Soap and Water to Hands and Face, -Eye Rinse, Nasal Irrigation and Gargling with Saline for COVID-19 with anecdotal evidence*

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Abstract
This paper provides a brief historical background of saline nasal irrigation (SNI), main modes of SARS-CoV-2 transmission and entry, and anti-infective properties of saline. It reviews the protective evidence associated with SNI and gargling against viral upper respiratory tract infection (URTI). SARS-CoV-2 presents as an URTI transmitted mainly via respiratory droplets and aerosols to the oro-nasal mucosa and indirectly after touching these entry sites from contaminated fomites. It can potentially be transmitted from the conjunctival mucosa to the nasal mucosa or from resuspension and inhalation from the facial area around the nose. SNI has antiviral, anti-inflammatory and mucociliary restorative properties. Numerous randomized controlled trials have reported that SNI, with and without gargling, prevents and treats viral URTI. Based on biological rationale and anecdotal evidence we suggest a protocol: Soap and Water to the Hands and Face-Eye Rinse Nasal Irrigation and Gargling with Saline (SWHF-ERNIGS) may limit the transmission SARS-CoV-2, and prevent and treat COVID-19 infection. Clinical considerations of the protocol are presented. The protocol is safe, straightforward and can be easily performed by healthcare workers and the general public; it uses readily available salt, water and soap. Formal studies of effectiveness and application of the protocol are warranted.

Key words: COVID-19, hand hygiene, hypertonic saline gargling, hypertonic saline nebulization, SARS-CoV-2, saline nasal irrigation, soap and water

Introduction
COVID-19 outbreaks throughout the world are unprecedented in modern times. This is due, in part, to the highly infectious nature and multiple mutations of the SARS-CoV-2 virus causing COVID-19, and to the fact those with difficult to detect presymptomatic and asymptomatic infections may have high viral loads with substantial viral shedding and transmission1-2. The largest case series in China of 44,672 confirmed cases showed only 14% had severe illness, 5% were critical and 2.3% died 3. A cytokine storm with increased levels of interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-2 receptor and tumor necrosis factor-alpha (TNF-α), occurs in severe disease, and is associated with a poorer prognosis 4,5. Even those with mild to moderate disease stress healthcare systems and economies worldwide.

High viral loads of the SARS-CoV-2 virus in the nasopharyngeal mucosa are seen in patients with COVID-19 infection 6. Persistence of a high VL is seen more frequently in hospitalized patients or those who have severe disease than in those who recover uneventfully 7,8. Therefore, any local treatment at the naso-pharyngeal level to prevent establishment of viral infection or to reduce viral load and replication may be beneficial in the prevention and treatment of SARS-CoV-2 URTI.

Saline nasal irrigation (SNI) without and with saline gargling or with an oral antimicrobial agent have been proposed for prevention and treatment of COVID-19 URTI 9-13. SNI is a common practice in the United States. One survey reported a large percentage (59%) of family physicians in the US state of Wisconsin prescribed SNI for viral URTIs 14. This paper describes the historic background of SNI and main modes of transmission of SARS-CoV-2, including potential modes of entry; the anti-infective properties of saline with SNI; and the literature associated with SNI and or gargling for viral
URTI. Based on this information, we propose a protocol incorporating gargling, SNI, saline eye rinse, and hand and face washing for prophylaxis and early treatment of COVID-19 infection and provide clinical considerations and anecdotal evidence supporting it.

**Historical background**

SNI emerged from an Ayurvedic practice called “Jala-Neti” and is believed to be over 1000 years old. Traditionally it was used as routine hygiene, and to treat sino-nasal symptoms associated with URTIs, allergies and for general well-being in Ancient India. Nasal irrigation came late to the West. In the 18th century, nasal irrigation was recommended for treatment of sino-nasal complaints. The “Report on Rhinology: The treatment of nasal and pharyngo-nasal catarrh” by a US surgeon Dr. J A Stucky, published in 1886, describes applying local agents to the pharyngeal cavities, fauces and tonsils by using spray applicators (Rumbold’s method). In the case of thick muco-purulent secretions, he first cleansed the area with a solution of sodium chloride, boric acid and cocaine. He quotes American laryngologist, Dr. J Co- hens, “The two great principles in the treating naso-pharyngeal catarrh were, first, to keep the parts clean, so as to let have a chance to get well of themselves, and second, to take care of the patient’s general health.” At the Central London Ear, Nose and Throat Hospital in 1901, Dr. W Wingrave, described six essentials of nasal irrigant “…1. The solution employed should, when practicable, be a solvent of the substance to be removed. 2. The reagent should be itself readily soluble in water and form a clear solution. 3. It should be non-irritating to mucous membranes and sensitive surfaces. 4. To ensure thoroughness it should possess the power of penetrating the surface tissues. 5. It should be miscible—i.e., chemically compatible with the most effective antisepsics. 6. It should be economical in cost and readily available.”. These views are consistent with current use of and recommendations for SNI.

