Caries Remineralizing Products: Caries Remineralizing Products: What is the Evidence? What is the Evidence?

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Course Objectives
• Review current commercial products claiming caries control/remineralization.
• Review evidence for effectiveness of these therapies in caries control.
• Discuss appropriate use of remineralization approaches in specific populations and clinical situations.

Caries Process
• Imbalance between pathological and protective factors resulting in dissolution and loss of tooth mineral content.
• Caries process follows a continuum.

Caries Continuum
Clinical
Health White Spot Cavitation Disease
Structural

Caries Risk Assessment
• Low socioeconomic status
• Previous history of caries
• High risk dietary behaviors
• Caregiver with high caries history
• Fluoride deficient
• High microbial count
• Chronic or serious systemic illness
• Enamel hypoplasia
• Abnormal salivary function

Caries risk Assessment Systems
• American Dental Association
• American Academy of Pediatric Dentistry
• Caries Management by Risk Assessment (CAMBRA)
• Cariogram – computerized caries assessment
Caries-Risk Assessment

- American Academy of Pediatric Dentistry:
  - Caries-risk assessment is an essential element of contemporary clinical care for infants, children and adolescents (2002).

AAPD- Caries-Risk Assessment

- Low Risk – no caries in 2 yrs, No visible plaque, no gingivitis, ↑ SES, regular dental care, optimal F
- Moderate Risk – caries in past 2 yr, irregular dental care, 1 enamel decalcification, gingivitis, Mid SES, sub-optimal F
- High Risk – caries 1 yr, multiple enamel decal, ↓ SES, sub-optimal F, no regular dental care, enamel defects, visible plaque on anterior teeth, frequent snacks, active caries in mother, ↑ S Mutans

Early Diagnosis Critical to Effectiveness

- Prior to cavitation and arrest and heal mineral loss through remineralization
- Diagnosis
  - Clinical
  - Radiographic
  - Transilumination
  - Quantitative light fluorescence

Radiographic Monitoring of Initial Lesions

<table>
<thead>
<tr>
<th>Radiolucent Lesions</th>
<th>% Clinically Cavitated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outer half of Enamel</td>
<td>Permanent</td>
</tr>
<tr>
<td>Inner half of Enamel</td>
<td>Primary</td>
</tr>
<tr>
<td>Outer half of Dentin</td>
<td>28%</td>
</tr>
<tr>
<td>Inner half of Dentin</td>
<td>96%</td>
</tr>
</tbody>
</table>

Pitts, 1992

Monitoring of Initial Lesions

Initial Detection of Lesions 1 year follow up

Clinical 360°: Technology

The new standard in caries diagnosis

Advances in caries detection technology are changing dentistry to make early diagnosis and preventive treatment the standard of care.

by Dr. John Flucke
**Prevention of Dental Caries**

- Mechanical plaque control
  - Brushing, Flossing
  - Professional Prophylaxis
- Chemotherapeutics
  - Fluorides
  - Antimicrobials (Chlorhexidine)
- Sealants
- Diet

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**Caries Continuum**

- Health
- White Spot
- Cavitation
- Disease

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**Demineralization/Remineralization**

- Demineralization:
  - Low pH
  - \( \text{Ca}^{++}, \text{PO}_4^{3-}, \text{H}^+ \)
- Remineralization:
  - Increased pH
  - \( \text{Ca}^{++}, \text{PO}_4^{3-}, \text{F}^- \)

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**Saliva – Critical player in remineralization**

- Has high concentrations of Ca and P for mineral deposition.
- Contains fluoride ions
- Provides transport mechanism to get ions to sites where they are required for activity

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**Saliva with low pH and Demineralization**

- Saliva
  - Substrate (sucrose)
  - S. mutans
- Enamel
  - Incipient caries lesion
  - F-rich layer

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**Salivary phosphopetides - Critical for Remineralization**

- Saliva
  - Statherin
- Enamel
  - Incipient caries lesion (demineralized)

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Remineralization Challenges

- Difficulty getting Ca and PO₄ ions into lesion as they tend to precipitate on the surface.
- Calcium compounds tend to be relatively insoluble.
- Search for the ideal solution.

What compounds, agents or approaches enhance remineralization?

