From:	Boateng, Sarah (HHS/OASH)
To:	Calsyn, Maura (HHS/OASH); Lesko, Max (HHS/OASH)
Subject:	FW: Briefing on fluoride - Dec 21, 2021
Date:	Monday, January 24, 2022 2:22:03 PM
Attachments:	References for ASH"s presentation Final.pdf 3 RDS short FINAL Community Water Fluoridation Current Evidence and Future Directions V5.pdf 2 ASH slides ASH briefing fluoride 122121 Taylor2.pdf

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These might be helpful

From: Wolfe, Mary (NIH/NIEHS) [E] <wolfe@niehs.nih.gov>
Sent: Tuesday, December 21, 2021 2:18 PM
To: Levine, Rachel (HHS/OASH) <Rachel.Levine@hhs.gov>; Howard, John (CDC/NIOSH/OD) <zkz1@cdc.gov>; Tabak, Lawrence (NIH/OD) [E] <lawrence.tabak@nih.gov>; O'Shaughnessy, Jacqueline A (FDA/OC) <Jacqueline.OShaughnessy@fda.hhs.gov>; D'Souza, Rena (NIH/NIDCR) [E] <rena.d'souza@nih.gov>; Berridge, Brian (NIH/NIEHS) [E] <brian.berridge@nih.gov>; States, Leith (HHS/OASH) <Leith.States@hhs.gov>; Iademarco, Michael (CDC/DDPHSS/CSELS/OD) <mai9@cdc.gov>; Woychik, Rick (NIH/NIEHS) [E] <rick.woychik@nih.gov>; Boateng, Sarah (HHS/OASH) <Sarah.Boateng@hhs.gov>
Cc: Taylor, Kyla (NIH/NIEHS) [E] <kyla.taylor@nih.gov>; Rooney, Andrew (NIH/NIEHS) [E] <andrew.rooney@nih.gov>; Fisher, Megan (HHS/OASH) <Megan.Fisher@hhs.gov>; Piacentino, John D. (CDC/NIOSH/OD) <gjt4@cdc.gov>; Joskow, Renee (NIH/NIDCR) [E] <joskowrw@nidcr.nih.gov>; Iafolla, Timothy (NIH/NIDCR) [E] <iafollat@nidcr.nih.gov>; Robin, Lauren (Posnick) (FDA/CFSAN) <Lauren.Robin@fda.hhs.gov>; Alraqiq, Hosam (NIH/NIDCR) [E] <hosam.alraqiq@nih.gov>; Wolpert, Beverly (FDA/CFSAN) <Beverly.Wolpert@fda.hhs.gov>; Hyman, Frederick N (FDA/CDER) <Fred.Hyman@fda.hhs.gov>
Subject: Briefing on fluoride - Dec 21, 2021
Good afternoon,
Attached are PDF files of the slides presented by Drs. D'Souza and Taylor. Also attached is a reference listed provided by Dr. D'Souza.
Please let me know if questions,
Mary

robinsMary S. Wolfe, Ph.D.
Acting Deputy for Policy and Communication
Director, Office of Policy, Review, and Outreach
Acting Director, Office of Workforce Development and Operations
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NIDCR List of Key References

Community Water Fluoridation (CWF)

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- Health Policy - Healthy People 2030 | health.gov

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Impact of CWF cessation on dental caries experience

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Fluoride and Oral Health:
Current Evidence and Future Research

Rena N. D'Souza, D.D.S., M.S., Ph.D.
Director, National Institute of Dental and Craniofacial Research, NIH

December 21, 2021

National Institute of Dental and Craniofacial Research

My Journey as a Clinician – Scientist

- A sense of intellectual curiosity
- Interest in using clinical questions (derived from chair side experiences) to drive scientific inquiry and the translation of discovery into practice
- *Lifetime dedication to better understanding the development and preservation of healthy dentition*
- A passion for mentoring and the dissemination of knowledge
- A commitment to diversity, equity and inclusion; the development of human potential
- A calling and the drive to make a difference

The Past, Present and Future.....

History
NIDR/NIDCR
Fluorides

Human Dentition

Dental Caries

Fluoride:
Mechanism of Action

Community Water Fluoridation

Public Health Burden of Disease

NIDCR (NIDR) Founded in 1948

- Statutory Authority - SEC. 453 [285h] Public Law 80-755
  - The general purpose of the **National Institute of Dental Research** is the conduct and support of research, training, health information dissemination, and other programs with respect to the cause, **prevention,** and methods of diagnosis and treatment of dental and oral diseases and conditions

"incredible epidemic of infectious disease of the oral cavity"—commonly known as tooth decay—that had disqualified men and women from military service in World War II as the impetus to form a dental research institute."

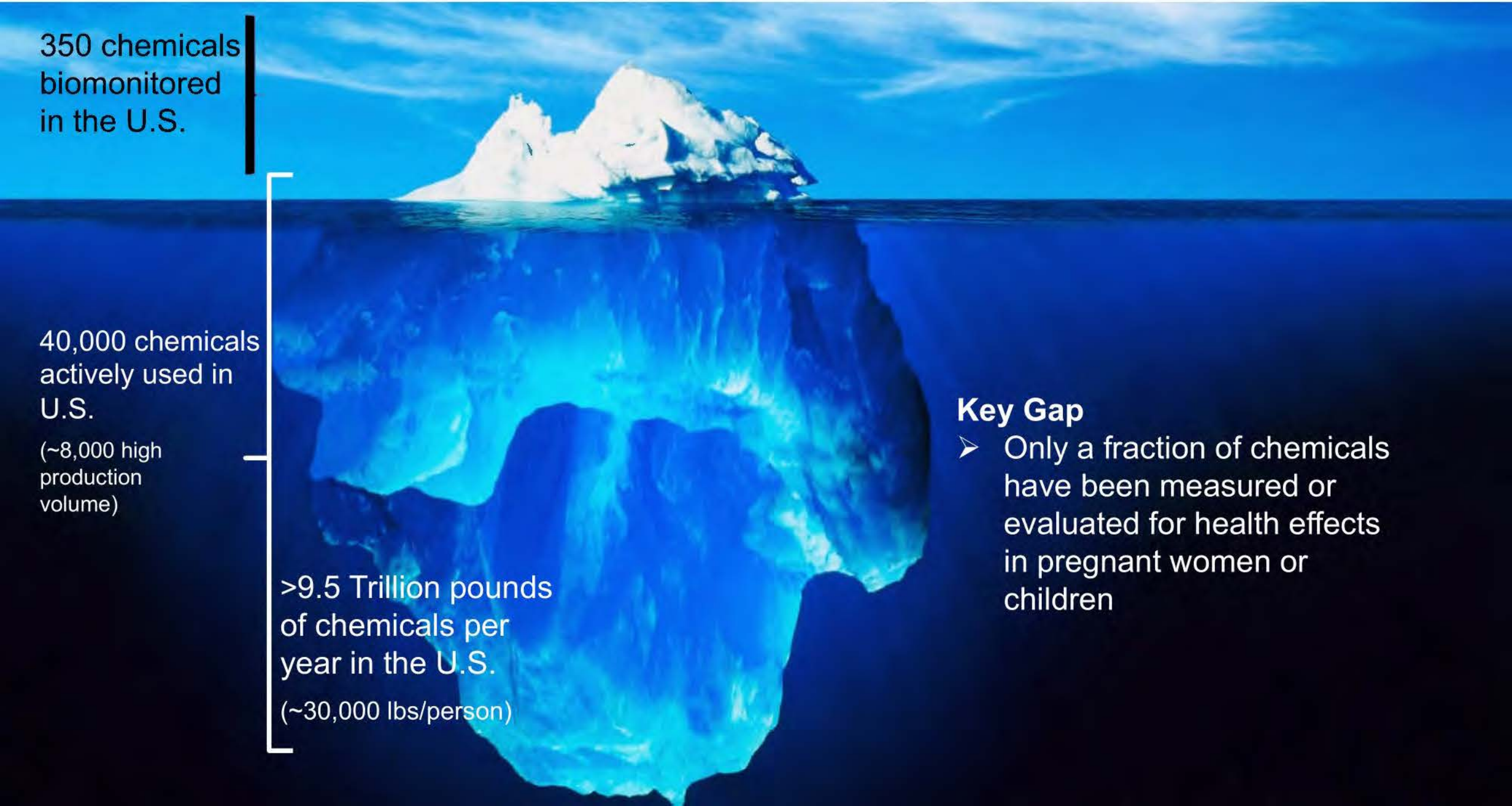
- The 1998 Omnibus Consolidated and Emergency Supplemental Appropriations Act

