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Silver Diamine Fluoride 38%

The Food and Drug Administration **has cleared** Advantage Arrest 38% Silver Diamine Fluoride for the treatment of dentinal hypersensitivity.

The Food and Drug Administration **has not cleared** Advantage Arrest 38% Silver Diamine Fluoride for the treatment of carious lesions.

This packet is provided to oral health professionals to allow them to understand the available peer-reviewed research that exists on the use of silver diamine fluoride worldwide for the treatment of caries. We are providing:

- Contact information for the Oral Health Information Department of Elevate Oral Care for any questions you might have following this review.
- The Advantage Arrest Package Insert.
- A systematic review article entitled: Silver Diamine Fluoride: A Caries “Silver-Fluoride Bullet”, J Dent Res 88(2): 116-125, 2009.
Download at: <http://www.elevateoralcare.com/dentist/JDR09>
- All known contrary references.
Download at: <http://www.elevateoralcare.com/Dentist/GISDF>
- All known references past 2009.

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We encourage you to direct any questions you have regarding this information to one of the contact points above.

For Total Body Health

Frequently Asked Questions

- 1. Does the application technique differ between the label indication of relief of dentinal hypersensitivity and the off label indication of caries control?**

In countries where silver diamine fluoride is used for the control of caries the application technique is identical to the instructions we provide in the Advantage Arrest Package Insert for the relief of dentinal hypersensitivity. No excavation, decay removal or anesthesia is required. The area to be treated should be “dry tooth brush” clean, free of plaque and debris. The area should be free of saliva, so as not to dilute the material. Transfer the material from a disposable plastic dappen dish to the surface to be treated and allow time to dry, which generally occurs in 30-60 seconds. If accelerated drying is required due to patient compliance use a low/weak air stream to dry the material.

The chemical action of the silver diamine fluoride occurs almost immediately in the outer layers of the softened dentin and can be confirmed by changes in the hardness and density of the dentin surface, similar to caries that arrests naturally because of positive changes in oral hygiene, diet, or daily application of fluoride in custom trays. The darkening of the lesion occurs over 24 hours and may increase over a week. Reexamination of the lesion at the next regular recall is appropriate and reapplication of silver diamine fluoride may be warranted. Repeat until the lesion has arrested

- 2. Is there a recommended frequency of application of silver diamine fluoride for caries control?**

Caries arrest studies were conducted with silver diamine fluoride applications of once and twice annually. Arrested lesions were retreated every six-months.

Clinicians have reported that they will recall their first cohort of silver diamine fluoride patients within 3-6 weeks to evaluate the application and action of the treatment. Once they have a feel for the predictability of the material with their application technique they will set recall appointments based on the risk level and caries activity of the patient with higher risk patients at 3-month intervals. Moderate to high-risk patients, where it appears that home care and diet counseling has had positive impact, are recalled at 6-months.

- 3. Does the application of silver diamine fluoride to a lesion cause discoloration?**

Yes, darkening of decayed, demineralized sites occurs as the lesion arrests. This is similar to what is seen when caries arrests from changes in diet or increased use of other fluorides. A recent study showed that patients see the discoloration as a clear indication that the treatment is working. Similar to the treatment of eroded and hypersensitive dentin, the treated area can be restored using glass ionomer or with a sandwich restoration of both glass ionomer and composite. In lab studies, bond strength of composite by itself to treated surfaces is reduced but the clinical importance is unknown.

38% silver diamine fluoride should not be diluted in an attempt to reduce discoloration. Studies have shown that diluted solutions may not be effective for caries arrest.

Ionic silver adsorbs onto almost any protein surface and is especially tenaciously bound to denatured proteins. This accounts for the specificity to carious collagen over normal collagen, but both will stain. The differentiator between these stains is that with silver diamine fluoride use, intrinsic pigmentation of a carious lesion occurs and surface protein staining occurs primarily on healthy tissue. These oxides are bound to the tissue and don't wash or polish away. This is why the blackened lesion retains its dark color for so long, and is most likely the reason the antimicrobial effect is long lasting.

The functional indicator of effectiveness is when the silver oxide is bound to the diseased collagen. If the surface doesn't turn black, the silver didn't bind and the antimicrobial effect will only be short lived.

4. Can Advantage Arrest be used on a prepared tooth just prior to restoration cementation?

Desensitizing agents, have been shown to be protective of the pulp when placed on crown preparations to reduce dentin permeability. Advantage Arrest, a desensitizer, has been shown safe to the pulp when placed on exposed dentin. In addition, studies have shown desensitization and efficacy in treating softened dentin before placing direct restorations. Usually the tooth is first treated with silver diamine fluoride 38% immediately followed by potassium iodide (without washing) to remove excess silver and reduce darkening of dentin. This provides the benefit of sealing tubules plus the antimicrobial benefits of both silver and fluoride

5. Are there any contraindications for the use of silver diamine fluoride for the control of caries?

Silver diamine fluoride should not be placed on exposed pulps. Other topical fluorides (e.g. fluoride varnish) should not be used in the same appointment. Studies have shown that 38% silver diamine fluoride conveys more effective protection against decay in other teeth than fluoride varnish with reduced overall fluoride exposure.

6. Is there evidence of caries prevention benefit to non-application sites following Advantage Arrest use for a patient?

Treating carious areas with silver diamine fluoride 38% acts as a whole mouth fluoride treatment. It can also be used in place of sealants in grooves. A protective effect has been shown to non-treated teeth and surfaces. These findings come from high quality randomized clinical trials.⁷⁸

7. Are there any post appointment instructions for the patient or the caregivers/guardians?

There are no postoperative limitations. Patients may eat or drink immediately. Patients may brush their teeth with fluoridated toothpaste on their regular schedule.

8. Does silver diamine fluoride stain skin, countertops, instruments etc.?

The capillary action of the applicator brush supplied with Advantage Arrest reduces dripping from the brush when transferring the material from a disposable plastic dappen dish. Patients should be protected with bibs and safety glasses as in any clinical procedure.

Contact to skin and oral tissue is not harmful but is likely to cause temporary tattooing. On skin and oral soft tissue the effect is not immediate, rather it will be noticed within hours. The staining will be limited to direct areas of contact and will fade over a period of 24-72 hours. If you believe you have touched the applicator to the skin of a patient it is good to advise them of possible tattooing.

When dispensing silver diamine fluoride it is a good idea to use an absorbent material that has a coated bottom, like a patient bib, under the dappen dish and applicator to avoid contact with metal trays and office countertops. If silver diamine fluoride comes in contact with instruments or countertops wash immediately with water, soap, ammonia or iodine tincture and then rinse thoroughly with water. Sodium hypochlorite (household bleach) can also be used for difficult stains.

9. *A contraindication in the Advantage Arrest Package Insert states that patients with more than six affected sites are recommended for exclusion. What are the safety implications for application of Advantage Arrest for a patient that has more than six sites to be treated?*

The Margin of Safety for the volume of product needed to treat six sites is within 130 times the NOAEL (no-observed-adverse-effect-level). Treating more sites in one visit will likely have little practical impact on patient safety. Like protocols for fluoride varnish application, the suspension for several days of fluoride supplements is advised.

10. *How does an arrested lesion treated with Advantage Arrest look like on radiographs?*

Arrested lesions look like a scar on radiographs. You will observe radio-opacity as the mineralization of the previously softened dentin increases. Ultimately the best test of arrest is still the color change and tactile hardness of the dentin surface.

It is advised that you educate your referring dentist about your use of Advantage Arrest since the appearance of a treated lesion might be new and confusing for many practitioners.

11. *How can Advantage Arrest be coded using CDT?*

There is a new CDT code for 2016 specifically for the use of caries arresting medicaments; the off-label use of Advantage Arrest.

Code D1354

The nomenclature reads: "Interim caries arresting medicament application," with the descriptor; "Conservative treatment of an active, non-symptomatic carious lesion by topical application of a caries arresting or inhibiting medicament and without mechanical removal of sound tooth structure."

It is common for insurance providers to initially not reimburse for new codes as they are developing usual and customary rates for the procedure. However, it's important the new code is used so the providers can see the volume of use and determine future coverage. There are several providers that have announced coverage in various states.

There are three other options to code the use of Advantage Arrest Silver Diamine Fluoride 38%. These codes are:

D1208 - Topical application of fluoride

Silver Diamine fluoride is categorized as a fluoride and can be used to treat site-specific locations. Its application and effect is very different than most fluorides, but the Off-Label indication is acceptable for this code use.

D 9910 - Application of a desensitizing medicament, per visit

Silver Diamine fluoride is indicated for dentinal hypersensitivity treatment and can be used to treat site-specific locations.

