

The Scientific Evidence for Fluoride's Developmental Neurotoxicity



February 10, 2020



American Environmental Health Studies Project

Chris Neurath

Research Director



FLUORIDEALERT.ORG
Fluoride Action Network

A dense, colorful micrograph of neurons. The image shows a complex network of cell bodies and long, thin processes. The neurons are stained with various fluorescent dyes, resulting in a vibrant display of colors including green, blue, red, yellow, and purple. The background is dark, making the brightly colored neurons stand out.

F neurotoxicity

Brain development is highly complex dynamic process

What is Developmental Neurotoxicity?

Image of neurons engineered to express multiple fluorescent colors.

F neurotoxicity

Brain development is highly complex dynamic process

Brain Development

“The wiring of brains is *staggeringly complex*. Our own brains have tens of billions of neurons connected through perhaps one hundred trillion synapses. *This circuitry is the result of our development and experience*”

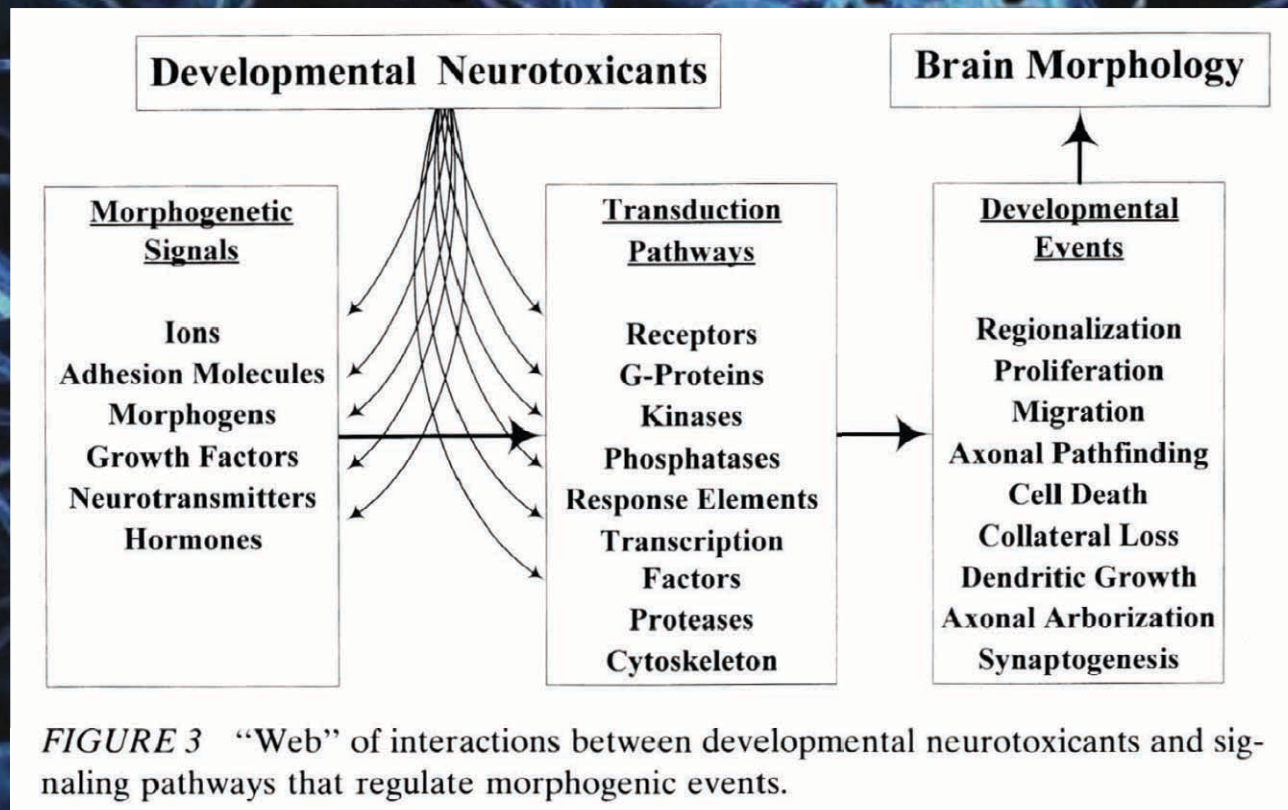
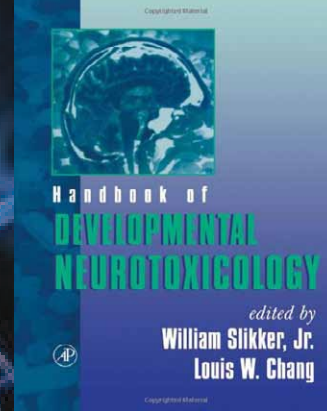
Harvard Center for Brain Science

Image of neurons engineered to express multiple fluorescent colors.

F neurotoxicity

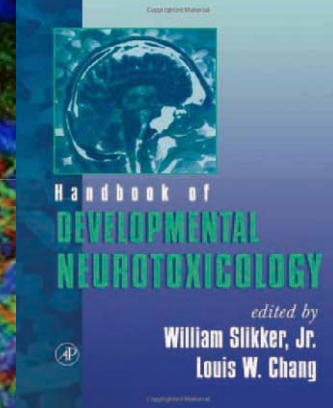
Brain development is highly complex dynamic process

Neurotoxicants can disrupt brain development in many ways



F neurotoxicity

Brain development is highly complex dynamic process



The fetal and infant brain is more susceptible than the adult to permanent harm from neurotoxic chemicals.

- The complex precisely timed neurodevelopment process offers many opportunities for disruption.
- The blood brain barrier is not well developed during the fetal period and the first 6 months of life.
- Disruption during even a short window of neurodevelopment can cause life-long permanent harm.



National Toxicology Program (NTP) draft systematic review and health assessment of the neurotoxicity of fluoride:

“Conclusions: NTP concludes that **fluoride is presumed to be a cognitive neurodevelopmental hazard to humans.** This conclusion is based on a **consistent pattern of findings in human studies** across several different populations showing that higher fluoride exposure is associated with **decreased IQ or other cognitive impairments in children.**”

F neurotoxicity

Large number
of studies

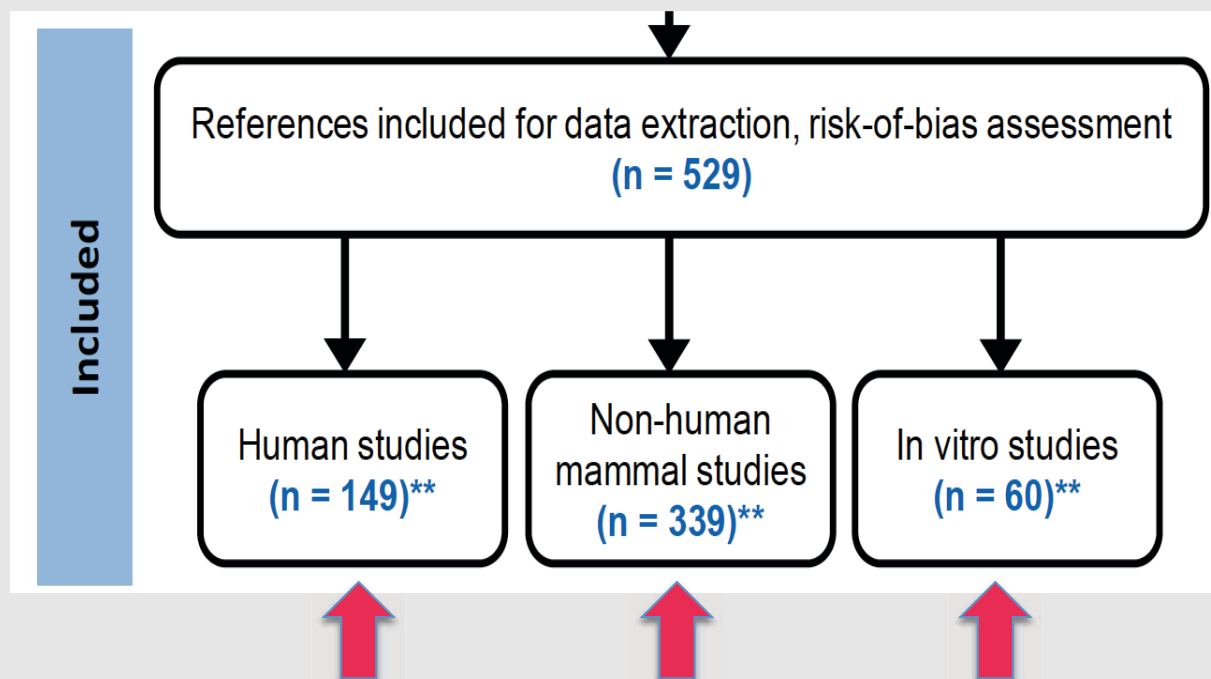


National Toxicology Program

U.S. Department of Health and Human Services

Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects

Figure 4. Study Selection Diagram



F neurotoxicity

Large number
of studies



National Toxicology Program
U.S. Department of Health and Human Services

Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects

Figure 5. Number of Epidemiological Studies by Outcome and Age Categories*

Outcome Category	Age Category					
	Child	Adult	Child/Adult Combined	Infant	Fetus	
Intelligence (IQ)	60	3				
Learning/Memory	4	3		1		
Cognitive Development	2			1		
Cognitive Impairment		5				
Attention/Hyperactivity/Behavioral Issues	5					
Motor/Sensory Function or Development	2	4		1		
Mood/Affect		1				
Visual-Spatial/Visual-Motor Function	2	2				
Brain Activity		1				
Brain Structure						2
Neurological Biochemical	2	1	1			1
Neurological Complications of Fluorosis		3				
Neurological Symptoms	1	3				
Birth Defects				3		
Thyroid Gland Function	12	5	2			
Thyroid Disease		2				

