessment Committee Glaucoma Panel is to investigate the disinfection methods for reusable tonometer prisms in eye care.

Background

Terminology

Cleaning, Disinfection, and Sterilization. Any procedure that involves contact of a medical device or surgical instrument with the patient's ocular surface may pose a risk for introducing infectious agents. Failure to disinfect or sterilize equipment may lead to the transmission of pathogens from either the environment or another person. Prevention of iatrogenic infection is based on a process of cleaning and then sterilizing or disinfecting reusable medical equipment. *Cleaning*, defined by the Centers for Disease Control and Prevention (CDC), is the removal of visible soil

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using water with detergents or enzymatic products. This process is followed by *sterilization*, the complete removal or destruction of all forms of microbial life, or by disinfection. The *disinfection* process eliminates many or all micro-organisms except bacterial or fungal spores. The efficacy of both sterilization and disinfection is affected by many factors: prior cleaning methods; the nature of the instrument or device (e.g., material properties; presence of a lumen, crevices, or both); the presence of biofilm on the device; the temperature, pH, and exposure time used; and in some cases, the humidity of the agent used to disinfect or sterilize.[1,2]

Critical, Semicritical, and Noncritical Devices. A classification system first devised by Spaulding in 1968[3] divides instruments for patient care into critical, semicritical, and noncritical categories, based on the risk of infection. *Critical* devices carry a high risk of infection if contaminated with any micro-organism. This category includes surgical instruments, implants, and needles for venipuncture or intravitreal injection. Instruments in this category either should be steam sterilized or purchased sterile. *Semicritical* instruments are defined as devices that come in contact with intact mucous membranes or nonintact skin. Intact mucous membranes generally are resistant to infection by common bacterial spores, but are susceptible to more virulent infectious agents. The CDC considers applanation tonometers to be semicritical devices.[1] Cleaning, followed by high-level disinfection, should eliminate enough pathogens to prevent transmission of infection as recommended by the CDC.[1] The CDC defines germicides as chemicals that inactivate all microbial pathogens, except large numbers of bacterial and fungal spores, as high-level disinfectants provided they are used according to the label. High-level disinfectants can be considered sterilants when used under the same contact conditions except for a shorter contact time.[2] The CDC considers high-level disinfection with a sterilant cleared by the United States Food and Drug Administration as the minimum requirement for the reuse of semicritical instruments. *Noncritical* items come in contact with intact skin, but not mucous membranes.[3]

Commonly Used Chemical Disinfectants in Eye Care

Ideally, the tonometer disinfection process should cover a broad antimicrobial spectrum; should act rapidly; should not damage the tonometer tip; and should be nontoxic to the user, patient, and environment. Three groups of commonly used disinfectants in eye care include alcohols, chlorine, and hydrogen peroxide.

Alcohols. Seventy percent isopropyl alcohol and 70% ethyl alcohol can be rapidly germicidal against bacteria, fungi, and viruses by denaturating proteins, but these disinfectants do not destroy bacterial spores. Both 70% isopropyl and 70% ethyl alcohol can inactivate human immunodeficiency virus (HIV), and 70% isopropyl alcohol kills *Acanthamoeba* cysts effectively. The CDC does not recommend alcohols for sterilizing medical and surgical materials because alcohols lack sporicidal action and they are not able to penetrate protein-rich materials.[1] The Food and Drug Administration does not consider alcohols or dilute bleach to be high-level disinfectants.[2]

Chlorine and Chlorine Compounds. Dilute bleach is a ubiquitous disinfectant. Dilute bleach is used in 1:10 and 1:20 concentrations for disinfection. Bleach has a broad spectrum of antimicrobial activity, does not leave toxic residues, is not affected by water hardness, and acts fast. Bleach oxidizes cell membranes and denatures proteins, which leads to loss of structure and cell lysis. Dilute bleach is biocidal against HIV, bacteria, bacterial spores, mycoplasma, mycobacterium tuberculosis, and fungi.[1]

Hydrogen Peroxide. Hydrogen peroxide's germicidal effect is attributed to destructive hydroxyl free radicals that oxidize membrane lipids, DNA, and other essential cell components.[1] Anaerobic and facultative anaerobes may be resistant to hydrogen peroxide in low concentrations.[1] Ten percent hydrogen peroxide deactivates a wide range of micro-organisms, including *Acanthamoeba* cysts, bacteria, yeasts, fungi, viruses, and spores.[1]

Damage to Tonometer Tips Caused by Disinfectants

All disinfectants, including dilute bleach, hydrogen peroxide, isopropyl alcohol (wipes or soaks), ethyl alcohol, prolonged soaking, heat (temperatures of more than 60°C), and ultraviolet light, have been identified as causing tonometer prism damage and may result in patient injury.[4–10]

