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Pharyngeal Antisepsis to Reduce COVID-19 Pneumonia

Antiseptic mouthwash use to control coronavirus disease 2019 (COVID-19) has been proposed, disputed, and dismissed without understanding the proposal and without serious consideration of merits and counterarguments. Adding a proven, safe, and evidence-based clinically reasonable measure to existing approaches of universal masking and social distancing, while awaiting a safe and effective vaccine, seems a constructive approach worth implementing and observing for efficacy. We describe how adding pharyngeal antisepsis, “washing the throat,” before sleeping, when healthy adults of all ages aspirate material from above the larynx, can help protect individuals against COVID-19 pneumonia and, hence, help protect society. We also address critiques presented against widespread adoption of pharyngeal antisepsis.

RATIONALE FOR PHARYNGEAL ANTISEPSIS

The morbidity and mortality associated with COVID-19 derive from its effects on the lower respiratory tract, sometimes with systemic complications. Discovery of upper respiratory tract infection is often called pre- or asymptomatic. However, when such asymptomatic persons who tested positive for infection via polymerase chain reaction (PCR) were subjected to thoracic CT scanning, COVID-19-consistent infiltrates were found in 55 out of 58¹ and 10 out of 10,² suggesting either cleared lower-tract debris resulted in upper-tract findings or simultaneous upper and lower infections. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virions can reach the lower tract either by direct inoculation from inhaled air unhindered in the upper tract passing through the vocal cords or by virions stopped in the upper tract, inhaled or contacted, that are subsequently aspirated. It is the latter, from the “droplets” repeatedly indicated as a common cause of COVID-19 infection, that pharyngeal antisepsis intends to prevent.

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Aspiration of pathogens inhabiting the pharynx is thought to be the mechanism of many bacterial pneumonias. Aspiration occurring in healthy adults, first demonstrated in 1978, occurred during sleep in at least 9 of 20 subjects studied a single night; 5 of 20 had indeterminate results.³ When 10 subjects were studied 2 different nights, 3 of 10 aspirated the first night and 4 of 10 the second night (2 aspirated both nights).⁴ Hence, evidence suggests sleeping aspiration is a common occurrence. For SARS-CoV-2 inhabiting the (naso)pharynx in previously healthy adults, sleep appears the at-risk time to acquire lower-tract disease.

A before-and-after randomized clinical trial of 60 seconds of swishing and gargling 20 mL of a mouthwash formulation effective for killing *Neisseria gonorrhoea* in vitro showed 16 of 33 mouthwash garglers (48%) became culture-negative 5 minutes later, compared to 4 of 25 saline garglers (16%; $P=0.013$, absolute risk reduction 32%, 95% confidence interval 4% to 51%).⁵ Branded and generic formulations containing the same 4 active ingredients, eucalyptol (0.092%), menthol (0.042%), methyl salicylate (0.06%), and thymol (0.064%), reduced SARS-CoV-2 replication of 3 human strains by >2.6 to >3.1 logs after a 30-second incubation.⁶ On a different continent with coronavirus 229E, a frequently used surrogate for SARS viruses, with incubations of 30, 60, and 120 seconds, the same components inhibited replication by >2 to >4 logs.⁷ The generic versions cost \$3 for 50 ounces, which breaks down to 4 (20 mL) to 6 (30 mL) cents/dose.

Hence, for persons without COVID-19 pneumonia but having acquired SARS-CoV-2 in their pharynx at bedtime, swishing and gargling the specified formulation, branded or generic, would be expected to substantially reduce virions capable of replication that can be aspirated during sleep, conferring advantage to the host. Long-term safety of such mouthwash use once daily is not disputed.

ARGUMENTS AGAINST RECOMMENDING OR SUGGESTING PERSONS PROTECT THEMSELVES WITH PHARYNGEAL ANTISEPSIS

These appear to be 3 arguments against pharyngeal antisepsis: 1) The infection is nasal so even if “throat washing”

were highly effective for virions residing there, new virions appearing during sleep could still be aspirated; 2) despite being an attractive approach, adoption should await a positive clinical trial; and 3) there are risks from this recommendation because it could detract attention and personal effort away from interventions with greater evidence, including social distancing and mask use, and would provide a false sense of security in individuals thinking that if they are gargling regularly with an antiseptic mouthwash, they are protected and don't need to as diligently apply such interventions. We address each of these in turn.

SARS-CoV-2 requires accessible angiotensin-converting enzyme 2 (ACE2) cell surface expression to enter cells and replicate. The absence of ACE2 surface expression in upper respiratory tissue samples⁸ or autopsied patients⁹ and presence of pulmonary infiltrates at diagnosis in asymptomatic persons who tested positive via polymerase chain reaction^{1,2} points to lower-tract mRNA fragments, exfoliated goblet cells, and other debris and not necessarily primary local upper-tract infection, explaining upper-tract findings. Typical metaplasia explains inducible ACE2 mRNA or antigen expression in upper-tract cell tissue culture. Regardless, even accepting the concept of nasal infection, the principle of debridement and washing is to reduce or eliminate pathogen prior to a risk period and not eliminate all risk. Thus, we wash hands before eating to reduce enteric pathogen risk despite awareness that food handlers may carry enteric pathogens. Pharyngeal antiseptics aims to reduce pharyngeal virus burden to tilt the balance in favor of the host for lower-tract defense, for a cost of 4-6 cents and a time of 60 seconds.

Clinical trials of interventions having solid preclinical evidence evaluate safety, efficacy, and analysis of resources the intervention requires. When there is no time, they are not done. Thus, our 9 injected influenza vaccines for the 2020-2021 season have not undergone clinical trials nor been efficacy-tested. The Centers for Disease Control and Prevention (CDC) reported effectiveness of 45% for the 2019-2020 vaccines¹⁰ and 29% for 2018-2019; yet, we again seek at least 150 million US persons to get vaccinated. Moreover, pharyngeal antiseptics highly effective against aspirated SARS-CoV-2 would be expected to fail to protect against COVID-19 pneumonia from inhalation indoors in at-risk settings.

The proportion of persons who might stop masking and social distancing upon using mouthwash before sleeping cannot be ascertained in advance. As clinicians we know patients with chronic obstructive pulmonary disease and healthy persons who follow multiple complex measures to preserve their health against dire outcomes. We know from news reports and photos that intelligence is no guarantee of following masking and social distancing. We practice medicine with the obligation to offer each patient our best advice, rather than withhold possibly helpful advice presupposing patients as a group would stop other healthful practices.

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