  - Changed the name to **NIDCR**

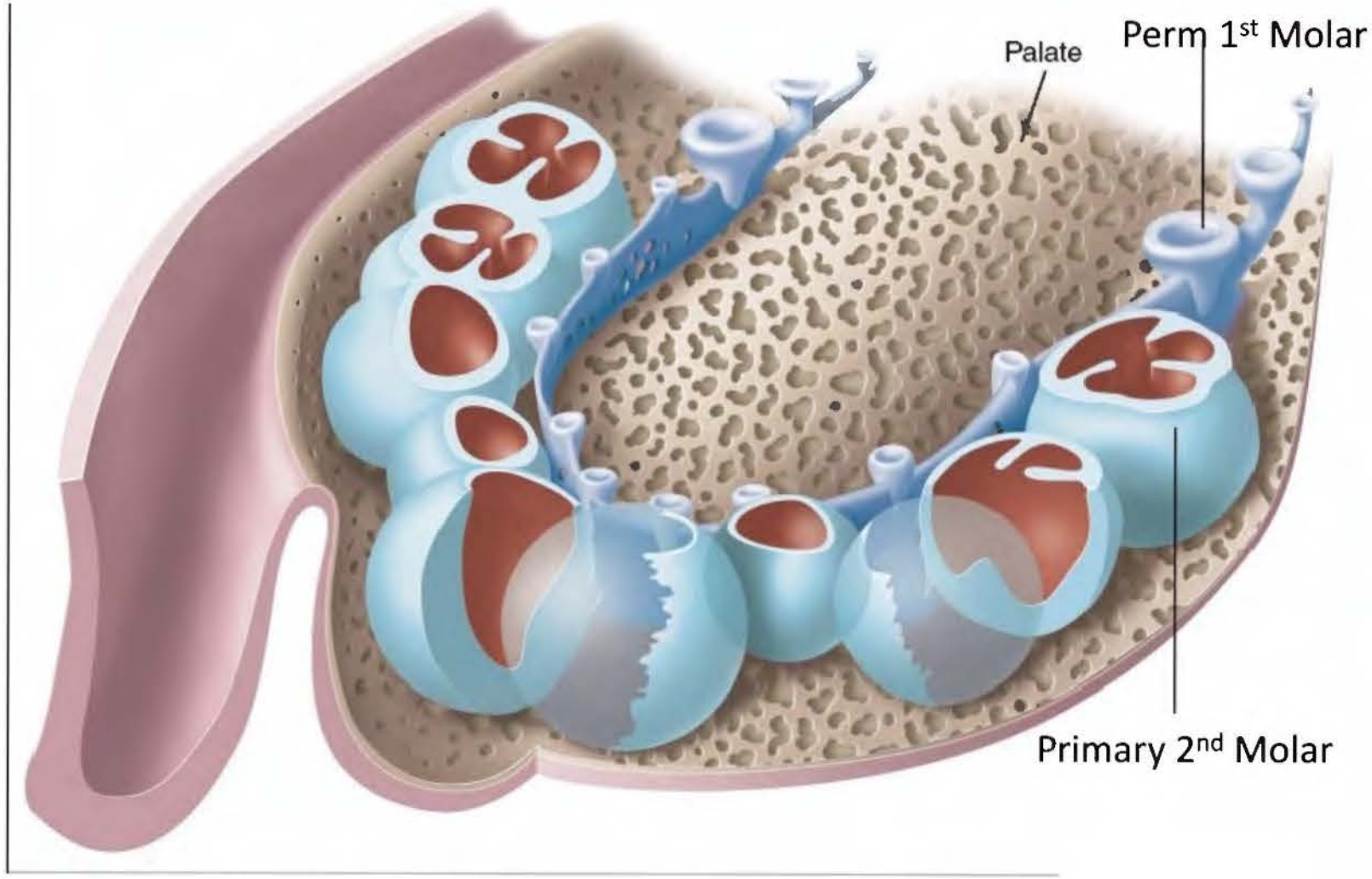
The Story of Fluoride and Tooth Decay

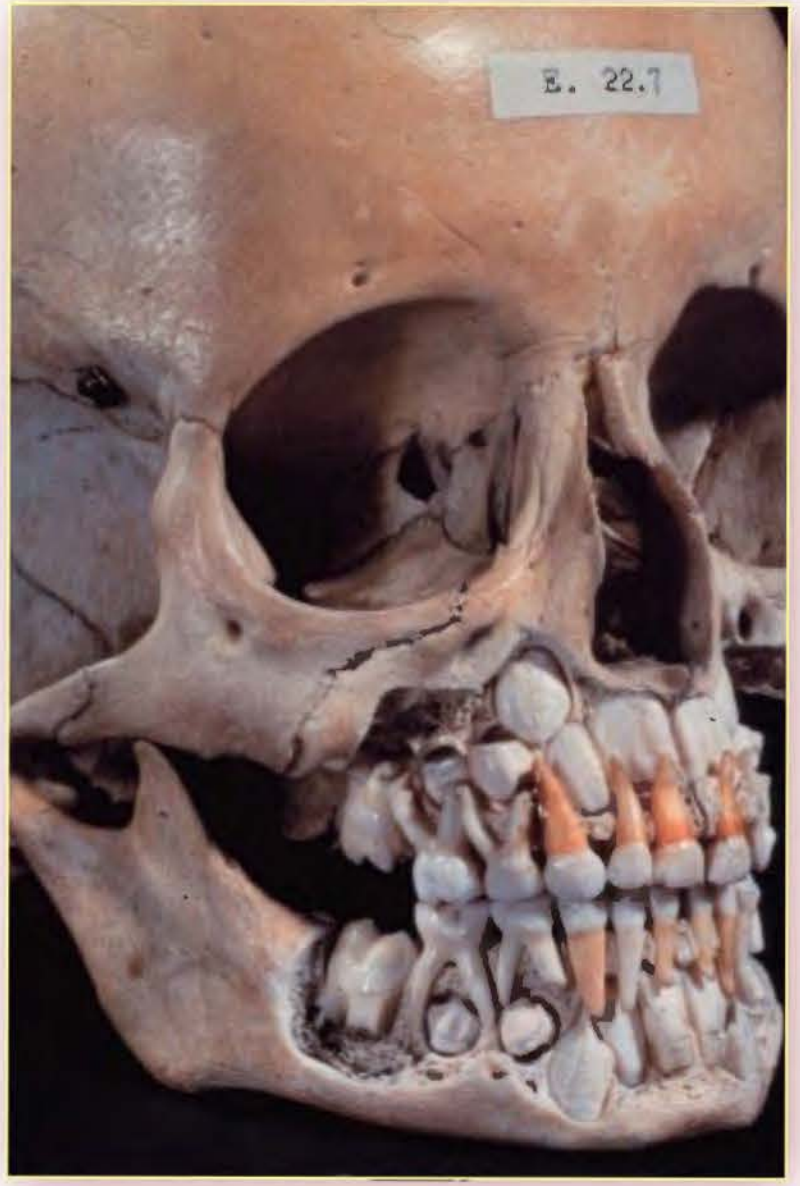
- **The Mysterious Disorder**
  - 1901-1931 Dr. Fred McKay
  - Mottled Enamel
- **A Fruitful Collaboration**
  - High Levels of Natural Fluoride
  - G.V.Black (Researcher)
- **New Questions Emerge**
  - Teeth made harder?
- **Fluoride Prevents Caries**
  - 4 pairs of US Cities
  - H. Trendley Dean's 21-city study
  - 1945 Grand Rapids, MI Study
- **A Lasting Achievement**
  - 1ppm (1mg/l) optimal level
  - 15 years later 50%-70% caries reduction in fluoridated communities; fluorosis low

NIDR dentists examined these Grand Rapids schoolchildren once a year to document the effects of fluoridation

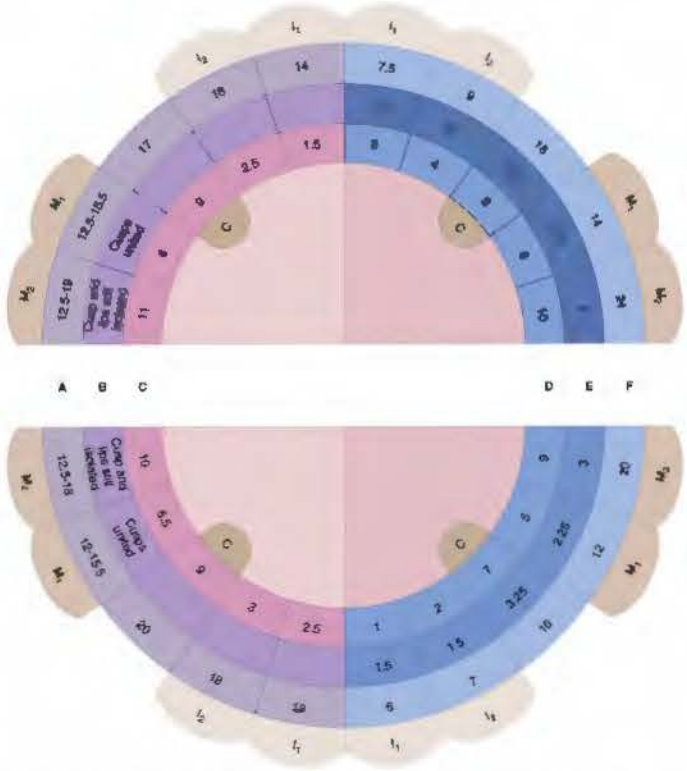

350 chemicals biomonitored in the U.S.
40,000 chemicals actively used in U.S.
(~8,000 high production volume)
>9.5 Trillion pounds of chemicals per year in the U.S.
(~30,000 lbs/person)
Key Gap
Only a fraction of chemicals have been measured or evaluated for health effects in pregnant women or children

HUMAN DENTITION





Chronology is Important



A B C D E F

FIGURE 10-29 Chronology of the human primary dentition. **A,** Mineralization begins (weeks in utero). **B,** Amount of enamel matrix found at birth. **C,** Enamel complete (months). **D,** Eruption sequence. **E,** Root completed (years). **F,** Emergence into the oral cavity (months). *C,* Canine; *I,* incisor; *M,* molar.

