Fluoride As a Nutrient of Public Health Importance

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• And thanks to John Himes and the rest of NFDIAS team for inviting us at Iowa to be a part of this project.
Fluoride

- One of the earth’s most abundant elements.
- Results in varying levels of fluoride occurring in all foods, water sources, and other beverages.
- Long known to have important effects on the teeth.
Fluoride

• Fluoride’s dental caries-preventive benefits were discovered in the early 20th century.
• Fluoride from many sources and in many forms has been largely responsible for the substantial decline in mean caries rates in most developed nations over the past 50-60 years.
Fluoride

• Among these sources are:
  – Water fluoridation
    • Naturally occurring
    • Adjusted community water fluoridation
  – Fluoridated dentifrice (toothpaste)
  – Dietary fluoride supplements (drops and tablets)
  – School water fluoridation
  – Fluoride mouthrinse- Rx and OTC
Fluoride

• Among these sources are:
  – Fluoride gel
    • Professional
    • Self-applied
  – Fluoride varnish
  – Salt fluoridation (not in U.S.)
  – Milk fluoridation (not in U.S.)
Topical vs. Systemic Fluorides
Topical Fluorides

- Water fluoridation
- Diet
- Dietary fluoride supplements (chew, swish, swallow)
- Dentifrice
- Mouthrinse
- Office (professional) application
- “Home gel”
Systemic Fluorides

- Water Fluoridation
- Diet
- Dietary Fluoride Supplements
- (Dentifrice)
Pre-eruptive vs. Post-eruptive
Dental Caries Decline

• Overall decline in last 50 years

• The decline in dental caries has not benefited equally all people in the U.S.

• The decline has not been universal internationally
Fluoride- Mechanism of Action

- Since caries rates initially were much lower in areas with naturally occurring fluoride in the water, the majority of the caries preventive effect was believed to be systemic.
Mechanism of Action

- Substantial epidemiological evidence, to go along with laboratory, animal and human clinical trial data, provides that topical fluorides can be extremely effective in caries prevention.
- Now fluoride understood to work primarily (perhaps 70-80%) by post-eruptive (topical) effects, rather than pre-eruptive.
- However, fluoride can be from an ingested (systemic) source, but topical mechanism of action, when it is redistributed to the oral environment through the saliva.
How Does Fluoride Work in Caries Prevention?

• Incorporated into developing crystal lattice.
• Reduces the activity of cariogenic bacteria.
• Inhibits demineralization.
• Enhances remineralization of demineralized enamel.
• Saliva is a major carrier of topical fluoride.
Sealants

- Pit-and-fissure sealants should also be mentioned as an important method of caries prevention for the biting surfaces of teeth.
- They have been used much more widely in the past 20 years.
Dental Fluorosis

• Early childhood ingestion of excessive fluoride, while dental enamel is still forming, is associated with the occurrence of dental fluorosis.
  – Severe form called “mottled enamel”, but most is mild.
  – Ingestion leading to dental fluorosis occurs several years before we see the teeth erupt.
  – Ingestion is difficult to quantify
    • Many sources
    • Dietary sources not labeled.
Risk Factors for Dental Fluorosis

- High fluoride water
- Optimally fluoridated water
- Dietary fluoride supplements (drops and tablets)
  - Developed for “replacing” fluoride intake for those without access to fluoridated water.
  - Ingestion as a bolus, rather than gradually throughout the day
- Fluoride dentifrice

Note: Total fluoride intake is the true risk factor
Relationships Among Fluoride Ingestion, Dental Caries, and Dental Fluorosis
Caries and Dental Fluorosis Prevalence Rates by Fluoride Concentration of Water, Comparison of Dean’s Data from 1930’s-1940’s to More Recent Data (Leverett, et al., 1991)
Dental Caries vs. Dental Fluorosis

- Only ~ 20% of children have about 80% of the total caries experience.
- Targeting of those at high risk is warranted in an effort to obtain cost-effectiveness in caries prevention and the best balance between caries and fluorosis.
Dental Caries
Dental Fluorosis
Fluoride Exposures and Intake

The optimal level of fluoride intake is not known accurately.
Water Fluoridation - U.S.