D1999 - Unspecified preventive procedure by report

From a third party payer perspective, this is the preferred code so providers can track the frequency of a procedure and develop usual and customary rates for future coverage.

It is also helpful to identify caries risk to justify the reimbursement with a recognized caries risk tool. Codes: D0601 (low), D0602 (moderate) and D0603 (high) codes are especially helpful in adult claims.

12. Can Advantage Arrest be used as a cavity Liner?

Silver Diamine Fluoride (SDF) is cleared in the same FDA category as cavity liners. Although there are no head to head clinical trials comparing SDF as a cavity liner, it has been used successfully in this way.

Silver Diamine Fluoride will not discolor intact enamel or dentin. SDF can discolor demineralized tooth structure brown/black. Some of this discoloration may shadow a restoration and can create less than optimal esthetic restorations.

13. Who is allowed to apply Silver Diamine Fluoride in clinical practice in my State?

Each State dental practice act is different. Since silver diamine fluoride is a fluoride containing product indicated for the control of dentinal hypersensitivity it should fit into the same rules as fluoride varnishes. Please confirm that within your own State's dental practice acts.

Advantage Arrest Package Insert

Advantage Arrest[®]

Silver Diamine Fluoride 38%

Professional Tooth Desensitizer

Rx Only

Desensitizing Ingredient: Aqueous Silver Diamine Fluoride, 38.3% to 43.2% w/v

Inactive Ingredients: Purified water

Clinical Pharmacology: Product forms insoluble precipitates with calcium or phosphate in the dentinal tubules to block nerve impulses.

Indication and Usage: Treatment of dentinal hypersensitivity. For use in adults over the age of 21.

Contraindications: This product is contraindicated in patients with ulcerative gingivitis or stomatitis, or known sensitivity to silver or other heavy-metal ions. Patients with more than six affected sites, patients having had full mouth gingivectomies and patients showing abnormal skin sensitization in daily circumstances are recommended for exclusion.

Warnings: This product is intended for local application only. Not for ingestion. Protect the patient's eyes. Use caution to avoid contact with skin or clothing. In the event of exposure to eyes or skin, flush the area copiously with water and immediately seek medical consultation. This product yielded positive cytotoxicity in standard testing.

Precautions for Use:

- 1). Advantage Arrest does not normally stain enamel or burnished dentin. Advise patients that soft dentin or margins of composite restorations may be stained. Staining may be reversed by gentle polishing with tincture of iodine (weak iodine solution).
- 2) Advise patients that air-drying and product application can cause momentary transient pain to hypersensitive areas. Advantage Arrest has not been shown to cause pulpal necrosis even when soft dentin is treated.
- 3) Minimize product contact with gingiva and mucous membrane by using recommended amounts and careful application. Advantage Arrest may cause reversible short-term irritation. When applying Advantage Arrest to areas near the gingiva, apply petroleum jelly or cocoa butter and use cotton rolls to protect the gingival tissues. Alternatively, a rubber dam can be used to isolate the area.
- 4) If accidental contact occurs, thoroughly wash the area with water, saline solution or ~3% hydrogen peroxide. This includes contact with skin, clothes, floors and cabinets.

Because Advantage Arrest is clear and thus may be difficult to see, use caution to avoid transferring the material from gloved hands to other surfaces.

Precautions for Handling:

1. Storage Precautions

- 1) Store in original packaging in a cool, dark place.
- 2) Replace cap immediately after use.
- 3) Use as soon as dispensed.

2. Advantage Arrest will stain skin, clothes, counter tops, floors and instruments brown or black. Refer to the following for stain removal:

- 1) Skin; wash immediately with water, soap, ammonia or iodine tincture and then rinse thoroughly with water. Do not use excessive methods in an attempt to remove difficult stains from skin as the stains will eventually fade.
- 2) Clothing/Countertops/Floors/Instruments; use the same procedures as with stained skin. Difficult stains may be treated with sodium hypochlorite.
3. If Advantage Arrest is dispensed into a separate container, be sure to wash or thoroughly wipe the container clean immediately after use.

Adverse Reactions: Transient irritation of the gingiva has rarely been reported.

Dosage and Administration:

1. Isolate the affected area of the tooth with cotton rolls or protect the gingival tissue of the affected tooth with petroleum jelly. Alternatively, a rubber dam can be used to isolate the area.
2. Clean and dry the affected tooth surface.
3. For up to 5 treated sites per patient, dispense 1-2 drops of solution into a disposable dappen dish. Transfer material directly to the tooth surface with an applicator.
4. Air-dry.

If needed, one or two reapplications may be administered at intervals of one week.

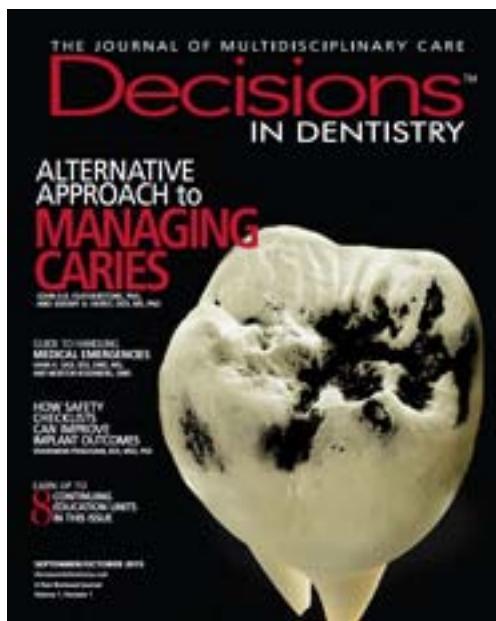
How Supplied: Single 10 mL dropper-bottle containing 8 mL of product. Not sterile.

Storage: Do not freeze or expose to extreme heat. Keep in an air-tight container in a dark place.

Caution: Federal law restricts this device to sale by or on the order of a dentist or physician.

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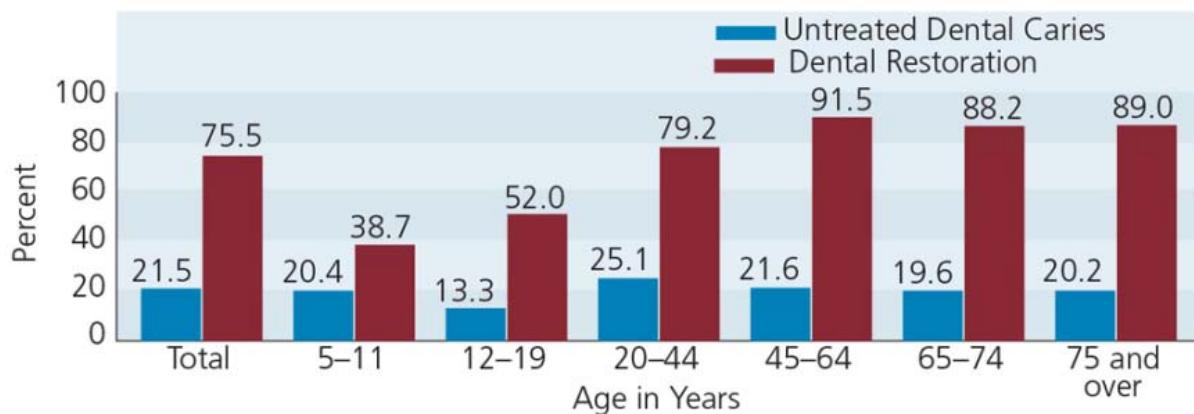


FRESH APPROACH TO CARIES ARREST IN ADULTS

October 5, 2015 John D.B. Featherstone, PhD Jeremy A. Horst, DDS, MS, PhD

Long used in other countries, silver diamine fluoride is now cleared for use in the U.S. While there is an assumption of use for pediatric caries control, here we explore indications for adults.

Although it may sound counterintuitive to some dental professionals, there is more untreated caries in adults than any other group. According to national data, the proportion of Americans age 20 and older with untreated tooth decay ranges from 20% to 25%, with younger adults experiencing more disease (Figure 1).¹ Indeed, the problem of tooth decay is more severe in U.S. adults than children, yet it has received less attention. The adult population has grown and longevity has increased, while tooth loss has decreased overall — signaling that burden of adult caries is on the rise.² Data show that 92% of the adult population has had at least one tooth restored, and decay in adults often occurs at the margins of these restorations.¹



Root decay is an increasing concern with advancing age, but no current national data are available on its prevalence. That said, we know root surface decay tends to appear in the same population that has experienced coronal decay, and is exacerbated by periodontal attachment loss and the polypharmacy of older age.³ A report from the Northwest Practice-based Research Collaborative found that 20% of middle-aged-and-older adults have root caries.⁴ A systematic review of existing studies suggested the rate was 24% among older adults.⁵ Thus, the root surface decay problem is likely as great as that of coronal decay. Silver diamine fluoride (38% weight per total volume (w/v) Ag(NH₃)₂F, 30% weight per total weight) is a colorless topical medicament comprising 25% to 29% (w/v) silver and 5% to 6% fluoride. This agent, which is pH 10,⁶ was only recently cleared for use in the U.S. The first product cleared by the U.S. Food and Drug Administration (FDA) became available in 2015 (Advantage Arrest, Elevate Oral Care, LLC).