Lingel and Coffey[7] conducted laboratory experiments studying damage to tonometers caused by disinfection using 1:10 dilute bleach, 3% hydrogen peroxide, and 70% isopropyl alcohol soaks. Three tonometer prisms each were soaked for 2 hours at a time, 4 times daily, 5 days weekly, for a total of 3 weeks. After each disinfecting soak, tonometers were rinsed with distilled water, dried with cotton, and inspected at a biomicroscope to grade for visual appearance and clarity. Tonometer damage by these 3 disinfectant soaks was compared with tonometer damage by 70% isopropyl alcohol wipes followed by a saline rinse. The tonometer prisms were noted to swell after disinfectant soaks. The increased diameter made it difficult to reinsert the tonometer prism into the holder. However, this did not affect intraocular pressure measurements. Seventy percent isopropyl alcohol soaks caused the most severe damage to the prisms, both to the glued parts and the prism surface, rendering them unusable for applanation after 4 days. Seventy percent isopropyl alcohol wipes caused damage to the glued ring structure of the prism, but did not affect accuracy. Soaking in both dilute bleach and 3% hydrogen peroxide left a hazy film over the prism surface. The film could be removed mechanically with a hard contact lens cleaner, but prisms soaked in dilute bleach retained a blue glow that diminished only after 3 weeks of air drying.

In summary, all disinfectants inevitably affect the glue that holds the hollow tip together and cause cracks in the rim of the tonometer tips. These cracks can irritate the cornea, harbor microbes, or allow disinfectants to get into the interior of the tonometer tip. The disinfectants then can leak

back onto the cornea, causing burns and abrasions. Therefore, routine inspection of tonometer tips should be performed at the slit lamp, and damaged tonometer tips should be replaced.

Common Causes of Ophthalmic Nosocomial Outbreaks

Ophthalmic nosocomial outbreaks are most commonly linked to adenovirus 8,[11–21] adenovirus 19,[16] and herpes simplex virus (HSV) 1.[16,17] Investigations into clusters of epidemic keratoconjunctivitis have identified tonometer tips, eye drop bottles, gonioscopy, minor surgical procedures, finger-to-eye contact, slit lamps, disinfection with 70% isopropyl alcohol wipes, and even individual health care providers as the sources of outbreaks.[11–18,21] Adenoviruses are especially hardy, and desiccated virus remains viable and can be recovered after 49 days on dried plastic or metal surfaces.[22] Other infectious agents with the potential to be transmitted during applanation include HIV, hepatitis C virus (HCV), enterovirus 70, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, *Acanthamoeba*, and prions.[17,23–29] Prevention of prion transmission is particularly challenging because patients may be asymptomatic for decades, and the prevalence of asymptomatic individuals is unknown. The CDC reports 4 cases of variant Creutzfeldt-Jakob disease (vCJD) in the United States.[30] Sporadic Creutzfeldt-Jakob disease (CJD) occurs at a rate of 1 to 1.5 cases per 1 million population per year.[31] Gill et al[32] tested 32 441 archived appendix samples in the United Kingdom for the presence of abnormal prion protein and detected 16 samples demonstrating positive results. Based on their findings, the authors estimated the number of asymptomatic carriers of prion disease to be 493 per 1 million population in the United Kingdom. The incubation period for prion disease may exceed 50 years by some estimates.[33] Corneal epithelial cells retained on tonometer prism surfaces may be a source of transmission of CJD.[34] Both ethyl and isopropyl alcohol are known to bind proteins to smooth surfaces, and therefore should be avoided to prevent prion transmission.[35]

Centers for Disease Control and Prevention and Manufacturer Guidelines for Disinfection of Tonometer Tips

In 2008, the CDC published guidelines for disinfection and sterilization in health care facilities based on the latest evidence available at that time.[1] The CDC removed several agents from the list of previously approved high-level disinfectants. Of importance for eye care professionals, 70% isopropyl alcohol and ethyl alcohol are no longer considered high-level disinfectants because of their inability to inactivate bacterial spores and because isopropyl alcohol does not inactivate hydrophilic viruses (i.e., poliovirus, coxsackie virus). Both 3% hydrogen peroxide and 70% isopropyl alcohol are no longer recommended by the CDC for tonometer disinfection because they have been associated with adenovirus epidemic keratoconjunctivitis outbreaks and because data suggest that they are ineffective against adenovirus. Ten percent hydrogen peroxide has been added to the list of recommended high-level disinfectants.