- Increase salivary flow rate
- Buffer pH to neutral more rapidly
- Increase bioavailability of Ca and P0₄ ions
- Enhance attraction of ions to microenvironment of demineralized crystallite surface

Characteristics of Ideal Remineralizing Agent

- Diffuses Ca and PO₄ into subsurface lesion
- Does not provide excess of Ca or favor calculus formation
- Functions at acidic pH
- Enhances inherent salivary mineralization properties

Fluoride Therapies: The Gold Standard in Remineralization

- Dental Caries
- Dental Erosion
- Dental Sensitivity

Fluorides and Safety Issues Continue to Make News

FOR IMMEDIATE RELEASE
Friday, January 7, 2011

HHS and EPA announce new scientific assessments and actions on fluoride

HHS’ proposed recommendation of 0.7 milligrams of fluoride per liter of water replaces the current recommended range of 0.7 to 1.2 milligrams.

Oregon and fluoridation: The go-to place for tooth decay

By Rick Attig, The Oregonian

April 23, 2009

AP: Oregon has one of the nation's lowest rates of fluoridated water and one of the highest rates of child dental decay. Hundreds of dentists gathered in Portland this week for a national conference on oral health. They came to the right place: Once San Diego follows through on plans to fluoridate its municipal water by May 2010, Portland will be the nation's largest city without fluoridated water.
**National Research Council Report on Fluoride Safety March 22, 2006**

Current EPA maximum contaminant level goal (MCLG) of 4 milligrams of fluoride per Liter (mg/L) of drinking water should be lowered to better protect people from health risks associated with high natural fluoride levels.

**Fluorine**

- 13th most abundant compound in nature.
- Most reactive element on earth.
- Atomic number 9
- Halogen
- Discovered by Karl Scheele in 1771 but not isolated until 1886 when Henri Moissan electrolysed potassium fluoride.

**Fluorides products for caries control are diverse.**

- Dentifrice
- Water fluoridation
- Mouth rinses
- Supplements
- Professional Applications – Gels, Foam, Varnish
- Restorative materials

**Fluoride Therapies and Products**

**What is the evidence that fluorides used in dentistry are safe and effective?**

- Water fluoridation – one of few disease prevention approaches tested at community level. 65 years of safety data
- Fluoride therapies: There have been hundreds of clinical trials evaluating various fluoride concentrations and formulations.
Fluorides: Evidence Based Dentistry

- Systematic Reviews of Topical Fluorides for Dental Caries:
- Over 150 systemic reviews of clinical trials identified with first publications in 1984.

Ijaz S, et al., Caries Research 44:579-592, 2010

Currently there are numerous therapeutic agents marketed claiming to enhance remineralization and caries control.

Remineralization Therapeutics

- Fluorides
- Salivary stimulation – chewing gum
- Amorphous calcium phosphate
- Tricalcium phosphate
- Casein Phosphoprotein
- Bioactive glass – calcium sodium phosphosilicate
- Arginine bibicarbonate – calcium carbonate complex
- Combinations

Remineralizing Agents

- Recaldent, MI Paste – casein phosphopeptides with amorphous calcium phosphate
- Novamin – calcium sodium phosphosilicate
- Caphosol – supersaturated rinse of soluble Ca and PO₄ ions. Primarily marketed for xerostomia

CPP-ACP - Currently has most research to evaluate

- Majority of research comes from Reynolds group at University of Melbourne
- In vitro and In situ caries models – many studies show products with CPP-ACP remineralize (GC Tooth Mousse, chewing gum)

Casein Phosphopeptides

- 10% W/W of the protein casein
- Low antigenicity
- Four major CPPs with phosphoserines can form complex with amorphous calcium phosphate
Casein Phosphoproteins

- Stabilization of calcium and phosphate ions by phosphoproteins ensures the ions are bioavailable.
- Statherine Asp-Ser(P)-Ser(P)-Glu-Glu
- CPP 8-12 Ser(P)-Ser(P)-Ser(P)-Glu-Glu
- CPP 63-68 Glu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)


Casein Phosphoproteins in the Enamel Lesion

- Evidence that CPP is able to penetrate into subsurface lesion.
- CPP-ACP complex size is compatible with enamel penetration.


Casein Phosphopeptide-Amorphous Calcium Phosphate

Clinical in-situ trials indicate a short-term remineralisation effect of CPP-ACP. The promising in-vivo RCT results suggest a caries-preventing effect for long-term clinical CPP-ACP use.


GC Tooth Mousse – MI Paste

- 10% recaldent W/V, water base, pH 7.8. Plus formula has 900 ppm F ion. Rx only
- CPP forms complex with ACP. CPP makes it sticky so forms film on tooth surface.
- Not a dentifrice and applied with finger.
- Leave for 3 minutes
- Limited clinical trial data at this time.


