Conquering COVID Part 2.0:
"Saline Nasal Irrigation (SNI)/Nasal Health & Gargling
Have Ongoing Clinical Trials?!"
(aka Learning from ELVIS & One Researched Reason
Why Children Could be More Protected Than Adults)
May 27, 2020

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"I am concerned, of course, but I am also incredibly optimistic."

Here we go! Buckle up! In the last article we talked about sleep and immune health and now we are going to talk nose and gargling health? Yup! In fact, we are primarily going to talk about the interesting world of saline and your nose. First, let me list the range of GENERAL educational references I utilized for this column (and then we can jump right into it):

- Bergmann C, et al. SN Comprehensive Clinical Medicine 2019;1:354-361.
- Carter A, et al. BMJ 2019; doi: 10.1136/bmj.l131.
- Jung M, et al. Asian Pac J Allergy and Immunol 2019; doi: 10.12932/AP-070918-0403.
- Succar EF, et al. Int Forum Allergy Rhinol 2019;9:S4-S8.
- Head K, et al. Cochrane Database of Systematic Reviews 2018, issue 6, Art. No: CD012597.
- Harvey R, et al. Cochrane Database Syst Rev 2007;3:CD006394.

Saline (from Latin "sal" meaning salt) is basically a combination of sodium chloride salt and water, and these products have become extremely popular. For example, the "Neti Pot" is now well-known and immersed in our over the counter (OTC) vernacular. **In the medical lexicon nasal "flushing" with saltwater (saline) has an official name and abbreviation - Saline Nasal Irrigation (SNI).** (This is sometimes also referred in the medical literature as NSI or nasal saline irrigation). It is also known as "nasal wash," "lavage," "rinse," or "shower" (okay I made that last one up). Basically, you are

rinsing the nasal cavity with saline and, apart from the Neti Pot, there are other simple to use sprays, pumps, or squirt bottles. One of my favorites to personally use, once in a while, is Simply Saline Sterile Nasal Mist (FYI - I have never communicated with or been paid by anyone at this company) or a generic version of it because it does most of the work for you. Basically, just place the tip of nozzle into each nostril, press the button, and magic (actually more specific directions and nasal or head positioning are on the website at: https://www.armandhammer.com/personal-care/nasal-saline-solutions/instant-relief/simply-saline-instant-relief-for-everyday-congestion-1-6-oz). There is also plenty of comforting quality control (QC) information on the website, which is critical for any OTC product or pill. QC transparency of any product sold OTC is a critical issue that needs to be regularly addressed (this is for another column). Whether you are choosing an OTC drug, supplement or any health care product including saline, knowing exactly what is inside or not inside the product is necessary today. Good companies will not shy away from QC, but instead encourage it. Sorry, I digressed a bit.

Keep in mind SNI solutions, in general, are **more commonly ISOTONIC** (approximately 0.9% NaCl), but there are also some companies that offer a **HYPOTONIC** (approximately 0.65% NaCl), or **HYPERTONIC** (greater than 0.9% NaCl) option. **Most research studies generally use ISOTONIC products** because increasing salt concentration beyond, or well beyond, this concentration could have more efficacy in some specific situations (discuss this with your doctor), but also could potentially create more side effects. The thought process with the lower than isotonic solution is that it could be less irritating or safer, but is it as effective? (This needs more research). There are also issues of how much (volume), how often (frequency), how long (duration), what pressure should be applied when using them, and the exact composition of the product, but again this should be worked out between you and your doctor. For example, some clinical trials suggest SNI solutions with larger volumes and lower positive pressure could be more effective than saline sprays for treatment of chronic nasal/sinus symptoms (Pynnonrn MA, et al. *JAMA Otolaryngol Head Neck Surg* 2007;133:1115-1120), which again is why everyone's situation is different and should be discussed with your doctor and not determined by a general informative health column.

What I love about SNI products, besides the fact that they are generally cheap (like me), is they are gaining acceptance in a variety of clinical recommendations or situations and continue to accumulate more research. In general, they have a good safety record with intermittent or occasional use (many pediatricians even recommend them for children with certain conditions) and, of course, they are a non-pill option that can be utilized at home. They have become partially symbolic of consumer or patient at-home health empowerment (yeah!).