SNI for sinus infections, nonallergic and allergic rhinitis, and assessment of its effects, became more formal in the 1990s. Early studies were conducted in environmental workers predisposed to sino-nasal complaints. After a number of positive randomized controlled trials for chronic rhinosinusitis, SNI with isotonic or hypertonic saline is now guideline-recommended as adjunctive treatment for acute bacterial rhinosinusitis in adults by The Infectious Disease Society of America (IDSA). These successes led to the assessment of SNI for viral URTI.

**Main modes of transmission and potential portals of entry of SARS-CoV-2**

SARS-CoV-2 virus is a respiratory human coronavirus which enters the cell to establish infection in the nasal and oral cavity via its surface spike glycoprotein interaction with the respiratory epithelial ACE-2 receptor. The virus is transmitted primarily by inhaling droplets ranging from >5-10 μm in diameter to smaller aerosols <5μm, especially in close contact (one meter) to the nasal and oral mucosa. Airborne transmission (>1 meter) occurs most often in indoor, crowded and inadequately ventilated settings. Indirect transmission occurs less frequently via touching the mucous membranes after contact with an infected individual or indirectly via contaminated fomites. Self-inoculation can occur from habitual face touching with contaminated hands to the mucous membranes. Face touching studies prior to and during COVID-19 pandemic show face touching can occur at an average rate of 10-23 touches per hour. This was observed in different populations (medical students, general public, outpatient clinics, family medicine clinicians and staff). In one study, 44% of touches involved mucosal areas: mouth (36%), nose (31%) and eyes (27%). In proximity coughing can transmit many viral particles on facial areas of susceptible individuals. A 3D fluid dynamic simulation model suggests the area of the human face close to the nostrils could result in self-inoculation via resuspension and inhalation of viral particles during physiological nasal air inspiration.

Systematic review and meta-analysis associates lesser acquisition of the SARS-CoV-2 virus and related viruses with: physical distancing of 1 meter or more (protection increases as distance lengthens) [adjusted odd ratio (aOR)= 0.18, 95% CI 0.09 to 0.38], face mask use (aOR= 0.15, 95% CI 0.07 to 0.34) and eye protection (aOR=0.22, 95% CI 0.12 to 0.39). Ocular mucosa may be a gateway to nasal epithelium through the nasolacrimal duct. Goggles worn during an outbreak of another respiratory virus, respiratory syncytial virus were found to be protective.

During the COVID-19 pandemic, myopic persons who wore glasses (>8 hours) were hospitalized less compared to those without myopia. There is much debate about whether SARS-CoV-2 is transmitted via the conjunctival mucosa. Content experts suggest a high potential based on the case of Dr. Wang Gaunfga, the Chinese pneumonia expert, who after unprotected eye exposure and despite wearing a N95 mask, developed COVID-19 with the first symptoms being conjunctivitis. Transmission via conjunctival mucosa is also suggested by the abundance of ACE-2 receptors in the ocular surface and finding of SARS-CoV-2 RNA in the conjunctival specimens.

**Antiviral, anti-inflammatory and mucociliary restorative properties associated with saline**

Saline (salt or NaCl in water solution) along with SNI has antiviral, anti-inflammatory and mucociliary restorative properties. SNI dislodges mucus; reduces the concentration of inflammatory mediators and microbial antigens; and can have positive effect on epithelial cell integrity in presence of additional ions (magnesium, zinc, potassium and bicarbonate). In vitro saline concentrations ranging from 10 to 100 millimoles...
(mM) (equivalent to 0.58g to 5.8g in 1 kg of water) inhibit the growth of both DNA and RNA enveloped and non-enveloped viruses by producing hypochlorous acid, an active ingredient of bleach (39). Saline at a strength of 260 mM NaCl (1.5%) inhibited 100% SARS-CoV-2 replication in Vero cells by causing a low energy state via plasma membrane depolarization leading to an overflow of Na⁺ and increased cytosolic Ca²⁺ within the cells (40). Additionally, in vitro sea-salt significantly reduced release of IL-8 in human bronchial gland cells by attenuating TNF-α and IL-1β release of IL-8 (41).