Dentition	Enamel Begins	Enamel Complete	Eruption
Primary	12 – 20 wks	1.5 – 10 mos	6 – 24 mos
Permanent	3 mos–10 yrs	3.5 – 13 yrs	6 –18 yrs

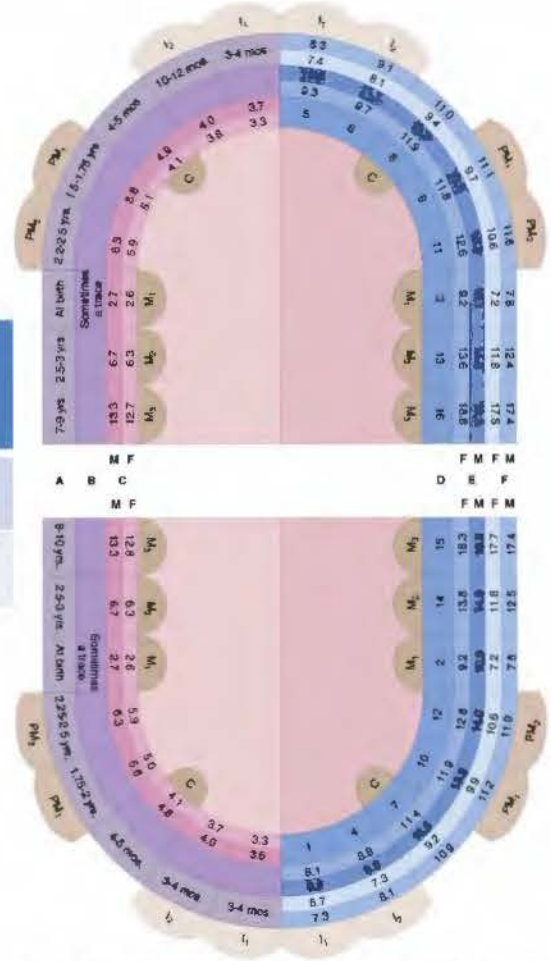
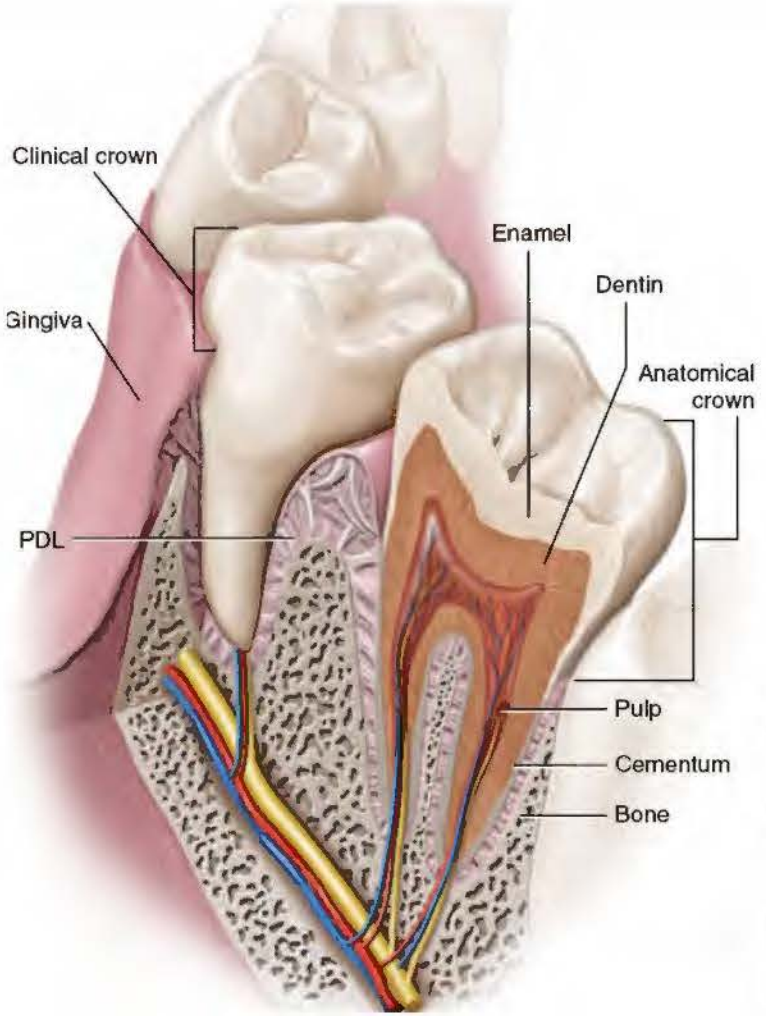
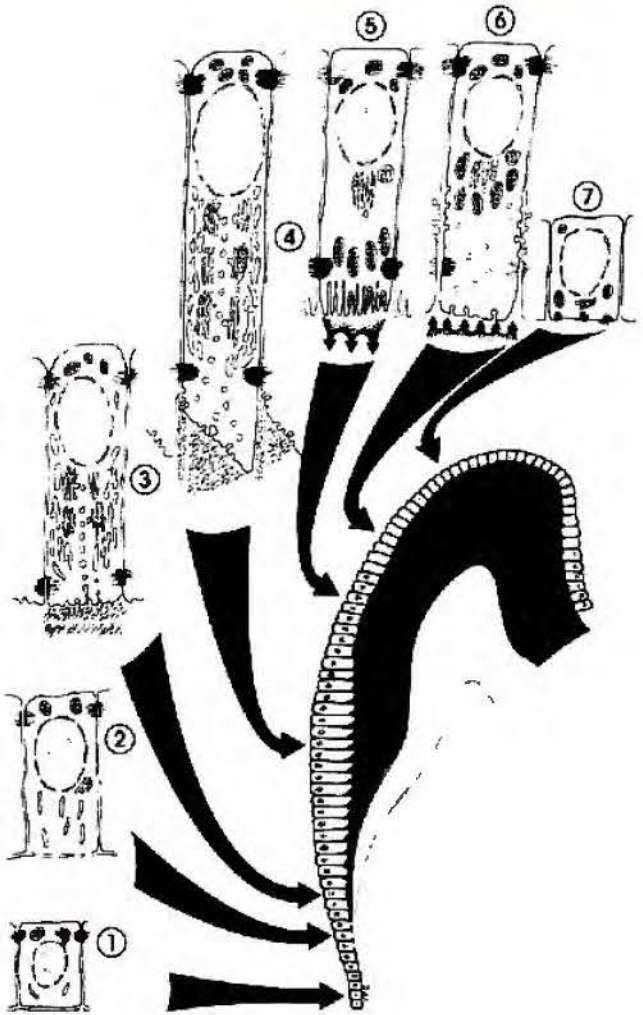
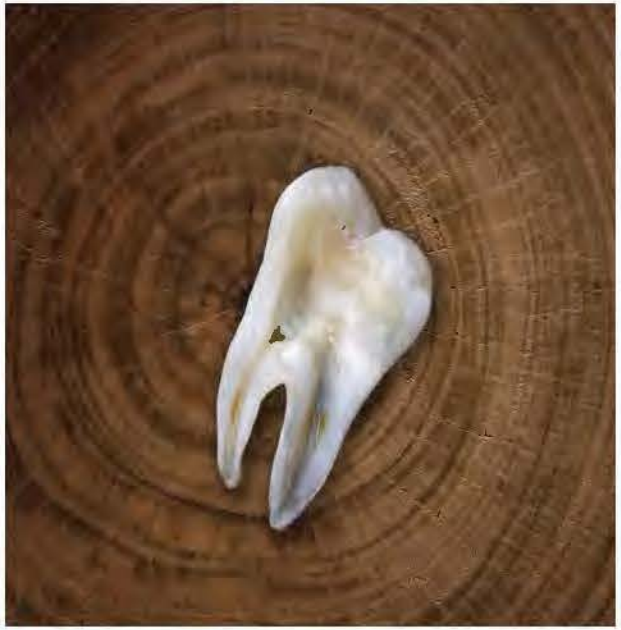


FIGURE 10-30 Chronology of the human permanent dentition. **A,** Mineralization begins. **B,** Amount of enamel matrix at birth. **C,** Enamel completed (years). **D,** Eruption sequence. **E,** Root completed (years). **F,** Emergence into the oral cavity (years). *F,* Female; *M,* male; *C,* canine; *I,* incisor; *M,* molar; *P,* premolar.

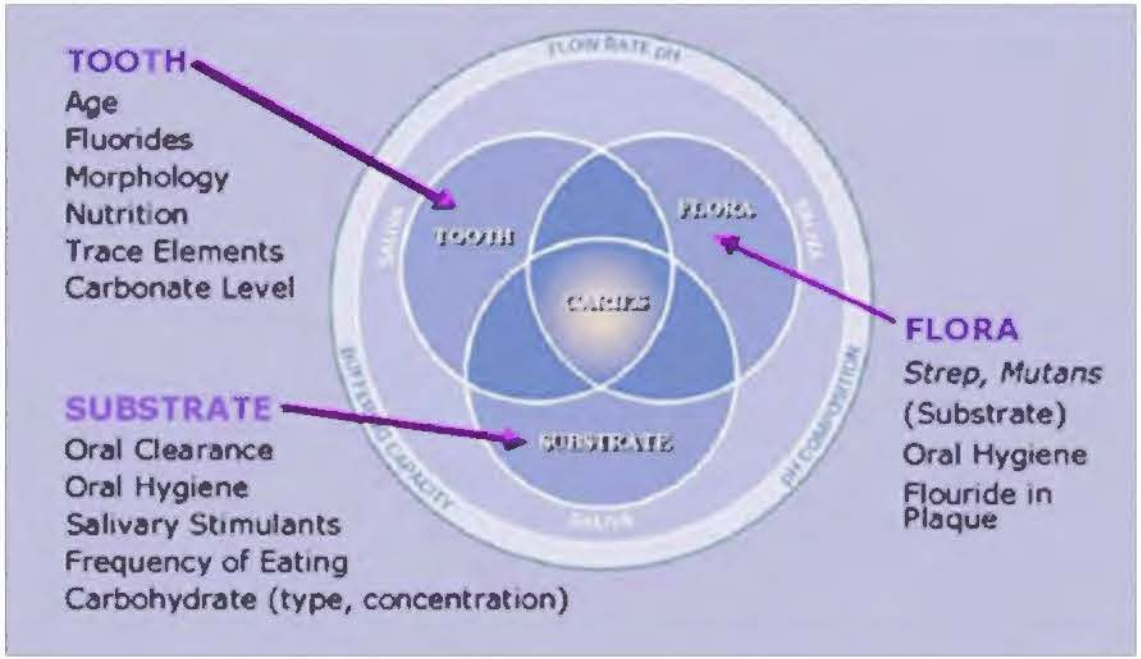
Nature's Reliable Biologic Hardware







Prenatal Oral Health



- Dental care safe and important during pregnancy
- Poor oral health in mother:
  - Preterm birth and low birth weight
- Mother's dental caries experience predictor of child's caries risk

Caries : A Disease of Childhood

Child's Age (Years)

