

“Squirt, Sniff, Burn”¹

Introduction

Zinc is a vital nutrient that serves many roles in the body. Present in many foods and dietary supplements, zinc aids the function of over 100 enzymes, has a presence in the immune system, helps heal wounds, and is a requirement for the synthesis of DNA and cell division (“Dietary Supplement Fact Sheet: Zinc”). Recently, zinc has also been used as the active ingredient in homeopathic cold remedies.

Zicam, an over-the-counter medicine that claims to reduce the severity and duration of the common cold, is applied intranasally and composed primarily of a diluted form of zinc gluconate. This particular remedy has enjoyed moderate popularity, selling over 35 million units since its introduction in 1999 (“Message to Consumers”).

Despite its widespread use, the intranasal application of zinc has recently produced safety concerns. In June 2009, the FDA warned the public against using three over-the-counter zinc products: Zicam Cold Remedy Nasal Gel; Zicam Cold Remedy Nasal Swabs; and Zicam Cold Remedy Swabs, Kids Size. The FDA attributed the recall to over 130 consumer reports of anosmia after Zicam use (“FDA Advises Consumers Not to Use Certain Zicam Cold Remedies”). Though cooperating with the FDA, Matrixx Initiatives, the maker of Zicam, maintains that its products are completely innocuous; the company argues that the anosmia being experienced by consumers is simply a side effect of malady that Zicam treats (“Message to Consumers”). Though the number one cause of anosmia is the common cold, evidence has surfaced suggesting that the intranasal application of Zicam may not be safe. Historical incidents,

¹ (Alexander and Davidson 217)

numerous case reports, and recent research on the effects of zinc gluconate on olfactory function reveal that the use of Zicam can in fact cause the user to lose his or her sense of smell.

Historical Evidence

Reports of zinc induced anosmia first surfaced in the 1930s during an outbreak of the polio virus. At the time, it was commonly thought that the polio virus entered the body through olfactory nerves in the upper nasal cavity. This prompted scientists to search for a method to avert the virus from inside the nose. E.W. Schultz discovered such a method. Through experiments with monkeys, he theorized that zinc sulfate could “coagulate” certain proteins in the olfactory epithelium and create a barrier in the nose that the polio virus could not penetrate. He noted that anosmia would be a side effect of the zinc sulfate application, but stressed that the effects would only be temporary (Jafek, Linschoten and Murrow 138).

Schultz’s potential treatment was tested in Toronto, Ontario during the late summer and early autumn months of 1937. About 5,000 children and a few adults were given either one or two doses of a 1% zinc sulfate solution administered intranasally with a pump-like device (see figure 1). Only 25 percent of those given treatment reported experiencing anosmia. However, several of those people reported some disruption to their sense of smell or taste after 2-6 months (Tisdall, Brown and Defries 60-62). This clearly contradicted Schultz’s

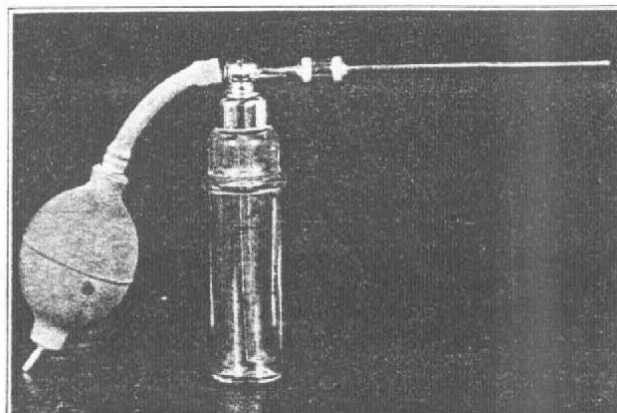


Fig. 1. The instrument recommended to apply the zinc sulfate solution in the 1930s. The long nozzle was engineered to forcefully expel the solution up to the “roof” of the nasal cavity. Image from F.F. Tisdall; Alan Brown; and R.D. Defries, "Persistent Anosmia Following Zinc Sulfate Nasal Spraying," *Journal of Pediatrics* (1938): 60-2, Web, 12 Nov. 2009.

assertion that anosmia caused by zinc sulfate lasted only temporarily; according to these reports, zinc can cause persistent anosmia similar to the anosmia being experienced by Zicam users.