The current Guideline for Disinfection and Sterilization in Healthcare Facilities[1] recommends that health care professionals "wipe clean tonometer tips and then disinfect them by immersing for 5 to 10 minutes in either 5000 ppm chlorine or 70% ethyl alcohol." Five thousand parts per million (ppm) chlorine is equivalent to 1:20 household bleach.

Tonometer manufacturers[36,37] recommend either 3% hydrogen peroxide or 1:10 dilute bleach for tonometer disinfection. Tonometer manuals further contain a warning not to use alcohols, acetone, ultraviolet radiation, steam sterilization, or ethylene oxide; to avoid immersion in any fluid for more than 1 hour; and to avoid temperatures of more than 60°C to prevent damage. Manufacturers also advise that tonometer prisms should be replaced 2 years after first use, after a maximum of 100 disinfection cycles with 1:10 dilute bleach, or immediately if damaged.

This Ophthalmic Technology Assessment was performed to evaluate critically the evidence in the literature supporting different disinfection methods used in eye care.

Question for Assessment

This purpose of this assessment was to address the following question: What is the evidence for current recommendations for disinfection of tonometer prisms?

Description of Evidence

Literature searches last conducted in October 2016 in the PubMed and Cochrane Library databases resulted in 64 potentially relevant citations. Thirty-eight articles were excluded because they were review articles or relevant to medical specialties other than ophthalmology. Sixteen of the remaining 26 citations were excluded because they were surveys (n = 7), case reports (n = 8), or non-English language articles (n = 1). The remaining 10 articles were laboratory studies relevant to the topic. The search terms used are as follows:

(*Infection Control*[MeSH] OR *infection control*[tiab] OR *Sterilization*[Mesh] OR *sterilization*[tiab] OR *Disinfection* [MeSH] OR *disinfection*[tiab] OR *cross infection* [MeSH] OR *cross infection*[tiab] OR *equipment reuse* [MeSH]) ((*tonopen* OR *goldmann* OR *applanation*)) AND (*Tonometry, Ocular*[MeSH] OR *tonometry* OR *tonometer**)

Published Results

The 10 articles included in the final review are laboratory studies that investigated various disinfection methods that can be applied to reusable tonometer tips: 9 studies used tonometer prisms, 1 study used steel discs, 5 studies focused on adenovirus 8 and 19, 2 studies evaluated enterovirus 70, 3 studies evaluated HSV 1 and 2, 1 study evaluated HIV type 1, 1 study evaluated HCV, and 2 studies focused on prion transmission (or CJD). All of the studies

included in this review were limited by small sample size (2 to 5 samples per experimental group).

Studies Testing Only Adenovirus 8

Craven et al[23] tested the efficacy of 6 cleaning methods and showed that all 6 were effective for the eradication of adenovirus 8 from tonometer tips. In this study, tonometers were inoculated for 15 seconds in an adenovirus 8 suspension (45 $TCID_{50}$/0.1 ml; TCID = tissue culture infective dose). Sets of 3 tonometer tips were subjected to 6 different cleaning techniques. The tips were processed immediately after inoculation using 1 of the following techniques: (1) 5-second wipe with dry tissue, (2) 5-second wipe with commercially available 70% isopropyl alcohol prep pads, (3) 5-second wipe with 1:1000 merthiolate-moistened tissue, (4) 15-minute soak in 1:10 dilute bleach followed by irrigation with 5 ml sterile water, (5) 15-minute soak in 70% isopropyl alcohol followed by irrigation with 5 ml sterile water, and (6) 15-minute soak in 3% hydrogen peroxide followed by irrigation with 5 ml sterile water (Table 1). The results were compared with the following controls: 3 tonometer tips that were recultured immediately and 3 tonometer prisms that were air dried for 15 minutes after inoculation and then cultured. None of the tonometer tips cleaned with any of the 6 methods described yielded any detectable adenovirus in culture, whereas adenovirus 8 was recovered from the controls. Wiping the contaminated tip with dry tissue was as successful as wiping with 70% isopropyl alcohol wipes. This study was critiqued for its small sample size and low virus concentration.[24]