The silver acts as an antimicrobial, the fluoride promotes remineralization, and the ammonia stabilizes high concentrations in solution.⁷ Application simply involves drying the surface, then applying sparing amounts of the liquid to the tooth, with no special instructions for post-application care.

Like fluoride varnish, the FDA label indication is for treating dentinal hypersensitivity in adults. There's another parallel to fluoride varnish, as silver diamine fluoride also shows promise for preventing and treating caries. As with other forms of off-label use, however, choosing silver diamine fluoride for this purpose falls under the purview of clinicians' professional judgment.

In Japan, Australia, Argentina and other nations, dentists have been placing silver diamine fluoride on caries lesions for more than 80 years. The value of silver ions to treat tooth decay has been known in this country for well over a century. Silver nitrate was commonly used by the forefathers of modern dentistry (e.g., G.V. Black, Percy Howe, Basil Bibby and others). In the past 20 years, dental scientists have more rigorously assessed its efficacy and safety.

Differences in nomenclature have led to confusion around this material. In order to systematically review the evidence, a literature review was designed to search PubMed and the International Association of Dental Research abstract archive with the following terms: "33040-28-7" OR "1Z00ZK3E66" OR "silver diamine fluoride" OR "silver fluoride" OR "silver diammine fluoride" OR "diammine silver fluoride" OR "ammonical silver fluoride" OR "ammoniacal silver fluoride." We found nine published randomized clinical trials of at least one year in duration evaluating silver diamine fluoride for caries arrest and/or prevention. Two studies focused on caries in adults.

PROMISING TECHNOLOGY

When applied every six months, silver diamine fluoride arrests more than 90% of caries.^{8,9} In children, applying silver diamine fluoride on active lesions once per year prevents caries in other teeth better than fluoride varnish placed four times per year on all surfaces.¹⁰ The same has been shown for direct prevention on noncarious surfaces.¹¹ Six large, randomized clinical trials demonstrated better caries prevention than other noninvasive materials, and six demonstrated better caries arrest than other noninvasive materials (three studies overlap in evaluating both prevention and arrest).¹² Silver diamine fluoride has shown similar performance in arresting caries as does the atraumatic restorative technique.^{9,12,13}

Many dentists have long held that, as a disease, dental caries must be "under control" in order for restorative efforts to succeed. This concept was updated by one of the authors with the postulation that caries arises when pathological factors (e.g., fermentable carbohydrates and oral bacteria, such as mutans streptococci and Lactobacilli) outweigh protective factors (e.g., salivary flow, fluoride and antibacterial therapy).^{14,15} The concept was formalized into Caries Management by Risk Assessment (CAMBRA) and has been shown to be an effective approach.¹⁶

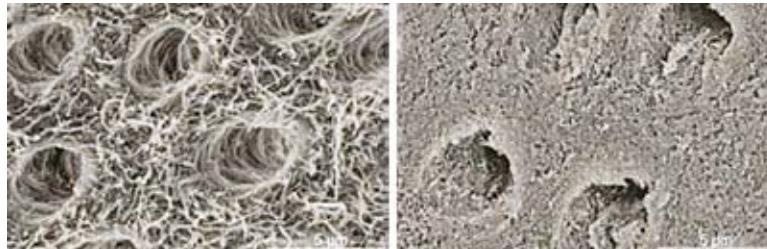
The implication is that reducing pathological factors and increasing protective factors reinstates a balance in favor of caries control, and provides an environment in which restorative care can be successful. In particular, fluoride alone is insufficient to swing the caries balance to the "no caries" side unless an antibacterial agent is added to the therapeutic mix. Silver diamine fluoride facilitates both goals in the CAMBRA strategy, wherein the silver decreases pathological bacteria and the fluoride promotes protective remineralization. Further, the low cost and profound ease of application enables widespread rapid adoption.

METHOD OF ACTION

Dental caries is a complex disease in which bacterial products cause demineralization and organic degradation. Once dentin is demineralized, the organic collagen matrix is exposed. Bacterial and host enzymes break down the organic components, and lesions advance.¹⁷

Without any excavation of soft dentin, silver diamine fluoride reacts with dentin protein and lays down a layer of silver protein that is resistant to bacterial acids and promotes the formation of hydroxyapatite and fluorapatite. The silver kills the bacteria,¹⁸ and treated surfaces are less susceptible to biofilm

formation.¹⁹ The decayed surface increases in mineral composition and hardness and the lesion gets smaller.²⁰ Figures 2A and 2B show microscopy images of a dentin surface degraded by demineralization compared to a surface treated with silver diamine fluoride.



FIGURES 2A and 2B. Scanning electron microscopy images showing the result of acid demineralization on dentin before (left) and after treatment (right) with silver diamine fluoride.

Courtesy of Ch Chu, University of Hong Kong

When used for treating hypersensitive dentin, topical application partially plugs dentinal tubules.²⁰ The resulting decrease in sensitivity among treated patients^{21,22} is consistent with the hydrodynamic theory of dentinal hypersensitivity.²³ In adults, sensitive teeth that are treated several times over a few weeks will show less response to an air blast and should be less sensitive to hot or cold stimuli.²¹ Comparing a range of studies, silver diamine fluoride appears more likely to decrease tooth sensitivity than fluoride varnish, desensitizers or oxalates.

For adult patients, the primary indications for topical treatment with silver diamine fluoride are:

- Treating dentinal hypersensitivity
 - Caries stabilization in a new patient whose disease is uncontrolled, and is therefore at high risk of experiencing new lesions (Figure 3)
 - Patients with extreme caries risk — for example, patients experiencing xerostomia from cancer treatment or taking multiple hyposalivatory medications (Figure 4)
 - Treating vulnerable surfaces, such as roots exposed from periodontal attachment loss, overdenture and partial denture abutments, or partially exposed third molars
 - Difficult-to-treat caries lesions (e.g., furcations or at the margins of fixed bridges)
 - Adults who cannot cooperate because of cognitive disabilities (e.g., patients with autism or dementia)
 - Patients without access to restorative dental services
- In these patients, silver diamine fluoride is not merely a substitute for fluoride varnish; it is an effective first-stage treatment.

EFFICACY IN ADULTS

Clinical research on silver diamine fluoride began in earnest in the late 1990s and its initial focus centered on early childhood caries. Randomized, double-blind, controlled clinical trials demonstrate that when treated every six months with silver diamine fluoride, even deep lesions in primary teeth are arrested in more than 90% of cases, with no damage to the pulp or abscess formation.⁷ Follow-up studies in both the primary and permanent dentition also demonstrate efficacy and safety. The effectiveness of this agent has been demonstrated in treating root caries,^{11,24} and in its use as an indirect pulp cap.²⁵ Studies also show the value of employing silver diamine fluoride in conjunction with addressing other protective factors (particularly oral health education),²⁴ and case reports have added to the evidence.²⁶

As part of the University of California, San Francisco School of Dentistry paradigm shift committee, we recently formalized best practices for use of silver diamine fluoride based on evidence and clinical experience.¹² When a caries risk assessment determines that an adult patient would benefit from treatment with silver diamine fluoride, food debris is rinsed away, individual caries lesions are isolated with cotton rolls, each lesion is dried, and one drop of the agent is applied with a microsponge. Care is taken to use the minimum amount needed to treat the lesion, and not apply the agent to the surrounding gingival tissue.

Note that no mechanical excavation is performed. The material is allowed to take effect for 1 to 3 minutes, and then the area is lavaged using water and high-volume suction. Lesions will harden and then turn dark brown or black within a week as the caries arrests (similar in appearance to naturally arrested lesions). A

curing light can accelerate the color change, allowing evaluation of whether the lesion is adequately treated. The agent only discolors infected and affected dentin, and will not stain intact tooth structure. Patients should be advised they are likely to experience a momentary metallic taste, which resolves by itself. Prior to treatment, they should also be informed about the permanent color change, and for this reason it is advisable to secure informed consent.