Prenatal

0

Primary Dentition

~6

Mixed Dentition (Primary and Permanent Teeth)

~15

Infancy (birth-2)

Early Childhood (3-8)

Middle Childhood (9-11)

Early Adolescence (12-15)

Effect of Mother's Oral Health on Child's Oral Health

Craniofacial and Tooth Defects, Dental Caries, Role of Parents on Diet and Oral Hygiene, Fluorides, Sealants, Inter-professional Care, Trauma

Dental Caries, Behavioral Health (Independence, Self-Esteem/Image, etc.), Diet and Eating Disorders, Oral Hygiene, Fluoride, Sealants, School-Based Care, Sport Injuries, Tobacco/e-Cigarettes, Vaccines (HPV)

Infants (0-2) and Early Childhood (3-8): Overview

- Primary teeth erupt (6 to 24 months
- Breast- and/or bottle-feeding
- Solid foods (use of sippy cup, etc.)
- Dependence on adult for diet and oral hygiene
- Early Childhood Caries
  - The most common chronic diseases of childhood
  - Diet-driven
  - OR : General Anesthesia (risky for young children; FDA 2016)
- Trauma
- Craniofacial defects

The Dental Project, 2017

Decisions in Dentistry, 2017 (Berg, J)

AAP, 2009 (Lee, Y)

Consequences of Untreated Dental Caries

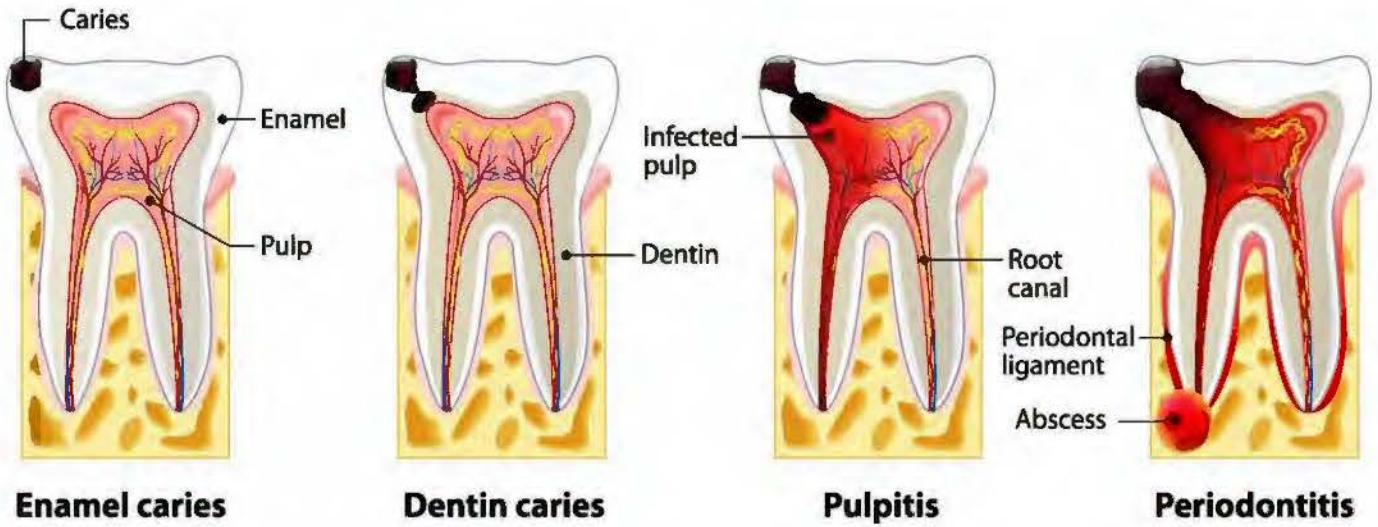
- Pain
- Infection (and possible death)
- Functioning
  - Impaired Chewing and Nutrition
  - Speaking
- Social
  - School absence
  - Poor school performance
  - Poor self-esteem
- Difficulty sleeping
- High Costs and Poor Access

For want of a dentist
By Mary Otto
Washington Post
February 28, 2007

Dental care remains costly and inaccessible to many, especially young children

Caries Persists in Adolescents, Adults and the Elderly

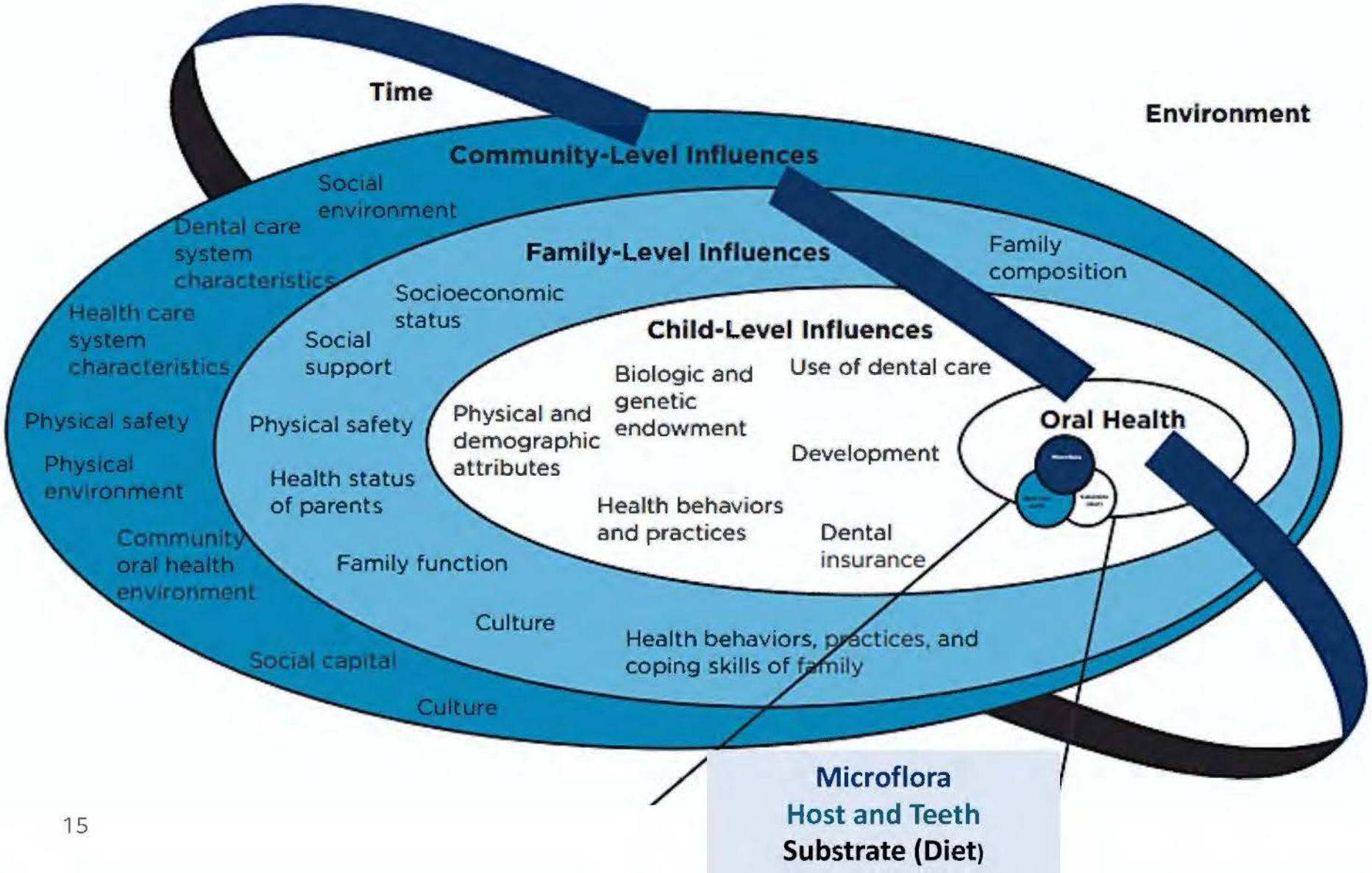
THE STAGES OF CARIES DEVELOPMENT



Dental Restorative – Recurrent Decay – Pulpitis/Pain - Abscess Root Canal Therapy - Brittle Tooth - Crown – Implant

Pain and Discomfort – Loss of Productivity - Health Decline / Pain Killers-ER Visits- Palliative Care – Recurrence

Conceptual Model of Multi-level Determinants of Oral Health



Influences on children's oral health: a conceptual model.
Fisher-Owens SA, Gansky SA, Platt LJ, Weintraub JA, Soobader MJ, Bramlett MD, Newacheck PW. Pediatrics. 2007 Sep;120(3):e510-20. doi: 10.1542/peds.2006-3084.
PMID: 17766495

Fluoride : Biological Mechanism of Action

Natural enamel: hydroxyapatite (HA), calcium-phosphate-based crystalline mineral: $\mathbf{Ca_{10}(PO_4)_6(OH)_2}$, forming microscopic prisms and lattices.