In another study using tonometer tips, Threlkeld et al[25] showed that 3 disinfectants (3% hydrogen peroxide, 70% isopropyl alcohol pads, and iodophor preparation) were effective against adenovirus 8 regardless of whether these disinfectants were used as wipes or soaks. The study evaluated the efficacy of various disinfectants for the elimination of adenovirus 8 (8.4×10^3–1.0×10^5 plaque-forming units [PFUs]/ml) from tonometer tips. The first part of the study evaluated various cleaning methods using wipes, and the second part of the study evaluated various cleaning methods using soaks. The first part of the study included 3 sets of experiments: tips either were processed immediately (control); air dried for 15 minutes (control); or subjected to a 5-second wipe with a dry gauze, 5-second wipe with a gauze soaked in tap water, 5-second wipe with a 70% isopropyl alcohol pad, 5-second wipe with a gauze soaked with 3% hydrogen peroxide, or 5-second wipe with an iodophor preparation pad. After exposure to 3% hydrogen peroxide and iodophor wipes, the tonometer tips were rinsed for 15 seconds in running cold tap water and air dried for 15 minutes. No virus was detected after wiping with cold tap water or using a 3% hydrogen peroxide wipe, 70% isopropyl alcohol wipe, and iodophor wipe on Goldmann tonometer tips compared with controls. Only wipes with dry gauze seemed to be ineffective for disinfection of tonometers. The data suggest that isopropyl alcohol wipes are superior to dry wipes and as effective as gauze wipes with tap water. This study was critiqued for its small sample size and low virus concentration.[24]

For the second part of the Threlkeld et al study,[25] which evaluated soaks, experiments also were performed in triplicate. Goldmann tonometer tips either were processed immediately (controls); air dried for 15 minutes and processed; or rinsed under running cold tap water for 5 seconds, soaked in cold tap water for 5 minutes, soaked in 3% hydrogen peroxide for 5 minutes, soaked in iodophor for 5 minutes, or soaked in 1:10 dilute bleach for 5 minutes. All tips soaked in disinfectant then were rinsed for 5 seconds under running cold tap water and air dried for 15 minutes. No virus was recovered after soaking tonometer tips in 3% hydrogen peroxide, iodophor, or 1:10 dilute bleach. Soaking in tap water or air drying did not reduce virus counts, whereas soaking in 1:10 dilute bleach or 3% hydrogen peroxide was effective.

Rutala et al[24] inoculated steel discs with adenovirus 8 solution. Based on data that demonstrated that adenovirus 8 was as hardy and viable on steel discs as on plastic surfaces,[22] steel discs were chosen to model applanation prisms. In this study, inoculated steel discs were air dried for 40 minutes and then either 50 μl of control solution or 1 of 21 different germicides were added for 1 or 5 minutes. Next, 5% fetal calf serum with neutralizer was added to neutralize the germicide. The inoculum was eluted and titrated in cell culture to determine loss in virus viability in log units. Each germicide was tested 2 to 5 times in this manner. The 7 germicides that demonstrated at least 3-log unit reduction of adenovirus 8 titer after 1-minute exposure were considered effective. They included the following: 0.55% ortho-phthalaldehyde (Cidex OPA; Advanced Sterilization Products, Irvine, CA), 0.2% peracetic acid (Steris 20 sterilant; STERIS Corporation, Mentor, OH), 2.4% glutaraldehyde (Cidex; Advanced Sterilization Products), 2.65% glutaraldehyde (Wavicide-01; Medical Chemical Corporation, Torrance, CA), 6000 ppm chlorine (0.6% bleach), 1900 ppm chlorine (Clorox Clean-up; Clorox Company, Oakland, CA), and 79.6% ethanol with 0.1% quaternary ammonium compound (Lysol brand II disinfectant spray; Reckitt Benckiser, Inc., Parsippany, NJ). The 2 germicides that showed at least 3-log unit reduction of adenovirus 8 titer after a 5-minute exposure, but less than 3-log unit reduction after a 1-minute exposure, included 70% ethanol and 65% ethanol with 0.63% quaternary ammonium compound (Clorox disinfectant spray; Clorox Company). The 12 germicides that were considered ineffective did not achieve at least a 3-log unit adenovirus 8 titer reduction. They included the following: 3% hydrogen peroxide, 0.0625% quaternary ammonium compound (TBQ; STERIS Corporation), 0.13% phenolic (Vesphene IIse; STERIS Corporation), 70% isopropyl alcohol, 10% povidone iodine (Novaplus; Novation LLC, Irving, TX), 0.24% and 0.12% chloroxylenol (Dettol; Reckitt Benckiser, Hull, United Kingdom), 4% chlorhexidine gluconate (BactoShield; STERIS Corporation), 0.5% triclosan (Medicated Soft 'N Sure; STERIS Corporation), 1% chloroxylenol (Acute-Kare; STERIS Corporation), 0.5% accelerated hydrogen peroxide (Accel TB; Virox Technologies, Inc., Oakville, Canada), 80 ppm chlorine (Microcyn; Sonoma Pharmaceuticals [formerly Oculus Innovative Sciences], Petaluma, CA), and 218 ppm chlorine (Sterilox; Sterilox Technologies, Radnor, PA). Rutala et al[24] noted that compared with other studies, they used higher adenovirus concentrations, longer air drying, and simulated organic matter (fetal calf serum) to make sterilization more challenging. The key findings of this 2006 study by Rutala et al were that 3% hydrogen peroxide and 70% isopropyl alcohol are not effective against adenovirus 8. Rutala is the lead author of the current CDC Guideline for Disinfection and Sterilization in Healthcare Facilities.[1]