Lesions should be retreated at regular recall intervals (at least twice per year), until they are restored. Difficult-to-treat lesions — in furcations, for example, or in situations in which restorative dentistry isn't feasible — can be maintained with this treatment. An example of the latter might include a patient with financial issues that delay definitive treatment.

In adults, untreated caries serve as an environmental niche that promotes growth of cariogenic microorganisms that can spread to cause new lesions. Treating caries with silver diamine fluoride kills the bacteria, thus reducing the potential for the lesion to advance or the bacteria to seed to surrounding dentition. Meanwhile, treated lesions serve as a reservoir of silver, which is reactivated once the bacteria attempt to recolonize. The treated lesion also acts as a reservoir for fluoride, which promotes mineralization and resistance to acid attack. In this sense, treated lesions help to maintain a therapeutic level of fluoride to reverse the effects of acidification following carbohydrate ingestion.

PRECAUTIONS AND SAFETY

Silver allergy is a contraindication. It is noted that nickel allergy is commonly misreported as a silver allergy, and consultation with the patient's physician may be relevant if the health history suggests a possible allergy. Relative contraindications include any significant desquamative gingivitis or mucositis that disrupts the protective barrier formed by gingiva or mucosa. Increased absorption and pain would be expected with contact. Heightened caution and use of a thin layer of petroleum jelly is recommended.

As noted by one study, following Japan's approval of a silver diamine fluoride product (Saforide, Toyo Seiyaku Kasei Co. Ltd.) decades ago, no adverse events have been reported in adults or children.²⁷ That said, universal precautions should be followed when using silver diamine fluoride. Topical application to the oral mucosa or skin can leave a temporary tattoo that will disappear without treatment over approximately two weeks. The agent may stain countertops and floors, though commercial cleaning agents can be used for stains not cleared by standard clinical disinfectants.

TREATMENT PLANNING

Phased treatment planning is recommended with high-risk caries patients, with the first goals being to arrest active decay and stabilize the caries balance. Often, patients with multiple caries lesions face long and complicated restorative treatment. While awaiting completion of care, new lesions may form and existing lesions may advance, thus further expanding the scope of treatment. In these situations, silver diamine fluoride can help arrest caries prior to comprehensive rehabilitation (Figure 3).



FIGURE 3. A 50-year-old male patient with extreme attrition and exposed dentin requiring reconstruction. The darkened surfaces were treated with silver diamine fluoride. *Courtesy of Peter Milgrom, University of Washington*

In today's economic environment, patients often face insurance benefit limitations and out-of-pocket costs that further prolong treatment. Others who have minimal dental benefits or lack insurance need a treatment to hold them until they can afford restorative care. This modality holds promise to address this need.

Lesions treated with silver diamine fluoride can be restored with any dental material (e.g., amalgam, resin, glass ionomer or cast restorations) to address plaque traps, esthetic concerns or occlusal function. Glass ionomer cement (GIC) is directly compatible without excavation, but placement of resin-based composites should follow enamel surface preparation with a bur to maximize bond strength. The dark color change brought on by silver diamine fluoride can show through semitransparent materials, including natural enamel. This can be masked using an opaque composite base or with a sandwich restoration of GIC and composite. It may be preferable to mechanically remove the discolored material, particularly along the dentin-enamel junction. Surprisingly, it is often reported that discolored dentin can be removed without anesthetic.

Special attention should be paid to anticipate recurrent caries at the margins of fixed bridges, partial denture abutments and overdenture abutments. When lesions occur in these areas, treatment with silver diamine fluoride may prove sufficient until more definitive treatment is feasible.

CONCLUSION

Patients with periodontal disease and others who have experienced attachment loss may report sensitivity and be at risk for root surface caries. Careful attention to the caries balance is required with these patients, and the clinical approach to sensitive surfaces and softened dentin is the same as for caries.

Considering this is a fluoride product, dental hygienists and dental assistants may be allowed to apply silver diamine fluoride. When used appropriately, silver diamine fluoride will not stain sound enamel or dentin. Superficial discoloration of adjacent fillings has been observed for some composites, and can be removed with prophylactic paste. Staining of leaking composite margins is likely and may warrant replacement.



FIGURE 4. A 65-year-old cancer patient with xerostomia and cervical caries treated with silver diamine fluoride. Courtesy of Peter Milgrom, University of Washington

For clinicians who treat cognitively or physically challenged adults, silver diamine fluoride may rapidly become a regular part of the armamentarium. Even in cases in which dental care under general anesthesia or heavy sedation is financially and medically appropriate, this modality can arrest and stabilize caries and reduce the burden on caregivers. For example, Figure 4 shows a cancer patient whose medical treatment greatly increased his caries risk. Silver diamine fluoride was used to restore caries balance for several years while his medical condition presented barriers to definitive restorative treatment. From a public health point of view, clinicians may find this to be an effective agent for treating patient populations that face barriers to care.

Silver diamine fluoride is a new evidence-based technology for U.S. dental practices. It is profoundly useful for managing caries in adult and pediatric populations, and is economically and practically feasible for use in outpatient settings as well as daily practice. Consistent with the CAMBRA principle, it appears to be particularly effective in stabilizing patients for whom caries control is challenging. Indications for this new tool include treating caries in extremely high-risk patients and surfaces, patients who are cognitively or physically challenged, and lesions that are difficult to restore.

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UCSF Protocol for Caries Arrest Using Silver Diamine Fluoride: Rationale, Indications and Consent

Jeremy A. Horst, DDS, PhD; Hellene Ellenikiotis, DDS; and Peter L. Milgrom, DDS

ABSTRACT The Food and Drug Administration recently cleared silver diamine fluoride for reducing tooth sensitivity. Clinical trials document arrest and prevention of dental caries by silver diamine fluoride. This off-label use is now permissible and appropriate under U.S. law. A CDT code was approved for caries arresting medicaments for 2016 to facilitate documentation and billing. We present a systematic review, clinical indications, clinical protocol and consent procedure to guide application for caries arrest treatment.

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Until now, no option for the treatment of dental caries in the U.S. besides restorative dentistry has shown substantial efficacy.¹ Silver diamine fluoride is an inexpensive topical medicament used extensively in other countries to treat dental caries across the age spectrum. No other intervention approaches the ease of application and efficacy. Multiple randomized clinical trials — with hundreds of patients each — support its use for caries treatment, thus substantiating an intervention that addresses an unmet need in American dentistry. In August 2014, the Food and Drug Administration (FDA) cleared the first silver diamine fluoride product for market, and as of April 2015, that product is available.

Since its approval in Japan more than 80 years ago,² more than 2 million containers have been sold. The silver acts as an antimicrobial, the fluoride promotes remineralization and the ammonia stabilizes high concentrations in solution.³

Because silver diamine fluoride is new to American dentistry and dental education, there is a need for a standardized guideline, protocol and consent. The University of California, San Francisco, School of Dentistry paradigm shift committee assembled a subcommittee with the following goals:

- Use available evidence to develop a list of clinical indications.
- Define a protocol that maximized safety and efficacy and minimized inadvertent staining of clinical facilities.

- Build an informed consent document at the eighth-grade reading level.

We conducted a systematic review, inquired of authors of published clinical and *in vitro* studies about details and considerations in their protocols and consulted experts in cariology and materials chemistry where evidence was lacking. The work of this committee resulted in the adoption of silver diamine fluoride use in the UCSF student clinics.

Methods

A literature review was designed by a medical librarian to search PubMed and the International Association of Dental Research abstract archive with the following search terms: "33040-28-7" OR "1Z00ZK3E66" OR "silver diamine fluoride" OR "silver fluoride" OR "silver diamine fluoride" OR "diammine silver fluoride" OR "ammonical silver fluoride" OR "ammoniacal silver fluoride". Differences in nomenclature have led to confusion around this material. Another review was completed with the terms "dental" OR "caries" AND "silver nitrate" AND "clinical."

Material

Silver diamine fluoride (38% w/v Ag(NH₃)₂F, 30% w/w) is a colorless topical agent comprised of 24.4-28.8% (w/v) silver and 5.0-5.9% fluoride at pH 10,⁴ and marketed as Advantage Arrest by Elevate Oral Care LLC (West Palm Beach, Fla.). Other companies may market silver diamine fluoride in the future following determination of substantial equivalence and FDA clearance.

