
UF
UNIVERSITY of
FLORIDA

Disclosure Statement

- I am an epidemiologist and an assistant professor at UF.
- I have studied fluoride and human health since early 2013.
- I do not have any conflicts of interest or disclosures related to the material in this presentation.

Today's Presentation

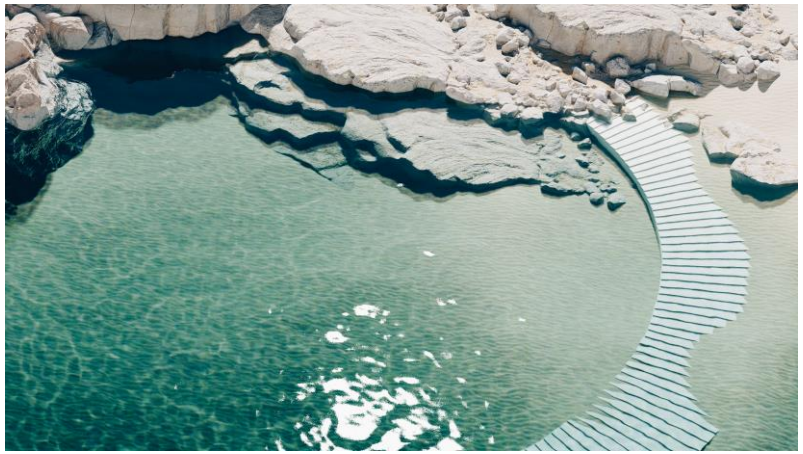
- **Fluoride and fluoridation additives**
- **Impacts of fluoride on health**
  - Bone and pineal gland
- **Fluoride and neurodevelopment**
  - The current state of the science shows that chronic fluoride exposure in early life is associated with worse child neurodevelopment, even at US levels

What is Fluoride?

- A mineral that naturally occurs in rock and soil
- Can leach and naturally occur in drinking water

F^-

(NRC,2006; ATSRD, 2014)



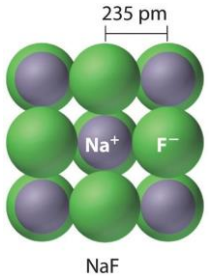
Community Water Fluoridation

- Fluoride can also be produced industrially
  - Fluorosilicic acid

  - Sodium fluorosilicate

Na_2SiF_6

  - Sodium fluoride



- The recommended concentration for fluoride in drinking water is 0.7 mg/L
  - Previously 0.7-1.2 mg/L but lowered in 2015

(Duchon, 2020; NSF, 2024; US Public Health Service, 2015)

Dental Fluorosis

- An outward manifestation of excess fluoride exposure
- Prevalence of **70%** among US children and adolescents in NHANES 2015-2016

(Dong et al., 2021)

› Int J Occup Environ Health. 2014 Apr-Jun;20(2):157-66. doi: 10.1179/2049396714Y.0000000062.
Epub 2014 Mar 20.

A new perspective on metals and other contaminants in fluoridation chemicals

Phyllis J Mullenix

PMID: 24999851 PMCID: PMC4090869 DOI: 10.1179/2049396714Y.0000000062

- **Hydrofluorosilic Acid**:
  - Arsenic (4.9-56 ppm)
  - Lead (<10-10.3 ppm)
  - Aluminum (212-415 ppm)

- **Sodium Fluoride**:
  - Barium (13.3-18 ppm)
  - Aluminum (3312-3630 ppm)

(Mullenix, 2014)

Fluoridation Chemicals

› Neurotoxicology. 2007 Sep;28(5):1023-31. doi: 10.1016/j.neuro.2007.06.006. Epub 2007 Jun 30.