F neurotoxicity

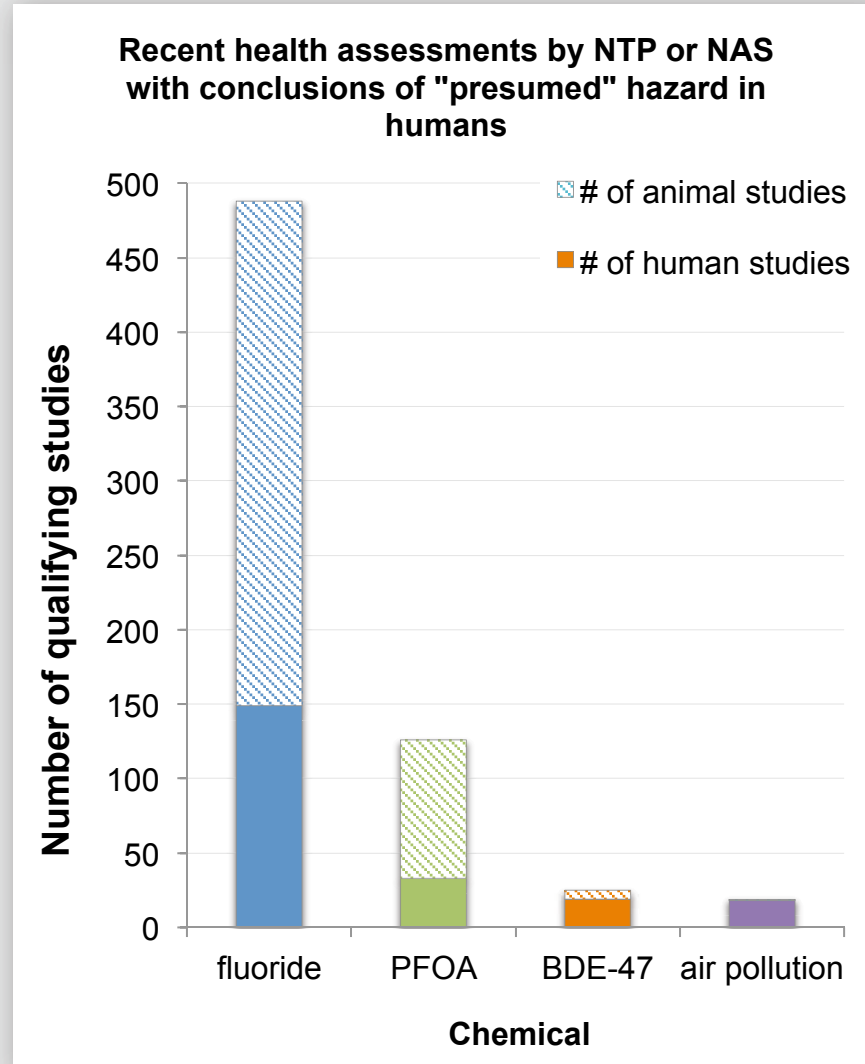
Large number
of studies

NTP found many more studies of F neurotoxicity compared to what it has found for other toxins in its recent reviews



National Toxicology Program
U.S. Department of Health and Human Services

Systematic Review of Fluoride Exposure and
Neurodevelopmental and
Cognitive Health Effects



F neurotoxicity

Large number
of studies

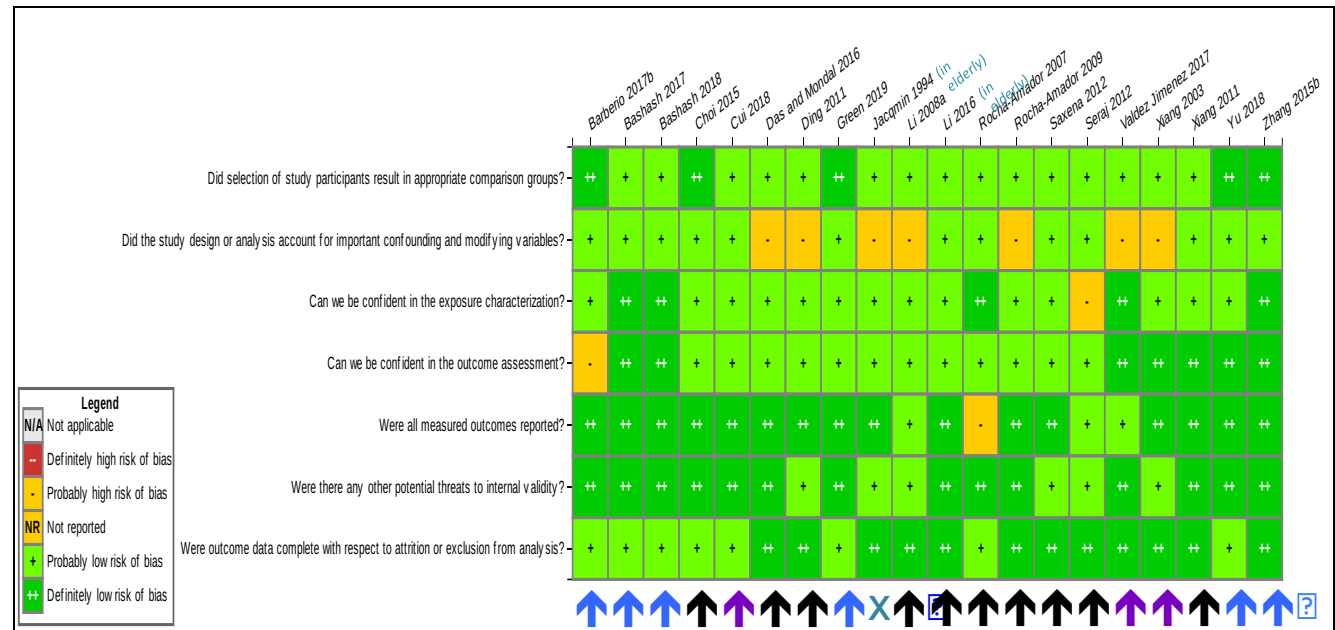
20 of the
studies
were
considered
high quality
(low Risk of
Bias).



National Toxicology Program
U.S. Department of Health and Human Services

Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects

Figure_A3-01 Human Risk of Bias scores (neurobehavioral, lower RoB studies)
from HAWC's NTP project "Fluoride 2019"



All studies except one found significant adverse effects

↑ = Study found adverse effects at exposure levels of 0.7 mg/L water F or equivalent

↑ = Study found adverse effects at exposure levels below 1.5 mg/L water F or equivalent

↑ = Study found adverse effects at exposure levels above 1.5 mg/L water F or equivalent

X = did not find statistically significant adverse effect

F neurotoxicity

Pre-conceptions



JAMA Editor's Podcast excerpts, on Green 2019:

Pre-conceptions that people who claimed that fluoridation is harmful were “nuts”.



Frederick P. Rivara, MD, MPH
Editor, *JAMA Networks Open*



Dimitri A. Christakis, MD, MPH
Editor, *JAMA Pediatrics*

F neurotoxicity

Pre-conceptions



[Open "JAMAPed clip A" to play](#)



Dr Rivara- “The paper is about fluoride, and maternal fluoride exposure during pregnancy, and its effects upon IQ scores of children at ages 3 and 4, which in itself is like a shocking title, because I had never known that there was even any concern that maternal fluoride use might affect children’s IQ.”

