ICODEN*
an innovative caries control strategy

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Definitions

• Primary Prevention
  – Methods to avoid occurrence of disease
    • Topical fluoride
    • Sealants

• Secondary Prevention
  – Methods to address an existing disease prior to the appearance of symptoms
    • Silver products applied to white spot lesion
Background

- Silver products (SN+F and SDF) are known to be effective at arresting caries
- It is unknown whether there is a “primary preventive” use for these products
- Silver ions do not precipitate into/onto sound enamel
- Fluoride component would have a primary preventive benefit, but fluoride varnish alone takes care of this
However...

• Clinical experience with silver products has demonstrated that these products “bleed” or “wick” into areas not believed to be carious.
• A lack of visible decalcification does not mean that the caries process has not begun.
• Pre-clinical porosities that are the result of a cariogenic process should “take up silver”.
“Collateral Benefit” from Treating Caries in Children with Silver Nitrate

2nd molar treated for deep caries in the fissures

“Collateral benefit” to the untreated 1st molar
Collateral Benefit in Kalona Study

• *In vitro* study looking at the chemical mechanisms of silver diammine fluoride (Raman spectroscopy)

**Findings:**
1. SDF works as a **caries-arresting** agent by forming Ag$_3$PO$_4$ and as a **caries-preventing** agent by forming fluoroapatite (FAP)
2. the time needed for SDF to work as a caries preventive agent is shorter than that needed to work as a caries-arresting agent
3. the presence of a thiol group (caries) delays the formation of Ag$_3$PO$_4$ and FAP.
Silver product formation at varying pH

- Ag$_3$PO$_4$ = Silver Phosphate (caries arresting agent)
- Ag$^+$ = Silver Ion (contributes to metallic silver precipitation, and blackening)
- AgNH$_3$$^+$ = Silver ammine
- Ag (NH$_3$)$_2$$^+$ = Silver diammine (important in formation of fluorapatite)
- Ag$_2$O(s) = Silver oxide (byproduct that causes blackening) – very stable product
Silver product formation at varying pH

Ag₃PO₄ = Silver Phosphate (caries arresting agent)
Ag⁺ = Silver Ion (contributes to metallic silver precipitation, and blackening)
AgNH₃⁺ = Silver ammine
Ag (NH₃)₂⁺ = Silver diammine (important in formation of fluorapatite)
Ag₂O(s) = Silver oxide (byproduct that causes blackening) – very stable product
Silver product formation at varying pH

\[ \text{Ag}_3\text{PO}_4 = \text{Silver Phosphate (caries arresting agent)} \]
\[ \text{Ag}^+ = \text{Silver Ion (contributes to metallic silver precipitation, and blackening)} \]
\[ \text{AgNH}_3^+ = \text{Silver ammine} \]
\[ \text{Ag} (\text{NH}_3)_2^+ = \text{Silver diammine (important in formation of fluorapatite)} \]
\[ \text{Ag}_2\text{O}(s) = \text{Silver oxide (byproduct that causes blackening) – very stable product} \]
• These finding suggest that the desired silver-containing intermediate (silver phosphate) forms preferentially at slightly acidic to neutral pH.
Fluorapatite formation at varying pH

\[ \text{Ca}_5(\text{PO}_4)_3\text{F} = \text{FAP} = \text{fluorapatite} \]

\[ \text{CaF}_2 = \text{calcium fluoride} \]
Fluorapatite formation at varying pH

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Fluorapatite formation at varying pH

Ca$_5$(PO$_4$)$_3$F = FAP = fluorapatite
CaF$_2$ = calcium fluoride
• These findings suggest that at neutral or higher pH the main product is Fluorapatite (primary prevention)
• At acidic pH, calcium fluoride is favored contributing to a caries arresting mechanism of action (secondary prevention)
• CaF$_2$, when followed in solution for 24 to 48 hours, is no longer detectable/available. At acidic pH, CaF$_2$ breaks down into calcium and fluoride which get integrated into the decalcified (carious) tooth structure.
Based on these findings we need to re-think the potential of silver products to act as a “primary preventive” agent.
Benefits of Silver/Fluoride Products in 1° Prevention

• Fluoride component will prevent caries
• True primary prevention
Benefits of Silver/Fluoride Products in 2° Prevention

• Fluoride component will prevent caries
• True primary prevention
• Silver component can act as a “disclosing agent”
  • Pre-clinical lesions and porosities will discolor
  • Silver will precipitate into lesions and (presumably) arrest early, pre-clinical caries
• This provides a “very early secondary prevention” benefit
Proposed Demonstration Project

Sample
• 0-3 population at high risk for caries

Methods
• Full dmfs/dmft status at baseline (record teeth, cavitated caries, white spot lesions, enamel defects)
• Low concentration silver/fluoride product (ICODEN) application to all tooth surfaces at baseline, and at 3 month intervals

Outcome variables of interest
• Appearance of silver-stained surfaces at recall
• Caries d2+incidence (caries into enamel or dentine)
• Restorations and extractions
• Change in GA cases, sedations, restorative visits for defined population
Preliminary Data Needed

Bench testing of varying concentrations of silver nitrate solution to find the lowest concentration at which visible staining occurs in demineralized surfaces without cavitation.
Safety

• What about safety/toxicity?
• Can silver products be used safely on very young children?
• What is the lowest concentration of Ag\(^+\) that will still be effective to disclose and treat very early demineralization?
Proposed Project Treatment Protocol: Silver/Fluoride application

• Brush teeth
• Isolate teeth
• Dry teeth
• Apply ICODEN solution for 2 minutes
Why two minutes?

- Unable to detect any silver phosphate formation before 90 seconds (Owais et al, 2017)
- The presence of a thiol group (representing bacterial component of caries) delays the formation of silver phosphate until all the formation of silver sulfide (Ag$_2$S) has occurred.
- When caries/bacteria are present, the first product that forms is a silver sulfide – which kills the bacteria. The remaining silver forms silver phosphate which arrests caries.
Challenges

• Precooperative age of subjects
Facilitators

• Many of the highest risk children in the U.S. are in group settings like Head Start and Early Head Start.
• Access to these children 3-4 times a year is quite feasible.
• The proposed treatment is simple and atraumatic.
• It could be accomplished in a non-dental clinic setting.
• Longitudinal follow-up for 1-4 years is feasible.
Thank you and acknowledgment

- Frank Mendoza, DDS
  - Pediatric Dentist with IHS in Warm Springs, OR
  - Developed and implemented “Warm Springs Model” for a medical management of caries in extremely high risk young children
  - Recipient of ADA Presidential Citation for the innovativeness and success of his work
Thank you and acknowledgment

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  – Pediatric Dentist with IHS in Warm Springs, OR
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  – Quest President
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