Effects of fluoridation and disinfection agent combinations on lead leaching from leaded-brass parts

Richard P Maas [1], Steven C Patch, Anna-Marie Christian, Myron J Coplan

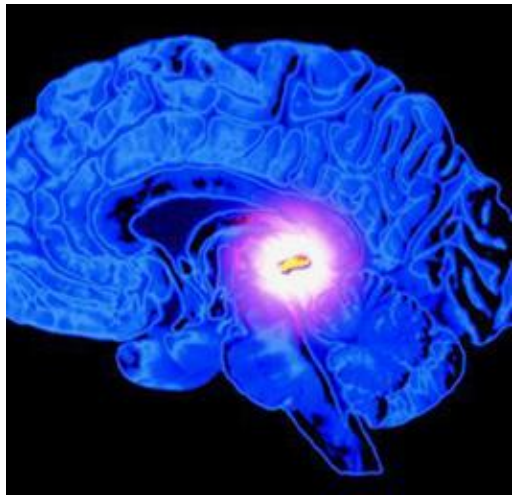
Affiliations + expand

PMID: 17697714 DOI: 10.1016/j.neuro.2007.06.006

Fluoride and Health

- Fluoride is beneficial for cavity prevention, particularly when applied to teeth

- When ingested, fluoride accumulates in bones, teeth and other calcium containing organs and glands, including the pineal gland and developing brain



(ATSDR, 2014; NRC, 2006)

Fluoride and Bone Health

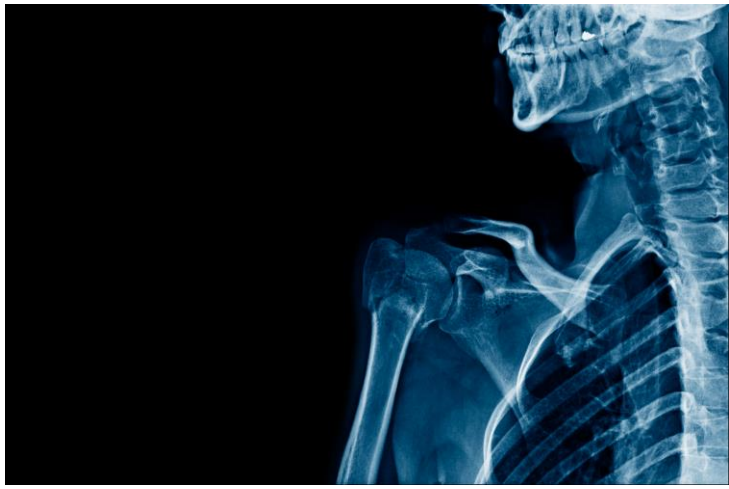
- Increases bone mineral density (BMD)

  -Trabecular bone

- Changes in bone quality

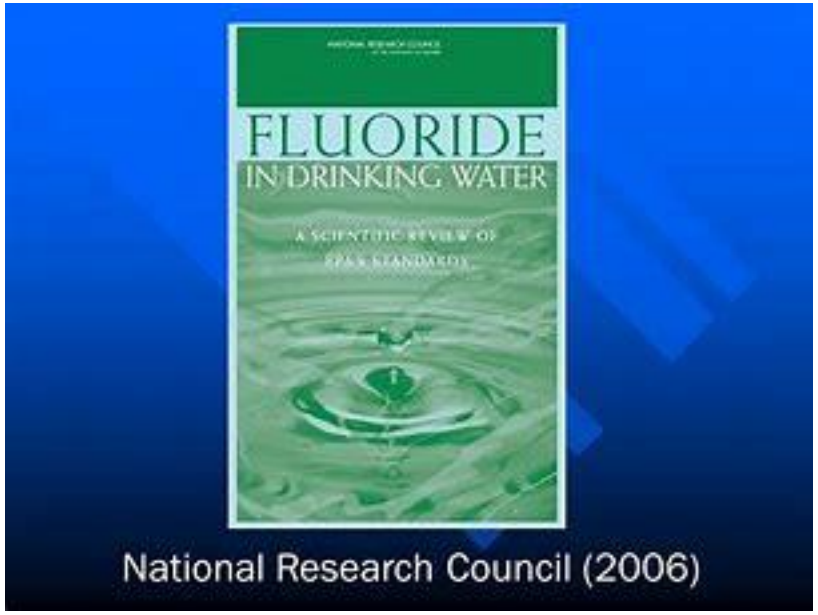
  -Bone weakness and <u>increased risk of fracture</u>