Pre-eruptive (systemic fluoride):

- F^- incorporated into crystal matrix during enamel maturation
- Pre-eruption exposure to fluoride can play a significant role in preventing decay in pits and fissures, the most susceptible surface of teeth
- Fluoride supplements: prescribed only for children who do not receive optimally fluoridated water

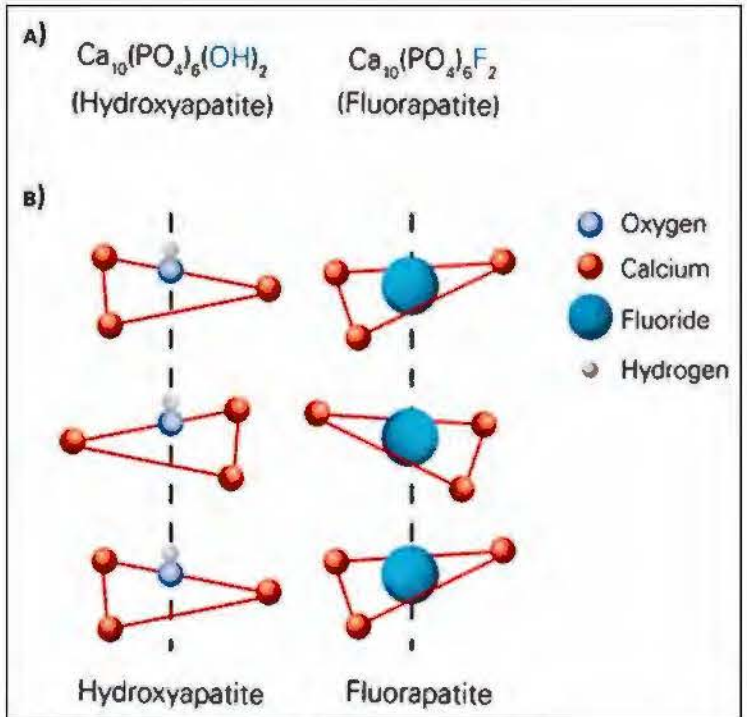
Fluoride : Biological Mechanism of Action

Post-eruptive (topical): At >50 ppm

F^- incorporated by exchange of OH^- ions to form fluoroapatite (FA) at the tooth surface:

$Ca_{10}(PO_4)_6F_2$.

- FA is harder, less soluble, more decay-resistant than HA
- Equilibrium **toward** remineralization using calcium and phosphate ions from saliva
- Inhibition of bacterial metabolism of glycogen
- Plays a significant role in preventing decay in pits/fissures, the most susceptible areas



Fluoride ions replace hydroxyl groups in hydroxyapatite to form fluorapatite. The replacement of hydroxide by fluoride creates a more stable crystal.

Community Water Fluoridation (CWF)

CWF is the process of adjusting the amount of fluoride in drinking water to a level recommended for preventing tooth decay

- Single most effective public health measure to prevent dental caries
- Dramatic decline in tooth decay over 75 years
- Named by CDC as one of the 10 great public health achievements of the 20th century
- In 2018, CWF to protect teeth against caries served more than 200 million people or 73% of those on public water supplies (63% of the total population)
- Healthy People 2030 Objective, OH-11: Increase the proportion of people whose water systems have the recommended amount of fluoride (goal: 77%)

Policy on Fluoride in Drinking Water

- 1950: CWF at 1 mg/L endorsed by
  - The U.S. Surgeon General
  - The American Dental Association (ADA)
  - The American Association of Public Health (APHA)
  - The Association of States and Territorial Dental Directors (ASTDD)
- 1962: Recommended CWF level changed to a range of 0.7 to 1.2 mg/L based on climate
- 2015 (Current PHS recommendation): CWF level changed to a single target of **0.7 mg/L**
- High dose prescription fluorides used in patients with autoimmune diseases, receiving chemotherapy and radiation for cancer. No toxicity.

Community Water Fluoridation is Cost-Effective

- Most cost-effective way to get fluoride to everyone in the community, regardless of age, educational achievement, income level
  - CWF annual cost per capita: $0.11 to $24.38 (highly dependent on size of water system)
  - Annual benefits per capita: $5.49 to $93.10
- Consistent evidence of caries prevention and cost savings for families and the health-care system
  - Average return of investment of $20 for every $1 spent
  - Savings of an average of $32 per person a year in averted treatment for cavities

CWF Safety and Health

- CWF is a safe practice, based on more than 75 years of research and experience*
  - Documented risks of CWF in the U.S are limited to dental fluorosis (mostly mild, cosmetic)
    - Numerous systematic reviews
    - US-CPSTF - 30 to 50% reduction in caries in children; stopping CWF led to 18% rise
    - UK MRC, Australia NHMRC; Cochrane Collaboration
  - Numerous studies have attempted to identify potential adverse health effects from CWF. None has found a significant association between the low levels of fluoride found in CWF and cancer, bone conditions, or neurotoxicity (NRC, 1993; 2006 – risk of bone fractures)

* McDonagh et al, 2000; National Health and Medical Research Council. 2017; Guth et al, 2020; National Health and Medical Research Council. 2017; Aggeborn et al, 2020.

Impact of CWF Cessation on Dental Caries Experience

- 2016 systematic review of 15 cases of CWF cessation in 13 countries between 1956 and 2003, overall, showed an increase in dental caries
- Calgary ended CWF in 2011. In 2018-2019, caries prevalence in the primary dentition of 2nd graders was significantly higher (64.8%) than in comparison – fluoridated Edmonton (55.1%). CWF renewed.

Why the long, strange debate over fluoride in tap water is about to resurface in Alberta

https://www.thestar.com/news/canada/2021/11/13/calgary-keeps-fighting-over-fluoride-in-tap-water-after-six-votes-and-a-decade-of-decay-will-it-finally-make-a-comeback.html

Highlights from NASEM's Review

- Much of the evidence in the NTP report comes from studies with high fluoride concentrations
- The revised monograph provides little or no conclusive information on the effects of fluoride at low exposure levels (less than 1.5 mg/L).
- NTP monograph focuses on hazard identification and not dose - response assessment
- Conclusion far-reaching and not supported by data

- A full dose–response assessment requires:
  - Detailed analyses of dose–response patterns, models, and model fit
  - Full evaluations of the evidence for supporting or refuting threshold effects
  - Assessment of the differences in exposure metrics and intake rates
  - More detailed analyses of statistical power and uncertainty
  - Evaluation of differences in susceptibility
  - Detailed quantitative analyses of effects of bias and confounding of small effect sizes

Research Directions

- Developing general guidelines for specifically designing and conducting population-based fluoride studies in the USA … diverse communities
- Identifying a valid biomarker for long-term fluoride exposure
- Delineating fluoride-specific effects from influences of other environmental factors; systemic vs. local applications of fluoride
- Collaboration of Interdisciplinary teams on fluoride and caries research (e.g., dentist-scientists, environmental epidemiologists, pediatricians, child development specialists)
- Need for sound prospective epidemiological studies at lower exposure levels (< 0.7 mg/L) ;
- Testing environmentally-relevant doses of fluoride in rigorous animal studies
- Recent literature exploring fluoride toxicity at high concentrations should be considered in context with the existing body of evidence to better assess risk : benefit ratios

Summary

- CWF is an effective and equitable approach to caries prevention
- CWF is recommended by public health, medical, and dental organizations including ADA, AAP, U.S. Public Health Service, and the WHO
- Research examining fluoride risks vs. benefits must continue
- Future research will continue to inform CWF recommendations
- Benefits and costs will be crucial factors that guide policies

Oral Health in America: Advances and Challenges

NIH & NIDCR release on 12/21/2021 High Level Dissemination and Impact

- Examines progress in oral health since the 2000 OSG Report
- Organized across the lifespan..challenges & opportunities, future vision and call to action

$55 billion in out-of-pocket expenses
Costs/person increased by 30% since 2000

50% reduction in 0 to 5 year-olds
Prevalence : 1 in 4 who are 6 yrs and older
9 of 10 by 50 yrs have caries
Severity and tooth loss declined

Questions? oralhealthreport@nih.gov
Q&A: https://www.nidcr.nih.gov/news-events/nidcr-news/2021/5-qas-about-oral-health-america-advances-challenges

Call to Action

- Reduce social, economic and systemic **inequities** affecting oral health behaviors and access to care
- Place significant efforts on **prevention-** caries, periodontal disease, HPV+oral cancers, opioid substance misuse
- **Integrate** health professional team, and provider facilities
- Focus on **continuum of care** through lifespan
- Support the evidence needed for best oral health practices by supporting the **BEST SCIENCE**

NIH National Institute of Dental and Craniofacial Research

Thank you……

National Institute of Dental and Craniofacial Research

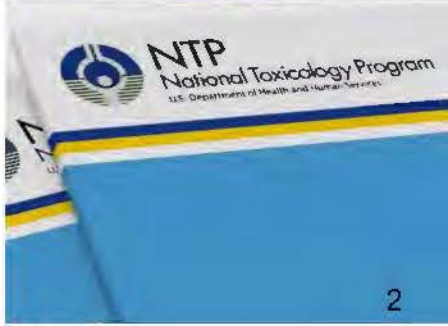
Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects

Kyla Taylor, Ph.D; Andrew Rooney Ph.D; John Bucher, Ph.D (retired)

Integrative Health Assessments Branch
Division of the National Toxicology Program
National Institute of Environmental Health Sciences

Fluoride

- Naturally occurring substance
- Added to municipal water supplies to prevent tooth decay
- Studies suggest potential developmental neurotoxic effects
- NTP systematically evaluated evidence of fluoride exposure and neurodevelopmental and cognitive health effects