Mechanisms

Silver diamine fluoride is used for caries arrest and treatment of dentin hypersensitivity. In the treatment of exposed sensitive dentin surfaces,

topical application results in the development of a squamous layer on the exposed dentin, partially plugging the dentinal tubules.⁵ High concentration aqueous silver has been long known to form this protective layer.⁶ Decreased sensitivity in treated patients^{7,8} is consistent with the hydrodynamic theory of dentin hypersensitivity.⁹

Dental caries is a complex progression involving dietary sugars, bacterial metabolism, demineralization and organic degradation. The collagenous organic matrix is

Silver diamine fluoride outperforms other anticaries medicaments in killing cariogenic bacteria in dentinal tubules.

exposed once a dentin surface is demineralized and destroyed by native and bacterial proteases to enable a lesion to enlarge.¹⁰ Upon application of silver diamine fluoride to a decayed surface, the squamous layer of silver protein conjugates forms, increasing resistance to acid dissolution and enzymatic digestion.¹¹ Hydroxyapatite and fluorapatite form on the exposed organic matrix, along with the presence of silver chloride and metallic silver.⁵ The treated lesion increases in mineral density and hardness while the lesion depth decreases.⁵ Meanwhile, silver diamine fluoride specifically inhibits the proteins that break down the exposed dentin organic matrix: matrix metalloproteinases,¹¹ cathepsins¹² and bacterial collagenases.⁵ Silver

ions act directly against bacteria in lesions by breaking membranes, denaturing proteins and inhibiting DNA replication.^{13,14} Ionic silver deactivates nearly any macromolecule. Silver diamine fluoride outperforms other anticaries medicaments in killing cariogenic bacteria in dentinal tubules.¹⁵

Silver and fluoride ions penetrate ~25 microns into enamel¹⁶ and 50-200 microns into dentin.¹⁷ Fluoride promotes remineralization, and silver is available for antimicrobial action upon release by re-acidification.¹⁸ Silver diamine fluoride arrested lesions are 150 microns thick.¹⁹

Artificial lesions treated with silver diamine fluoride are resistant to biofilm formation and further cavity formation, presumably due to remnant ionic silver.^{20,21} More silver and fluoride is deposited in demineralized than nondemineralized dentin. Correspondingly, treated demineralized dentin is more resistant to caries bacteria than treated sound dentin.²² When bacteria killed by silver ions are added to living bacteria, the silver is re-activated so that effectively the dead bacteria kill the living bacteria in a "zombie effect."²³ This reservoir effect helps explain why silver deposited on bacteria and dentin proteins within a cavity has sustained antimicrobial effects.

Clinical Evidence

Silver Nitrate Plus Fluoride Varnish

Before the FDA cleared silver diamine fluoride, some U.S. dentists sequentially applied silver nitrate then fluoride varnish to dentinal decay as the only available noninvasive option for caries treatment. Duffin rediscovered silver nitrate from the early literature,²⁴ which had been lost

to modern cariology. Surprisingly, there is no mention of silver nitrate in either of the American Dental Association Council on Scientific Affairs reports on *Nonfluoride Caries-Preventive Agents*²⁵ or *Managing Xerostomia and Salivary Gland Hypofunction*,²⁶ and it is not part of standard dental school curricula. Case series of carious lesions arrested by silver nitrate date to the 1800s. For example, in 1891, 87 of 142 treated lesions were arrested.²⁷ Percy Howe, DDS, then director of the Forsyth Institute in Boston, added ammonia to silver nitrate, making it more stable and effective as an antimicrobial for application to any infected tooth structure from early cavitated lesions to infected root canals.²⁸ Duffin added the application of fluoride varnish following silver nitrate, simulating silver diamine fluoride. While his clinic doubled in patients, cases needing general anesthesia disappeared. His review of randomly selected charts showed only seven of 578 treated lesions progressed within two and a half years to the point that extractions were needed.²⁴ Thus, with the exception of Duffin's and one other report, attention to silver nitrate largely disappeared by the 1950s. The lore is that use and teaching of this intervention were lost with the introduction of effective local anesthetic to enable painless restorations and fluoride for caries prevention. Because no high-quality clinical trials have been performed, we did not include the silver nitrate plus fluoride varnish regimen in our recommendation.

Silver Diamine Fluoride

We found nine published randomized clinical trials evaluating silver diamine fluoride for caries arrest and/or prevention of at least one year in duration. These

studies each involved hundreds of children aged 3 to 9 or adults aged 60 to 89 (FIGURES 1 and 2). Most participants had low (< 0.3 ppm) fluoride in the environmental water and reported using fluoride toothpaste (e.g., 73 percent).²⁹ Silver diamine fluoride was applied with cotton isolation. Lesions were detected with mirror and explorer only. All studies were registered and met the Consolidated Standards of Reporting Trials requirements. Clinical cases and studies not meeting these criteria can be found elsewhere.³⁰ Caries Arrest

When stannous fluoride was used to activate color change, a break in the black color within a lesion at six months was highly sensitive and specific for active caries.

Caries arrest increased dramatically after reapplication from one year posttreatment³¹⁻³³ to one and a half years,^{31,34} and increasingly to two to three years (FIGURE 1).^{29,31,35} Single application without repeat lost effect over time in the elderly.³¹ Twice per year application resulted in more arrest than once per year.^{31,35} Twelve percent silver diamine fluoride was markedly less effective.³²

Darkening of the entire lesion indicated success at follow-up and is suggested to facilitate diagnosis of caries arrest status by nondentists. A longitudinal study reported that color activation of silver diamine fluoride with 10% stannous fluoride resulted in less first molar caries.³⁶ Tea extract was used in one group to activate color change for improved follow-up diagnosis; no differences

in arrest were seen.³² Indeed, when stannous fluoride was used to activate color change, a break in the black color within a lesion at six months was highly sensitive and specific for active caries.³⁷

Silver diamine fluoride greatly outperformed fluoride varnish for caries arrest²⁹ and was equivalent or better than glass ionomer cement (GIC) (FIGURE 1).^{31,33} The addition of semiannual intensive oral health education with the application of silver diamine fluoride in the elderly increased the arrest of root caries (FIGURE 1).³⁸

Caries Prevention

When silver diamine fluoride was applied only to carious lesions, impressive prevention was seen for other tooth surfaces.^{29,35} Fluoride-releasing GIC can have this effect but it is limited to surfaces adjacent to the treated surface and of short duration. Direct application to healthy surfaces in children also helps prevent caries (FIGURE 2).^{29,35,39} Two studies show great difference in the level of prevention in the elderly;^{38,40} the difference is hard to reconcile. As seen for arrest, prevention is less after one year without repeat application.⁴¹

Annual application of silver diamine fluoride prevented many more carious lesions than four-times-per-year fluoride varnish in both children²⁹ and the elderly.⁴⁰ Prevention was roughly equivalent to twice-per-year varnish in one study (FIGURE 2).³⁹ The addition of semiannual intensive oral health education in a study of the elderly increased prevention.³⁸ Although many fell out, GIC or resin sealants outperformed silver diamine fluoride in preventing caries in the first molars of children,^{39,41} though the cost was ~20 times more.

Ongoing Trials

Unpublished reports of clinical studies unanimously confirm better caries arrest and/or prevention by silver diamine fluoride over control or other materials. A one-year report of a study of the elderly demonstrated that the addition of a saturated solution of potassium iodide (SSKI) to decrease discoloration did not significantly alter caries arrest or prevention.⁴² This was confirmed in the two-year examinations (personal communication, Edward Lo). A one-year report of a study in children showed that the application once per week for three consecutive weeks, once per year, was more effective than that of single annual application.⁴³ Other studies have recently begun to evaluate the ability of silver diamine fluoride to arrest interproximal carious lesions, to compare the relative efficacy of silver diamine fluoride to the combination of silver nitrate plus fluoride varnish and to compare the effects on populations with or without access to fluoridated water. Final reports from these studies will follow in the coming years.

Recommendations From the Literature on Clinical Efficacy

These studies show that 38% silver diamine fluoride is effective and efficient in arresting and preventing carious lesions. Application only to lesions appears to be similarly effective in preventing cavities in other teeth and surfaces as applying directly. Single application appears insufficient for sustained effects, while annual re-application results in remarkable success, and even greater effects with semi-annual application. From these data, we recommend twice-per-year application, only to carious lesions without excavation, for at least the first two years.