  -Even at levels similar to the United States



(Aaron et al., 1991; Grynpas, 1990; Helte et al., 2021; NRC, 2006; Riggs et al., 1990)

Fluoride and Endocrine Effects



- "**Fluoride is therefore an endocrine disruptor** in the broad sense of altering normal endocrine function or response"

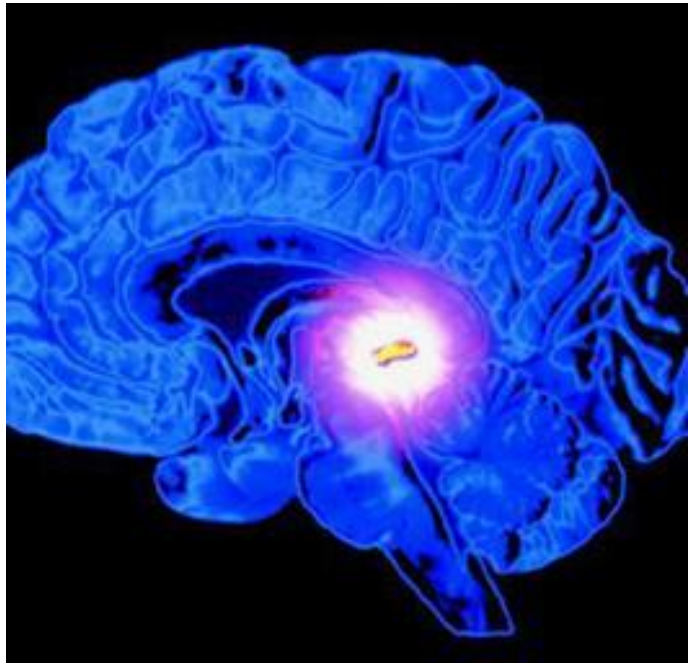
- "Fluoride is likely to **cause decreased melatonin production and to have other effects on normal pineal gland function**, which in turn could contribute to a variety of effects in humans"

(NRC, 2006, p. 26 & p. 267)

Fluoride and Pineal Gland Health

- Accumulates highly in the pineal gland
  - Small gland at the base of the brain
  - Produces melatonin, a hormone that regulates sleep

- Associated with pineal gland calcification
    - Sleep disturbances and neurological problems
      - Alzheimer's Disease, schizophrenia, pediatric brain tumor, multiple sclerosis



(Bersani et al., 1999; Kitkhuandee et al., 2014; Luke, 2001; Tharnpanich et al., 2014; Mahlberg et al., 2008, 2009; Sandyk & Awerbuch, 1994; Sandyk & Awerbuch, 1991; Tuntapakul, 2016)

Pergamon

Neurotoxicology and Teratology, Vol. 17, No. 2, pp. 169–177, 1995

0892-0362/95 $9.50 + .00

0892-0362(94)00070-0

Neurotoxicity of Sodium Fluoride in Rats

PHYLLIS J. MULLENIX,*†[1] PAMELA K. DENBESTEN,‡ ANN SCHUNIOR* AND WILLIAM J. KERNAN§

*Toxicology Department, Forsyth Research Institute, Boston, MA 02115
†Department of Radiation Oncology, Harvard Medical School, Boston, MA 02115
‡Department of Pediatric Dentistry, Eastman Dental Center, Rochester, NY 14621
§Veterinary Diagnostic Laboratory, Iowa State University, Ames, IA 50011

Malin and Till *Environmental Health* (2015) 14:17
DOI 10.1186/s12940-015-0003-1

ENVIRONMENTAL HEALTH

RESEARCH Open Access

Exposure to fluoridated water and attention deficit hyperactivity disorder prevalence among children and adolescents in the United States: an ecological association

Ashley J Malin* and Christine Till

"**Parents reported higher rates of medically-diagnosed ADHD in their children in states in which a greater proportion of people receive fluoridated water from public water supplies.** The relationship between fluoride exposure and ADHD warrants future study."

| Research | 19 September 2017

Prenatal Fluoride Exposure and Cognitive Outcomes in Children at 4 and 6–12 Years of Age in Mexico

This article accompanies LOW PRENATAL EXPOSURES TO FLUORIDE: ARE THERE NEUROTOXIC RISKS FOR CHILDREN?.

