

Intranasal Xylitol, Recurrent Otitis Media, and Asthma: Report of Three Cases*

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ABSTRACT: Upper respiratory problems have been increasing since the early 1970s, owing to environmental factors that include poorly conceived drug therapy. Otitis media, asthma, sinusitis, and allergies can all be related to chronic faulty hygiene in the nasopharynx. A nasal spray, consisting of xylitol (a naturally occurring food substance) in saline, has been developed to aid the self-cleansing mechanism of the nasopharynx and to reduce local pathogens. The preventive value of the nasal spray is demonstrated in 3 case reports.

Introduction

The spectrum of problems we term upper respiratory infections (URIs) are the most common presenting complaints to primary care physicians. Beginning with nasopharyngeal colonization, bacteria extend down the Eustachian canal to cause otitis media, through the ostiomeatal complex to cause sinus infections, and nasal bacteria that are aerosolized or aspirated cause bronchitis (although this is properly a lower respiratory infection). The treatment of these conditions is the primary reason for the use of antibiotics, and their overuse is the primary source of antibiotic resistance.

Besides the infectious problems, allergens and irritants in the nasopharynx cause allergic disorders, and they, together with viral URIs and chronic sinus disease, are the major triggers for asthma. Another major trigger, gastro-esophageal reflux, causes a reflex inflammation in the nasopharynx.

Since the early 1970s, we have experienced steady increases in these problems. Documented by the National Center for Health Statistics for otitis¹ and by the Centers for Disease Control for asthma,² these conditions have been increasing at about 5% to 6% per year since the 1970s (see Figures 1 and 2). Specialists in their respective areas have tried to find reasons for the increases. Day-care use is seen as the primary reason for increases in ear infections³ and increases in allergies as the reason for increases in asthma. Since allergies are a major trigger for asthma, this explanation tends to be circular, and most accept that the underlying reasons for the increases remain unclear. A recent observation compounding this problem is that asthma increases are not seen in Eastern Bloc countries such as Russia and Albania.⁴

* After observing the benefit described in this article, I applied for and received a patent on the method of xylitol delivery intranasally.

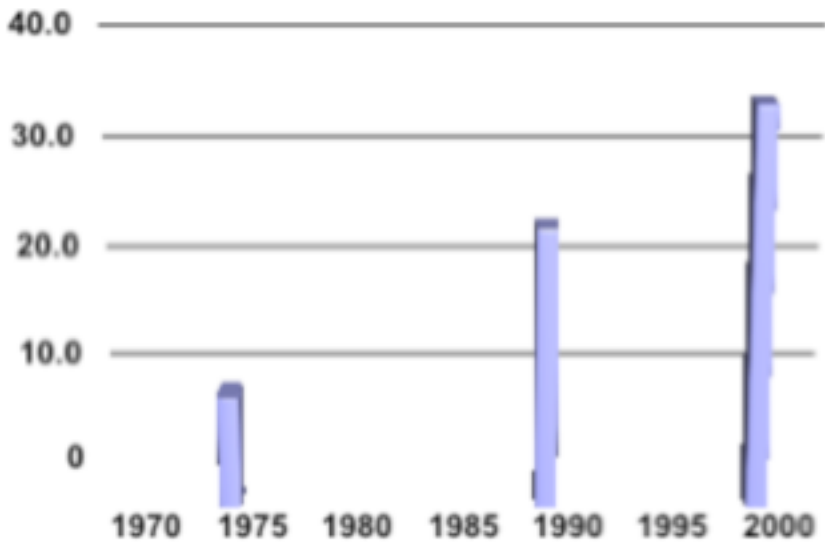


Figure 1 Increases in Otitis Media in U.S. (2000 — extrapolated)

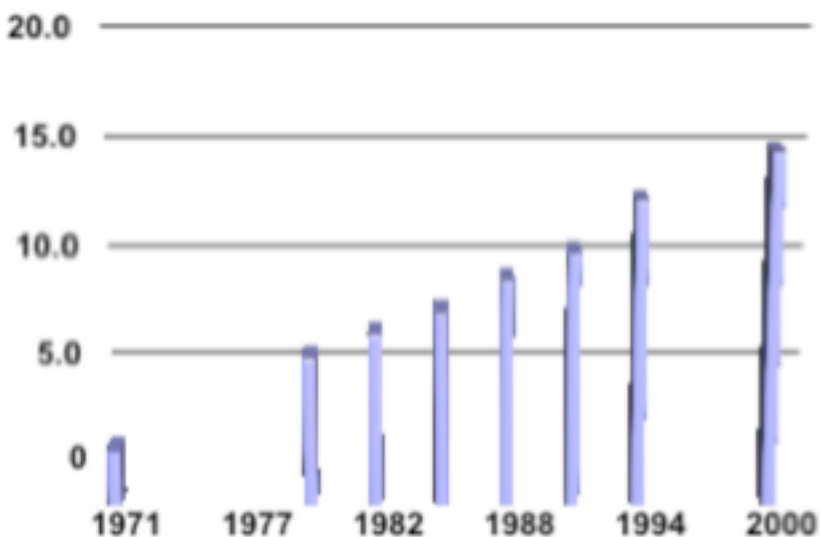


Figure 2 Increases in asthma in the U.S. (1971 and 2000 are extrapolated)