- 52% adjusted water fluoridation
- 4% natural fluoridation
- 7 states have < 25% fluoridated water
- 20 states and D.C. > 75% fluoridated
Bottled Water

- For drinking and reconstitution of formulas and beverages
- Most < 0.3 ppm F
- Some ≥ 1.0 ppm F
- Tested once per year, fluoride levels not listed
Home Water Filtration Systems

- Usually carbon or charcoal, do not remove fluoride
- Distillation and reverse osmosis remove the majority of fluoride
Fluoride in Milk

- Breast milk: 0.004 to 0.01 ppm F
- Cow’s milk: 0.01 to 0.05 ppm F
- More fluoride if reconstituted with fluoridated water.
Infant Formula

- Concern about high levels in the 1970s.
- U.S. manufacturers voluntarily lowered their F concentrations.
- Reconstitution of concentrated formulas with fluoridated water could substantially increase intake.
- For example, ingestion of about 1 liter of milk-based formula daily from liquid concentrate reconstituted with 1 ppm F water would result in about 5 times the intake from formula made with distilled water.
Other Products High in Fluoride

- Tea
- Dry Infant Cereals
- Chicken Products
- Fish Products
- Seafoods
• Limited information from manufacturers
• Tracking of fluoride content and assessment of intake complex
• ‘Halo effect’ or ‘diffusion effect’ (and vice-versa)
Fluoride Dentifrices

- More than 90% contains fluoride
- Concentrations 1000-1100 ppm F
- National Health Interview Survey showed use of fluoride dentifrices by
  - 33% under age 2
  - 91% aged 2 - 4
Iowa Fluoride Study


• Goals of relating longitudinal patterns of F intakes (and exposures) to dental fluorosis and caries:
  • first of the primary teeth at age 4½-5
  • now of the early-erupting permanent teeth at age 8½-9
  • then the later-erupting permanent teeth at age 13.
Iowa Fluoride Study

• Prospective cohort study
• 1,375 mothers with newborns successfully recruited beginning in 1992
• Parent questionnaires completed at baseline, 6 weeks, 3, 6, 9, 12, 16, 20, 24, 28, 32 and 36 months of age, and then every 6 months
• Currently, about 750 parents of children aged 9 to 12 actively participating
Selected Iowa Fluoride Study Results
## Results - Bottled Waters

<table>
<thead>
<tr>
<th>F Level (ppm)</th>
<th>% of Samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.3</td>
<td>83</td>
</tr>
<tr>
<td>0.3-0.07</td>
<td>7</td>
</tr>
<tr>
<td>0.71-1.0</td>
<td>1</td>
</tr>
<tr>
<td>&gt;1.0</td>
<td>9</td>
</tr>
</tbody>
</table>
## Results - Juices/Juice Drinks

<table>
<thead>
<tr>
<th>Fluoride (ppm)</th>
<th>Percent</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.30</td>
<td>48</td>
<td>0.13</td>
<td>1.11</td>
</tr>
<tr>
<td>0.30 - 0.60</td>
<td>9</td>
<td>0.45</td>
<td>0.45</td>
</tr>
<tr>
<td>0.61 - 1.00</td>
<td>24</td>
<td>0.82</td>
<td>0.82</td>
</tr>
<tr>
<td>&gt; 1.00</td>
<td>19</td>
<td>1.40</td>
<td>1.21</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100</td>
<td>0.65</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Note: The overall range was 0.02-2.80ppm
Note: Published article had error with mean and median values reversed
Fluoride Concentrations According to Grape Juice as an Ingredient

<table>
<thead>
<tr>
<th>Flavor</th>
<th>%</th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Grape</td>
<td>4</td>
<td>1.33</td>
<td>1.40</td>
<td>0.15-2.80</td>
</tr>
<tr>
<td>Red Grape</td>
<td>12</td>
<td>1.00</td>
<td>0.66</td>
<td>0.05-2.45</td>
</tr>
<tr>
<td>No Grape</td>
<td>84</td>
<td>0.57</td>
<td>0.32</td>
<td>0.02-2.64</td>
</tr>
</tbody>
</table>
## Effects of Water Sources on Manufactured Products of One Company