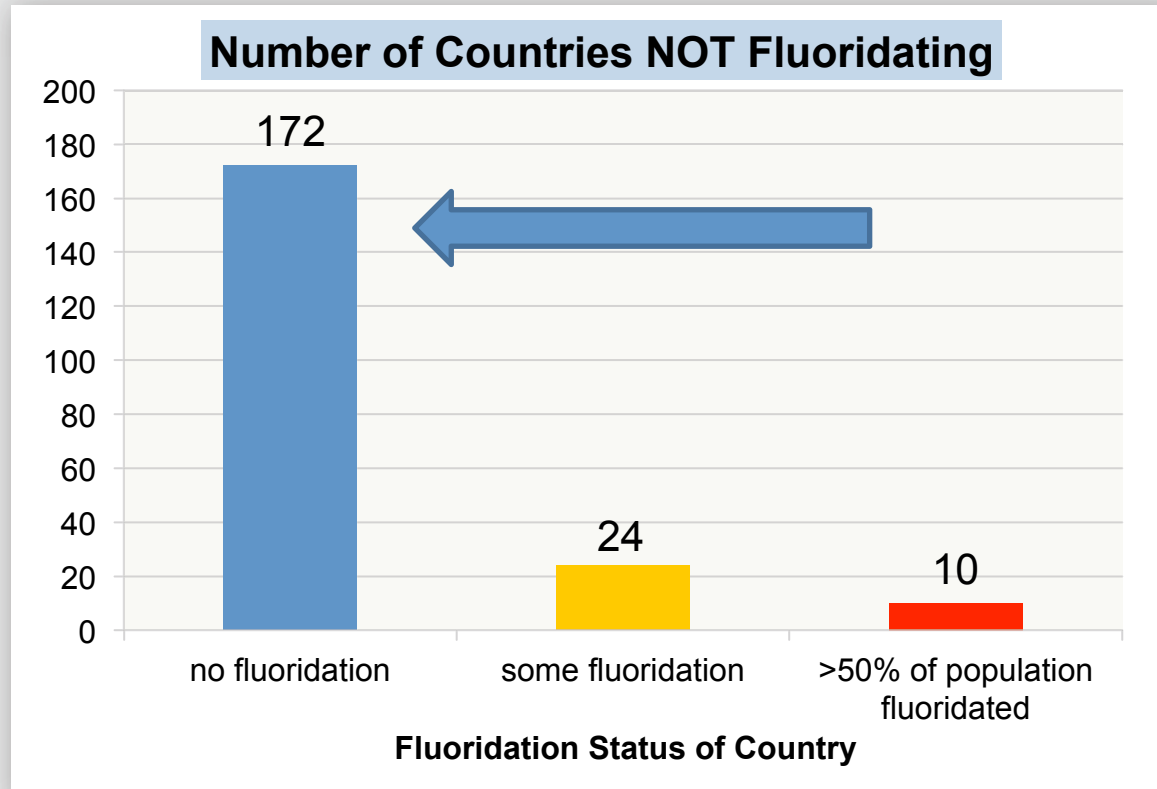


Dr Christakis- “... the traditional teaching when I was going through residency in my early professional career was that fluoride was completely safe, all these people that are trying to take it out of the water are nuts, its the best thing that’s ever happened for children’s dental health, and we just need to push back and get it into every water system.”
“So when I first saw this title my initial inclination was **‘What the hell?’**”

F neurotoxicity

“in Europe only 3% of municipal water supplies are fluoridated”

Editors surprised by just how much of the world does *NOT* fluoridate.



F neurotoxicity

“in Europe only 3% of municipal water supplies are fluoridated”



[Open "JAMAPed clip B" to play](#)

Editors surprised by just how much of the world does *NOT* fluoridate.



Dr Rivara- “... this was from Canada and they picked some large cities in Canada; these were Montreal, Vancouver, Kingston, Toronto, Hamilton and Halifax; so I’m a little surprised that those places did not [all] have fluoridated water supplies.”

Dr Rivara- “And the other interesting thing that came out, like in the editorial and in this paper, was that in Europe only 3% of municipal water supplies are fluoridated.”



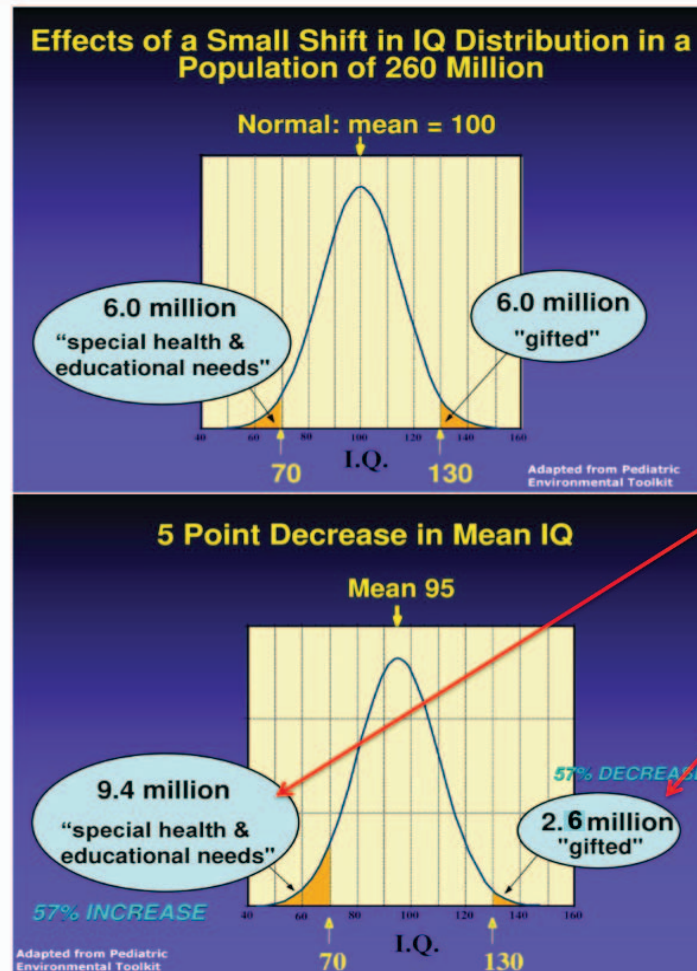
Dr Christakis- “Right, so again this was to me sort of eye-opening, that you know, I sort-of thought that ‘everyone did it’; certainly all developed countries, everyone that was at any level of sophistication was putting fluoride in the water.”

F neurotoxicity

A sizable effect “on par with lead”
“that’s a real concern”

Editors “really startled” at size of effect.

For an increase of 1 mg/L in maternal urine fluoride concentration, boys lost 5 IQ points.



How 5 IQ point average loss shifts the IQ distribution and dramatically changes numbers of children at each “tail”.

3.4 Million MORE special needs people

3.4 million FEWER gifted people (geniuses)

Steven Rosenberg, M.D., M.P.H.
Everything You Always Wanted to
Know About Childhood Lead Poisoning
(but Were Afraid to Ask)
SlideShare-June 21, 2007

F neurotoxicity

**A sizable effect “on par with lead”
“that’s a real concern”**



[Open "JAMAPed clip C" to play](#)



Dr Rivara- “... a 1 mg/L increase in the maternal urinary fluoride concentration was associated with a 5 point lower score on the boys’ IQ.”

Dr Christakis- “Right. An effect size which is sizable, on a par with lead”

Dr Rivara- “Right, it is.”

Dr Rivara- “The effect size is really quite large, because when you think about it really in terms of not the individual child so much as the shift in the curve ... the shift in the curve, now, being shifted to the left, for boys, that’s a real concern”

Dr Rivara- “the results are really startling”



Dr Christakis- “... there have been other observational studies that have shown this, and there have been animal models as well, that have shown this idea that fluoride could be a neurotoxin; which again was totally news to me because I thought it was junk science, anyone would ever say such a thing.”

F neurotoxicity

Editor's advice: Pregnant mothers should avoid fluoridated water



F neurotoxicity

Editor's advice: Pregnant mothers should avoid fluoridated water



[Open "JAMAPed clip D" to play](#)



Dr Rivara- “So, if mothers now come into their doctor’s offices and ask the pediatrician what to do, what are you going to say?”

Dr Christakis- “I think I would advise them to drink bottled water, or filtered water, because its not a particularly odious thing to do, and potentially does reduce the risk.”

Dr Rivara- “Yea, you know the other thing is that some people may not be able to afford bottled water, it could be a financial burden to some low-income families, and we need to think about that as well.”

“Well, its going to get a lot of attention, and I’m very proud that you published it.” 18