A randomized trial showed that nasal irrigation with atomized saline used four times daily restored mucociliary function to a greater physiological level (p<0.001) when compared to nasal lavage in acute rhinosinusitis (42). In a similar context, nebulized hypertonic saline helps in clearing luminal mucous in small airways that occurs in patients with cystic fibrosis, asthma, COPD, viral, fungal and mycobacterial pneumatic infections and restores airway surface liquid depletion (43). Hypertonic saline nebulization is a standard of care for treating patients with an acute exacerbation of cystic fibrosis (44).

**Literature review**

A Cochrane review of SNI for URTI suggests possible symptom benefits and recommended larger, less biased studies be done (45). A meta-analysis of hypertonic and isotonic SNI showed hypertonic saline has greater symptom reduction than isotonic saline in sino-nasal infections (standard mean difference [SMD] = -0.58, CI: -0.76 to -0.40) (46). A meta-analysis of studies in children showed a benefit of SNI for some nasal symptoms (SMD = -0.29 CI: -0.45 to -0.13) with a decreased use of antibiotics and decreased acute rhinosinusitis and its complications (47). The study showed no significant improvement in respiratory symptoms or overall health status.

The intervention arm of a randomized pilot trial prepared a hypertonic saline solution and performed hypertonic SNI and gargling (HSNIG) four times daily beginning within 48 hours of URTI symptom onset (48). Results in the HSNIG intervention arm showed significant reductions in symptoms by 1.9 days (p=0.01), use of over-the-counter medications by 36% (p=0.004), transmission within household contacts by 35% (p=0.006), and a higher proportion had a >=0.5 log10/day decrease in viral shedding compared to the control arm (73% vs. 43%; p=0.04). Ninety-three percent of the intervention arm found HSNIG useful and 86% reported performing it outside their homes. Sixty-one percent said they would perform HSNIG again if they had a cold but would have had a higher uptake if the procedure was more convenient. After the COVID-19 pandemic began, the investigators performed a post-hoc analysis of 15 patients that were infected with the non-pandemic strains of human coronavirus (not SARS-CoV-1/2) causing URTI, 7 in the intervention arm and 8 in the control arm (49). Analysis showed improvement in hoarseness, cough and blocked nose (p <0.05), and duration of illness (mean improvement 2.6 days, p =0.05) in the intervention arm. However, the sample size is small, and the authors interpreted the results with caution.

A prospective multicenter randomized trial in children 6-10 years of age compared a commercial isotonic nasal saline nasal (seawater) wash plus standard treatment to standard treatment alone during an acute viral URTI (50). The saline nasal wash was well-tolerated, and participants had few complaints. The preventive phase of the study showed the groups using an isotonic saline nasal spray plus standard treatment, three times daily had statistically significantly fewer (p<0.05) URTI illnesses (31% vs 75%), school absences (17% vs 35%) and complications (8% vs 32%) when compared to controls. Patients randomized to the saline group were evaluated in three delivery strength subgroups: medium jet flow, fine spray, and a dual formula for eye and nose wash with a fine spray. When compared to controls, all three saline groups showed significant improvement (p<0.05) in sore throat, nasal secretions, nasal secretion type and nasal breathing. The children showed a preference for the fine nasal spray. A second study of children <2 years (mean age 9.0 ± 3.9 months) found significant improvement in the two treatment groups of isotonic and sea-salt nasal saline irrigation when compared to the control group in nasal congestion, rhinorhea, weakness, nutrition, sleep quality and diet (p<0.05) (51). There was no significant difference in cough symptoms between the three groups (p>0.05).

