I’m Chris Neurath and I’m the Research Director for the American Environmental Health Studies Project. I’m going to give an overview of the scientific evidence for fluoride’s developmental neurotoxicity.
I’m going to start with some amazing and beautiful pictures ... and the question: What exactly is developmental neurotoxicity ... and why is it such a focus of current research on fluoride?
Brain development starts with a few cells in the early fetus and continues rapidly in a highly complex dynamic process through infancy. Indeed the rate of neurodevelopment in humans is extremely rapid in utero, but is even faster in the first months after birth. This formation of the wiring of our brains is “staggeringly complex” as described by the Harvard Center for Brain Science. “Our own brains have tens of billions of neurons connected through perhaps one hundred trillion synapses.”
There are many critical processes during neurodevelopment, which all have to take place with precise timing and coordination with the other processes. A disruption from a toxic chemical to any process, even during a brief window of time, can cause permanent harm. Reduced IQ is one symptom of such harm.
The fetal brain and the infant brain is more susceptible to disruption than the adult brain because of this complex neurodevelopment process but also because the blood-brain barrier, which can limit access of toxic chemicals to the brain in adults, is not well developed until after age 6 months. Disruptions to neurodevelopment can cause life-long harm which often can not be repaired.
The best place to start is with the recently released National Toxicology Program, or NTP, a systematic review of fluoride’s neurotoxicity. This was a very thorough review that has been 5 years in the making. They concluded that fluoride is a presumed neurotoxin.
Their conclusion is based on a very large amount of evidence that would probably surprise most people who have not studied fluoride’s adverse effects. The NTP identified 149 human studies and 339 laboratory animal studies.
Of the human studies, there was a wide variety of developmental neurotoxic endpoints, with the largest number being studies of IQ in children with 60 such studies.
It is worth comparing this NTP review of fluoride neurotoxicity to NTP reviews of other toxic chemicals. The NTP’s main purpose is to assess the toxicity of chemicals and they have issued several recent reports on other chemicals that concluded they were “presumed” hazards. But fluoride turns out to have many more studies than any of these other chemicals. The other chemicals shown are PFOA which is a perfluorinated chemical, BDE-47 is a brominated fire retardant, and “air pollution” which includes PM 2.5.
The NTP carefully assessed every study and gave them scores for several domains. Of the 149 human studies, they determined that 20 were high quality, or in their terminology, at “low Risk of Bias”. When comparing this number of high quality human studies to the number available for other developmental neurotoxins, or for toxins of any type, this is a very large number. The EPA, for example, has determined that some chemicals are neurotoxins without a single high quality human study available.

The green in the graphic essentially means “good” and low Risk of Bias for that domain. Yellow and red indicate higher Risk of Bias. Of the 20 high quality studies, 18 were in children and all 18 found statistically significant adverse effects. This is the high level of consistency cited by the NTP in their conclusion of “presumed” neurotoxic in humans.

The graphic is from the NTP report but I have added the colored arrows that are blue, purple, and black. They indicate the exposure levels at which harm was found and are related to the exposure levels found in the USA, due largely to artificially fluoridated water. The blue arrows indicate studies that found adverse effects at 0.7 mg/L water fluoride concentrations or the equivalent in urine fluoride. 0.7 mg/L is currently the most common level of fluoridation in the USA. The NTP also considered that levels below 1.5 mg/L are relevant to exposures in the USA. I’ve marked those in purple. Half of the high quality studies found that exposures common in the USA were associated with harm, mostly lowered IQ.
I now want to discuss the reaction to the rapidly emerging evidence that fluoride is neurotoxic and can lower IQ of children. The single study which has received by far the most attention is the Green 2019 study published in *JAMA Pediatrics* in August 2019. You’ve probably heard about it and may have read it. I found the *JAMA* editors reactions to it to be very revealing of where most people, including health professionals, beliefs about fluoride have been ... and where they can move to when they have an open mind. I’m going to give excerpts from their Podcast discussion of the paper.
Excerpts from their Podcast: audio clip A.

Open "JAMAPed clip A" to play
The editors were surprised at how many cities and countries do not fluoridate their water. In fact, the large majority of the world does not fluoridate.
Excerpts from Podcast: audio clip B.

Open "JAMAPed clip B" to play
The editors noted with concern that the loss of IQ from fluoridation is “on par with lead”. They also point out that even a small average drop of IQ of a few points, can produce a large increase in those on the lower tail of the distribution who need special education, and a halving of the number of gifted children on the high end distribution tail.
F neurotoxicity
A sizable effect “on par with lead”
“that’s a real concern”

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 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.”