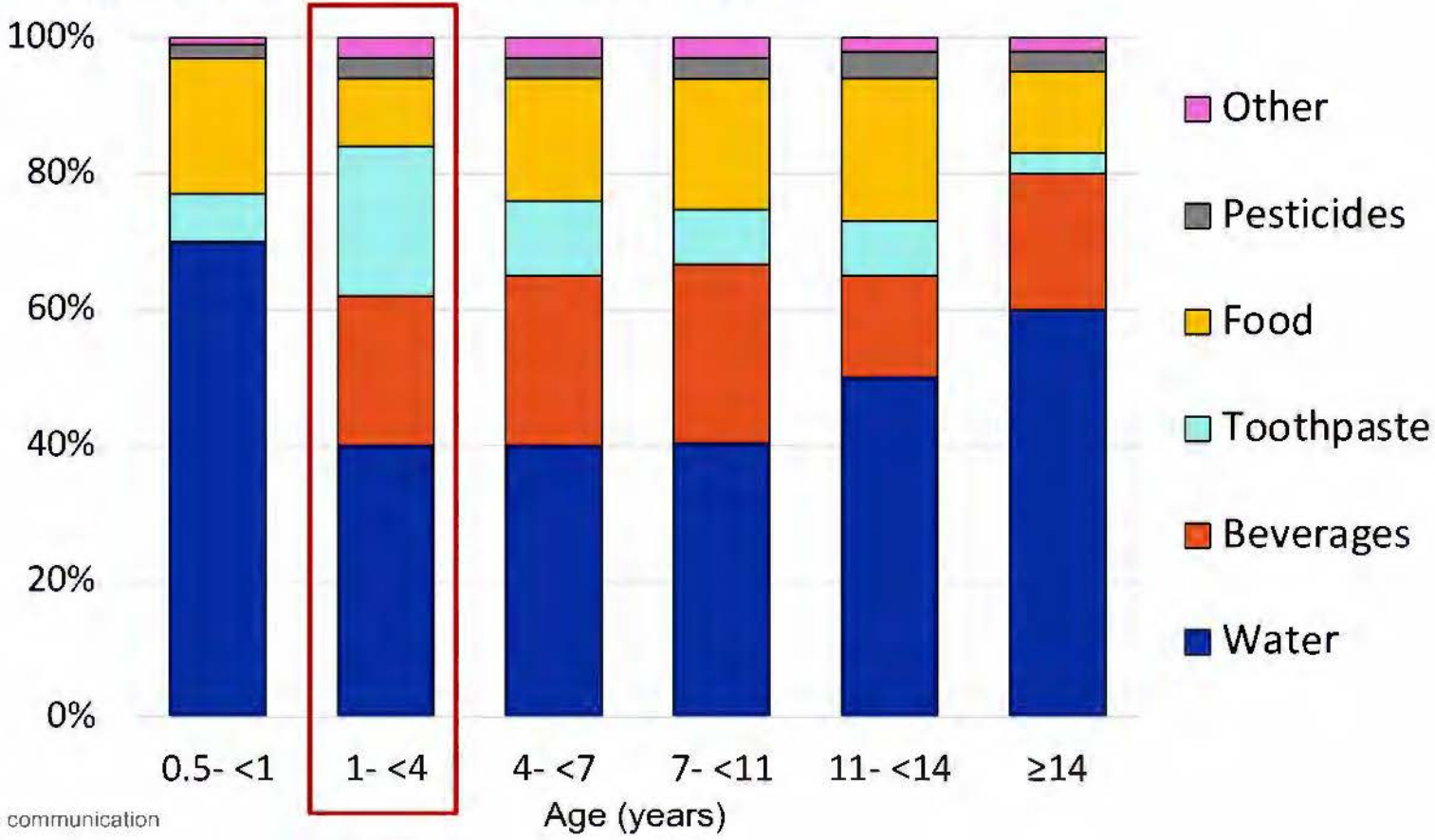


Many sources of fluoride

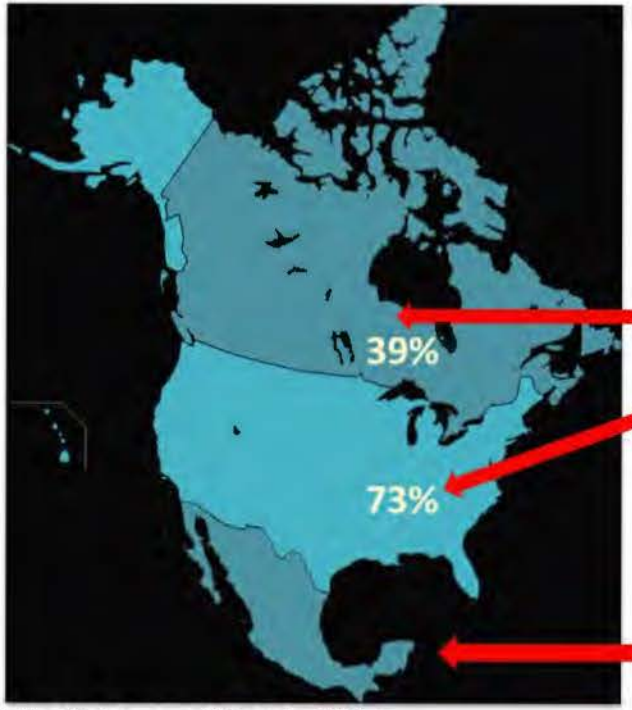
Topical sources

Systemic sources

% fluoride intake from various sources



Sources of *added* fluoride in North America



Optimal level: 0.7 mg/L
(in drinking water)

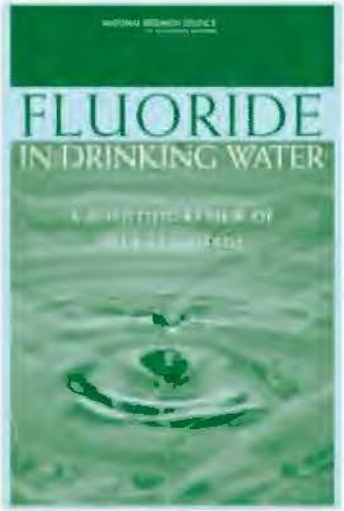
Salt supply is fluoridated

Public Health Agency of Canada, 2017

Does fluoride cause neurotoxic effects?

- **2006:** A National Research Council (NRC) report found suggestive evidence of neurotoxic effects in animals and humans

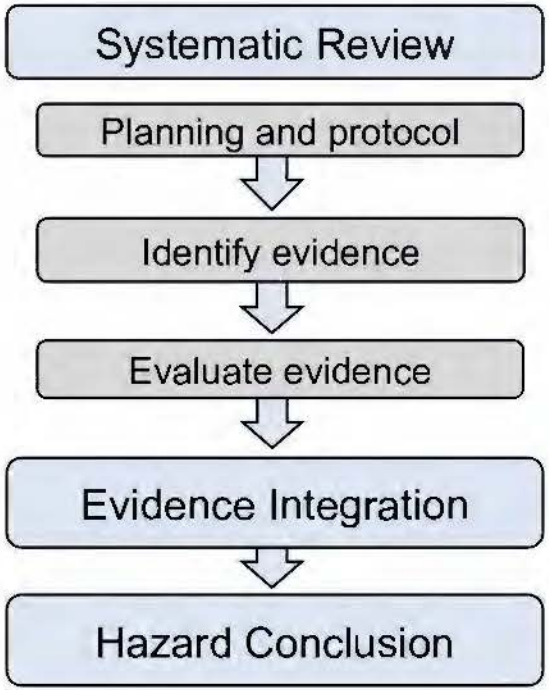
- **2016:** NTP systematic review of experimental animal studies found low to moderate evidence of adverse effects on learning and memory



Current systematic review evaluates potential neurodevelopmental & cognitive effects of the human, animal, and mechanistic/*in vitro* literature

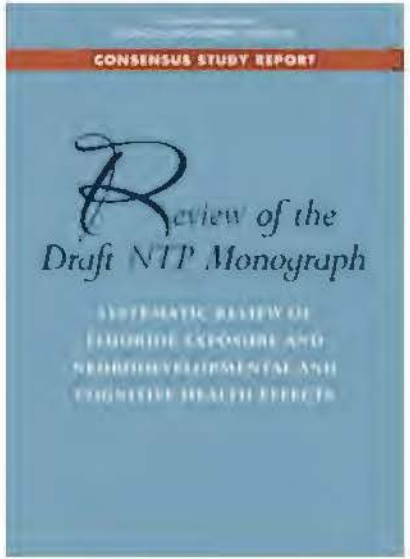
NTP systematic review methods

- Systematic review
  - Predefined, multi-step process to identify, select, critically assess, and synthesize evidence to answer a specific question
- Evidence integration
  - Integrate evidence from human and animal studies with consideration of mechanistic data
  - Develop confidence and level of evidence ratings
- Hazard conclusion
  - Develop evidence-based conclusion on 4-point scale (*known, presumed, suspected, and not classifiable*)
- Scientific peer-review



NTP fluoride systematic review

- National Academies of Science, Engineering, Medicine committee reviewed initial (2019) and revised (2020) drafts that reached hazard conclusion of *presumed*
  - Recommended a meta-analysis, dose-response analysis
  - Provided extensive comments
  - Data not presented clearly enough to support a hazard conclusion



"*The committee's finding did not mean that NTP's conclusions were incorrect; rather, further analysis or reanalysis would be needed to support the conclusions*"

In response to NASEM peer-review report

- Revised into State of the Science Report (2021)
  - Removed hazard conclusions
  - Summarize and critically evaluate evidence
  - Characterize quality of studies, consistency of data
- Meta-analysis and dose-response analysis are being published separately

Both documents, the State of the Science report and Meta-analysis, are currently in peer review

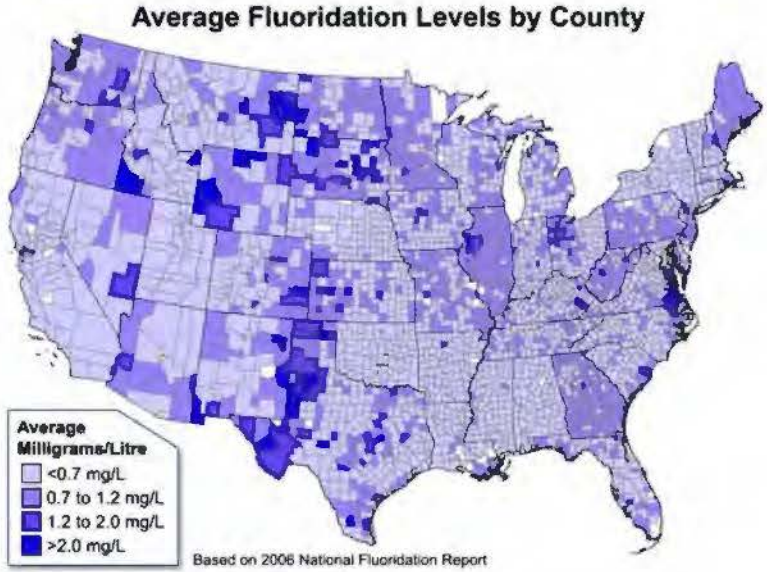
Next 11 pages are Withheld in Full pursuant to Exemption (b)(5)

(b)(5)