In an adult crossover prevention study, three puffs of an isotonic nasal spray in each nostril twice daily significantly prevented URTI episodes during the spray period when compared to observation period (0.7 vs 1.0, p=0.05) (52). Nasal blockage and secretions decreased on average from 11 days during the observation period to 6.4 days during the spray period (p=0.027). The decrease in all URTI symptoms (9.4 days vs 13.4 days, p=0.069) was not significant. The authors attributed this to the fact that nasal spray predominantly affected nasal symptoms. When compliance was increased to >70% (p=0.02) during the spray period, the symptoms decreased further to 5.8 days.

A randomized control trial in Japan, where gargling is a socially accepted practice, found gargling three times daily with 20ml water alone significantly decreased the risk of URTI (hazard ratio = 0.60, 95% CI=0.39-0.95) and reduced bronchial symptoms (p=0.055) (50). Further analysis of water gargling found no significant prevention of influenza-like illnesses (ILI) (hazard ratio= 0.72, 95% CI: 0.30-1.61) (53). This was attributed, in part, to the low prevalence of ILI among study participants.

Univariate analysis of a retrospective case control study among healthcare workers in Beijing, China performed early in the SARS-CoV-1 outbreak found a nasopharyngeal wash effective in preventing SARS-CoV-1 infection (4.7% vs. 14.8%, p<0.001) (54). Multivariate analysis showed not performing nasal wash
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1 infection (OR=2.41, CI=0.98-5.93, p=0.056). The Handbook of Covid-19 Prevention and Treatment by The First Affiliated
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recommends healthcare workers flush eyes or gargle with saline or .05% iodophor after unprotected conjunctival and / or oral mucosal exposure to SARS-CoV-2 virus (53). They also recommend wiping the nasal cavity with a cotton swab dipped in 75% alcohol.

Two clinical trials in adults found no benefit of saline nasal irrigation or water gargling (54,55). One study of adults presenting to family practice clinics found mean days of wellness and symptom scores were not statistically significant among the three study groups: a 2% hypertonic saline nasal spray, isotonic or normal saline nasal spray and observation (54). The study found high rates of nasal burning in the hypertonic nasal saline group (32%) compared to 13% in the isotonic saline group. Late recruitment into the study after onset of infection, type of nasal saline preparation used (i.e., canning/pickling salt, baking soda and water) and side effects potentially biased the results. A second randomized control study of Vitamin D3 use, and water gargling showed gargling alone did not reduce the mean duration of symptoms or improve time to symptom resolution in both clinically diagnosed (p = 0.69) and laboratory confirmed URTIs (p = 0.43) (55). Overall, similar results were seen in the vitamin D3 group, except that vitamin D3 did reduce significantly the incidence of laboratory confirmed URTI (p=0.007). The authors did not monitor compliance with the protocol and mentioned that twice daily gargling was probably insufficient.

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In a study of children with URTI (3 weeks to 2 years of age) the
average nasal scores taken 2 days apart significantly improved in all the 3 groups: saline nose drops; medicated phenylephrine nose drops and controls (p<0.01) (56). Respiratory scores also improved significantly in the saline nasal drop and control group (p<0.01) but not in the phenylephrine nose drops group (p>0.10). The saline nose drop group showed the greatest improvement in nasal and respiratory scores. The authors attributed misclassification bias due to the fact the saline nose drops may have been used as needed by the control group, resulting in the control group showing significant improvement as well. They concluded that medicated phenylephrine nose drops are not essential for URTI treatment and recommended cheaper, harmless and physiological saline drops. Other drawbacks of the study include the small sample size, several of the children received antibiotics for otitis media, as well as a high attrition rate as 38% of participants did not return for the second visit.

Soap and Water to Hands and Face-Eye Rinse Nasal Irrigation and Gargling with Saline (SWHF-ERNIGS) protocol
The SWHF-ERNIGS protocol was developed for use in the pre-
vention and early local treatment of COVID-19 infections based
on the research cited above and portals of entry of the virus
(Table 1).

Clinical considerations regarding use of SWHF-ERNIGS protocol
There are medical contraindications to using saline nasal lavage
and gargling, including dementia, stroke, inadequately healed
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Table 1. Soap Water to Hands Face-Eye Rinse Nasal Irrigation and Gargling with Saline (SWHF-ERNIGS) protocol.