Casein Phosphopeptide-Amorphous Calcium Phosphate

- Exp - 54 mg CPP-ACP gum – Control gum without CPP-ACP - 3X day for 10 minutes.
- 2,720 subjects from 29 schools randomly assigned and BW radiographs taken at baseline and 24-month
- CPP-ACP gum the odds of a surface experiencing caries progression were 18% less

Morgan et al., The anticariogenic effect of sugar-free gum containing CPP-ACP nanocomplexes on approximal caries determined using digital bitewing radiography. Caries Res. 2008;42(3):171-84
**CPP-ACP and Orthodontic Demineralization?**

- 60 adolescent patients with decalcifications at debracketing
- 10% casein phosphopeptide-amorphous calcium phosphate vs 1100ppm toothpaste 1 time/day
- Both groups showed remineralization (QLF) but CPP-ACP was not superior to toothpaste


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**Alternative uses of CPP-ACP in caries control**

- Add 1% CPP-ACP to sugar confectionary consumed 6x day
- Intra-oral caries test model
- Two randomized, double-blind, crossover studies
- Stopped lesion progression and promoted remineralization

Walker GD et al., Casein phosphopeptide-amorphous calcium phosphate incorporated into sugar confectons inhibits the progression of enamel subsurface lesions in situ. Caries Res. 44(1):33-40, 2010

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**Bottom Line on CPP-ACP for Caries Prevention**

- There is substantial in situ evidence supporting a benefit
- The weak clinical evidence does not support recommending the use of CPP-ACP for caries prevention.
- Does that mean you never use it?
- Cost $12 - 30 for 2 oz tube

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**Allergies to Milk Proteins**

- It is advised not to use products containing Recaldent if you suffer from allergy or severe sensitivity to milk, milk protein or milk-based products. The risks are serious and can lead to life-threatening allergic reaction.

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**ACP Addition to Sealants and Fluoride Varnish**

- Enamel Pro-Varnish (Premier) – ACP in 5%NaF varnish. No clinical data
- Aegis Sealant with ACP (Bosworth). Smart remineralization? No clinical evidence

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**Incorporation ACP in Dental Materials**

- Orthodontic bracket bonding resin Aegis Ortho® (The Bosworth Co.) vs Concise® (3M Dental Products) on premolars for 30 days
- Extracted and did microhardness testing
- Significantly greater hardness around ACP resin than control.

On-line Testimonials Dr. Bicuspid

Tri-calcium Phosphate Fluoride Varnish

- 3M ESPE 5% NaF Varnish with tricalcium phosphate.
- New formulation of Vanish
- Claim more available fluoride
- No clinical data

Tri-calcium Phosphate Fluoride Toothpaste

- 3M ESPE 5000ppm NaF toothpaste with tricalcium phosphate.
- No clinical data
- In-vitro studies suggest as good or better than CPP-ACP formulation

Tri-calcium Phosphate Research

- Karlinsky RL,
- Indiana Nanotech, LLC, 351 West 10th Street, Suite 309, Indianapolis, IN 46202, USA. rkarlins@gmail.com

Indiana Nanotech LLC
Designing and Manufacturing Tailored Materials for Life Science Applications

NovaMin - calcium sodium phosphosilicate

- Bioactive glass available since the 1960s and was designed for bone repair.
- Used for bone grafting and ridge augmentation.
- Key components SiO₂, Na₂O, CaO, P₂O₅

NovaMin - calcium sodium phosphosilicate

- Marketed primarily to manage tooth sensitivity.
- Effective at occluding dentinal tubules
- Reported more effective than potassium nitrate and fluoride dentifrice. (JADA 141:995-999, 2010)
- Now in multiple toothpastes (Restore, Renew)

Karlinsey et al., In vitro remineralization efficacy of NaF systems Containing unique forms of calcium Am J Dent. 22(3):185-8 2009.

DuraShield Plus (Sultan Dental)
- 5% NaF varnish
- 10% Novamin wt%
- Came out in 2008 and marketed for those patients needing a varnish and who have dentinal sensitivity.

CaviStat: Sugarless mint (arginine bicarbonate calcium carbonate complex)
- Two clinical trials – 1 chewing gum and 1 lozenge.
- Significantly larger caries reductions in Cavistat group (p < 0.001).


Mechanism of Action: arginine bicarbonate calcium carbonate

Not currently available in US but to be marketed as BasicMints Ortek Therapeutics Inc.

Chewing gum and Caries Control
- Evaluating multiple clinical trials suggests that caries reduction in permanent teeth is significant compared to not chewing gum (about 40% caries reduction)
- What is the mode of action and does the sweetener make a difference?