Meta-analysis results

Dose-response analysis

- More confidence in our results if there is a dose response
- Statistically significant dose-response between fluoride level in water or urine and children's IQ
- Higher fluoride exposure associated with decreased IQ for
  - All studies **(p<0.001)**
  - High-quality studies **(p<0.05)**
  - Low exposures
    - High quality urinary fluoride studies at <1.5 mg/L **(p-value<0.05)**
    - High-quality water fluoride studies <2.0 mg/L **(p-value=0.07)**

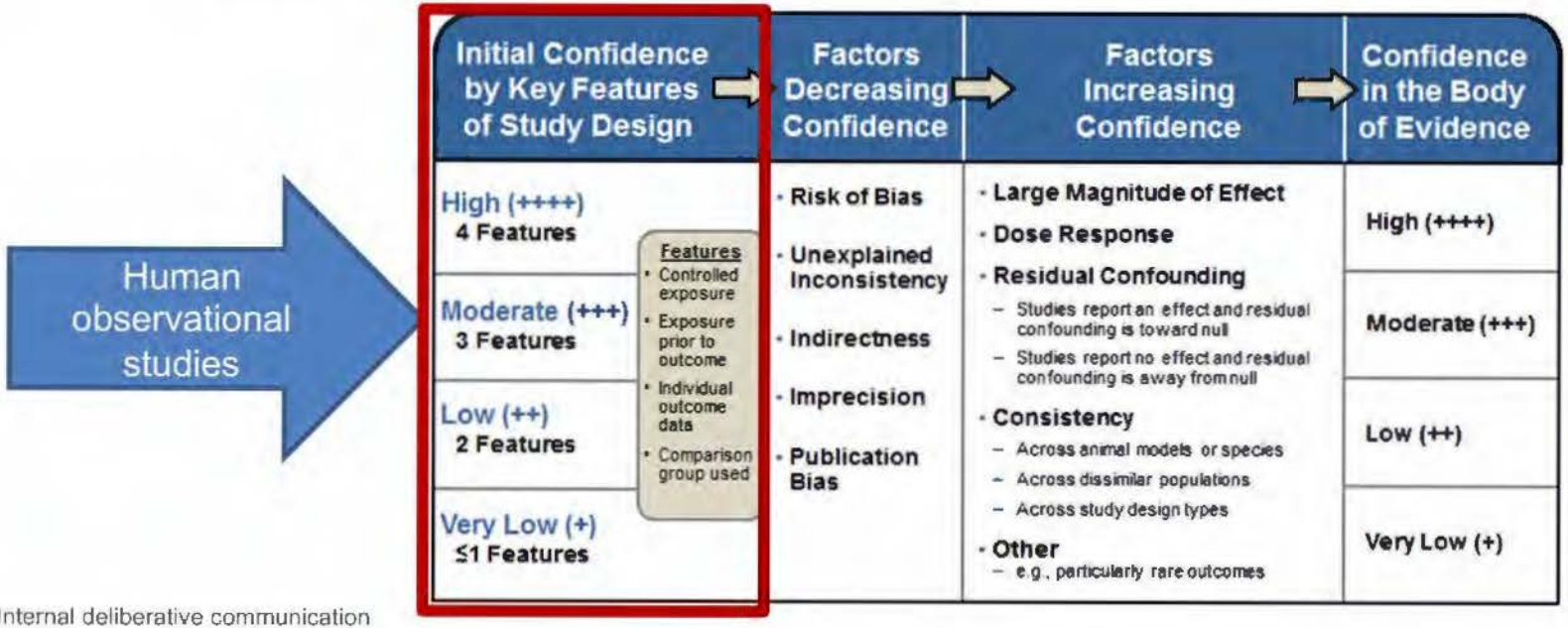


Water systems with ≥ 1.5 mg/L naturally occurring fluoride serve 0.59% of U.S. pop. (~1.9 million ppl)

https://www.cdc.gov/fluoridation/data-tools/reporting-system.html

Final step: Rate confidence in each body of evidence

- Measure of confidence that overall findings reflect the true exposure-effect relationship
  - Performed for bodies of evidence on outcome basis



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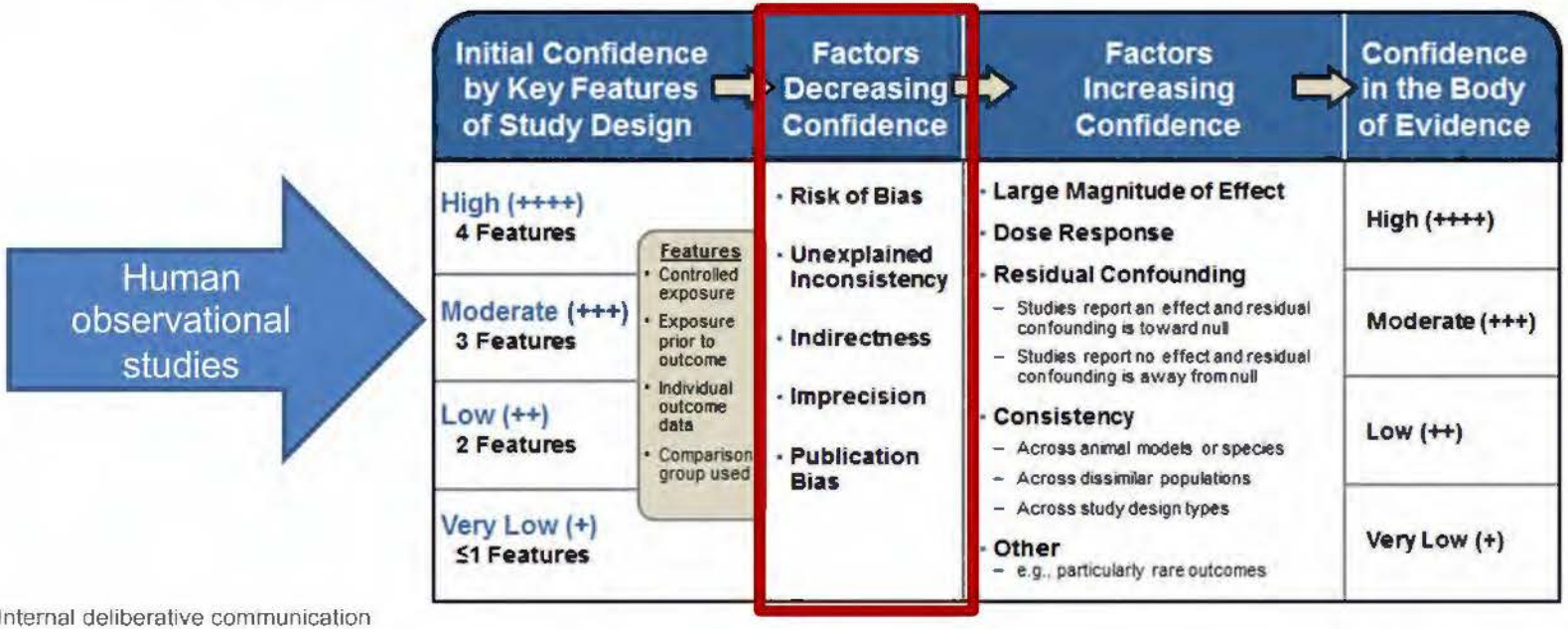

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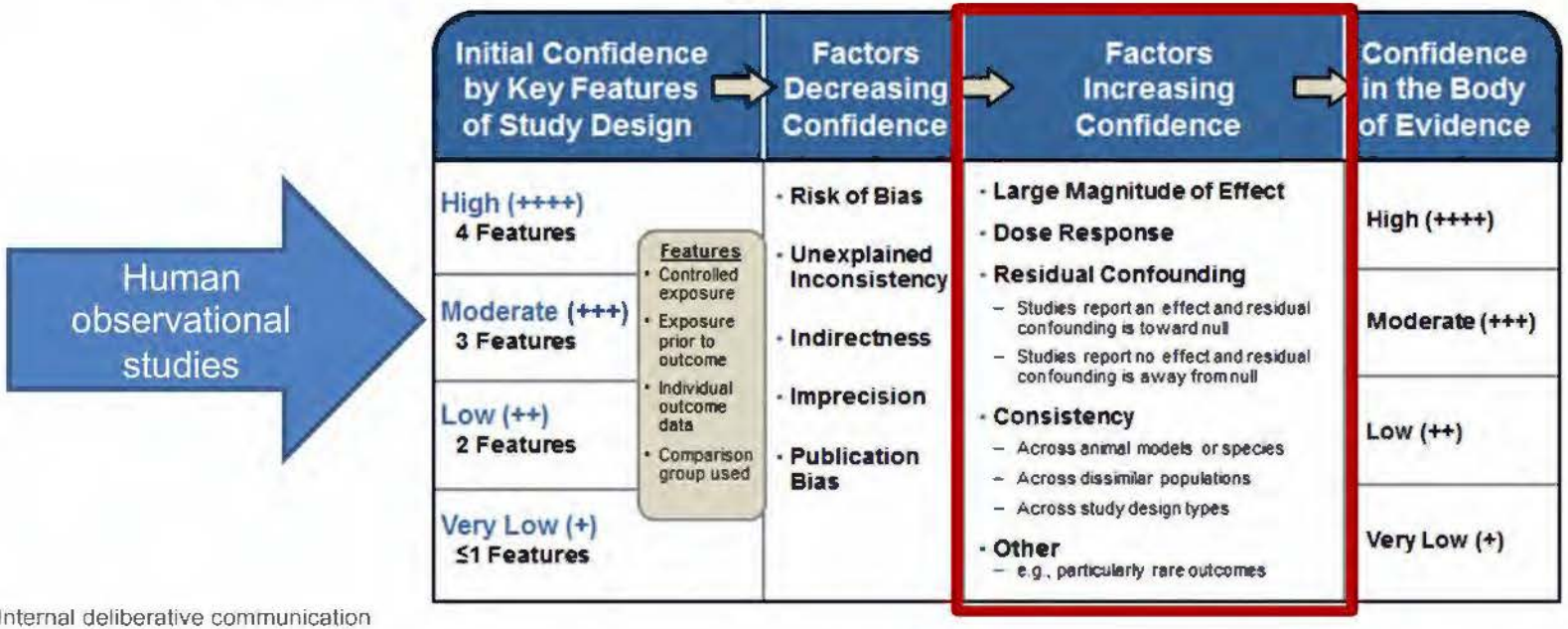