Individual Studies



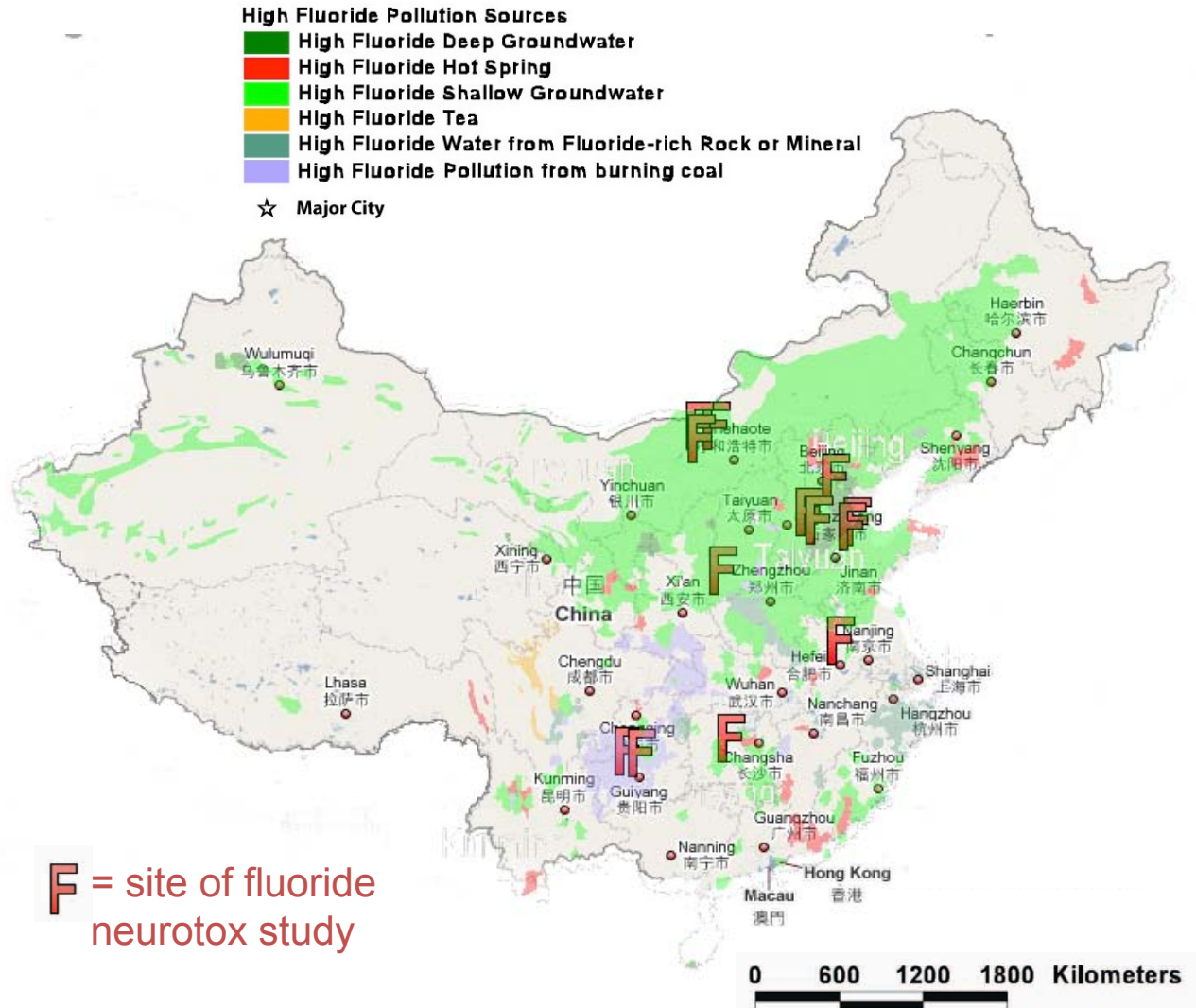
F neurotoxicity

First studies from China

In the 1980s China started investigating F neurotoxicity because it had 100 million people living in endemic fluorosis areas due to natural F in groundwater.

No artificial fluoridation in China.

High Fluoride Pollution Sources in the People's Republic of China



F neurotoxicity

Xiang 2003

High quality
study with
individual level
data; China.

EFFECT OF FLUORIDE IN DRINKING WATER ON CHILDREN'S INTELLIGENCE

Q Xiang,^a Y Liang,^a L Chen,^b C Wang,^b B Chen,^a X Chen,^b M Zhou^c
Shanghai, P.R. China

F and IQ

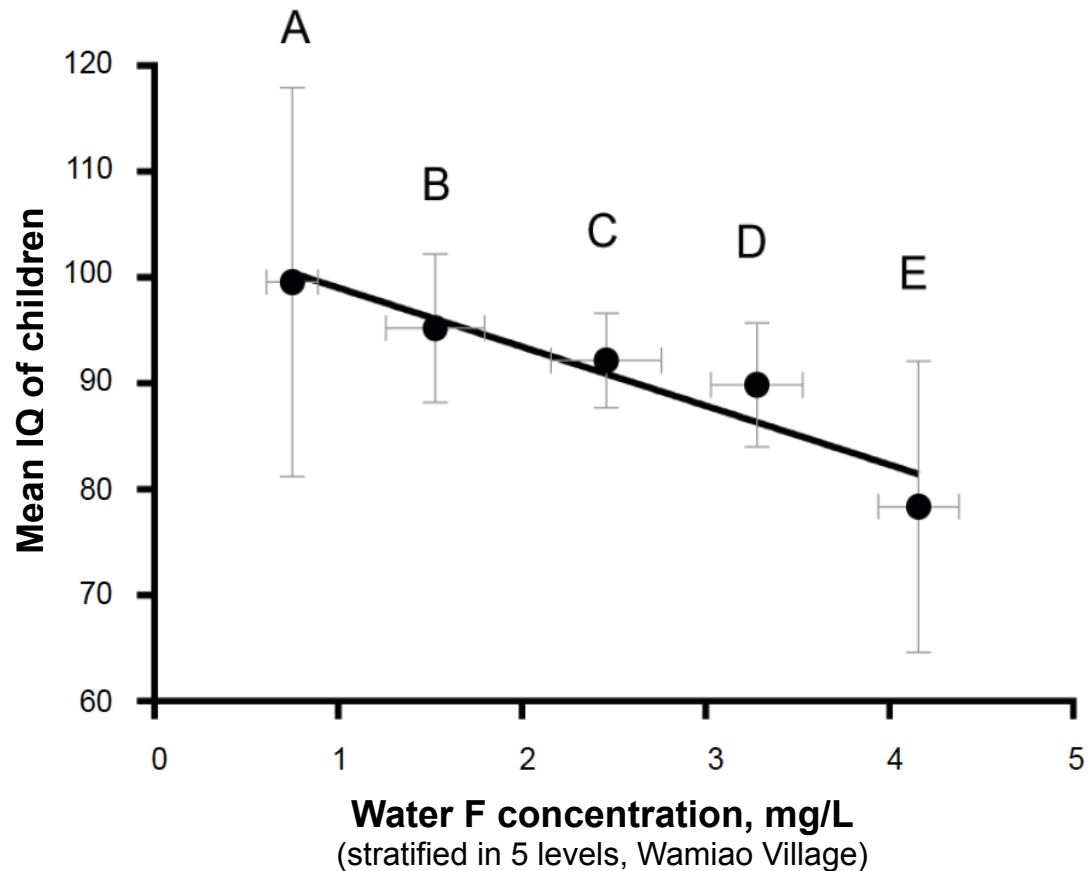


Figure adapted
from Hirzy
2016 based on
data reported
in Xiang 2003.

F neurotoxicity

Xiang 2003

High quality
study with
individual level
data; China.

84 Fluoride Vol. 36 No. 2 84-94 2003 Research Report

EFFECT OF FLUORIDE IN DRINKING WATER ON CHILDREN'S INTELLIGENCE

Q Xiang,^a Y Liang,^a L Chen,^b C Wang,^b B Chen,^a X Chen,^a M Zhou^c
Shanghai, P.R. China

F and % IQ below 80

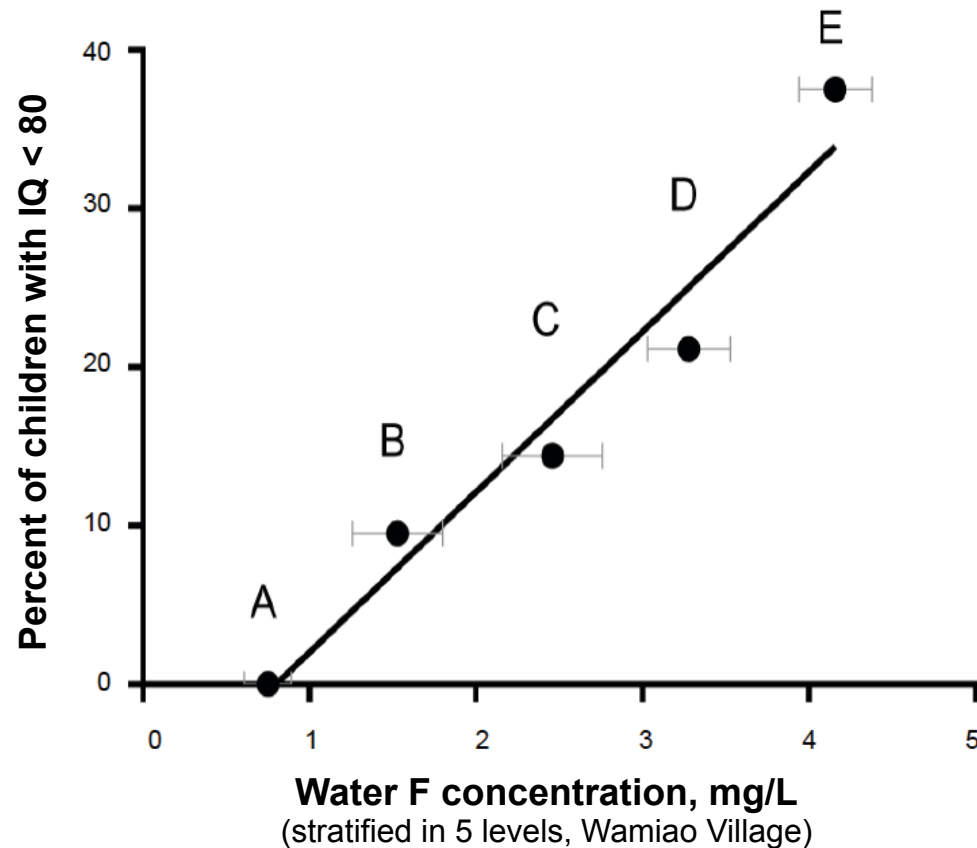


Figure adapted
from Hirzy
2016 based on
data reported
in Xiang 2003.