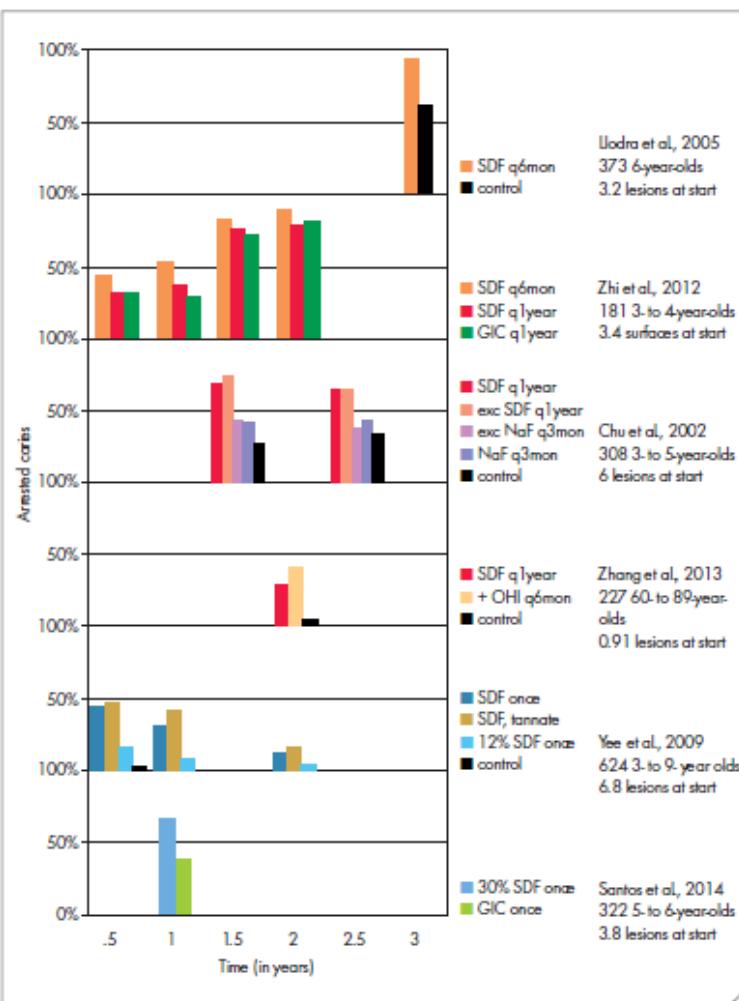


FIGURE 1. Graphic summary of randomized controlled trials demonstrating caries arrest after topical treatment with 38% silver diamine fluoride (SDF). Studies are arranged vertically by frequency of silver diamine fluoride application. Caries arrest is defined as the fraction of initially active carious lesions that became inactive and firm to a dental explorer. SDF (38% unless noted otherwise); q6mon, every six months; q1year, every year; q3mon, every three months; GIC, glass ionomer cement; NaF, 5% sodium fluoride varnish; + OHI q6mon, SDF every year and oral hygiene instructions every six months.

For any patient with active caries, we recommend considering replacement of fluoride varnish as the primary means to prevent new lesions, with application of silver diamine fluoride to the active lesions only. For patients without access

to both sealants and monitoring, silver diamine fluoride is the agent of choice for prevention of caries in permanent molars — particularly as there is no margin to leak and thereby facilitate deep caries and it does not stain sound enamel.



FIGURE 2. Graphic summary of randomized controlled trials demonstrating caries prevention after topical treatment of carious lesions with 38% silver diamine fluoride. Prevented caries is defined as the fraction of new carious lesions in treatment groups as compared to those in the placebo or no treatment control group. Chlorhex, 1% chlorhexidine varnish.

Longer studies are needed to determine whether caries arrest and prevention can be maintained with decreased application after two to three years, and whether more frequent use would enhance efficacy. Traditional or

nontraditional restorative approaches, such as the atraumatic restorative technique (ART)⁴⁴ and Hall crowns,⁴⁵ should be performed as dictated by the response of the patient, disease progression and the nature of individual lesions.

Safety

Maximum Dose and Safety Margin

The margin of safety for dosing is of paramount concern. In gaining clearance from the FDA, female and male rat and mouse studies were conducted to determine the lethal dose (LD₅₀) of silver diamine fluoride by oral and subcutaneous administration. Average LD₅₀ by oral administration was 520 mg/kg and by subcutaneous administration was 380 mg/kg. The subcutaneous route is taken here as a worst-case scenario. One drop (25 µL) is ample material to treat five teeth and contains 9.5 mg silver diamine fluoride. Assuming the smallest child with caries would be in the range of 10 kg, the dose would be 0.95 mg/kg child. Thus, the relative safety margin of using an entire drop on a 10 kg child is 380 mg/kg LD₅₀/0.95 mg/kg dose = four-hundredfold safety margin. The actual dose is likely to be much smaller, for example 2.37 mg total for three teeth was the largest dose measured in six patients.⁴⁶ The most frequent application monitored in a clinical trial was weekly for three weeks, annually.⁴³ Thus, we set our recommended limit as one drop (25 µL) per 10 kg per treatment visit, with weekly intervals at most. This dose is commensurate with the Environmental Protection Agency's (EPA) allowable short-term exposure of 1.142 mg silver per liter of drinking water for one to 10 days (Agency for Toxic Substances and Disease Registry, ATSDR, 1990).

Cumulative exposure from lower-level acute or chronic silver intake has no real physiologic disease importance, but the bluing of skin in argyria should obviously be avoided. The EPA set the lifetime exposure conservatively at 1 gm to safely avoid argyria. The highest applied dose for three teeth measured in the pharmacokinetic study, 2.37 mg, would enable > 400 applications.⁴⁶ Silver

nitrate (typically a 25% solution) has been used for more than 100 years in the U.S. without incident, including acceptance by the ADA, and in other countries for arresting dental caries.³

Adverse Effects

Not a single adverse event has been reported to the Japanese authorities since they approved silver diamine fluoride (Saforide, Toyo Seiyaku Kasei Co. Ltd., Osaka, Japan) more than 80 years ago.⁴⁷ The manufacturer estimates that more than 2 million multi-use containers have been sold, including > 41,000 units in each of the last three reporting years.

In the nine randomized clinical trials in which silver diamine fluoride was applied to multiple teeth to arrest or prevent dental caries, the only side effect noted was for three of 1,493 children or elderly patients monitored for one to three years who experienced "a small, mildly painful white lesion in the mucosa, which disappeared at 48 [hours] without treatment."^{29,31-33,35,38,40,41,48} The occurrence of reversible localized changes to the oral mucosa was predicted in the first reports of longitudinal studies.⁴⁹ No adverse pulpal response was observed.

Gingival responses have been minimal. In a pharmacokinetic study of silver diamine fluoride application to three teeth in each of six 48- to 82-year-olds, no erythema, bleeding, white changes, ulceration or pigmentation was found after 24 hours. Serum fluoride hardly went up from baseline, while serum silver increased about tenfold and stayed high past the four hours of measurement.⁴⁶ In a two-site hypersensitivity trial of 126 patients in Peru, at baseline 9 percent of patients presented redness scores of 2 (1 being normal, 2 being mild to moderate redness and 3 being severe); and after one day, 13 percent in silver diamine fluoride treated patients versus 4 percent

in controls. All redness was gone at seven days. Meanwhile, gingival index improved slightly in silver diamine fluoride treated patients.⁷ Nonetheless, gingival contact should be minimized. In our experience, it has been adequate to coat the nearby gingiva with petroleum jelly, use the smallest available microsponge and dab the side of the dappen dish to remove excess liquid before application.

Concerns for fluoride safety are most relevant to chronic exposure,⁵⁰ whereas this is an acute exposure. Chronically high systemic fluoride results in dental

mucositis that disrupts the protective barrier formed by stratified squamous epithelium. Increased absorption and pain would be expected with contact. Heightened caution and use of a protective gingival coating may suffice.

A saturated solution of potassium iodide (SSKI) is contraindicated in pregnant women and during the first six months of breastfeeding because of the concern of overloading the developing thyroid with iodide; thyroid specialists suggested a pregnancy test prior to use in women of childbearing age uncertain of their status.

Nonmedical Side Effects

Silver diamine fluoride darkens carious lesions. At least for children, many parents have seen the color changes as a positive indication that the treatment was effective.²⁹ Application of an SSKI immediately following silver diamine fluoride treatment is thought to decrease staining (patent US6461161). This is an off-label use; potassium iodide is approved as an over-the-counter drug to facilitate mucus release to breathe more easily with chronic lung problems and to protect the thyroid from radioactive iodine in radiation emergencies. In our clinical experience, SSKI helps but does not dramatically effect stain; arrested lesions normally darken. Most stain remains at the dentin-enamel or cementum-enamel junction. However, SSKI maintains resistance to biofilm formation or activity in laboratory studies.⁵⁰ Also, SSKI maintained caries arrest efficacy in the early results of an ongoing clinical trial.⁴² Meanwhile, silver diamine fluoride-treated lesions can also be covered with GIC or composite (see below for discussion on bonding).