The parallel increases of both asthma and otitis should raise the obvious question of what happened in the early 1970s to prompt them. Since otitis and asthma are wholly different processes, the increase in incidence suggests that there is something the respective illnesses have in common. We may be missing the forest for the trees. The nasopharynx appears to be the central nidus where both the infectious and allergic processes have their origin.

The following case reports are from my own experience and practice using a nasal spray containing an 11% solution of xylitol with 0.65% saline that stimulates the washing of the nasopharynx.

Case Reports

Case 1

H. was 5 months old when her parents placed her in day care. She was breast-fed until she was 2 years old. Neither parents nor day-care workers smoked. Within 2 months of beginning day care, she had an ear infection that resolved with oral amoxicillin. But infections recurred, and within 5 months she had experienced 4 more. Learning problems are associated with recurrent ear infections in this critical time of life. These problems occur even when ear infections are treated appropriately,⁵ and ventilation tubes do not affect the learning problems.⁶ Parents and day-care workers cooperated in washing (spraying) H.'s nose every time they changed her diaper. She had no further ear infections until about 6 months later when a new day-care worker had been hired who was not aware of the spraying routine. Reestablishing regular nasal washing resolved this problem without the need for antibiotics. H. continues to use this spray on a regular basis and has had only 2 febrile episodes in the 3 years since beginning the regular nose washing, far less than the 6 URIs per year described as normal for children attending day care. H.'s only antibiotic use in the last 2 years was for streptococcus-antigen-positive tonsillitis.

After this story appeared in a local paper, I soon had many other similar children in my practice and was able to get follow-up information on 10 of them. The parents reported a total of 43 ear infections in the 5 months prior to my seeing them, an incidence of 0.86 a month. Over an average of 11 months follow-up, the parents reported a total of 7 ear infections, an incidence 0.06 per month. Of the infections that did occur, 3 were in 1 child and 3 occurred when the use of the spray was interrupted.

Case 2

B. was 8 years old when she came to my attention.

She was receiving 5 different medications for her asthma, including regular nasal and frequent systemic steroids. She visited an emergency room about every 6 weeks. After hearing about the xylitol spray, her mother began spraying the child's nose regularly 3 times a day. About a week later B. had an episode where some of the material filling her nasopharynx broke loose gagging her in the process. Her mother, and others who have had similar episodes with this spray, described it as a frightening experience, but the next week B. did not have any trouble with her asthma. A week later her mother stopped all of her asthma medications. Six months later B. was actively playing basketball and doing gymnastics without any trace of asthma. About 2 years after B. began using the spray, I called to ask for a progress report. She had experienced only 1 asthma attack and was no longer using the spray.

Case 3

C., aged 42 years, has had diabetes and asthma for about 20 years. She had been receiving multiple medications for her asthma, including steroids that make her diabetes harder to manage. She had been in the hospital for her asthma and related pulmonary infections an average of 2 times annually for the past 10 years. She began using the spray regularly and in the ensuing year did not experience any asthma and did not require any asthma medication. Her peak flow remained at 150 to 200 L/min for about 6 months but was 350 L/min after a year of regular use of the spray.

Discussion

Normal nasal cleaning

Mucociliary clearance is the primary means of removing pollutants from the nasopharynx. Environmental factors affecting this mechanism will be reflected by the incidence of problems. Cigarette smoke, for example, causes more problems because it is cilia toxic. Most upper respiratory conditions occur in the fall, after the first cold spells. Turning on the heat in our homes and businesses dries the air we breathe, and in turn makes the mucus drier and harder to clear. The greatest incidence of otitis media and chronic suppurative otitis in this country is in the Native American people of Alaska. Healthcare workers dealing with these people reported that these problems did not exist prior to their becoming "civilized," (D.Knudsen, personal communication). While there are many factors involved with "civilizing," which included decreased breastfeeding and some group child care, one factor was certainly housing with central heat. Going from a winter dwelling where the relative humidity is close to 100% to a home where it is closer to 20% was apparently too much for these people, who had otherwise adapted to their environment in a healthy way. Day care and crowded working conditions led to increased sharing of bacteria that taxes the mucociliary apparatus. Breastfeeding is protective for most upper airway problems not only because of the preventive influence provided by the immunoglobulins, but because breast milk provides more water than commercial formulas. When pollution, from allergens or pathogens, is too much for mucociliary clearance, mast cells are triggered that release histamine, tryptase, and other enzymes. Histamine opens the proximal venules, leading to an extravasation of fluid and immune complexes. Christor Svensson⁷ has studied this process and points out that:

Topical histamine induces extravasation of plasma from the subepithelial microvessels. The plasma exudate first floods the lamina propria and then moves up between epithelial cells into the airway lumen. This occurs without any changes in the ultrastructure or barrier function of the epithelium. *We have therefore forwarded the view of mucosal exudation of bulk plasma as a physiological airway tissue response with primarily a defense function.* (Emphasis added)

In a commonsense interpretation of this description, the tryptase is the soap and the histamine turns on the water for nasopharyngeal washing; for the body, the solution to pollution is dilution. Current Treatment

On the other hand, this washing does cause some symptoms, and drugs are traditionally used to reduce them. More than 60 years ago, the role of histamine in allergic and inflammatory conditions was discovered, and antihistamines were developed to block the response. Histamine was seen as the reason for the symptoms and not as a defensive response of the body. The number of antihistamines and decongestants multiplied, and many of them became available over the counter and have been readily available for the past 30 years. They rapidly became the standard treatment for colds and congestion. More recently, nasal steroids were added to deal with inflammation.

All of this happened at the critical time period in the early 1970s when the above-noted increases in nasopharyngeal problems began. Eastern Bloc nations have not had exposure to Western television advertising nor to the wholesale use of these drugs; and they have not had the increases in asthma that we in the Western world have experienced. What these drugs are designed and intended to do is block the histamine-induced rhinorrhea and shrink swollen membranes to allow easier draining of sinuses and Eustachian canals. What the drugs *do*, in effect, is to turn off nasopharyngeal washing. Decongestants close down the leaking blood vessels—turning off the water. Nasal steroids turn off the immune system, which then fails to respond to the pollution in the nasopharynx.

For more than 25 years, we have been systematically turning this normal defensive washing off; and we have experienced close to a 3-fold increase in the problems originating in this area. The cost of treating ear infections in 1990 was estimated to be between 3 and 4 billion dollars' and that of asthma to be \$5.8 billion in 1994:

Extrapolating these costs over the 25-year period reveals that the added costs, over the baseline of the incidence in 1975, are on the order of \$100 billion. That does not include the costs of sinus or allergic diseases. The late Senator Dirksen is reported as saying, "A billion dollars here, and a billion dollars there, and pretty soon you're talking about real money." Clearly we need to stop blocking this normal process, and doing so should substantially reduce the incidence of upper respiratory problems. If, however, we learn from our mistakes, an even better response would be to facilitate nasopharyngeal washing.

Washing the Nose

Saline nasal sprays have been available for over 25 years. They have been shown to improve the quality of life and decrease the incidence of sinus problems when used regularly. They have no reported effect on otitis or asthma. Hypertonic saline solutions are more effective at cleaning the nasopharynx. Saccharin transit time, a measure of mucociliary transport, is decreased, indicating that this function is accelerated. The problem with saline, especially hypertonic saline, is 2-fold. First, the body's own antibiotic substances in the airway surface fluid work better when saline concentration is low.⁹ Secondly, a normal saline concentration slows ciliary activity. A 7% solution paralyzes them temporarily and a 14% solution paralyzes them permanently.¹⁰ A 3% hypertonic saline is commercially available that speeds the clearing of mucus from the nose because of its irritant effect, but it is expensive. On the other hand, it is easy to make. However, many people believe that if a little of something is good, more may be even better. Therefore it may be wiser not to advise patients to make up their own saline solutions.

Silber and his colleagues¹¹ studied the effect of hyperosmolar solutions in the nose in the late 1980s, using a solution of mannitol that was approximately 3 times the osmolarity of normal body fluids. When 5 ml was put into the nasopharynx for a few seconds, then removed, these researchers found increased histamine and an increase in volume of the recovered fluid. Looking at this in terms of nasopharyngeal washing, we can see some obvious advantages. Not only does this solution turn on the washing by stimulating the release of histamine, it also increases the amount of water, enabling the washing to be more effective. There were no ill effects felt by the subjects in this study. Mannitol is not easy to obtain, but xylitol, a polyol similar to mannitol, is commonly available. It has some pronounced advantages when used nasally.

Zabner⁹ used a 5% (near isotonic) solution of xylitol sprayed 4 times a day into the nostrils of normal subjects and found after only 4 days that it decreased bacteria counts of coagulase negative Staphylococci. He and his colleagues believe that such a spray may be beneficial to people with cystic fibrosis because it lowers the saline content of the airway surface fluid and allows the innate antibacterial properties of that fluid to work more effectively. These researchers

also showed that xylitol was not absorbed, indicating that the actions were mechanical and due to the osmotic properties of the xylitol. While mentioning the osmotic properties, Zabner and his colleagues gave little credit to the inherent antibacterial properties of xylitol, which are significant.