Table 1. Cleaning and Disinfection of Tonometers

Type of Agent	Manufacturer and Location	Adenovirus	Herpes Simplex Virus	Enterovirus 70	Human Immunodeficiency Virus	Hepatitis C Virus
Agents effective in elimination of viral pathogens:						
Sodium hypochlorite soak (1:10 dilute bleach)		15 mins effective[23] 5 mins effective[25] 1 min effective[24]	Effective[27]			
0.05% sodium hypochlorite soak		2 mins effective[17]	2 mins effective[17]	2 mins effective[17]		
Cidex OPA*	Advanced Sterilization Products, Irvine, CA	1 min effective[24]				
Steris 20 sterilant*	STERIS Corporation, Mentor, OH	1 min effective[24]				
Cidex*	Advanced Sterilization Products, Irvine, CA	1 min effective[24]				
Wavicide-01*	Medical Chemical Corporation, Torrance, CA	1 min effective[24]				
Clorox Clean-up*	Clorox Company, Oakland, CA	1 min effective[24]				
Lysol II disinfectant spray*	Reckitt Benckiser, Inc., Parsippany, NJ	1 min effective[24]				
Clorox disinfectant spray*	Clorox Company, Oakland, CA	5 mins effective[24]				
70% ethanol soak†		5 mins effective[24]				
Agents with controversial evidence, ineffective for viral pathogens in at least 1 study:						
3% hydrogen peroxide wipe		Effective[25]			Effective[28]	
3% hydrogen peroxide soak		15 mins effective[23] 5 mins effective[25] 5 mins ineffective[24]				99.5% reduction[29]
70% isopropyl alcohol wipe†,‡		Effective[23,25]	Effective[27]		Effective[28]	Ineffective[29]
70% isopropyl alcohol soak†,‡		15 mins effective[23] 5 mins ineffective[17,24]	Effective[27]			99.5% reduction[29]
Phenyl mercuric (borate or nitrate)‡		Wipe: effective[23] Soak: ineffective[17]	Ineffective[17]	Ineffective[17]		
10% povidone iodine wipe		Effective[25]				95% reduction[29]
10% povidone iodine soak		5 mins effective[25] 5 mins ineffective[24]				
Dry wipe		Effective[23] Ineffective[25]	Ineffective[27,28]		Ineffective[28]	
Other agents apparently effective in eliminating viral pathogens:						
Water wipe		Effective[25]				99% reduction[29]
Agents ineffective for eliminating viral pathogens after 5 mins (or not tested for viral pathogens):						
TBQ	STERIS Corporation, Mentor, OH	Ineffective[24]				
Vesphene IIse	STERIS Corporation, Mentor, OH	Ineffective[24]				
Dettol	Reckitt Benckiser, Hull, United Kingdom	Ineffective[24]				
BactoShield	STERIS Corporation, Mentor, OH	Ineffective[24]				
Medicated Soft 'N Sure	STERIS Corporation, Mentor, OH	Ineffective[24]				
Acute-Kare	STERIS Corporation, Mentor, OH	Ineffective[24]				
Accel TB	Virox Technologies, Inc., Oakville, Canada	Ineffective[24]				
Microcyn	Sonoma Pharmaceuticals (formerly Oculus Innovative Sciences), Petaluma, CA	Ineffective[24]				

(*Continued*)

Table 1. (Continued.)

Type of Agent	Manufacturer and Location	Adenovirus	Herpes Simplex Virus	Enterovirus 70	Human Immunodeficiency Virus	Hepatitis C Virus
Sterilox	Sterilox Technologies, Radnor, PA	Ineffective[24]				
Sekusept	Ecolab Healthcare UK, Northwich, United Kingdom	Not tested				
Pantasept	Haag-Streit International, Koeniz, Switzerland	Not tested				
Ultraviolet radiation[†]		Eradication after 90 mins[26]		Eradication after 1.5 mins[26]		
Water soak		Ineffective[25]				
Air drying		Ineffective[25,26]	Inactivation after 120 mins[27]	Undetectable after 4 hrs[26]		

*Not registered by the United States Food and Drug Administration as a high-level disinfectant or chemical sterilant for disinfection of medical devices in contact with mucous membranes.
†Tonometer prism manufacturers warn users to avoid these disinfectants because they are incompatible with the polymethyl methacrylate material of the prism. This warning includes use of any alcohols (ethanol and isopropyl alcohol), acetone, ultraviolet radiation, steam or ethylene oxide sterilization, immersion in fluid for more than 1 hour, and temperature of more than 140°F (60°C).
‡Associated with adenovirus outbreaks.