<table>
<thead>
<tr>
<th>Site of Manufacture</th>
<th>Water Source</th>
<th>Infant Juice</th>
<th>Size</th>
<th>Fluoride (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>City, non-fluoridated</td>
<td>Apple-grape</td>
<td>4 oz</td>
<td>0.28</td>
</tr>
<tr>
<td>N</td>
<td>City, non-fluoridated</td>
<td>Apple-grape</td>
<td>25.3 oz</td>
<td>0.20</td>
</tr>
<tr>
<td>L</td>
<td>City, fluoridated</td>
<td>Apple-grape</td>
<td>64 oz</td>
<td>0.88</td>
</tr>
<tr>
<td>S</td>
<td>City, non-fluoridated</td>
<td>Apple</td>
<td>4 oz</td>
<td>0.06</td>
</tr>
<tr>
<td>N</td>
<td>City, non-fluoridated</td>
<td>Apple</td>
<td>4 oz</td>
<td>0.03</td>
</tr>
<tr>
<td>L</td>
<td>City, fluoridated</td>
<td>Apple</td>
<td>64 oz</td>
<td>0.57</td>
</tr>
</tbody>
</table>
Variation in Fluoride Levels of the Same Product Manufactured at Different Production Sites.

Coca-Cola

Pepsi-Cola

Production Sites

Mean Fluoride Levels (ppm)

PA WI FW AB LX CN SL CR NK WT UG LN
## F Concentration of 206 RTE Infant Foods

<table>
<thead>
<tr>
<th>Food Type</th>
<th>No. of Samples</th>
<th>Range</th>
<th>Median</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruits &amp; Desserts</td>
<td>88</td>
<td>.01-.49</td>
<td>.03</td>
<td>.10</td>
</tr>
<tr>
<td>Vegetables</td>
<td>48</td>
<td>.01-.42</td>
<td>.08</td>
<td>.12</td>
</tr>
<tr>
<td>Mixed Foods</td>
<td>42</td>
<td>.01-.63</td>
<td>.13</td>
<td>.21</td>
</tr>
<tr>
<td>Meats (including poultry)</td>
<td>19</td>
<td>.01-8.38</td>
<td>.05</td>
<td>1.46</td>
</tr>
<tr>
<td>Chicken</td>
<td>6</td>
<td>1.05-8.38</td>
<td>4.04</td>
<td>4.40</td>
</tr>
<tr>
<td>Cereals</td>
<td>9</td>
<td>.01-.31</td>
<td>.02</td>
<td>.08</td>
</tr>
</tbody>
</table>
Fluorosis and Dietary Sources

- Concentrated infant formula reconstituted with fluoridated water associated with elevated risk of fluorosis of primary teeth (molars).
- First published data to show this.
Fluoride and Bone

• Fluoride’s effects on bone are not well understood.

• Overall, studies have demonstrated conflicting results, with some reporting increased bone density and reduced fractures, while others decreased bone density and increased fractures.

• Fluoride appears to delay bone turnover, enhancing total bone quantity.

• Fluoride could affect cortical and trabecular bone differently, enhancing trabecular bone density and diminishing cortical bone density.
Fluoride and Bone

• Fluoride intake associated with reduced hip fractures and more wrist fractures (*Phipps, et al.*, 2000)
• Very high fluoride levels probably associated with reduced bone health at all sites.
• Many limitations and concerns with measuring fluoride intake and bone health in these studies
• Conflicting results also for sodium fluoride as a therapeutic agent for osteoporosis -- perhaps dependent on the specific fluoride regimen
• The bottom line is that at low dosages (such as in fluoridated water), fluoride appears to have little effect on bone health.
Dual-energy X-ray Absorptiometry (DXA)