Xylitol was first studied by the Finns, who showed that oral xylitol reduces tooth decay.¹² Orally administered xylitol in syrup¹³ and in chewing gum¹⁴ reduced the incidence of ear infections by 30% and 42%, respectively. Early studies attributed these benefits to the fact that the bacterial group of alpha streptococci, which includes *Streptococcus mutans*, the primary cause of tooth decay in the mouth, and *Streptococcus pneumoniae*, in the nose, are found to ingest xylitol, but they cannot metabolize it.¹⁵ In human terms, they get indigestion. Further studies of these two bacteria showed that their adherence to their respective surfaces is decreased in the presence of xylitol. In a study looking specifically at nasal pathogens, a 5% solution of xylitol reduced their adherence to cultured nasal cells by 68% for *Streptococcus pneumoniae* and 50% for *Haemophilus influenzae*.¹⁶ This study makes the nasal use of xylitol very sensible. At its conclusion the authors point out that high concentrations of xylitol are needed to produce these effects. Spraying seems to be the logical way of placing it in the nasopharynx.

Most of the studies of the bacterial effects of xylitol have been performed on *S. mutans*, but xylitol's effect on other bacteria has been increasingly investigated since its preventive benefit on the incidence of otitis has emerged. The results of recent dental studies point to the possibility of more profound benefits. A two-year study¹⁷ was carried out in Belize using six different types of gum on children around the time they lost their primary teeth. At the end of the study, the children chewing the xylitol gum had better dental health than all other subjects. There were no surprises in this study. But five years later, the dental researchers returned to Belize and examined the children again.¹⁸ They found that the group of children who had chewed the xylitol gum and whose permanent teeth erupted during the second year of the study, or after the study was completed, had 90% fewer cavities. These children had no access to xylitol during the 5-year period after the first study.

It is difficult to explain this benefit using the short-term effects of bacterial indigestion or decreased adherence described earlier. These long-term benefits, which occurred in the absence of continued exposure to xylitol, suggest either a change in the type or nature of the bacteria. Both have been shown to occur in laboratory studies. The nature of the bacteria can change because a type of resistance does develop in *S. mutans*—it learns not to eat the xylitol. But in the process, it also loses some of its virulence and no longer makes the acid that initiates the tooth decay.¹⁹ We also know that the type of bacteria can change because of xylitol. Soderling and associates²⁰ found that mothers who chewed xylitol gum passed significantly less *S. mutans* to their infants. At age five, these children had 70% fewer cavities without ever being directly exposed to xylitol.²¹ Whether these long-term benefits will carryover for *S. pneumoniae* remains for future studies to determine.

Our experience with this spray began after reading the first article describing the reduction in otitis with xylitol chewing gum. The direct effect of the xylitol on the nasal pathogenic bacteria seems to be the strongest benefit for preventing infectious problems. But the calculated osmolality of the xylitol in this solution is 723 mOsm, which is high enough to reproduce both Silber's washing and Zabner's osmolyte effects. The small amount of the spray is not irritating, and if used in both nostrils every hour, 24 hours a day, would deliver about as much xylitol as is in half of a plum.

Xylitol is a food substance with two-thirds the calories of sucrose. It is found in many fruits, such as plums, and has been given the safest rating by the World Health Organization and the Food and Drug Administration as a food additive. The average person makes about 10 grams

daily in the cells of the body. When xylitol is given intravenously, the usual dosage is 25 mg/kg/hr, and even twice that much is a safe dose.²²

While it makes sense to assist the immune system in this way, the benefits seen in the reduction of tooth decay, to say nothing of the reductions in otitis, sinusitis, allergies, and asthma, are "drug" benefits. Classifying commonly available foods as drugs is not financially feasible. No "drug" studies have been done with xylitol, and there is neither pharmaceutical nor industry interest in doing any. No advertising can be done claiming a "drug" benefit without xylitol being manufactured as a drug, but people use the gum to prevent tooth decay because they know about the studies showing its effectiveness. A solution of xylitol and saline is commercially available that is intended only to help the immune system wash the nose.

Conclusion

According to the Centers for Disease Control, handwashing is the most effective means of preventing the spread of communicable disease, since it protects the nose from the contamination associated with putting our hands to our faces. It makes as much sense to wash the nose regularly. Using xylitol in a nasal spray is a very effective way of both assisting and stimulating the body's own natural nasopharyngeal washing, and reducing both bacterial colonization and allergenic pollution, with their accompanying problems.

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