Again, they are often recommended by health care professionals to use alone or in combination with other treatments. Over the years they have become recommended by some health care professionals as a part of the greater therapy for the following (partial list):

- Common Cold or inflammation of the sinuses and nasal cavity (chronic rhinosinusitis for example)
- Allergic rhinitis
- After some nasal surgeries (reduce postoperative debris)
- Help clear mucus from nose/sinuses, reduces crusting, and moisturize area
- Flush out nasal allergens (decreasing antigen load, or proteins known to cause inflammation) and even bacteria that could be problematic
- Reduce antibiotic prescriptions for acute/chronic sinus infections
- Reduce the need or amount of other medications such as decongestants
- Often used before utilizing a topical nasal steroid to treat inflammatory problems of the nose and sinuses (if nasal steroid is used first and saline right after it would wash out and negate the effects of the medicine).
- Etc. Etc. Etc.

So, why am I covering SNI in a COVID-19 column? We are getting there my friends. It is interesting that Upper Respiratory Tract Infections (URTI) can lead to Lower Respiratory Tract Infections (LRTI) so early effective and safe treatment could potentially prevent a mild infection from becoming a more serious infection. Laboratory studies have suggested the impact of NaCl or saline on having anti-viral effects. For example, it may have more direct cytotoxic effects in the nose, or it may allow cells to utilize chloride ions to produce disinfectant type compounds in the body. Even sodium from the saline could have an anti-microbial impact. There are many theories as to how saline might work. Past studies have also suggested saline could have the ability to reduce some types of viral shedding (**this has NOT been tested with COVID-19**), which could reduce personal risk as well as other contact risks in the house (Ramalingam S, et al. *Sci Rep* 2019; 9:1015). Perhaps just flushing out the bad dudes from your nose once in a while does something?

Before we talk about COVID-19 please keep in mind that everything in life comes with some kind of catch or warning or disclaimer and we need to cover that before we move on. The potential side effects of SNI (especially the more you use them) includes nasal irritation, generally minor nosebleed, ear or nasal

discomfort, and saline dripping out several minutes after use. In other words, again some people use them too frequently and that can create its own set of problems. Everything in moderation folks!

Additionally, another reason I am more of a fan of picking a known commercial product like Simply Saline or a generic equivalent from a reputable company is due to ongoing concerns of what is known as “SNI hygiene”, especially with homemade products, because they may have been, in rare cases, associated with dangers or risks. There has been a potential association with SNI and primary amebic meningoencephalitis (PAM), which is a parasite that can come from warm fresh water sources, for example, and when it gets in your nose it can travel to other locations and do a lot of damage (Google if you want, but it is so rare that I do not want to scare you). The first apparent two cases of PAM occurred in 2011 in Louisiana and may have come from a home water supply. Homemade products have a risk of getting contaminated (with bacteria or other unfriendly things) and people should follow CDC guidelines when using their own water source at home. Again, using a well utilized commercial product is associated with less concerns in my opinion. I have no expertise in recommending a homemade SNI product, or type of water, and I do not want to gain any expertise in this area and this is why I also recommend talking to your doctor and sticking with a reputable product that takes care of all the preparation and QC for you.

Okay, now that you and I have achieved a PhD in the pros and cons of SNI it is easy to see why at least three medical centers (NYU Langone, Stanford, and Vanderbilt) in the U.S. are conducting some form of SNI research against COVID-19. In fact, at the time of this writing two (NYU Langone and Vanderbilt) of the U.S. studies are now already recruiting participants for these separate clinical trials! Another separate clinical trial is also recruiting currently in the United Kingdom, which is remarkable because multiple clinical studies on SNI is simply fabulous! Yes, but why, more specifically, is there so much interest in SNI and COVID-19?

The viral concentration (load) with the coronavirus that causes COVID-19 (also known as “SARS-CoV-2”) appears to be initially highest in the nose and nasopharynx. In fact, fascinating research published just days ago from the Icahn School of Medicine at Mount Sinai, New York (Bunyavanich S, et. al. *JAMA* 2020; doi: 10.1001/jama.2020.8707) preliminarily found LOWER levels of the specific receptors in the nose, which SARS-CoV-2 utilizes to bind to human cells to gain entry, in younger children versus adults of a variety of ages. Thus, the numbers of these receptors in the nose utilized by the virus increased with increasing age! Again, this is preliminary, but it may be just part of the reason children have consisted of less than 2% of COVID-19 disease cases thus far. In other words, researchers know that older age and co-

morbidities places one at a higher risk of being impacted by COVID-19, but more specifically, why? There are an infinite number of theories about different hormones, receptors, and immunologic issues and other vulnerabilities as you get older. However, there is still not enough definitive proof as to why younger people are more protected from COVID-19. For example, in some epidemics or even pandemics, such as 1918, younger people were dramatically impacted in large numbers where the average age of death was just 28 years of age (Gagnon A, et al. *PLoS One* 2013; doi: 10.1371/journal.pone.0069586).