Authors: Morteza Bashash, Deena Thomas, Howard Hu, E. Angeles Martinez-Mier, Brisa N. Sanchez, Niladri Basu, Karen E. Peterson, ... SHOW ALL ..., and Mauricio Hernández-Avila | AUTHORS INFO & AFFILIATIONS

Publication: Environmental Health Perspectives • Volume 125, Issue 9 • CID: 097017 • https://doi.org/10.1289/EHP655

JAMA Pediatrics | Original Investigation

Association Between Maternal Fluoride Exposure During Pregnancy and IQ Scores in Offspring in Canada

Rivka Green, MA; Bruce Lanphear, MD; Richard Hornung, PhD; David Flora, PhD; E. Angeles Martinez-Mier, DDS; Raichel Neufeld, BA; Pierre Ayotte, PhD; Gina Muckle, PhD; Christine Till, PhD

Each 1 mg/L increase in maternal urinary fluoride across pregnancy is associated with a 4-5-point IQ reduction in children

Prenatal Fluoride Exposure in North America

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Prenatal fluoride exposure and attention deficit hyperactivity disorder (ADHD) symptoms in children at 6–12 years of age in Mexico City

Morteza Bashash[a,*], Maelle Marchand[a], Howard Hu[a,1], Christine Till[b], E. Angeles Martinez-Mier[c], Brisa N. Sanchez[d], Niladri Basu[e], Karen E. Peterson[d,f,g], Rivka Green[b], Lourdes Schnaas[h], Adriana Mercado-García[i], Mauricio Hernández-Avila[i], Martha María Téllez-Rojo[i]

Fluoride exposure during pregnancy from a community water supply is associated with executive function in preschool children: A prospective ecological cohort study

Deborah Dewey [a,b,c,d,*,1], Gillian England-Mason [a,b,1], Henry Ntanda [b], Andrea J. Deane [a,b], Mandakini Jain [e], Nadia Barnieh [b], Gerald F. Giesbrecht [a,b,c,f], Nicole Letourneau [a,b,c,g,h], APrON Study Team

NeuroToxicology 59 (2017) 65–70

Contents lists available at ScienceDirect

NeuroToxicology

Full Length Article

In utero exposure to fluoride and cognitive development delay in infants

L. Valdez Jiménez[a], O.D. López Guzmán[b], M. Cervantes Flores[b], R. Costilla-Salazar[c], J. Calderón Hernández[a], Y. Alcaraz Contreras[d], D.O. Rocha-Amador[d,*]

[a] Coordinación para la Innovación y Aplicación de la Ciencia y la Tecnología (CIACYT), Universidad Autónoma de San Luis Potosí, San Luis Potosí, Mexico
[b] Facultad de Ciencias Químicas, Universidad Juárez del Estado de Durango (Unidad Durango), Victoria de Durango, Mexico
[c] División de Ciencias de la Vida, Universidad de Guanajuato, Guanajuato, Mexico
[d] División de Ciencias Naturales y Exactas, Universidad de Guanajuato, Guanajuato, Mexico

Published in final edited form as:
Environ Res. 2022 August ; 211: 112993. doi:10.1016/j.envres.2022.112993.

Domain-specific effects of prenatal fluoride exposure on child IQ at 4, 5, and 6–12 years in the ELEMENT cohort

Carly V. Goodman[a], Morteza Bashash[b], Rivka Green[a], Peter Song[c], Karen E. Peterson[c], Lourdes Schnaas[d], Adriana Mercado-García[e], Sandra Martínez-Medina[d], Mauricio Hernández-Avila[f], Angeles Martinez-Mier[g], Martha M. Téllez-Rojo[e,*], Howard Hu[b], Christine Till[a]

Dietary fluoride intake during pregnancy and neurodevelopment in toddlers: A prospective study in the progress cohort

Alejandra Cantoral [a], Martha M. Téllez-Rojo [b,*], Ashley J. Malin [c], Lourdes Schnaas [d], Erika Osorio-Valencia [d], Adriana Mercado [b], E. Ángeles Martínez-Mier [e], Robert O. Wright [c], Christine Till [f]