1. Post-exposure and Prophylactic Use: Begin the protocol immediately after a known exposure and use at least 1-3 times a day prophylactically depending upon exposure risk.
2. After acute URTI symptoms: begin the protocol use as soon as possible after symptoms appear, use at least 4-6 times a day and as many times as needed for symptom relief.
3. Prepare a saline solution (0.9% - 3%) for nasal irrigation and gargling. For nasal irrigation use either distilled or boiled tap water, or a commer-
cial sterile nasal spray. If using tap water, boil for 1 minute and cool. If the elevation is >6500 feet, boil the water for 3 minutes and cool. The saline solution for gargling may be made using distilled or potable tap water (boiling is not necessary).
Note: A hypertonic solution (3% w/v), equal to 1 teaspoon (5-6gm) of salt (preferably sea-salt) in 7oz (200ml) water is recommended. If this strength is not bearable then the highest tolerable strength is recommended.
4. Wash and decontaminate all surrounding surfaces and containers before and after following the protocol using proper infection control practises. Particularly for nasal irrigation devices, rinse with distilled or boiled water only (56).
5. Wash the hands and face with soap and water.
6. Gargle three times with the saline solution at each use.
7. Irrigate each nostril three times at each use, using any of the following methods7: sniffing, spraying, nasal lavage (with a Neti pot or other commercial lavage system), or an atomizer (56,57).
8. Use an optic saline spray in each eye or place each eye in a shallow container containing the saline solution, open and close the eyelid, and repeat three times. Repeat with the other eye using a fresh solution. (Eye rinse is for prophylaxis only and SWHF-NIGS can be used for early infection).
9. If making larger volume solutions use glass lined flasks or bottle and make fresh solutions daily (46).

7 weblinks to sniffing and neti pot techniques are with the references 46 and 57, respectively.

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onal and musculoskeletal conditions (57). Inhaled nebulized hypertonic saline should be considered in those subsets of patients and further studies are needed. There is a risk of lethal amoebic meningoencephalitis caused by Naegleria fowleri when contaminated water is used for nasal irrigation (56). While this has been reported, it is exceedingly rare. The CDC recommends that clean water be used for nasal irrigation in the following order: distilled, boiled, filtered or chemically disinfected water (56).

Although no serious adverse events have been reported with SNI, there are side effects, including a sense of discomfort, nervousness during first use, ear fullness, stinging of nasal mucosa and rare epistaxis (57). Transient conjunctival redness and irritation has been observed with saline eye rinse by one of the authors (SP). Side effects can be ameliorated by decreasing the saline concentration from 2-3% to 0.9% and altering one’s technique for SNI (57). Easier methods of nasal irrigation may also be used from nasal lavage (the most difficult to perform) to sniffing, use of a nasal spray or an atomizer.

Nasal irrigation cups and bottles can become contaminated (59). It is recommended washing them with distilled, or boiled water and to make a fresh solution daily (59,60).

**Anecdotal evidence**

This protocol was used by three health care providers in different settings: one in a long-term care center (lead author SP); another in a cardiology practice and one in a family physician’s practice during the peak of the pandemic. In each of these high-risk exposure settings, those performing part or all the protocol remained negative from infection. The lead author (SP), despite being in multiple long term care outbreaks and being exposed to infected patients and other health care staff, remained COVID-19 negative. A cardiologist from Las Vegas, Nevada and a family physician and her nurse in Karachi, Pakistan, also reported using the protocol fully or partly, and remained COVID-19 negative. The cardiologist and the nurse did not perform eye rinse. The cardiologist and the nurse did not perform eye rinse. The cardiologist reported all his other four colleagues, and the family physician reported her office work area (the receptionist and other 2 providers) became positive for COVID-19. The author (SP) and cardiologist tested antibodies from a commercial laboratory, and both were negative prior to getting the COVID-19 vaccine. The author (SP) and family physician also have observed anecdotal success of the protocol in many patients with COVID-19 infection.