Matrixx Initiatives responds to the studies in the 1930s on zinc sulfate and anosmia in the following manner:

Certainly no conclusion can be determined from these studies relative to Zicam, which involves a different compound (zinc gluconate), in a different concentration, applied differently, in a different dose, to a different part of the nasal anatomy. It is also important to note that no scientific studies have ever shown that use of Zicam Cold Remedy intranasal products or zinc gluconate applied intranasally can cause loss of smell. (“FDA Questions”)

Unfortunately, the company’s arguments do not sufficiently prove that Zicam has no effect on the sense of smell.

For example, in a 1982 study by Paul Catalon involving the effects of various salts on the olfactory cells of catfish, Catalon asserted that it was the actual Zn^{2+} cation that harmed the olfactory epithelium. He made that conclusion based on the fact that both the compounds $ZnSO_4$ and $ZnCl_2$ produced similar damage in the nose. He also observed that the effects were “concentration independent” (Jafek, Linschoten and Murrow 139). Since zinc gluconate, the main ingredient of Zicam, contains the same Zn^{2+} cation, it is entirely possible that Zicam in any concentration could cause anosmia.

Furthermore, Matrixx Initiatives’s statement referring to its product’s application “to a different part of the nasal anatomy” does not account for human error. When used as directed, the Zicam gel does not come close to the olfactory nerves in the nose. However, a nasal pump

(see Figure 2) is used in the application of zinc gluconate. This instrument could force some zinc onto the olfactory epithelium if inserted too deeply into the nasal cavity.



Fig. 2. The nasal pump used in the application of Zicam. This pump forcefully expels solution in a similar manner to the pump used in the 1930s.

Image from “Zicam Review. Does Zicam Cold Remedy Really Work?,” Product Review Ratings, n.p., 10 Dec. 2008, Web, 12 Nov. 2009

These observations support the notion that zinc gluconate can adversely affect the sense of smell, just as zinc sulfate did over 70 years ago.

Case Reports

Since Zicam’s introduction in 1999, there have been relatively few complaints of anosmia in relation to the total population of Zicam users.

Matrixx Initiatives dismisses these cases as results of the common cold and not the application of zinc gluconate (“FDA Questions”).

Nevertheless, many of the claims against Zicam may have some merit.

Aside from numerous anecdotal reports of consumers losing their sense

of smell, there have been case studies and evaluations performed by

medical professionals that isolate zinc gluconate as the cause of

anosmia in several patients.

Seventeen patients claiming to be anosmic as a result of Zicam use were evaluated by Dr. Thomas Alexander and Dr. Terence Davidson at the University of California San Diego Nasal Dysfunction Clinic. All of the subjects reported squirting a zinc gluconate nasal gel into their nostrils, sniffing the gel deeper into their nasal cavity, and then experiencing an acute burning sensation, with anosmia following within a couple of days. Through physical examinations, CT scans, and other observations, the principal investigators were able to rule out any inflammatory conditions or infections that could have caused the anosmia in fifteen patients. Alexander and Davidson excluded the possibility of post viral anosmia mainly because burning is not a characteristic of anosmia caused by a cold. Additionally, patients who realize they have lost their

sense of smell after an infection do so after about two weeks, not within a few days.

Furthermore, six of the people evaluated never experienced the symptoms of a cold (Alexander and Davidson 217-20).

The Department of Otolaryngology at the University Of Colorado School Of Medicine evaluated seven men and three women who reported anosmia after using Zicam. These subjects also reported the symptoms observed in Alexander and Davidson's study; their anosmia was characterized by a squirt, a sniff, and a burning sensation. Through a questionnaire, the staff at the University of Colorado was also able to rule out any other factors influencing the loss of smell in the patients (Jafek, Linschoten and Murrow 138).