Studies Testing Adenovirus 8 and 19, Enterovirus 70, Herpes Simplex Virus 1 and 2, Human Immunodeficiency Virus 1, and Hepatitis C Virus

Hara et al[26] used tonometer tips to evaluate the efficacy of various disinfectants against adenovirus 19 and enterovirus 70 (Table 1). Adenovirus 19 (10^5 $TCID_{50}$/ml) or enterovirus 70 (10^8 PFU/ml) were applied to 6 Goldmann tonometer tips, after which the tips were air dried at room temperature. Using air drying as the control group, they investigated the effect of disinfection using ultraviolet light or heat (90°C) on adenovirus 19 and enterovirus 70. No enterovirus 70 was recovered after 4 hours of air drying, whereas adenovirus 19 maintained the same initial infectious level for 11 days. Viral disinfection of tonometers using ultraviolet light achieved complete inactivation of enterovirus 70 within 1.5 minutes. Adenovirus 19 was 60 times more resistant to ultraviolet light than enterovirus 70, and therefore ultraviolet light was not effective against adenovirus. Although heat (90°C) was effective against adenovirus 19 and enterovirus 70, manufacturers do not advise temperatures of more than 60°C because excessive heat can damage the tonometer tips.

Nagington et al[17] studied the efficacy of 3 disinfectants for the eradication of adenovirus 8, enterovirus 70, and HSV 1 from tonometer tips. Adenovirus 8 (viral concentration not given), enterovirus 70 (10^{4-5} TCD_{50}), and HSV 1 (viral concentration not given) were applied onto tonometer prisms to investigate the efficacy of 0.05% sodium hypochlorite (1:20 dilute bleach), phenyl mercuric borate, and isopropyl alcohol as disinfectants. The applied tonometer tips were dipped into the disinfectant and removed after intervals to test for viral activity. Two minutes in 0.05% sodium hypochlorite rendered adenovirus 8, enterovirus 70, and HSV 1 undetectable. No reduction in viability was observed with phenyl mercuric borate. Isopropyl alcohol was highly effective against HSV 1, but had a negligible effect as a disinfectant for adenovirus 8 and enterovirus 70.

Ventura and Dix[27] evaluated the efficacy of 10% Clorox, 70% isopropyl alcohol swabs, and dry wipes for the eradication of HSV 1 from tonometer prisms. One thousand PFUs of HSV were placed on 10 to 12 tonometer tips to determine HSV 1 viability for up to 120 minutes. Plaque-forming units began to decline with natural drying after 60 minutes; no viable HSV 1 was detected at 120 minutes. In contrast, a humid environment prolonged HSV 1 survival. Five microliters of various eye drop solutions placed on inoculated tonometer tips had no virucidal effect. Herpes simplex virus 1 was completely eliminated by both 5 μl 1:10 dilute bleach and 5 μl 70% isopropyl alcohol applied to tonometer tips. Wiping tonometer tips with dry gauze did not eliminate HSV 1.

Pepose et al[28] studied the elimination of HIV type 1, HSV 1, and HSV 2 from tonometer prisms using either dry wipes, 70% isopropyl alcohol wipes, or 3% hydrogen peroxide. An unreported number of used and new Goldmann tonometer tips were submerged in 500 μl of 5×10^5 IU cell-free or cell-associated HIV type 1 or incubated with 10 μl of 10^4 PFU HSV 1 or HSV 2 for 10 minutes at room temperature. The tonometers were air dried for 10 minutes and either wiped with dry gauze, wiped with gauze soaked in 3% hydrogen peroxide, wiped with 70% isopropyl alcohol pads, or processed as untreated controls. Next, the tonometer tips were incubated within virus-specific growth media and periodically assayed for HIV type 1-specific

antigens for up to 30 days and assayed for HSV 1 and 2 for 72 hours. Sterile gauze and tissue wipes were not effective for the test viruses. Both 70% isopropyl alcohol wipes and 3% hydrogen peroxide wipes were effective disinfectants for eliminating HIV type 1, HSV 1, and HSV 2.