F neurotoxicity

Zhang 2015

High quality study; first
with gene-F interaction;
China.

**Found 5x greater
loss of IQ for those
with specific
genotype**

Genotype	N	IQ points lost per 1 mg/L urine F	p-value
combined	108	-2.42	0.030
val/val	28	-9.67	0.003

F and IQ
all genotypes combined

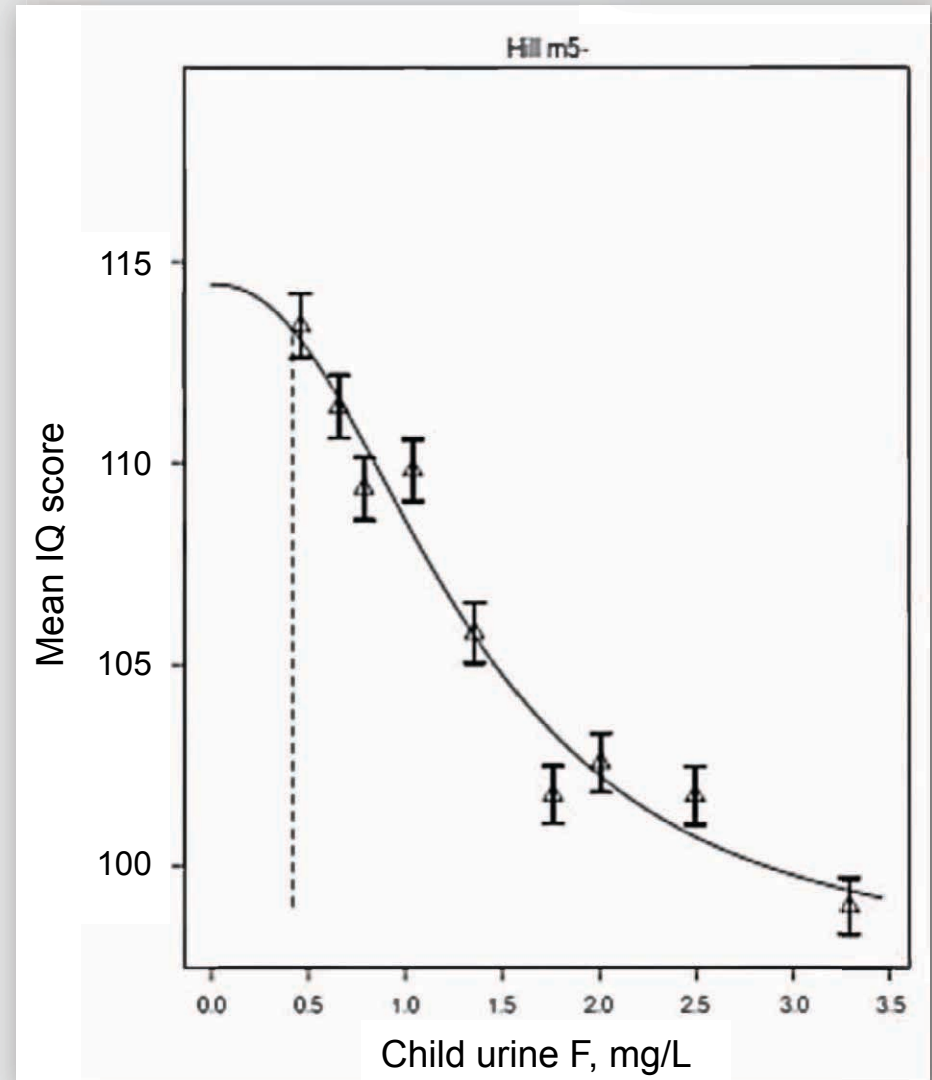


Figure based on Zhang 2015, Figure 1, with Benchmark
Dose analysis using PROAST method.

F neurotoxicity

Valdez-Jimenez 2017

High quality study; first mother-offspring longitudinal cohort; Mexico.

F and IQ

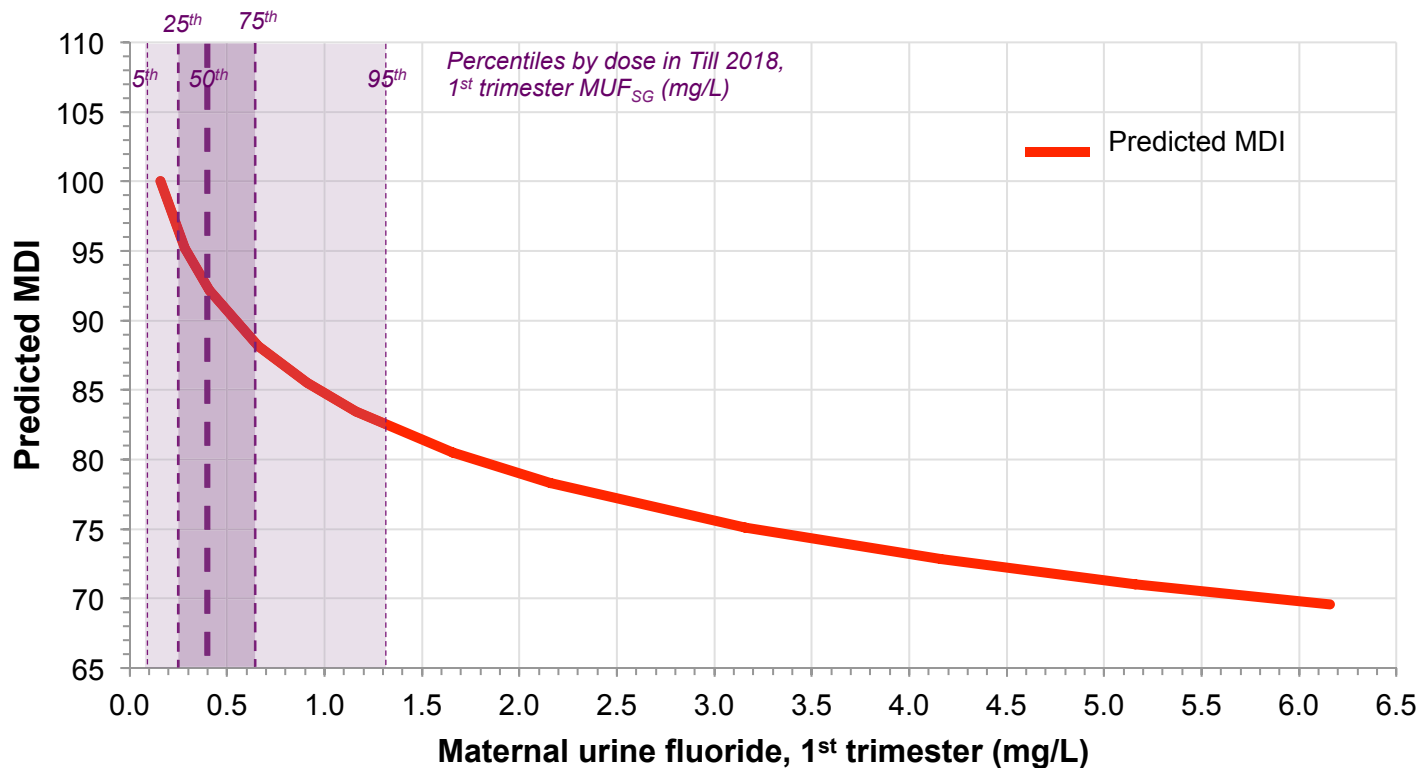
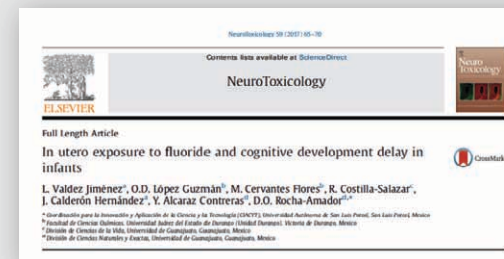


Figure based on Valdez-Jimenez 2017, Table 4, with overlay of Till 2018 exposure levels in Canada.