• Areal bone mineral density
  \[ \text{aBMD} = \frac{\text{BMC}}{\text{BA}} \]
  – Mineral mass of bone per unit area of the two-dimensional projection image
  – Dependent on bone area (cm\(^2\)), not volume (cm\(^3\))
  – Bone size dependent measure
    • Difficult to interpret in children
    • Short children have lower aBMD than age-matched peers despite normal bone structure
Outcomes: DXA scans of spine, hip, and whole body at age 5:
- Spine BMD
- Spine BMC
- Hip BMD
- Hip BMC
- Whole body BMC
IFS – Bone and Fluoride: Methods

- Predictors: Fluoride intake in mg and mg/kg bw – at individual time points and combined (area-under-the-curve)
- Sample size: 310
- Analyses: Spearman correlation coefficients and multiple linear regression models
IFS- Results: 2004 IADR – Levy et al.

• A few significant weak associations in bivariate analyses.
• Most of these non-significant after adjusting for demographics and body size.
• Associations reduced further after additional adjustment for vigorous physical activity.
Peripheral Quantitative Computed Tomography (pQCT)

- Volumetric bone mineral density
  \[ vBMD = \frac{BMC}{\text{bone volume}} \]
  - Mineral mass of bone per unit volume of bone cross-sectional slice
  - Differentiates cortical bone from trabecular bone
- Bone parameters
  - Cortical bone area
  - Cortical thickness
  - Cortical density
  - Total cross-sectional bone area
  - Bone component circumferences
Fluoride Intake and Cortical Bone Characteristics in Young Children Pilot Study (Gilmore, et al.) - Methods

- N = 189 (98 F/91 M)
- Cortical bone assessments (20% radius) at age 9 years
  - Bone mineral content
  - Bone area
  - Cortical thickness
  - Periosteal circumference
  - Endosteal circumference
- Fluoride exposure (birth – 5 years)
Fluoride Intake and Cortical Bone Characteristics in Young Children Pilot Study - Initial, Interim Results

• F intake from all sources at age 5 years
  – Mean = 0.77 mg/day
  – Range = 0.18 – 2.50 mg/day

• Associations with cortical bone assessments (20% radius) at age 9 years – age-, gender- and body size- adjusted
  – Inverse Bone mineral content
  – Inverse Bone area
  – Inverse Cortical thickness
  – Positive Periosteal circumference
  – Positive Endosteal circumference
Summary Comments- Fluoride

• Much is known about fluoride exposures, intake, dental fluorosis, and caries
• Fluoride probably studied more than any other element
• However, more gaps remain
Conclusions- Fluoride

• Fluoride exposures and intake are extremely complex.
• Good data are not currently available to relate more recent fluoride intake patterns (with less supplement and dentifrice ingestion) to dental fluorosis and caries.
• Water fluoridation is the most cost-effective and efficient way to provide fluoride’s benefits.
Challenges Due to Lack of Existing Fluoride Databases

• Planning of future studies is hindered substantially by the logistical difficulties in designing an approach to dietary fluoride assessment.
  – Few qualified laboratories
  – Very labor-intensive
  – Expensive
  – Water sources used in production and reconstitution at home.

• Difficult to reach “NIH standard” for scientific rigor for funding, given these difficulties.
The National Fluoride Database and Intake Assessment Study

• Will provide a national snapshot of fluoride levels of beverages and foods.

• Will allow researchers to use national and regional average fluoride levels concerning important beverages and foods.

• Will guide researchers toward a better understanding of the aspects of their projects needing local, project-specific efforts (e.g., local water source fluoride values, filtration).
The National Fluoride Database and Intake Assessment Study (cont.)

• Will provide a framework for the questions needed concerning these aspects warranting more individualized assessment.

• Will allow researchers to choose to purchase a contract with MNDS for the online use of the survey instruments and fluoride results.
Recommendations for Using Fluoride to Prevent and Control Dental Caries in the United States

Process

• 11 Member Work Group
• Scientific Review of Manuscript by 23 Fluoride Experts
• Extensive Outside Review of Report
• MMWR, 2001:50 (No. RR-14):1-42

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PDF format:
http://www.cdc.gov/mmwr/PDF/rr/rr5014.pdf