Environmental Research 200 (2021) 111315

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Critical windows of fluoride neurotoxicity in Canadian children

Linda Farmus [a], Christine Till [a,*], Rivka Green [a], Richard Hornung [b], E. Angeles Martinez Mier [c], Pierre Ayotte [d,e], Gina Muckle [d,f], Bruce P. Lanphear [g,h], David B. Flora [a]

Malin *et al. Environmental Health* (2023) 22:74
https://doi.org/10.1186/s12940-023-01026-2

Environmental Health

RESEARCH

Open Access

Urinary fluoride levels and metal co-exposures among pregnant women in Los Angeles, California

Ashley J. Malin[1*], Howard Hu[2], E. Angeles Martínez-Mier[3], Sandrah P. Eckel[2], Shohreh F. Farzan[2], Caitlin G. Howe[4], William Funk[5], John D. Meeker[6], Rima Habre[2], Theresa M. Bastain[2] and Carrie V. Breton[2]

Fluoride Exposure Assessment

- Urinary fluoride level (Valdez Jiménez, 2017; Bashash, 2017,2018; Green, 2019)
- Water fluoride (Dewey et al., 2023; Green et al., 2019)
- Dietary fluoride intake (Cantoral et al., 2021)

What About Infant Exposures?

Environment International 134 (2020) 105315

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Fluoride exposure from infant formula and child IQ in a Canadian birth cohort

Christine Till[a,*], Rivka Green[a], David Flora[a], Richard Hornung[b], E. Angeles Martinez-Mier[c], Maddy Blazer[a], Linda Farmus[a], Pierre Ayotte[d,e], Gina Muckle[d,f], Bruce Lanphear[g,h]

Till et al. 2020

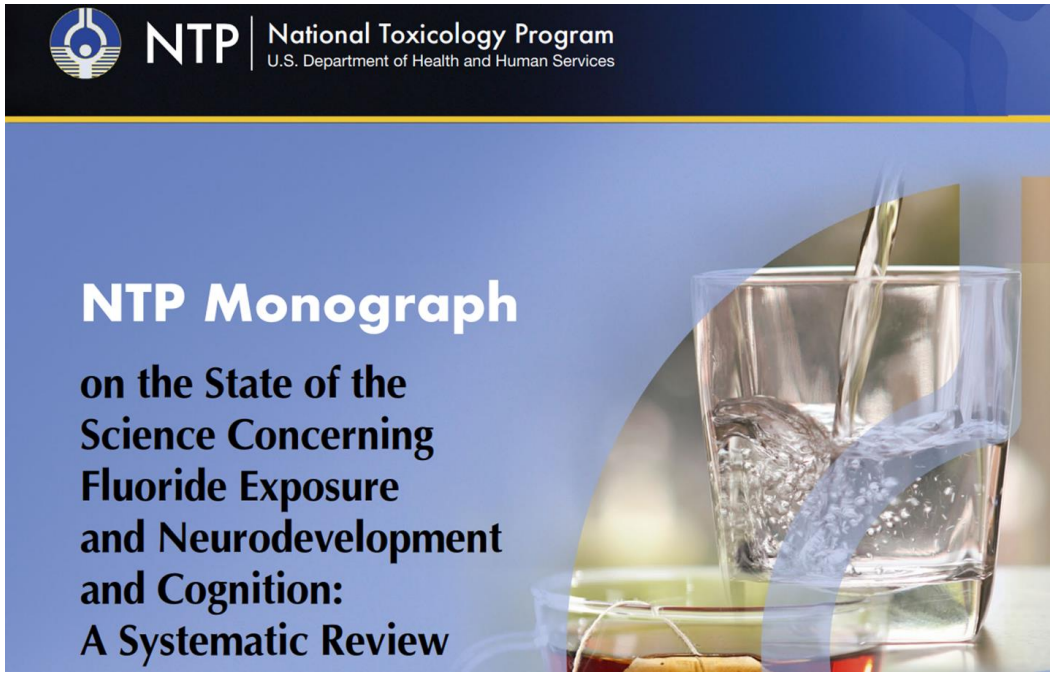
- An **increase of 0.5 mg/L in water fluoride concentration** in infancy was associated with:

- A **9.3-point decrement in Performance IQ (PIQ)** among formula-fed children(95% CI:−13.77, −4.76)

- A **6.2-point decrement** in PIQ among breast-fed children (95% CI: −10.45, −1.94)

National Toxicology Program (NTP) Report

- Comprehensive systematic review on early life fluoride exposure and child neurodevelopment
- Included studies published by 2023
- 72 total studies on fluoride and IQ
  - 64 found that higher fluoride was associated with lower child IQ
- 19 high quality studies
  - 18 found that higher fluoride was associated with lower child IQ



(NTP, 2024)

NTP Report

- "there is **moderate confidence** in the body of evidence that estimated fluoride exposure is **inversely associated with IQ in children**"

- "the moderate confidence in the inverse association between fluoride exposure and children's IQ is **relevant to some children living in the United States**, including **at a minimum those living in areas where fluoride in drinking water is known to be at or above 1.5 mg/L"**

(NTP, 2024)

NTP Report

- Associations between drinking water fluoride levels below 1.5 mg/L and children's IQ remain "**unclear**"

- It is plausible that pregnant women and children living in optimally fluoridated communities could have a total fluoride intake at or above the level of those living in a community with a water fluoride level of 1.5 mg/L or higher.

(NTP, 2024)

NTP Meta-Analysis

Research

JAMA Pediatrics | Original Investigation

Fluoride Exposure and Children's IQ Scores
A Systematic Review and Meta-Analysis

Kyla W. Taylor, PhD; Sorina E. Eftim, PhD; Christopher A. Sibrizzi, MPH; Robyn B. Blain, PhD; Kristen Magnuson, MESM; Pamela A. Hartman, MEM; Andrew A. Rooney, PhD; John R. Bucher, PhD

NTP Meta-Analysis

- **Urinary fluoride concentrations *below* 1.5 mg/L are consistently associated with lower child IQ**
  - When considering all studies or only the high-quality ones

- The findings show that a **dose-response relationship** between higher fluoride exposure and lower child IQ exists

(Taylor et al., 2025)

- The NTP report highlighted a need for more US-based studies on fluoride and neurodevelopment

JAMA Network | Open

Original Investigation | Public Health

Maternal Urinary Fluoride and Child Neurobehavior at Age 36 Months

Ashley J. Malin, PhD; Sandrah P. Eckel, PhD; Howard Hu, MD, MPH, ScD; E. Angeles Martinez-Mier, PhD, DDS, MSD; Ixel Hernandez-Castro, PhD; Tingyu Yang, MS; Shohreh F. Farzan, PhD; Rima Habre, ScD; Carrie V. Breton, ScD; Theresa M. Bastain, PhD

Higher prenatal fluoride exposure is associated with more neurobehavioral problems (anxiety, temper tantrums, symptoms of autism, and headaches/stomach aches) among 3-year-old children in Los Angeles, California.

JAMA Network | Open

Original Investigation | Public Health

Maternal Urinary Fluoride and Child Neurobehavior at Age 36 Months

Ashley J. Malin, PhD; Sandrah P. Eckel, PhD; Howard Hu, MD, MPH, ScD; E. Angeles Martinez-Mier, PhD, DDS, MSD; Ixel Hernandez-Castro, PhD; Tingyu Yang, MS; Shohreh F. Farzan, PhD; Rima Habre, ScD; Carrie V. Breton, ScD; Theresa M. Bastain, PhD

- Pregnant women whose **urinary fluoride levels were approximately 1.2 mg/L had children with nearly double the odds of exhibiting clinically relevant neurobehavioral problems** by age 3 when compared with pregnant women whose urinary fluoride levels were approximately 0.5 mg/L

(Malin et al., 2024)

Mechanisms of Developmental Neurotoxicity

- Fluoride can readily cross the placenta
- Accumulates in brain regions implicated in **learning, memory, mood, attention** and **executive function**