**Discussion**

The biological rationale, prior relevant laboratory studies and randomized clinical trials with URTIs, and anecdotal COVID-19 evidence suggest SWHF-ERNIGS may be an effective prophylaxis and treatment of COVID-19 viral URTI. While anecdotal evidence provides low strength of recommendation in evidence-based practice, it can be complementary to formal research evidence and must be acknowledged, studied and utilized (60). Saline gargling and eye rinse are recommended in Chinese guidelines for post-exposure prophylaxis in healthcare workers and SNI is not mentioned (59). The source of these recommendations is unreferenced. It can be argued that SARS-CoV-2 is different from regular non-epidemic viruses and most previous studies were done with non-epidemic viral strains except in the case control study that showed nasal wash was protective in SARS-CoV-1 infection (52). Interim analysis of a small open randomized trial using nasal irrigation with hypertonic saline (HS), hypertonic saline with surfactant (HSS) in COVID-19 non-hospitalized outpatients showed significant reduction in median time to nasal congestion compared to non-intervention group (NI) [NI=14 days, HS=5 days and HSS=7 days, p=0.04] (61). There was a nonsignificant trend in the intervention group towards earlier symptom resolution, decreased cough and fatigue. Also, there is another pre-printed, unblinded, randomized uncontrolled study (n=79) using pressured nasal irrigation within 24 hours of symptom onset in outpatients greater than 55 years of age with either sodium bicarbonate or povidone iodine added to isotonic saline for nasal irrigation. Results suggest that death and hospitalization were significantly less in these two groups when compared to the national data in nearly the same age group (>50 years) and timeframe (10.6% vs 1.27%; p<0.006) (62). It needs to be determined whether a persistent high viral load seen in the oro-nasal mucosa in severe disease and hospitalized patients is associated with cytokine storm, COVID-19 morbidity and mortality. Early and aggressive use of the protocol may help to decrease these viral levels. A recent retrospective study that showed intranasal corticosteroid use decreased hospitalization, ICU admission and in-hospital deaths with COVID-19 indirectly would support such a hypothesis (63).

The protocol can be initiated prior to SARS-CoV-2 virus testing on any of the first symptoms of COVID-19 URTI (sore throat, headache, fatigue, nasal symptoms, dry cough, fever) (64). Acute loss of olfactory flavor perception (85-91%), loss of sense smell (17.5%-85.6%), and taste loss (35%) with or without fever, cough and shortness of breath have been identified in the literature as some of the early onset symptoms of COVID-19 infection (64-66). There are diagnostic dilemmas associated with RT-PCR testing. At symptom onset RT-PCR can have a high false negative rate (38%; CI: 18-65%) and some patients can be repeatedly RT-PCR negative (67,68). Also, there may be situations in which testing may be unavailable, delayed or not done and PPE may be inadequate or improperly used (69). In these situations, the protocol will be beneficial.

Both homemade and commercial preparations of saline have been used in formal studies. Saline strengths ranged from
isotonic (0.9%) to hypertonic (3%). Reviewed studies used different nasal irrigation techniques, i.e., sniffing, spray, lavage with a Neti pot, or atomizer. Common to all were the use of a saline preparation equal to or greater than isotonic saline (0.9%). Many studies used sea-salt. Additive beneficial effects of sea-salt have been attributed to its mineral richness (HCO₃⁻, K⁺, Ca²⁺ and Mg²⁺) as well as to its anti-inflammatory properties when compared to other forms of saline (25-29,30). Other agents like intranasal corticosteroids and antiseptics (povidone-iodine, hydrogen peroxide, cetlypyridinium chloride, ethanol) that have in-vitro activity against SARS-COV-2 are also being considered and studied (33,63,70). One interesting candidate is copper enhanced nasal saline irrigation that retains the antiviral properties of povidone-iodine without having detrimental effect on the mucociliary function seen with povidone-iodine (71). Compared to other agents the components of SNI are readily available, and safety and tolerability of SNI are well established (71,72).

Hypertonic saline nebulization can be considered in the setting of those who can’t do nasal irrigation and/or gargling early in infection or those with lower respiratory tract symptoms. Clinical trials are being performed with inhaled hypertonic saline nebulization in intubated critical COVID-19 infections (clinicaltrials.gov). A sea-salt prepared hypertonic saline nebulization should be evaluated because of its strong in vitro anti-inflammatory effect (73). The optimal saline concentration, derivation and delivery, requires further study in SARS-CoV-2 infected patients. The SWHF-ERNIGS protocol described above encompasses all SARS-CoV-2 portals of respiratory entry: oral, nasal, conjunctival and transfer by the hands to facial mucosal surfaces. The protocol is a combination of the universally recommended standard of care practice of hand hygiene (with washing with soap and water), well-studied interventions to the oral and nasal mucosa (with SNI and gargling) and the new application of rinsing the eyes (with saline) and of washing the face (with soap and water) (74). Cleansing these areas mirrors CDC’s advice to avoid touching unwashed hands to the nose, eyes and mouth as a prevention against COVID-19 (72). Face touching is an unavoidable habitual human behavior and virus may also be transmitted from the nasal facial skin via resuspension and inhalation (75-78). Researchers have hypothesized that washing one’s face and hands may reduce COVID-19 infection (79). Hence the protocol serves as a terminal cleansing procedure. It can be used by the general public and healthcare workers, and can be started immediately after a suspected or proven exposure. It can be used in situations where there is a high risk of acquiring or spreading of infection e.g., during institutional or family outbreaks or in patients transitioning from one highly prevalent healthcare setting to another COVID-19 infection free or naïve setting. Trials in all these important settings should be considered with the protocol.