F neurotoxicity

Bashash 2017

**High quality, mother-offspring
longitudinal cohort study;
Mexico City.**

**First NIH-funded study of
F developmental
neurotoxicity.**

**Found large, statistically
significant effects on IQ.**

**Average IQ losses of 4-6
points for each 1 mg/L
increase in mother's
urine F.**

F and IQ

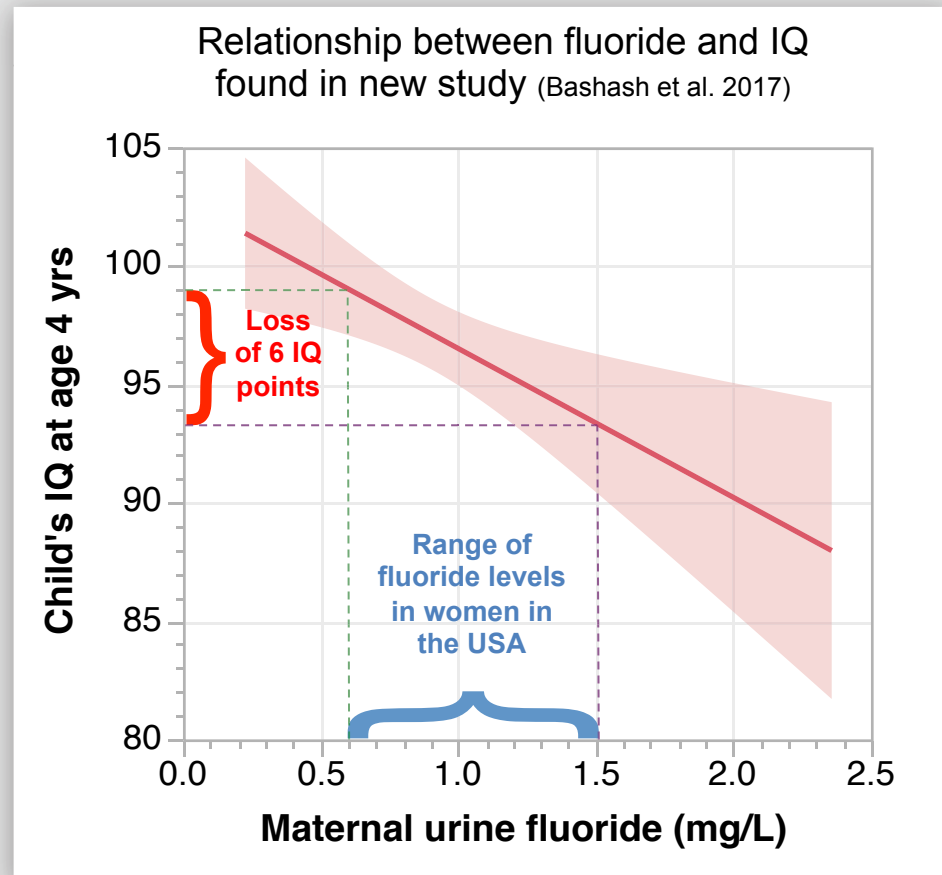


Figure based on Bashash 2017, Figure 2.

F neurotoxicity

Bashash 2017



Many potential confounders considered and/or adjusted for:

Child characteristics:

1. gestational age
2. weight at birth
3. sex
4. parity (being the first child)
5. age at outcome measurement

Maternal characteristics:

6. smoking history (ever smoked vs. nonsmoker)
7. marital status (married vs. others)
8. age at delivery
9. maternal IQ
10. education,
11. cohort (Cohort 3-Ca, Cohort 3-placebo and Cohort 2A)
12. HOME score (Home Observation for the Measurement of the Environment)
13. child's urine F at outcome assessment
14. SES (Socio-Economic Status)
15. maternal bone lead
16. maternal blood mercury
17. calcium supplement

Excluded from study if:

18. history of psychiatric disorders
19. high-risk pregnancies
20. gestational diabetes

or reported current use of:

21. daily alcohol
22. illegal drugs
23. continuous prescription drugs

or were diagnosed with:

24. preeclampsia
25. renal disease
26. circulatory diseases
27. hypertension
28. seizures during the index pregnancy

F neurotoxicity

Bashash 2017

**High quality, mother-offspring
longitudinal cohort study;
Mexico City.**



“Conclusion

In this study, higher levels of maternal urinary fluoride during pregnancy (a proxy for prenatal fluoride exposure) that are in the range of levels of exposure in other general population samples of pregnant women as well as nonpregnant adults were associated with lower scores on tests of cognitive function in the offspring at 4 and 6-12 y old.”

F neurotoxicity

Cui 2018

High quality study; with
gene-F interaction; China.

F and IQ

- Second study to ever look at gene-F interaction. Also found much greater susceptibility to IQ loss for those children with a gene variant:

10 IQ point loss for 1 mg/L increase in urine F.

- 4x greater loss than for all children combined.
- 14% of children had susceptible TT gene variant.

Cui 2018, dose-response for TT genotype
stratified by quintile of exposure

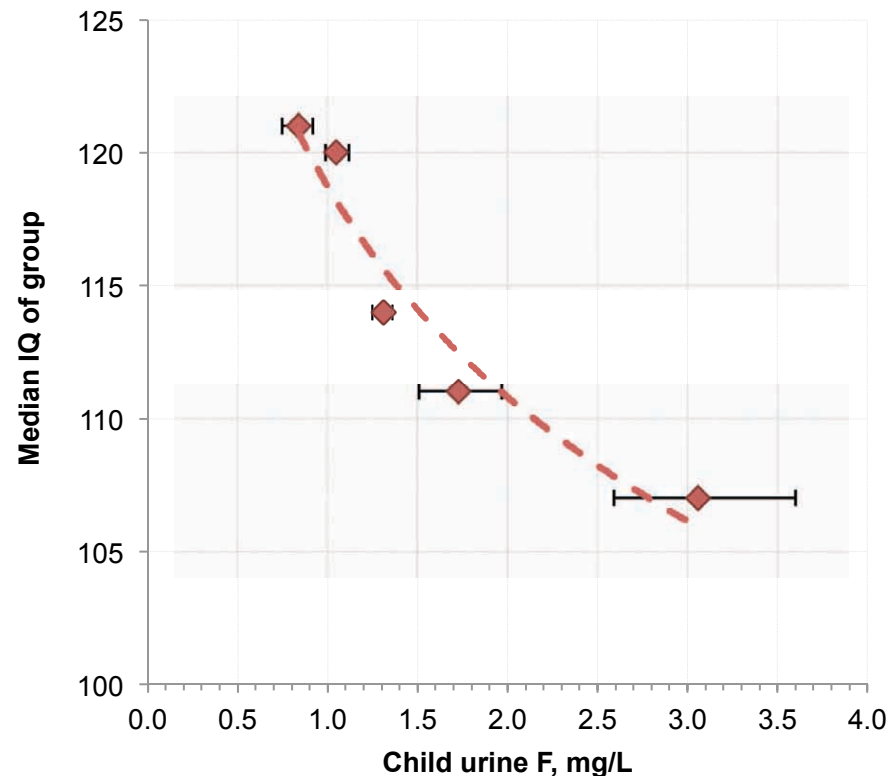


Figure based on
Cui 2018, Table
1 and Table 4.



F neurotoxicity

Green 2019

High quality, mother-offspring longitudinal cohort study;
Canada.

- Second NIH-funded study of F developmental neurotoxicity.
- Found large, statistically significant effects on IQ.
- Average IQ loss of 4.5 points in boys for each 1 mg/L increase in mother's urine.
- Average IQ loss of 3.7 points for each 1 mg/day increase in mother's F ingestion.

Research

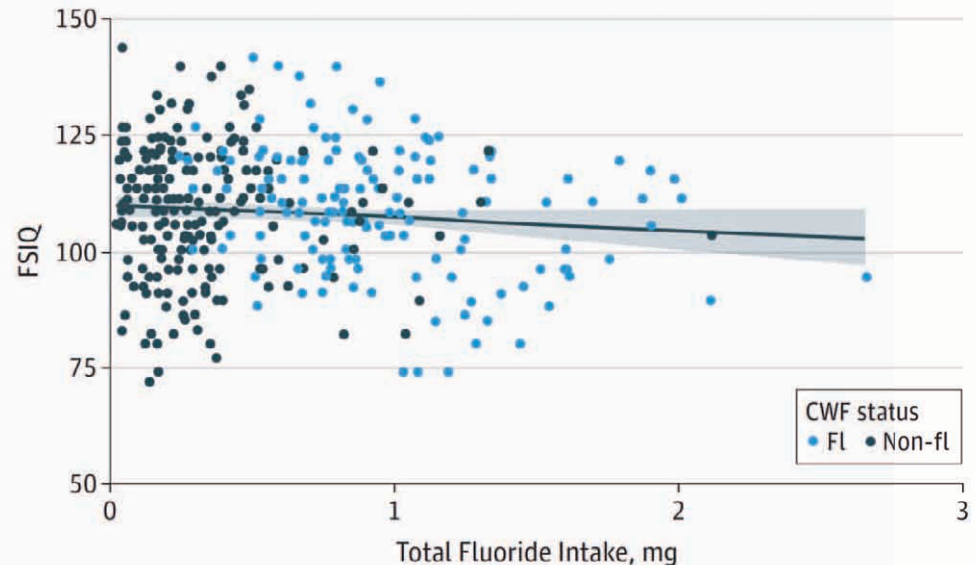
JAMA Pediatrics | Original Investigation

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

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

F and IQ

B Total fluoride intake



F neurotoxicity

Malin 2019

1st study of F and sleep patterns; adolescents in USA.

- **Altered sleep patterns in adolescents** linked to levels of fluoride in the drinking water in the USA.
- Study used nationally representative NHANES data collected by CDC.
- Animal studies suggest F may impair melatonin production in pineal gland.



