

**In Response: "Perioperative COVID-19 Defense: An Evidence-Based Approach for Optimization of Infection Control and Operating Room Management"**

**D**r Maguire<sup>1</sup> considers the use of patient decolonization to aide in the prevention of perioperative viral transmission.<sup>2</sup> The evidence, outlined below, favors our recommended approach, given the Coronavirus Disease 2019 (COVID-19) pandemic.<sup>2</sup>

First, the patient reservoir is a critical factor contributing to disease transmission that must be addressed.<sup>3-5</sup> We evaluated the impact of an evidence-based, multifaceted approach on perioperative *Staphylococcus aureus* transmission and surgical-site infections (SSIs) in a randomized clinical trial.<sup>6</sup> Attention to improved hand hygiene, patient decolonization, vascular care, and environmental cleaning generated substantial reductions in *S. aureus* transmission and SSIs, especially when optimized by surveillance of transmission.<sup>6</sup>

Second, povidone-iodine and chlorhexidine have broad-spectrum activity. Povidone-iodine is a complex of povidone, hydrogen iodide, and elemental iodine that targets structures needed for survival and replication (eg, neuraminidase for viral propagation via infection of noninfected cells and hemagglutinin for attachment). This results in multimodal activity.<sup>7</sup> Povidone-iodine has rapid and effective virucidal activity against the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Modified Vaccinia Virus Ankara (MVA) with at least a 4 log<sub>10</sub> (99.99%) inactivation of both pathogens within 15 seconds.<sup>7,8</sup> This represents more antiviral potency than alcoholic and nonalcoholic hand sanitizers and soaps.<sup>7</sup> Our reason for using chlorhexidine gluconate was that it is available in the US as Peridex oral rinse. While chlorhexidine gluconate is less effective than povidone-iodine,<sup>8</sup> it has activity against enveloped viruses on skin and in the oral cavity (0.12%) with viral inactivation in as little as 30 seconds.<sup>9</sup> The inactivity of chlorhexidine rinse against the poliovirus is presumed to be related to lack of an envelope.<sup>9</sup> Because the COVID-19 virus is enveloped, chlorhexidine gluconate 0.12% is likely to have similar activity against the virus as it does against other enveloped viruses.<sup>10</sup>

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Conflicts of Interest: R. W. Loftus reported research funding from Sage Medical Inc, BBraun, Draeger, and Kenall, has one or more patents pending, and is a partner of RDB Bioinformatics, LLC, and 1055 N 115th St #301, Omaha, NE 68154, a company that owns OR PathTrac, and has spoken at educational meetings sponsored by Kenall (AORN) and BBraun (APIC). M. C. Parra is affiliated with RDB Bioinformatics, LLC, as R. W. Loftus' spouse. The remaining authors declare no conflicts of interest.

Third, povidone-iodine and chlorhexidine gargle reduce the spread of viruses. The MERS outbreak showed that human-to-human transmission often involved close contact and the health care arena.<sup>7,8</sup> Therefore, improvements in hygiene practices, such as patient decolonization, can help combat the spread of COVID-19. Povidone-iodine preparations reduce viral loads of the patient skin, oropharynx, and nasopharynx.<sup>7,8</sup> The agent is included in the World Health Organization's list of essential medicine for addressing the spread of other viral pathogens of global concern (ie, hepatitis A, influenza, and the MERS).<sup>7,8</sup> Povidone-iodine is provided in both skin preparation and oral gargle formulations, has anti-inflammatory activity, has an excellent safety profile, and no resistance identified to date.<sup>7,8</sup> Finally, povidone-iodine and alcohol-based hand rubs are more effective than soap-based hand washes for hand hygiene in the presence of transmissible viruses<sup>11,12</sup> and povidone-iodine has been shown to prevent the spread of contagious conjunctivitis.<sup>13</sup>

Fourth, nasal povidone-iodine is formulated to prevent nasal irritation.<sup>14</sup> Nasal povidone-iodine is thickened, and pH balanced, to be nonirritating, to have a sustained effect, and to address the physiology of the nose.<sup>14</sup> We observed no issues with sneezing or coughing induced by nasal povidone-iodine<sup>14</sup> in our randomized trial.<sup>6</sup> The product<sup>14</sup> was well tolerated and without adverse events. The authors are unaware of reports suggesting otherwise.

Fifth, the authors are unaware of evidence suggesting that chlorhexidine gluconate 0.12% oral rinse is associated with inducing cough. This hypothetical concern raised by Dr Maguire<sup>1</sup> should be balanced against the substantial evidence that the oral reservoir contains a high viral load that should be attenuated to prevent the spread of COVID-19 and that 0.12% chlorhexidine gluconate may be useful in achieving this goal.<sup>7-9</sup> Whether the alternative of povidone-iodine oral rinse is more effective is currently unknown.<sup>7,8,11,12,15</sup>

In conclusion, the evidence shows a favorable risk/benefit profile for our recommendation of patient decolonization with nasal povidone and oral chlorhexidine rinse to help mitigate the perioperative spread of COVID-19.<sup>7-12</sup> If substantial concerns remain (eg, sneezing and/or coughing), we would recommend using the agents after patient induction and stabilization. Given the severity of the COVID-19 pandemic, we believe that it would be ill-advised to avoid use of these evidence-based preventive measures. These steps are part of a comprehensive program that stands on a solid body of published evidence established during the past 14 years.<sup>2-6</sup>

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