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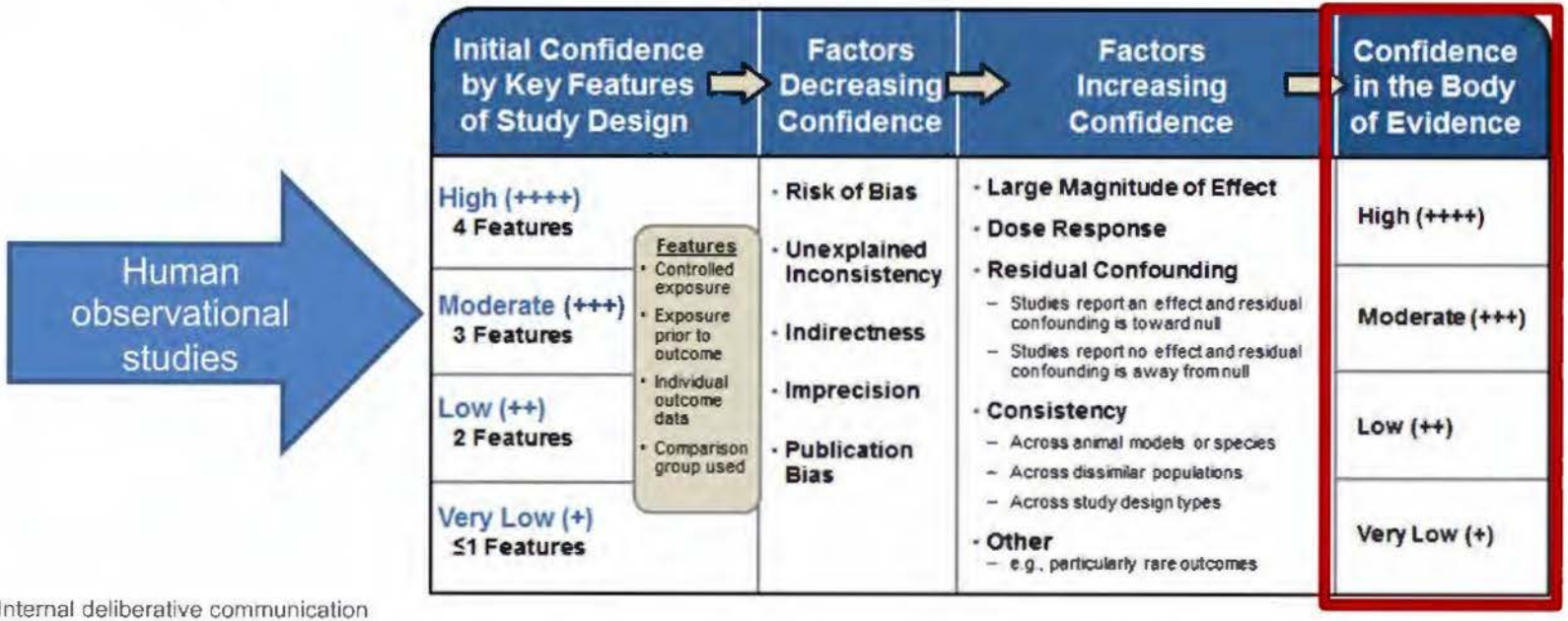

Confidence ratings for each body of evidence

1

IQ in children

(n=66)

Moderate confidence

2

Other cognitive effects in children (n=14)

Low confidence

3

Cognitive effects in adults (n=9)

Low confidence

Confidence ratings

IQ studies in children

1

n=66 studies

Moderate confidence

- Higher fluoride exposure and lower children's IQ consistently associated across:
  - Study location (China, India, Iran, Canada, Mexico)
  - Study population
  - Study design (prospective cohort, cross-sectinal)
  - Study quality/risk of bias determination
    - 18 of 19 high quality studies
    - 41 of 47 low quality studies
  - Exposure measure (water fluoride, urinary fluoride)
  - Type of exposure data (group & individual-level)

Other cognitive effects in children

2

n=14 studies

Low confidence

- Some evidence that fluoride is associated with other cognitive neurodevelopmental effects (eight of nine high quality studies)
- Heterogeneity in measured outcomes, methods used
- Additional studies on ADHD and other attention-related disorders needed

Cognitive effects in adults

n=9 studies

Low confidence

- Literature limited
  - Two high quality studies with inconsistent results
  - Heterogeneity in measured outcomes, inconsistency in results among low quality studies

Summary

Confidence in fluoride affecting children's cognition & neurodevelopment

- **NRC 2006:** Expressed concern, **low confidence** in the evidence based on mostly low-quality cross-sectional studies from China with highly exposed populations

- **NTP 2021:** Reached **moderate confidence** in the evidence based on:
  - Consistent statistically significant associations between higher fluoride and lower IQ in children
  - Expanding database, more precise exposure information
  - High-quality prospective cohort studies of different populations
  - More data at lower exposures (e.g., <1.5 mg/L)

- State of the Science Report report and Meta-analysis represent current science, and more studies are continually published

Current status

- State of the Science report
  - Describes systematic review in detail
  - No hazard conclusions
  - Currently in peer-review
  - Publication expected in early 2022
- Meta-analysis of fluoride exposure and children's IQ
  - Submitted for publication

Thank you--Questions?

From:	Iademarco, Michael (HHS/OASH)
To:	States, Leith (HHS/OASH); Calsyn, Maura (HHS/OASH)
Cc:	Levine, Rachel (HHS/OASH); Boateng, Sarah (HHS/OASH); Balbus, John MD, MPH (OS/OASH/OCCHE); Mataka, Arsenio (HHS/OASH)
Subject:	FW: Request Nominations for the Working Group of the NTP BSC
Date:	Thursday, June 16, 2022 5:12:17 PM
Attachments:	2022-06 OASH Review.docx fluoride_May 2022 draft meta-analysis supplemental material_May 31_Draft_060222 OASH.pdf Fluoride_SoS_Monograph08_Pre-Publication.pdf fluoride_May 2022 draft meta-analysis manuscript_May 31_Draft_060222 OASH.pdf

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Please add or revise my review ("OASH Review") and suggest names (see my yellow highlight) as requested by Monday COB. See my attached draft response and I am working with CDC to come up with some SMEs for the BSC workgroup. Michael

From: Woychik, Rick (NIH/NIEHS) [E] <rick.woychik@nih.gov>

Sent: Wednesday, June 15, 2022 8:39 PM

To: Schwetz, Tara (NIH/OD) [E] <tara.schwetz@nih.gov>; D'Souza, Rena (NIH/NIDCR) [E] <rena.d'souza@nih.gov>; O'Shaughnessy, Jacqueline A (FDA/OC) <Jacqueline.OShaughnessy@fda.hhs.gov>; Howard, John (CDC/NIOSH/OD) <zkz1@cdc.gov>; Hannan, Casey J. (CDC/DDNID/NCCDPHP/DOH) <clh8@cdc.gov>; Hacker, Karen (CDC/DDNID/NCCDPHP/OD) <pju3@cdc.gov>; Wolfe, Mary (NIH/NIEHS) [E] <wolfe@niehs.nih.gov>; Berridge, Brian (NIH/NIEHS) [E] <brian.berridge@nih.gov>; Iademarco, Michael (HHS/OASH) <Michael.Iademarco@hhs.gov>

Cc: Archer, Trevor (NIH/NIEHS) [E] <archer1@niehs.nih.gov>; Woychik, Rick (NIH/NIEHS) [E] <rick.woychik@nih.gov>

Subject: Request Nominations for the Working Group of the NTP BSC

Dear Drs. Schwetz, D'Souza, O'Shaughnessy, Howard, Hannan, Hacker, Wolfe, Berridge and RADM Lademarco

Prior to the release of the State of the Science Monograph (which is a qualitative systematic review of the literature) and the accompanying meta-analysis paper (which is meant to be a quantitative systematic review of the epidemiologic literature) for publication, Adm Levine asked that these documents undergo an internal review within HHS by key stakeholders within the OASH, CDC, FDA, NICHD, and the NIH-OD. To ensure that the review comments from the key stakeholders are carefully evaluated, in consultation with OASH and NIH leadership, I have made the decision to engage the National Toxicology Program (NTP) Board of Scientific Councilors (BSC) to specifically to review the stakeholder comments on these two documents. I have consulted with Dr. David Eaton, Chair of the NTP BSC, who will be coordinating this effort. Dr. Eaton will assemble a special working group of the BSC with a range of specific subject matter expertise related to the content of these two documents. This is not meant to be a thorough peer review of both manuscripts but rather will be a focused effort of the working group dedicated to be: a) primarily an adjudication of the written comments from key stakeholders from NIDCR, NIH-OD, FDA, CDC, and the OASH, and, b) secondarily to provide any additional insights into the quality of the work.

As key stakeholders, I am writing to solicit nominations of individuals who you feel would have the subject matter expertise to serve on this special working group. We are specifically interested in individuals that have expertise in the biology, toxicology and environmental epidemiology relevant to the assessment of the potential human health effects of fluoride, as well as other areas that you may feel are relevant to address concerns amongst stakeholders across HHS. However, to ensure objectivity, we are not considering authors or close collaborators of authors of either the State of the Science or the Meta-analysis papers, or anyone who previously participated in the NASEM reviews of the earlier documents. I will then work with Dr. Eaton to assemble this working group. We would like to get this effort under way as quickly as possible. **Therefore, would you please send your nominations to me by COB on Friday, June 24th. If you cannot make this deadline, please let me know.**

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(b)(5)