RESEARCH

Open Access

Fluoride exposure and sleep patterns among older adolescents in the United States: a cross-sectional study of NHANES 2015–2016

Ashley J. Malin^{1*}, Sonali Bose^{2,3}, Stefanie A. Busgang¹, Chris Gennings¹, Michael Thorpy⁴, Robert O. Wright^{1,2}, Rosalind J. Wright² and Manish Arora¹



F neurotoxicity

Till 2020

High quality, mother-offspring
longitudinal cohort study;
F in infant formula;
Canada.

Dramatic lowering of IQ



**NEW STUDY:
FLUORIDATION LOWERS IQ OF FORMULA-FED BABIES**



Till 2020

**High quality, mother-offspring
longitudinal cohort study;
F in infant formula;
Canada.**

Children who were formula-fed and lived in fluoridated areas as babies have dramatically lower IQ compared to those who lived in non-fluoridated areas.



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

Christine Till^a, Breka Green^a, David Flores^a, Richard Horwang^b, E. Angeles Martinez-Mier^c,
Blanca Ayala^a, Gina Macklin^d, Bruce Lymphon^{a,b}

[illegible]

ABSTRACT

Background: Infant consumption of formula reconstituted with fluoridated water can be a source of fluoride exposure. We examined the association between fluoride exposure in infants and tooth decay.

who lived at the same time and in the same place as the Victorian and American writers. The methodology was identical: both authors tried to depict the Victorian and American in their own way, without separating drinking off wine. We examined every possible combination of the two, looking for their representation in various media: articles in British and American newspapers, books, the *Illustrated Primary and Secondary* (and other) magazines, and the *Illustrated London News*. We found that various brands of wine had the impact of something like 2 and 3 times the quantity of alcohol consumed. A serious accident occurred like someone who had been drinking for 2 and 3 days.

[illegible]

...the impact of ...

100

and 74% is associated with 30% of reactive

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F neurotoxicity

Till 2020

High quality, mother-offspring
longitudinal cohort study;
F in infant formula;
Canada.

F and IQ

Very large loss of IQ with increasing tap
water F for *formula-fed infants*:

-9 IQ points (Full Scale IQ) for each 1 mg/L increase in
tap water F.

based on Till 2020, Table 2



F neurotoxicity

Till 2020

High quality, mother-offspring
longitudinal cohort study;
F in infant formula;
Canada.

***Recommendation: no fluoridated
water for infants***

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^{a,c}, Gina Muckle^{a,c}, Bruce Lanphear^{a,b}

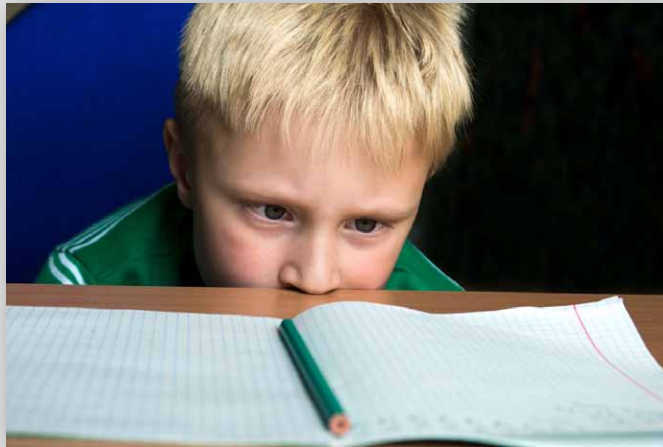
“After adjusting for fetal exposure, we found that fluoride exposure during infancy predicts diminished non-verbal intelligence in children. In the absence of any [dental] benefit from fluoride consumption in the first six months, it is prudent to limit fluoride exposure by using non-fluoridated water or water with lower fluoride content as a formula diluent.”

**NEW STUDY:
FLUORIDATION LOWERS IQ OF FORMULA-FED BABIES**

F neurotoxicity

Fluoride and ADHD

Three studies of Fluoride and ADHD



F neurotoxicity

Malin 2015

F and ADHD

1st study of F and ADHD; ecological; USA.

Dramatic rise in ADHD prevalence as percent of state fluoridated increased.

About 50% higher ADHD rate in states with most fluoridation compared to those with least.

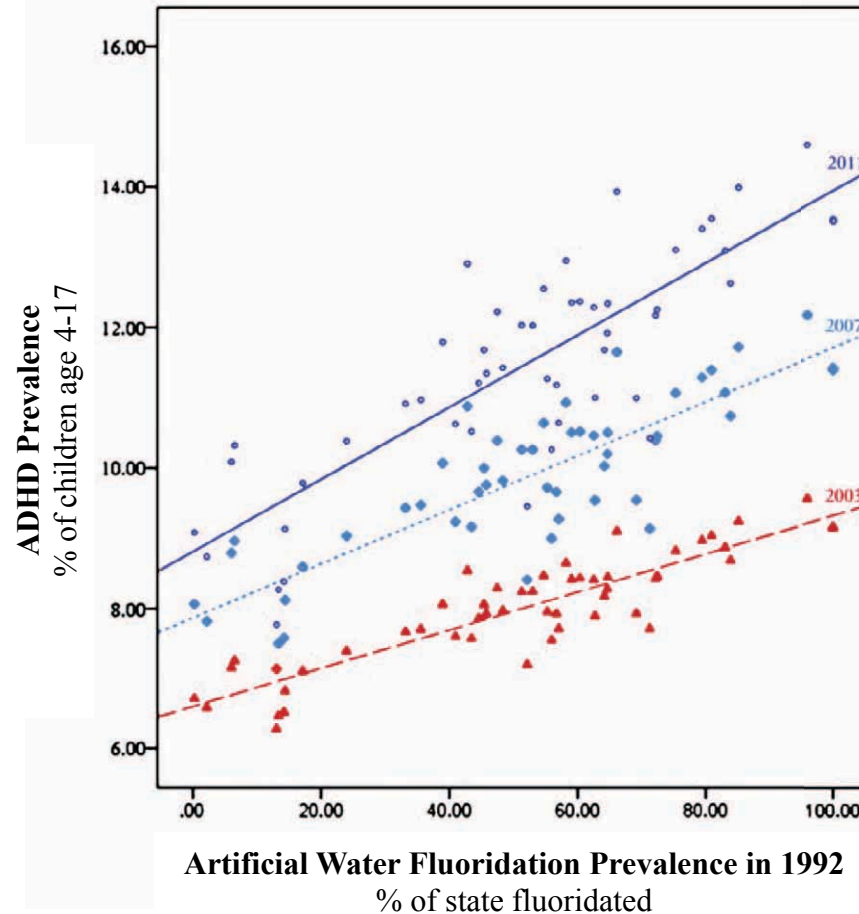


Figure 1. Artificial fluoridation prevalence predicting ADHD prevalence after adjusting for 1992 median household income, by state. For three survey years: 2003, 2007, 2011.

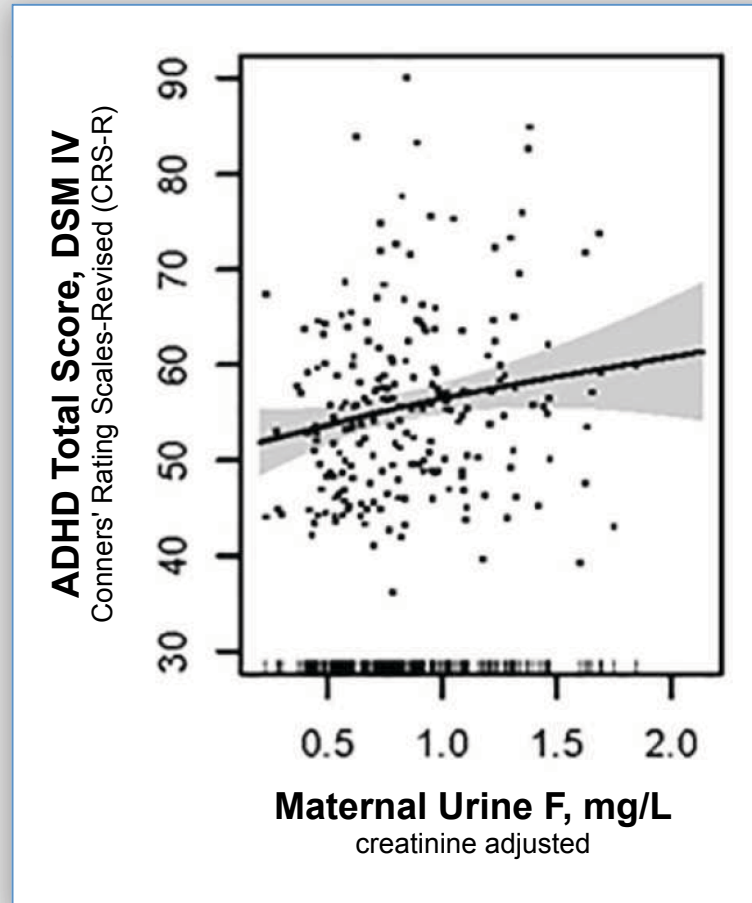
F neurotoxicity

Bashash 2018

1st high quality
study of F and
ADHD; Mexico.