(Bartos et al., 2018, 2022; Chen et al., 2003; Mullenix, 1995; Sun et al., 2018)

Impacts on Neurochemistry at Low Levels

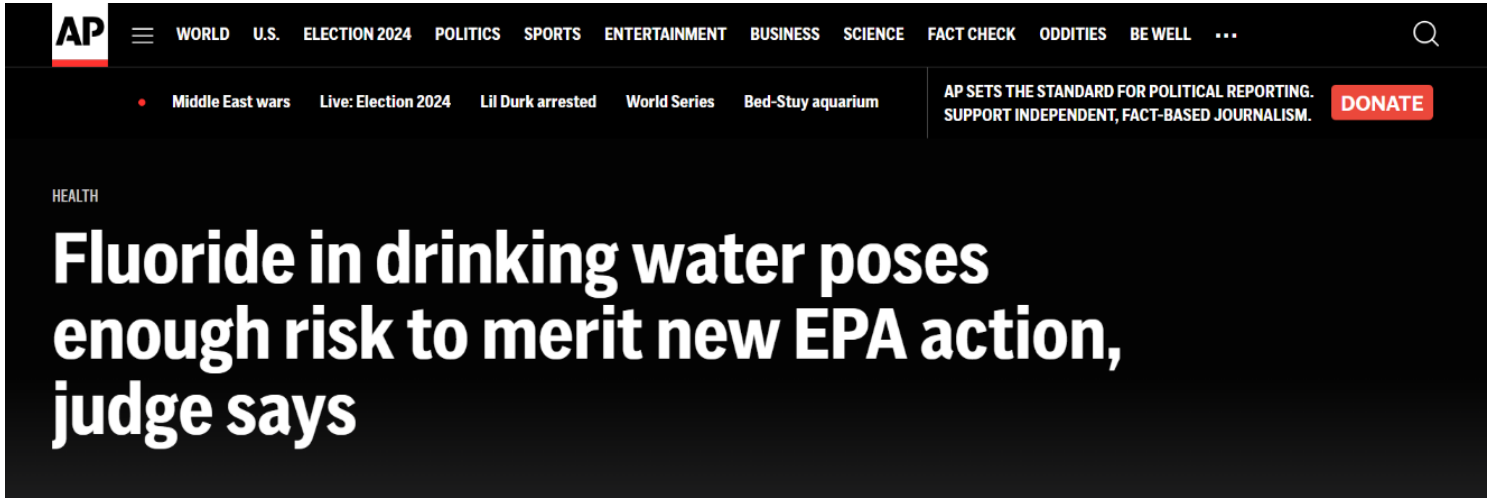
- Alters cholinergic activity
  - Important for attention, learning, memory
- Alters glutamate metabolism
- Contributes to mitochondrial dysfunction
- Increases oxidative stress

(Bartos et al., 2018, 2022; Chen et al., 2003; Liu et al., 2010; Mullenix, 1995; Sun et al., 2018)

Criteria for Causality

- Strength of the association ✓
- Consistency ✓
- Temporality ✓
- Biological plausibility ✓
- Dose-response relationship ✓
- Coherence ✓
- Experimental evidence

(adapted from Hill, 1965)



- "the Court finds that fluoridation of water at 0.7 milligrams per liter ("mg/L") – the level presently considered "optimal" in the United States – poses an **unreasonable risk of reduced IQ in children.**"

- "The scientific literature in the record provides **a high level of certainty that a hazard is present**; **fluoride is associated with reduced IQ.**"

(Case 3:17-cv-02162-EMC Document 445)

Federal Ruling Implications

- There is not enough of a margin of safety between the hazard level (i.e., 1.5 mg/L) and exposure level (i.e., 0.7 mg/L) of fluoride in drinking water for dental cavities prevention

- The EPA's default standard is for there to be *at least* a **factor of 10** between the hazard level and exposure level

Federal Ruling Implications

- According to the EPA's default standard:

  The fluoride concentration in drinking water would need to be **0.15 mg/L or lower** to provide enough of a margin of safety **to protect child IQ**

Questions:

ashleymalin@ufl.edu