Enhance Salivary Remineralizing Potential
- Chewing gums increase salivary flow and thus have the potential to reduce caries.
  - Numerous clinical trials evaluating sucrose-free polyol gum (e.g. sorbitol, manitol, xylitol or combinations)

Twetman S. Consistent evidence to support the use of xylitol and sorbitol containing chewing gum to prevent dental caries. Evid Based Dent. 2009;10(1):10-1

Primary action of chewing gum to enhance remineralization
- Increase salivary flow rate
- Buffer pH to neutral more rapidly
- Increases rate of food clearance
- Increase bioavailability of Ca and P0_4 ions

Primary action of chewing gum to enhance remineralization

- Clinical trials suggest that xylitol (64% caries reduction) is more effective than sorbitol (36% caries reductions) or sorbitol-manitol combinations.

Is this due to action of xylitol or differences in patient compliance and amount of chewing, dosage differences or other factors?

Xylitol and Caries Prevention

- Numerous randomized clinical trials.
- Most trials Strep Mutans levels and pH are outcome and not caries.
- Gums, lozenges and syrups tested

Xylitol and Caries Clinical Trial

- 100 9-15 month old children randomized into 3 groups.
- Xylitol syrup 2 or 3 per day 4gr or 2.6gr.
- Decayed teeth were 1.9 control group, 1.0 Xyl-3x group, and 0.6 Xyl-2x group.
- Difference to control significant – Tx groups - no significant difference


Xylitol Daily Dose for Effectiveness

- 6 grams per day is being recommended but lower levels in small children appear to be of benefit.
- Gums vary in Xylitol content
- Epic gum 1.06 gram per stick.
- Trident 170mg per stick

Xylitol in Toothpaste and Mouthrinse

- No clinic evidence that the addition of xylitol in dentifrice or mouthrinse reduces caries.

Spiffies with Xylitol

- Marketed for cleaning infant mouths
- Very sweet flavored disposable towelet
- Parents report infants like them
- No evidence they create a health effect
- Are there concerns about exposing infants to very sweet substances?

Taste Buds and Dental Caries

- Clinical study shows significant association of certain taste bud gene polymorphisms and dental caries.


Increasing Use of Artificial Sweetners and Risk of Obesity and Diabetes

- Epidemiological data have demonstrated an association between artificial sweetener use and weight gain
- Randomized controlled trials in children are very limited, and do not clearly demonstrate either beneficial or adverse metabolic effects


Xylitol and Acute Otitis Media Prevention

- Systematic review: of 44 trials - four randomized controlled trials met inclusion criteria.
- Significant treatment effects: Xylitol generally well accepted prophylaxis for AOM.
- 10grams 5X day


Chewing Gum Risks vs Benefits

- Safety – potential choking hazard and AAP recommends against gum prior to age 4yrs.
- Effectiveness – 5-14 yr olds chewing 10-20 after meals
- Chewing gum abuse can cause hypertrophy of temporalis and other masticatory muscles
- Noncaloric sweeteners have been linked to obesity and diabetes

So how does one use different caries control therapeutics?

- Does the evidence support any of these remineralizing therapies are superior to fluoride?
- Can they be used in place of traditional fluoride approaches?
- What is the basis for using them?

Caries Risk Assessment

- Additional benefit may be gained using some non-fluoride caries control approaches in patients at high caries risk.
- Caries risk assessment is critical for developing an appropriate and customized preventive oral health treatment plan.
**Caries Risk Assessment**

- Low socioeconomic status
- Previous history of caries
- High risk dietary behaviors
- Caregiver with high caries history
- Fluoride deficient
- High microbial count
- Chronic or serious systemic illness
- Enamel hypoplasia
- Abnormal salivary function

**Fluoride Treatment in Saliva Deficient Patients**

- Acidic topical treatments (APF gels/foam) are contraindicated as there will be no saliva to slowly dissolve the CaF$_2$ surface reaction products and deliver the F$^-$ ion to the demineralized enamel.
- Adjunctive remineralizing therapies might be helpful

**Incorporating Remineralizing Products in Your Caries Prevention Protocols**

- Evidence supports the use of chewing gum after meals or snacks for the prevention of dental caries.
- Clinical trials provide weak evidence that xylitol lozenges are effective.
- There is insufficient clinical trial evidence to support recommending any of the mineral formulations for caries reduction.

**New Products for Caries Control**

- It is highly likely that several of the new calcium phosphate remineralizing approaches will prove to be effective.
- Stay Tuned!!!

**Thank You**