Led by the discovery that HCV can be detected in tears, Segal et al[29] studied disinfectants for their potency to eliminate HCV from Goldmann tonometer prisms. In this study, 5 μl or 3.5 μl of HCV 2×10^7/ml were placed on Goldmann tonometers and left to dry for 20 minutes or 1 hour, respectively. Wiping tonometer tips with dry gauze or 70% isopropyl alcohol (5 seconds or 15 seconds) was not effective against HCV. Wiping with povidone iodine 10% (5 or 15 seconds) or washing with cold water for 10 seconds removed more virus (95% and 99%, respectively). In a second set of experiments, HCV-inoculated tonometer tips were soaked for 5 minutes either in 3% hydrogen peroxide or 70% isopropyl alcohol, or they were washed with cold water for 15 seconds. Soaking in 3% hydrogen peroxide or 70% isopropyl alcohol reduced HCV by 0.05% or less compared with controls. None of the disinfectants used completely eliminated HCV from tonometer tips. This study did not examine the efficacy of hypochlorite, but 1:10 dilute bleach was found to be very effective against HCV in a nonophthalmic context.[38]

Studies Addressing Risk of Prion (Variant Creutzfeldt-Jakob Disease) Transmission through Retained Cellular Debris on Tonometers

Lim et al[39] investigated the retention of corneal epithelial cells on tonometer prisms as an indicator for risk of vCJD transmission. They compared Goldmann prisms after intraocular pressure measurements of 10 patients who routinely were taking glaucoma medications (reference group) with those of 10 patients who were not using any eye drops. The authors found more epithelial cells on prisms from patients using glaucoma medications (mean, 156 cells; range, 0−470 cells) compared with patients not using eye drops (mean, 14 cells; range, 4−57 cells; $P = 0.004$). The tonometer prisms from patients using glaucoma medications were selected for further studies. Using the reference group with a mean of 156 cells for comparison, they found that an immediate dry-tissue wipe of 10 tonometers reduced cell numbers to a mean of 9 cells (range, 2−35 cells; $P = 0.004$). An immediate dry-tissue wipe of 10 tonometers, followed by a 10-minute soak in 0.05% sodium hypochlorite, did not further reduce retained cell counts (mean, 10 cells; range, 4−35 cells; $P = 0.003$). If tonometers first were allowed to dry for 24 hours, subsequent delayed dry wiping was less effective in reducing cell counts (delayed dry wiping: mean, 116 cells; range, 23−320 cells; $P = 0.5$) than immediate dry wiping. However, tonometers dried for 24 hours and then soaked in 0.05% bleach for 10 minutes yielded fewer retained cells (mean, 11 cells; range, 1−42 cells; $P = 0.004$). Ten tonometer tips, which were washed with running water immediately after applanation, dry wiped with tissue, and then soaked for 10 minutes in 0.05% bleach, also retained a low cell count (mean, 7 cells; range, 2−26 cells; $P = 0.003$). The reduction of cell counts was comparable among these procedures (except for 24-hour air drying followed by dry wiping), but none of the tested disinfection methods reduced cell counts to 0.

Amin et al[40] used 12 disposable acrylic tonometer tips to applanate patients and studied protein retention and the implied risk for vCJD transmission. They compared tips with no cleaning (n = 4), tips soaked for 5 minutes in 1 ml ultrapurified water (n = 4), and tips rinsed for 5 minutes with 50 ml ultrapurified water (n = 4). The amount of protein recovered varied substantially among patients (mean, 7.6 μg; standard deviation, ±8.4 μg; range, 4.3−>20 μg). Soaking the tip in 1 ml ultrapurified water decreased protein retention, which was reduced further when tips were rinsed using 50 ml ultrapurified water. Applying a 70% isopropyl alcohol swab tended to reduce protein quantity further, but did not completely eradicate protein carryover. The statistical significance of the procedures described could not be determined because of the small sample size and wide interpatient variability.

The risk of prion transmission from retained epithelial cells on tonometers currently is unknown. The prion load conveyed to the recipient of a full-thickness corneal graft is far greater than that conveyed by 9 to 10 epithelial cells on a tonometer tip.[41] Furthermore, a study[42] using Western blot analysis on the eyes of patients who had sporadic CJD and vCJD confirmed earlier results (in human eyes) that β-structure-rich insoluble conformer prion protein could be detected only in the retina and not in the cornea or sclera. The literature on this topic is scant; evidence from animal studies is variable; and host genetic factors, such as homozygosity at codon 129, may determine risk of susceptibility.[43]

Conclusions

The CDC standard for high-level disinfection of tonometer applanation prisms is based on a classification system that was published in 1968 and classifies instruments into critical, semicritical, and noncritical categories.[3] Applanation tonometers are categorized as semicritical devices and are assumed to carry a risk of transmission of infectious disease similar to instruments that come into contact with mucous membranes (e.g., endoscopes). The laboratory studies included in this assessment represent the best knowledge on disinfection of tonometers available at the time of the literature search. Although extrapolation from the laboratory data presented in this Ophthalmic Technology Assessment to actual clinical infection rates is difficult, the data from these studies nevertheless can help us to develop best practices to protect our patients.