Patients note a transient metallic or bitter taste. In our experience, with judicious use, the taste and texture

At least for children, many parents have seen the color changes as a positive indication that the treatment was effective.

fluorosis. The ubiquitous use of fluoride-based gas in general anesthetics has shown that the first acute response is transient renal holding, and is rare.⁵¹ Concerns have been raised about poorly controlled silver diamine fluoride concentrations⁵² and fluorosis appearing in treated rats.⁵³ However, silver and fluoride levels are closely monitored for the U.S. product, and the Health Department of Western Australia conducted a study that found no evidence of fluorosis resulting from long-term proper use of silver diamine fluoride.⁵⁴ Therefore, we have concluded that the development of fluorosis after application of the U.S.-approved product is not a clinically significant risk.

Silver allergy is a contraindication. Relative contraindications include any significant desquamative gingivitis or

response is more favorable than the response to fluoride varnish.

Even a small amount of silver diamine fluoride can cause a "temporary tattoo" to the skin (on the patient or provider), like a silver nitrate stain or henna tattoo, and does no harm. Stain on the skin resolves with the natural exfoliation of skin in two to 14 days. Universal precautions prevent most exposures. Long-term mucosal stain, local argyria akin to an amalgam tattoo, has been observed when applying silver nitrate to intraoral wounds; we anticipate similar stains with submucosal exposure to silver diamine fluoride.

Silver diamine fluoride stains clinic surfaces and clothes. The stain does not come out once it sets. Spills should be cleaned up immediately with copious water, ethanol or bleach. High pH solvents such as ammonia may be more successful. Secondary containers and plastic liners for surfaces are adequate preventives.

Effects on Bonding

Using a contemporary bonding system, silver diamine fluoride had no effect on composite bonding to noncarious dentin using either self-etch or full-etch systems.⁵⁵ In one study, simply rinsing after silver diamine fluoride application avoided a 50 percent decrease in bond strength for GIC.⁵⁶ In another study, increased dentin bond strength to GIC was observed.⁵⁷ Silver diamine fluoride decreased dentin bonding strength of resin-based crown cement by approximately one-third.⁵⁸ Thus, rinsing will suffice for direct restorations, while excavation of the silver diamine fluoride-treated superficial dentin is appropriate for cementing crowns.

Indications

Countless patients would benefit from conservative treatment of nonsymptomatic active carious lesions. We discuss the following indications.

First, extreme caries risk is defined as patients with salivary dysfunction, usually secondary to cancer treatment, Sjogren's syndrome, polypharmacy, aging or methamphetamine abuse. For these patients, frequent prevention visits and traditional restorations fail to stop disease progression. Similar disease recurrence occurs in severe early childhood caries.

Second, some patients cannot tolerate standard treatment for medical or psychological reasons. These include the preoperative child, the frail elderly, those with severe cognitive or physical

Countless patients would benefit from conservative treatment of nonsymptomatic active carious lesions.

disabilities and those with dental phobias. Various forms of immunocompromise mean that these same patients have a much higher risk of systemic infection arising from untreated dental caries. Many only receive restorative care with general anesthesia or sedation and others are not good candidates for general anesthesia due to frailty or another medical complexity. The Centers for Disease Control and Prevention (CDC) estimates 1.4 million people in the U.S. live in nursing homes and 1.2 million live in hospice.⁵⁹ These individuals tend to have medical, behavioral, physical and financial limitations that beg a reasonable option.

Third, some patients have more lesions than can be treated in one visit, such that new lesions arise or existing lesions become symptomatic while

awaiting completion of treatment. This is particularly relevant to the dental school setting where treatment is slow. American dentistry has been desperately lacking an efficient instrument to be used at the diagnostic visit to provide a step toward controlling the disease.

Fourth, some lesions are just difficult to treat. Recurrent caries at a crown margin, root caries in a furcation or the occlusal of a partially erupted wisdom tooth pose a challenge to access, isolation and cleansability necessary for restorative success.

Following the above considerations, we developed four indications for treatment of dental caries with silver diamine fluoride:

1. Extreme caries risk (xerostomia or severe early childhood caries).
2. Treatment challenged by behavioral or medical management.
3. Patients with carious lesions that may not all be treated in one visit.
4. Difficult to treat dental carious lesions.

Finally, these indications are for our school clinics. They do not address access to care. The U.S. Department of Health and Human Services estimates 108 million Americans are without dental insurance, and there are 4,230 shortage areas with 49 million people without access to a dental health professional.⁶⁰ Unlike fillings, failure of silver diamine fluoride treatment does not appear to create an environment that promotes caries, and thus needs to be monitored. Thus, a final important indication is:

5. Patients without access to dental care.

Clinical Application

We considered practical strategies to maximize safety and effectiveness in the design of a clinical protocol for the UCSF dental clinics (**FIGURE 3**).

The key factor is repeat application

Silver Diamine Fluoride (SDF)

UCSF Protocol for Arresting Dental Carious Lesions or Treating Tooth Sensitivity

Material: Advantage Silver Arrest (38% SDF, purified water) from Elevate Oral Care.
Shelf life: three years unopened. Do not refrigerate. Avoid freezing or extreme heat.

Indications:

1. Extreme caries risk (xerostomia or severe early childhood caries).
2. Treatment challenged by behavioral or medical management.
3. Patients with carious lesions that may not all be treated in one visit.
4. Difficult to treat dental carious lesions.
5. Patients without access to dental care.

Maximum dose: 25 µL (1 drop) / 10kg per treatment visit.

SDF Contraindication: Silver allergy.

SDF Relative Contraindications: Ulcerative gingivitis, stomatitis.

SSKI Contraindications: Pregnancy, breastfeeding.

Considerations:

- Decayed dentin will darken as the caries lesions arrest. Most will be dark brown or black.
- SDF can stain the skin, which will clear in two to three weeks without treatment.
- SDF can permanently stain operatory surfaces and clothes.
- A control restoration (e.g., GI via ART or other material) may be considered after SDF treatment.
- Saturated solution of potassium iodide (SSKI, Lugol's Solution, various sources) can be used after SDF to decrease color changes.
- Re-application is usually recommended, biannually until the cavity is restored or arrested or the tooth exfoliates.

Procedure:

1. Plastic-lined cover for counter, plastic-lined bib for patient.
2. Standard personal protective equipment (PPE) for provider and patient.
3. One drop of SDF into the deep end of a plastic dappen dish
 (also obtain one drop of SSKI in a separate dappen dish if selected).
4. Remove bulk saliva with saliva ejector.
5. Isolate tongue and cheek from affected teeth with 2-inch by 2-inch gauze or cotton rolls.
6. If near the gingiva, consider applying petroleum jelly with a cotton applicator for safety.
7. Dry affected tooth surfaces with triple syringe or if not feasible dry with cotton.
8. Bend microsponge, immerse into SDF, remove excess on side of dappen dish.
9. Apply directly onto the affected tooth surface(s) with microsponge.
10. Allow SDF to absorb for up to one minute if reasonable, then remove excess with gauze or cotton roll.
 (If using SSKI, apply with a different microsponge. Repeat one to three times until no further white precipitates are observed.
 Wait five to 10 seconds between applications. Remove excess with cotton.)
11. Rinse with water.
12. Place gloves, cotton and microbrushes into plastic waste bags.

FIGURE 3. Clinical protocol for the UCSF dental clinics.

over multiple years. We believe that dryness of the lesion during application is also important. Isolation with gauze and/or cotton rolls is sufficient, while air drying prior to application is thought to improve effectiveness. Allowing one to three minutes for the silver diamine fluoride to soak into and react with a lesion is thought to effect success.

Allowing only a few seconds to soak in due to the cooperation limits of very young patients commonly results in arrest. Application time in clinical studies does not correlate to outcome. However, our committee decided to be cautious in our recommendations for initial use. Longer absorption time also decreases concerns about removing silver

diamine fluoride with a posttreatment rinse. Removing any excess material with the same cotton used to isolate is routine to minimize systemic absorption.

Many clinicians place silver diamine fluoride at the diagnostic visit, then at one and/or three-month follow ups, then at semiannual recall visits (six, 12, 18, 24 months). Whether application needs

to continue after two or three years to maintain caries arrest is not known. Another approach is simply to substitute silver diamine fluoride for any application of fluoride varnish to a patient with untreated carious lesions. Increased frequency with higher disease burden follows the caries management by risk assessment (CAMBRA) principles.⁶¹ It is relevant to take photographs to track lesions over time.