The role of asymptomatic infection is increasingly recognized as an important factor in the spread of SARS-CoV-2 infection (78). A case has been published of a physician who after an asymptomatic COVID-19 infection, started HSNIG and remained asymptomatic (80). He became negative by PCR after 3 days and remained SARS-CoV-2 IgG antibody negative at 2 months. One advantage of the SWHF-ERNIGS protocol is that it uses common and readily available household materials such as soap, salt and water. The saline solution is easy, inexpensive to prepare and use, and has no serious demonstrated side effects. It is not toxic to the respiratory epithelium compared to oral antiseptic agents which may be, and it fulfills all the Wingrave’s principles of a successful irrigant (17,23,77). Because of this, we and many others are advocating its current application during this ongoing pandemic as an economical public health measure and can be a powerful mitigation strategy (9-13,40,61,62,74).

The SWHF-ERNIGS protocol, or any such measure at the oronasal mucosal level, should not be considered a substitute for vaccines or CDC, WHO or FDA approved treatment modalities, but its use can be adjunctive and complementary. Such a protocol may be especially useful in resource limited settings, in those for whom the vaccine is not approved or contraindicated, in those who prefer a more natural treatment, vaccine refusers, during outbreaks of new viruses or variant strains and during large gatherings/events where there is a potential of an outbreak.

Conclusion
Saline nasal irrigation, an ancient Ayurvedic practice, was practiced in the West since at least the 18th century for diseases of the upper respiratory tract. IDSA guidelines recommend SNI as an adjunctive treatment for chronic sinusitis. Randomized SNI and gargling studies support its use for both prevention and treatment of viral URTI. SNI’s effects are multifactorial: mechanical, direct antiviral, anti-inflammatory (with sea-salt) and mucociliary restorative. SARS-CoV-2 transmits primarily by droplets/aerosols through the oro-nasal entry sites or indirectly to it via touching contaminated surfaces and by face retouching which many studies have shown is an unavoidable human behavior. Also, potential routes include the conjunctiva via the nasolacrimal duct, and nasal skin via resuspension and inhalation. Based on the literature review and biological rationale, we propose consideration of the SWHF-ERNIGS protocol as a simple and safe hygiene strategy to prevent and treat COVID-19 infection via cleansing the primary sites of acquisition, replication and transmission - the oral and nasal mucosa; and indirect sites of transmission-the hands, face and conjunctival mucosa. This is consistent with CDC recommendations of avoiding touching these mucosal surfaces. All salinities from the preferred hypertonic (3%) to isotonic (0.9%) have been shown to be effective in viral URTI trials.

Our anecdotal success of the protocol among healthcare workers as prophylaxis and in acute COVID-19 infection as well
as small SNI open-label randomized trials of acute COVID-19 infections suggests the possible utility of the protocol and SNI against COVID-19. Controlled trials (clinicaltrials.gov) are underway with HSNIG which is an essential component of our protocol. Formal assessment using clinical trial methodology is needed to assess the utility of our protocol in different scenarios (general public and healthcare worker prophylaxis, post-exposure prophylaxis, community/institutional outbreaks, early infection, asymptomatic infection). The ease of use, biological plausibility, and low cost (especially important in low resource settings) suggest that healthcare authorities consider and recommend application of this simple strategy.

**Authorship contribution**
All authors (SP, LD, DR) were involved in designing, drafting, critically revising for important intellectual content and of the final approval of the version submitted. SP contributed to the initial conception and design of the study.

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