Statistically
significant increase in
ADHD Total Score
(inattentive and
hyperactive-impulsive
behaviors combined)
with higher maternal
urine F.

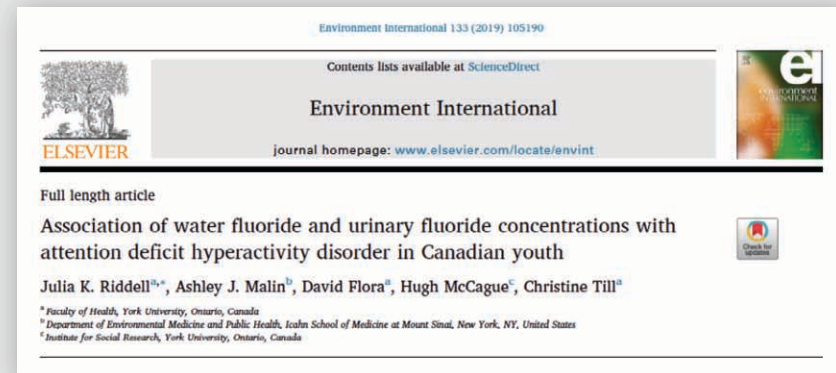
F and ADHD



F neurotoxicity

Riddell 2019

High quality study of F
and ADHD; Canada.



F and ADHD

Found almost **300% higher risk of ADHD** for those living in fluoridated areas in national sample of Canadian children.

Found **600% higher risk of ADHD** for every 1 mg/L increase in tap water F.

“In conclusion, we found that higher tap water fluoride levels and fluoridation of municipal water supplies were associated with a higher risk of an ADHD diagnosis as well as increased symptoms of hyperactivity and inattention, especially among adolescents.”

The Scientific Evidence for Fluoride's Developmental Neurotoxicity . . .



is Overwhelming



F neurotoxicity

Should we care?

What are the implications of a few IQ points lost per person?

Should we care?



F neurotoxicity

Population-wide IQ loss



Estimate of total IQ points lost in the USA due to fluoridated water

Using similar methods as Bellinger 2012 used for other risk factors.

Assume steady-state conditions of exposure.

Loss of IQ for infants fed formula made up with fluoridated tap water:

8.8 IQ points loss per 1.0 mg/L increase in tap water F (Till 2020)

0.46 mg/L difference in water F between fluoridated and non-fluoridated areas (Till 2020)

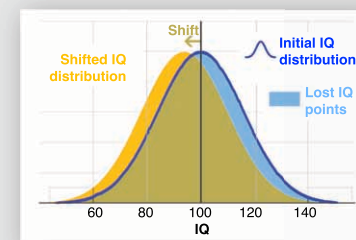
$8.8 \times 0.46 = 4.1$ **IQ point average loss in fluoridated areas**

50% of infants formula-fed in first 6 months (Till 2020)

70% of USA has fluoridated tap water

$50\% \times 70\% = 35\%$ formula-fed and have fluoridated water

3.8 million children born in USA each year



3.8 million children \times 35% who are formula-fed and have fluoridated tap water \times 4.1 IQ points loss =

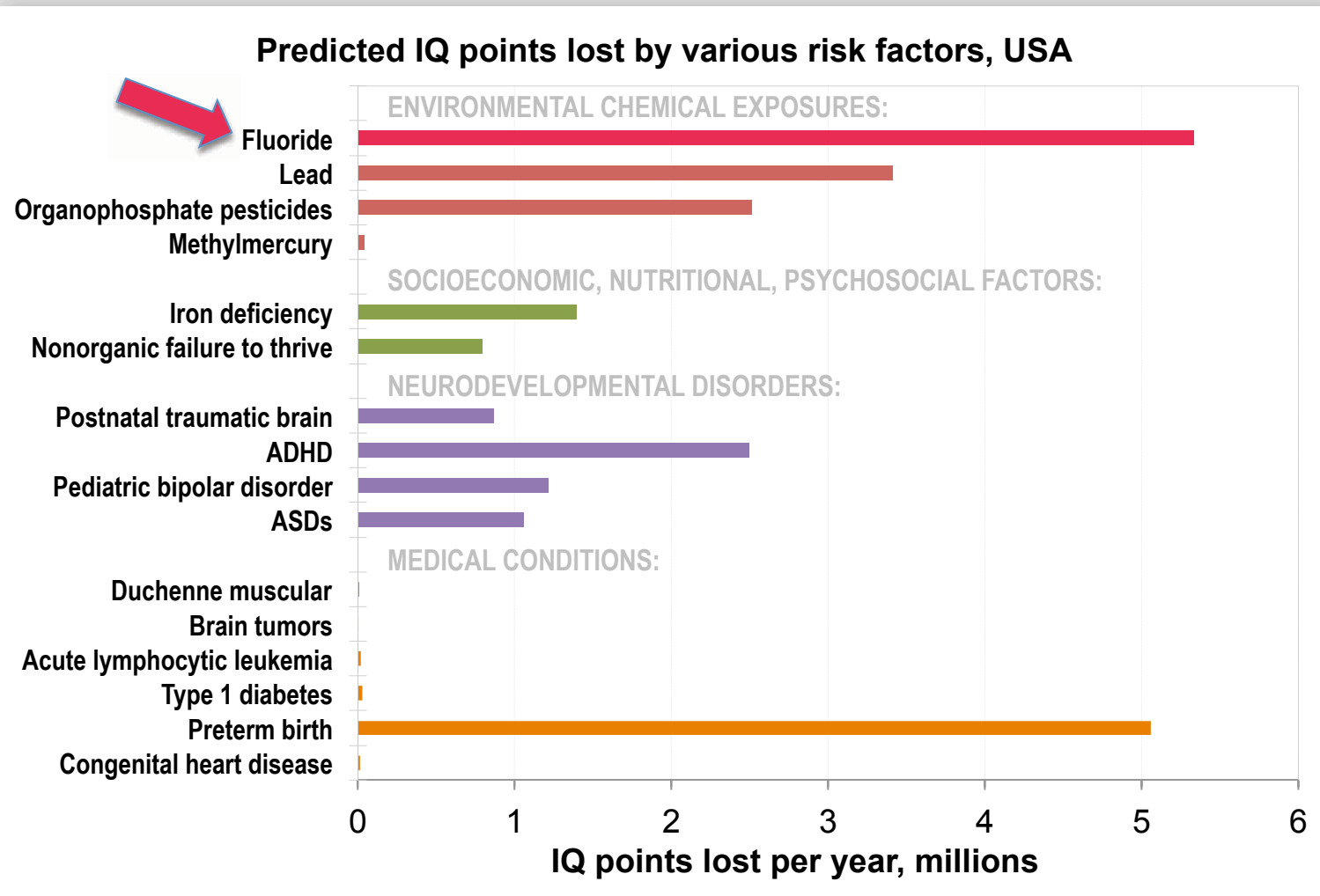
5.4 million IQ points lost per year in the USA
due to water fluoridation



F neurotoxicity

Comparison

*Water fluoridation
causes greater loss of IQ
in the USA than any
other risk factor*



All risk factors except fluoride based on Bellinger 2012, Table 2.

F neurotoxicity

**Population-wide
economic cost**

**\$\$\$ cost of
Fluoridation?**

Estimate of total dollar cost due to IQ loss from fluoridated water and subsequent lower lifetime incomes, in the USA.



F neurotoxicity

Population-wide economic cost

\$\$\$ cost of Fluoridation?

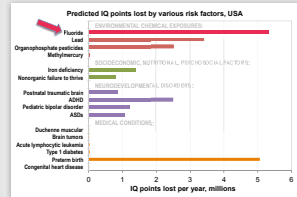
Estimate of total dollar cost due to population-wide IQ loss from fluoridated water and subsequent lower lifetime incomes, in the USA.

\$20,000	lifetime earnings lost per 1 IQ point reduction per person
79 years	average life expectancy
\$254	earnings lost per year per person per 1 IQ point reduction
327 million	population of USA
50%	percent of infants who drink formula
70%	percent living in fluoridated area as infants
35%	percent of persons who had formula and lived in fluoridated areas as infants
114 million	number of persons in USA who had formula and lived in fluoridated areas as infants
-4.1	average IQ point loss for formula-fed infants in fluoridated areas compared to non-fluoridated
-\$117 billion	annual earnings loss for USA (assuming steady state exposure and costs)

Over \$100 billion per year in USA

F neurotoxicity

Should we care?



- **4.5 million IQ points lost per year; more than any other risk factor.** Fluoridation is causing more economic harm due to lowered intelligence and achievement than any other IQ risk factor, including lead, mercury, and preterm birth.

- **\$100 billion per year; much more harm than good.** Water fluoridation is causing much more economic harm from IQ loss than any dental benefit it might provide.

- **Easier to solve than any other environmental problem.** Water fluoridation can be stopped immediately at virtually no cost. No other environmental harm is so easily solved.

Pregnant mothers and children should be protected from the risks posed by fluoride.

F neurotoxicity

Should we care?

We must