Efforts to improve the penetration of silver diamine fluoride into affected dentin by chemical cavity preparation have not been studied but are being explored clinically. Pretreatment with ethylenediaminetetraacetic acid (EDTA) to remove superficial hydroxyapatite in affected dentin may open the dentinal tubules to further silver diamine fluoride penetration. Pretreatment with hypochlorite (bleach) may help breakdown bacteria and exposed dentin proteins, but this may be redundant to the action of the silver. Hypochlorite to decrease discoloration after silver diamine fluoride treatment is not recommended, as the color comes from silver that cannot be broken down like organic chromophores and might break down dentin proteins stabilized against the effects of bacteria and acid by interactions with silver.

Experience with the combination of silver nitrate plus fluoride varnish (see above) has many practitioners asking about a topical varnish after silver diamine fluoride placement to prevent silver diamine fluoride taste and keep the silver diamine fluoride in the lesion. We see no evidence that varnish would help achieve either goal. Varnish does not seal. Rather, allowing more time for residence and diffusion of silver diamine fluoride to react with and dry into the lesion is more likely to improve effectiveness. Also, in our experience, silver diamine fluoride results in less aversive taste and texture responses than to fluoride varnish.

Decreased darkening of lesions in the esthetic zone improves acceptance. SSKI is an option if the patient is not pregnant, though significant darkening should still be expected. SSKI and silver diamine fluoride are not to be combined prior to application — SSKI can be placed after drying the silver diamine fluoride-treated tooth. Silver diamine fluoride does not prevent restoration of a lesion, thus it does not prevent esthetic options. While silver diamine fluoride has been shown to be more effective than ART or interim restorative treatment

In our experience, silver diamine fluoride results in less aversive taste and texture responses than to fluoride varnish.

(IRT),³³ the two are compatible and can be combined across one or more visits.

The California Business and Professions Code permits dental hygienists and assistants to apply silver diamine fluoride for the control of caries because they are topical fluorides (Section 1910.(b)). Physicians, nurses and their assistants are permitted to apply fluorides in California and in many other states and federal programs. The recent decision of the Oregon Dental Board to allow dental hygienists and assistants to place silver diamine fluoride under existing rules for topical fluoride medicaments sets a precedent. Dental hygienists and assistants in Oregon were barred from providing silver nitrate in a previous decision. All providers need to be trained. Applications should be tracked if applied to the same patient by multiple clinics.

Documentation and Billing

A new code, D1354, for "interim caries arresting medication application" was approved by the Code on Dental Procedures and Nomenclature (CDT) Code Maintenance Commission for 2016. The code definition is "Conservative treatment of an active, nonsymptomatic carious lesion by topical application of a caries arresting or inhibiting medicament and without mechanical removal of sound tooth structure." The CDT Code is the U.S. HIPAA standard code set and is required for billing. The Commission includes representatives from the major insurers, Medicaid, ADA, AGD and specialty organizations. Insurers are in the process of evaluating coverage for this treatment.

Legal Considerations

Silver diamine fluoride is cleared by the FDA for marketing as a Class II medical device to treat tooth sensitivity. We are discussing off-label use as a drug to treat and prevent dental caries. This is a parallel situation to fluoride varnish, which has the same device clearance but is ubiquitously used off label by dentists and physicians as a drug to prevent caries. The same public health dentists who achieved the FDA device clearance are now applying for a dental caries indication. However, this is a more complicated process, normally only carried out by large pharmaceutical companies, and is likely to take longer.

Consent

Because silver diamine fluoride is new in the U.S., it is important to communicate effectively. In the UCSF clinics, we are using a special consent form (**FIGURE 4**) as a way to inform patients, parents and caregivers, and

UCSF Dental Center Informed Consent for Silver Diamine Fluoride

Facts for consideration:

- Silver diamine fluoride (SDF) is an antibiotic liquid. We use SDF on cavities to help stop tooth decay. We also use it to treat tooth sensitivity. SDF application every six to 12 months is necessary.
- The procedure: 1. Dry the affected area. 2. Place a small amount of SDF on the affected area. 3. Allow SDF to dry for one minute. 4. Rinse.
- **Treatment with SDF does not eliminate the need for dental fillings or crowns to repair function or esthetics. Additional procedures will incur a separate fee.**
- I should not be treated with SDF if: 1. I am allergic to silver. 2. There are painful sores or raw areas on my gums (i.e., ulcerative gingivitis) or anywhere in my mouth (i.e., stomatitis).

Benefits of receiving SDF:

- SDF can help stop tooth decay.
- SDF can help relieve sensitivity.



Risks related to SDF include, but are not limited to:

- **The affected area will stain black permanently.** Healthy tooth structure will not stain. Stained tooth structure can be replaced with a filling or a crown.
- Tooth-colored fillings and crowns may discolor if SDF is applied to them. Color changes on the surface can normally be polished off. The edge between a tooth and filling may keep the color.
- If accidentally applied to the skin or gums, a brown or white stain may appear that causes no harm, cannot be washed off and will disappear in one to three weeks.
- You may notice a metallic taste. This will go away rapidly.
- If tooth decay is not arrested, the decay will progress. In that case the tooth will require further treatment, such as repeat SDF, a filling or crown, root canal treatment or extraction.
- These side effects may not include all of the possible situations reported by the manufacturer. If you notice other effects, please contact your dental provider.
- Every reasonable effort will be made to ensure the success of SDF treatment. There is a risk that the procedure will not stop the decay and no guarantee of success is granted or implied.

Alternatives to SDF, not limited to the following:

- No treatment, which may lead to continued deterioration of tooth structures and cosmetic appearance. Symptoms may increase in severity.
- Depending on the location and extent of the tooth decay, other treatment may include placement of fluoride varnish, a filling or crown, extraction or referral for advanced treatment modalities.

**I CERTIFY THAT I HAVE READ AND FULLY UNDERSTAND THIS DOCUMENT
AND ALL MY QUESTIONS WERE ANSWERED:**

(signature of patient) _____ (date)
(signature of witness) _____ (date)

FIGURE 4. UCSF special consent form.

to standardize procedures because we have so many inexperienced student clinicians. All practices have established procedures for consent and an extra form may not be needed in the community. The normal elements of informed consent

apply. We sought to ensure awareness of the expected change in color of the dentin as the decay arrests, likelihood of reapplication and contraindications in the presence of silver allergy and stomatitis. Note the importance of distinguishing

between allergy to nickel and other trace metals rather than silver allergy, which is rare. We used readability measurements to guide intelligibility and included a progressively discolored lesion to show stain of a lesion but not healthy enamel.

Conclusion

Silver diamine fluoride is a safe, effective treatment for dental caries across the age spectrum. At UCSF, it is indicated for patients with extreme caries risk, those who cannot tolerate conventional care, patients who must be stabilized so they can be restored over time, patients who are medically compromised or too frail to be treated conventionally and those in disparity populations with little access to care.

Application twice per year outperforms all minimally invasive options including the atraumatic restorative technique — with which it is compatible but 20 times less expensive. It approaches the success of dental fillings after two or more years, and again, prevents future caries — while fillings do not. Silver diamine fluoride is more effective as a primary preventive than any other available material, with the exception of dental sealants, which are > 10 times more expensive and need to be monitored.

Saliva may play a role in caries arrest by silver diamine fluoride. Lower rates of arrest are seen in geriatric patients.³⁸ The elderly tend to have less abundant and less functional saliva, which generally explains their higher caries rate. In pediatric patients, higher rates of arrest are noted for buccal or lingual smooth surfaces and anterior teeth.³¹ These surfaces bathe more directly in saliva than others. It is surprising that silver chloride is the main precipitant in treated dentin, as chloride is not a common component of dentin or silver diamine fluoride, so may come from the saliva.

Traditional approaches often provide only temporary benefit, given the highest rates of recurrent caries are in patients with the worst disease burden. The advent of a treatment for nonsymptomatic caries not requiring general anesthesia or sedation addresses long-standing

concerns about the expense, danger and practical complexity of these services.

Experience suggests that dryness prior to application enhances effectiveness. Good patient management is still profoundly relevant to the very young and otherwise challenged patients, though this one-minute intervention is more tolerable than other options. Silver diamine fluoride can readily replace fluoride varnish for the prevention of caries in patients who have active caries. This as a powerful new tool in the fight against dental caries, particularly suited for those who suffer most from this disease.

Clinical evidence supports continued application one to two times per year until the tooth is restored or exfoliates, and otherwise perhaps indefinitely. Some treated lesions keep growing, particularly those in the inner third of the dentin. It is unclear what will happen if treatment is stopped after two to three years and research is needed. ■

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