Researchers from this new study from Mount Sinai sampled the nasal epithelium of 305 individuals aged 4-60 years (51% female), and they specifically looked at the gene expression of the receptor that COVID-19 virus utilizes to get into the body (known as "ACE2"). **In other words, if one of the most common methods of entry of this virus is from a receptor found in the nose (and elsewhere), and the older you are, then the more you express this receptor in the nose, then again it helps to PARTIALLY or slightly explain why older is tantamount to more vulnerable with this specific virus**. Thus, trying to stop the virus, inside the nose itself, before it can gain access to the rest of the respiratory tract or body also appears to make some sense (with or without this latest study from New York).

For example, researchers at Vanderbilt University Medical Center in Nashville, Tennessee are currently recruiting for an interesting study of SNI. These researchers at Vanderbilt argue that, since no targeted local therapy in the nasal cavity against the COVID virus exists, then this study also has additional merit (they have a point). Again, since some studies have suggested saline nasal irrigations could reduce viral shedding in the nose with some other viruses, then why not try this in a clinical trial? **Since the SARS-CoV-2 virus is an ENVELOPED VIRUS** (it uses an "envelope" or covering or shield to improve survival) then using a compound that can penetrate this envelope would be interesting. Thus, the hypothesis of the Vanderbilt researches is that using saline nasal irrigation (with or without a small amount of baby shampoo) could theoretically reduce viral concentrations, transmission, secondary bacterial infections and inflammation in those infected with SARS-CoV-2. Interestingly, these researchers commented that a tiny amount of baby shampoo added to saline may also theoretically help clean out the sinonasal cavity even further. There is a theory with bacteria, for example, that if a small amount of baby shampoo is added to saline rinses, then the baby shampoo acts as a SURFACTANT, which means the potential for the rinse to penetrate the biofilms or more oily layer surrounding some bad bacteria are broken down and they get harmed or flushed out. For example, a suggestion from a researcher at the Baylor College of Medicine (https://www.bcm.edu/news/head-and-neck/new-ways-to-flush-sinus-infection) suggests only a half a teaspoon of baby shampoo is needed for 8 ounces of

saline **but everyone should consult with their doctor before trying this, and keep in mind I would not try this until this clinical trial at Vanderbilt and others give us more clarity**. Interestingly, past study from the University of Pennsylvania and several other medical research centers (Chiu AG, et al. *Am J Rhinol* 2008;22:34-37.; or Rosen PL, et al. *Am J Rhinol Allergy* 2013;27:177-180.; or Isaacs S, et al. *Am J Rhinol Allergy* 2011;25:e27-29.) found that the use of baby shampoo nasal irrigations could potentially help against some hard to treat bacteria in the nose. **Please do not** use baby shampoo for your SNI (this is a study).

There will be three groups in this Vanderbilt clinical trial of approximately 90 participants. There will be a control group that receives no nasal irrigation, a saline nasal irrigation group utilizing the product twice a day, and then the third group will use twice a day saline nasal irrigation mixed with a half teaspoon of baby shampoo. This study will be for patients that tested positive for COVID-19 at Vanderbilt and are planning to self-quarantine at home working with a doctor (so more mild disease cases).