Clearly, not all of the consumer reports alleging zinc-induced anosmia can be attributed to infections or other causes. Matrixx Initiatives should address the possibility that its product causes a life-altering side effect.

Recent Experiments

Before 2009, only one major study had been published that tested the direct effects of zinc gluconate on the olfactory epithelium in animals. In this 2007 experiment, Burton Slotnick and his colleagues found that only large amounts of Zicam could cause olfactory dysfunction when various volumes of zinc gluconate solution were applied into the nasal cavities of mice. Additionally, the principal investigators reported that the affected mice recovered normal olfactory function within three weeks (Slotnick et al. 743-49). These findings had seemed to discredit the allegations against Zicam.

However, a new study on Zicam yielded conflicting results. Scientists at the University of Washington also used zinc gluconate nasal irrigation to test the effects of Zicam on the sense of smell in mice, and they found that Zicam caused significant damage to the olfactory cleft. Even

after two months, the mice treated did not regain normal olfactory function. Many of the methods used by Slotnick were questioned in this new study as well. For example, the principal investigators of the 2009 study found it difficult to evenly distribute a solution over the whole surface area of the olfactory cleft in mice when small values of solution were used. Slotnick administered doses as small as 2 μ l; it is possible that little to no zinc gluconate actually reached the olfactory epithelium of the mice in his study (Lim et al.). The objectivity of Slotnick's study should also be questioned considering the fact that it was funded in part by Matrixx Initiatives (Slotnick et al. 743).

Conclusion

The FDA recall of Zicam is a cause for concern. With no warning on the drug's label other than the generic "use as directed" note, millions of consumers unexpectedly purchase a product that could significantly affect one of the five senses. Additionally, many assume that homeopathic products are safe. What many don't know is that these "safe" remedies actually undergo less testing and scrutiny than mainstream pharmaceuticals. In order to fulfill its mission to protect public health, the FDA should put into place more regulations on homeopathic medicines such as Zicam, so potentially dangerous products will not be marketed for years with their hazards undiscovered.

Works Cited

- Alexander, Thomas H and Terence M Davidson. "Intranasal Zinc and Anosmia: The Zinc-Induced Anosmia Syndrome." *Laryngoscope* 116.2 (2006): 217-20. Print.
- "Dietary Supplement Fact Sheet: Zinc." *The National Institutes of Health Office of Dietary Supplements Website*. The National Institutes of Health Office of Dietary Supplements, 7 Nov. 2008. Web. 17 Nov. 2009.
- "FDA Advises Consumers Not to Use Certain Zicam Cold Remedies." *U.S. Food and Drug Administration Website*. U.S. Food and Drug Administration, 16 June 2009. Web. 8 Nov. 2009.
- "FDA Questions." *Zicam Official Website*. Matrixx Initiatives, n. d. Web. 19 Nov. 2009.
- Jafek, Bruce W, Miriam R Linschoten and Bruce W Murrow. "Anosmia after Intranasal Zinc Gluconate Use." *American Journal of Rhinology* 18.3 (2004): 137-41. Web. 12 Nov. 2009
- Lim, Jae H, et al. "Zicam-Induced Damage to Mouse and Human Nasal Tissue." *PLoS One* 4.10 (2009). n. pag. Web. 14 Nov. 2009.
- "Message to Consumers." *Zicam Official Website*. Matrixx Initiatives, 16 June 2009. Web. 10 Nov. 2009.
- Slotnick, Burton, et al. "Olfaction and Olfactory Epithelium in Mice Treated With Zinc Gluconate." *Laryngoscope* 117.4 (2006): 743-49. Print.
- Tisdall, F.F., Alan Brown and R.D. Defries. "Persistent Anosmia Following Zinc Sulfate Nasal Spraying." *Journal of Pediatrics* (1938): 60-2. Web. 12 Nov. 2009.