Ophthalmic nosocomial outbreaks commonly are linked to adenovirus 8 and 19, and tonometer tips have been identified as sources of such outbreaks. Adenoviruses are especially hardy, because desiccated virus remains viable and can be recovered after 49 days on dried plastic or metal surfaces.[22] Proper tonometer disinfection against adenovirus was evaluated in 5 publications. Although these 5 studies were limited by varying adenovirus concentrations and differences in laboratory protocol, all of the 4 studies that tested 1:10 dilute bleach concluded that it was effective against adenovirus.[17,23−25] Four studies tested 70% isopropyl alcohol (e.g., alcohol wipes) as a disinfectant for adenovirus 8. Two of these studies[24,25] found that 70% isopropyl alcohol and 3% hydrogen peroxide were effective against adenovirus 8, but these studies not only used lower virus concentrations, but also immediately wiped non-desiccated adenovirus 8, which is easier to remove than desiccated adenovirus. In contrast, 2 other adenovirus studies[17,24] demonstrated that 70% isopropyl alcohol and 3% hydrogen peroxide were not effective in eliminating

adenovirus. In summary, studies suggest that elimination of adenovirus is best achieved by using sodium hypochlorite (1:10 dilute bleach). Use of 70% isopropyl alcohol (e.g., alcohol wipes) is not sufficient to eliminate adenovirus (especially in desiccated form or at high concentrations) and has been associated with adenovirus outbreaks.[21]

Herpes simplex virus 1 also has been associated with infectious spread via tonometer tips. Sodium hypochlorite (1:10 dilute bleach) eliminates HSV 1 and enterovirus 70 effectively,[17,24] and 70% isopropyl alcohol wipes eliminate HIV and HSV 1 effectively.[27,28] No study on tonometers to date has tested if HIV and HCV are eliminated effectively by 1:10 dilute bleach; however, 1:10 dilute bleach is known to eradicate HIV and HCV effectively in nonophthalmic medical settings.[44] To date, there has been no reported case of HIV or hepatitis C transmission via a tonometer tip.

Although there has been no reported case of CJD transmission associated with applanation tonometry, prions are extremely resistant to disinfection. Isopropyl alcohol and ethanol are not suitable for preventing prion transmission because both can cause epithelial cells to adhere to the tonometer tip surface, making these cells more difficult to remove.[35] Both mechanical cleaning and 1:20 (dilute bleach) can reduce the number of epithelial cells retained on tonometer tips; however, because neither can completely eradicate retained epithelial cells, neither can be viewed as effective for the prevention of prion transmission.[39] Therefore, in patients with suspected prion disease, disposable tonometer covers or single-use tonometers should be used rather than reusable tonometers.[13,32]

Dilute bleach at 1:10 concentration, 70% isopropyl alcohol, 3% hydrogen peroxide, ultraviolet light, and even water soaks can cause varying degrees of damage to tonometer prisms. To avoid patient injury, the tonometer tip should be inspected for microscopic cracks, dissolution of acrylate glue, warping, and opacification of the prism. If sodium hypochlorite is used, it is imperative to soak the tip for no more than 5 minutes because of the risk of the disinfectant dissolving the glue and causing cracks, which can be especially apparent at the circular rim. Cracks in the tonometer tip may allow the hollow tip to harbor disinfectants and microbes, which then could leach back out during applanation and increase the risk of corneal injury or infection. If the disinfectant has not completely evaporated or is not rinsed off thoroughly with water, corneal damage or conjunctival irritations also can ensue.

In summary, based on the currently available evidence, 1:10 dilute bleach is a single high-level disinfectant with broad efficacy against common infectious agents encountered in eye care. Only 1:10 dilute bleach is recommended by both the tonometer manufacturers and the CDC for disinfecting applanation tonometers. In patients with suspected prion disease, disposable tonometer covers or single-use tonometers should be used. Because dilute bleach in any concentration, 70% isopropyl alcohol, and 3% hydrogen peroxide all can damage tonometer tips, reusable tonometers must be checked for damage before applanation to prevent patient harm. Given limitations in the number and adequacy of studies on this topic, future well-designed studies may provide evidence that will modify current recommendations for tonometer disinfection.

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Abbreviations and Acronyms:
CDC = Centers for Disease Control and Prevention; **CJD** = Creutzfeldt-Jakob disease; **HCV** = hepatitis C virus; **HIV** = human immunodeficiency virus; **HSV** = herpes simplex virus; **PFU** = plaque-forming unit; **ppm** = parts per million; **vCJD** = variant Creutzfeldt-Jakob disease.

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