Studies are also looking at other types of nasal washes or irrigations, such as hypertonic saline to see if that could be more effective. **There are also studies that are using SNI and mouth gargling with various compounds (including saline) that could have anti-microbial activity**. For example, there was a recent PRELIMINARY study of hypertonic SNI and gargling (then always spitting it out) multiple times a day that appeared to reduce the duration of common cold by almost two days, other OTC medical use, transmission in the household, and viral shedding. Furthermore, another follow-up look at this study suggested that some benefits appeared to also include colds not just caused by rhinoviruses, but those caused by other types, such as other coronaviruses, which is why it needs to be researched against the newest coronavirus that causes COVID-19 (Ramalingam S, et al. *J Glob Health* 2020; doi: 10.7189/jogh.10.010332; & Ramalingam S, et al. *Sci Rep* 2019;9:1015). This interesting and wonderful study, and I am not kidding here because you cannot make this stuff up, is known by the acronym **"ELVIS"** (Edinburgh and Lothians Viral Intervention Study). Thus, SNI and gargling are receiving more ongoing research interest around the globe because of **ELVIS** and numerous other studies. In other words, **"it's now or never"** (sorry joke that reflects my age) for more SNI and/or gargling studies to be initiated to determine if they truly prevent and/or reduce the progression of common cold and other viral infections. Basically, it is time for **"a little less conversation"** and I get **"all shook up"** or excited just thinking about these studies. In fact, there was even a randomized trial of **gargling with just water** published 15 years ago that demonstrated some preliminary potential efficacy with this method to prevent some upper respiratory tract infections and even the progression of them (of course not with COVID-19), which is so fascinating

(Satomura K, et al. *Am J Prev Med* 2005;29:302-307). My final advice when you gargle and spit with anything, mouthwash or water, for example, is to hit the sink and not get any of it on your **"blue suede shoes."** Please **"don't be cruel"** because my Elvis jokes were not that bad, and most people **"can't help falling in love"** with them…eventually.

If you and the health care team you trust with your health believes an SNI/nasal saline irrigation product or gargling some product could help you in some way, then it could become a part of your health prevention treatment. **However, please keep in mind, again, that the research with SNI and COVID-19 are studies without any current human results, which means this approach could ultimately be found to be effective. or not effective, or even dangerous to use with COVID-19. We have no idea until we get those results, so please do not become a clinical trial of one**.

Finally, more specific scientific research studies to determine why younger people are less likely to be impacted by this specific virus are now being conducted, which could ultimately lead to better prevention and treatments to protect vulnerable populations (regardless of age or situation). For example, there is a new study launching now known as "HEROS" (Human Epidemiology and Response to SARS-CoV-2), funded by the National Institute of Allergy and Infectious Diseases that will follow 6000 children to determine more specific risk factors for COVID-19 (https://www.nih.gov/news-events/news-releases/study-determine-incidence-novel-coronavirus-infection-us-children-begins). Elvis is about to leave the column.

Thank you for reading my latest installment and I wish you and your family the best of health. **I am concerned, of course, but I am also incredibly optimistic!** I look forward to modern day science and you of course, kicking COVID-19 and cancer in the gluteus maximus!

All of my best always,

Mark A. Moyad MD, MPH

Please pay attention to all of the CDC recommendations that can be found at https://www.cdc.gov/coronavirus/2019-ncov/index.html

Read my previous COVID-19 articles at:

- Coronavirus Part 1 (Hopefully There is No Part 2 Because We Will Have Conquered Corona Quickly)

- Coronavirus Part 1.1 (The Countless Unsung Heroes in the Battle to Beat this Thing Has Begun! [aka Almost 100 Clinical Studies and Counting])

- Conquering COVID Part 1.2: “Drug Repurposing” clinical studies are happening right now! (aka Hydroxychloroquine, Tocilizumab … & even Viagra Versus COVID-19?)

- Conquering COVID Part 1.3: “Starkloff Social Distancing Saves Lives Now!”(aka as the curve becomes critical so does the history lesson)

- Conquering COVID Part 1.4: “40+ reasons why a vaccine could & should work?!” (aka the virus is currently NOT a chameleon)

- Conquering COVID Part 1.5: “Research has spoken: time for clean, breathable, effective (CBE) mask utilization!” (aka Dodgeball without rules/masks? No thanks!)

- Conquering COVID Part 1.6: “Vaccine Repurposing & now 70 potential vaccine candidates?!” (aka the test tube Is half-full, not half-empty)

- Conquering COVID Part 1.7: "Now over 900 clinical studies- including a Gout pill?!" (aka a few weeks ago it was 100 clinical

studies - the pros & cons of a "natural" medicine)

- **Conquering COVID Part 1.8 A & B (HBOT Double Issue!): “HBOT for some cancer side effects or COVID-19?!” (aka more medical centers face "pressure” to offer this option)**

- **Conquering COVID Part 1.9 A & B (Another Double Issue): "Sleep & 33% or one-third of your entire life?!" (aka Sleep Health = Better Software Updates & Immune Health)**

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www.ustoo.org/covid