Excerpts from Podcast: audio clip C.

Open "JAMAPed clip C" to play
The editors concluded with the advice that pregnant mothers should not drink fluoridated water.
F neurotoxicity
Editor’s advice: Pregnant mothers should avoid fluoridated water

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 it’s not a particularly odious thing to do, and potentially does reduce the risk.”

Dr Rivara: “Yes, 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, it’s going to get a lot of attention, and I’m very proud that you published it.”

Excerpts from Podcast: audio clip D.

Open “JAMAPed clip D” to play
I’m now going to briefly go over some of the most important individual studies. These will just be ones that the NTP rates high quality and low risk of bias.
Studies of fluoride’s developmental neurotoxicity started in China in the 1980s. That’s because large areas of China with a population of about 100 million used groundwater for drinking that had elevated fluoride levels. China and WHO consider water fluoride concentrations above 1.5 mg/L elevated. The map shows the large areas with elevated groundwater fluoride as light green. It shows other sources of fluoride exposure in other colors. Purple shaded areas are a special localized situation where people cook indoors using coal briquettes that are made from a mix of clay and coal. The clay is the source of the high indoor fluoride levels. Normal coal combustion, such as from power plants, is not a significant source of fluoride exposure. The large red “F” markers show the locations of neurotox studies, which are spread throughout China in many different populations. Almost all of the studies found reduced IQ in the children with higher fluoride exposure.
The earliest studies in China were often of relatively unsophisticated design, but by about 2000, stronger study designs were being used. The Xiang 2003 study is the earliest study to be rated high quality in NTP’s review. As shown in the graph, as the water fluoride increased, IQ steadily decreased. Loss of IQ is even apparent at concentrations below 1.5 mg/L.
But Xiang 2003 also found an even more worrying effect by looking at the percentage of children with IQ below 80, as shown in this graph. At the lowest water fluoride level of about 0.8 mg/L, shown as group “A”, no children had IQ below 80. At the next higher level, group “B”, at about 1.5 mg/L, 10% of children had IQs below 80, and at the highest exposure level almost 40% of children had IQ below 80.
Of the 18 studies in children that NTP considers to be of high quality, I’m only going to discuss those that have some special feature. All 18 found statistically significant adverse effects. The Zhang 2015 study shown here was the first study to look at interactions between fluoride and genes. That is, it looked to see whether individuals with particular genetic variants were more susceptible to loss of IQ from fluoride than more common genetic variants. It found a 5-fold greater loss of IQ for a specific gene variant. The table on the lower left shows that for all children with all variants the loss of IQ was 2.42 points per 1 mg/L increase in urine fluoride, but for the val/val variant, the loss was 9.67 IQ points. About a quarter of the population had the val/val variant. The figure on the right shows how IQ drops in the susceptible group as urine fluoride increases. There is a substantial drop in IQ even at the lowest urine fluoride levels which are well below 1.5 mg/L.
This study is noteworthy because it is the first mother-offspring longitudinal cohort study. It measured fluoride in the mothers during pregnancy and then assessed the neurodevelopment of the infants. There was a steep drop in infant’s neurodevelopment score, especially in the range of maternal urine fluoride below 1.5 mg/L. This study was in Mexico, but the exposure levels can be related to those in Canadian pregnant women or pregnant women in the USA, for that matter. The purple shading indicates urine fluoride levels found in a Canadian study. Much of the loss of IQ occurs within the shaded purple range.
This study, Bashash 2017, was the first funded by the US National Institutes of Health, or NIH, with a grants totaling about $3 million. It is a very high quality study and found a large, statistically significant effect of fluoride on IQ. The average loss was 4 to 6 IQ points for each 1 mg/L increase in mother’s urine fluoride. The graph shows the dose-response relationship found for children tested at age 4 years. It also shows in the blue bracketed region the range of fluoride levels expected in the USA and the resulting loss of IQ of 6 IQ points is shown in the red bracketed region.

To date, there have not been any published studies of maternal urine fluoride levels in the USA so the range sown here is based on studies in artificially fluoridated areas of Canada and New Zealand.
As just one indication of the high quality and rigor of the Bashash 2017 study, this is a listing of all the potential confounders that were considered and adjusted for if necessary.

### 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
The study concluded: “higher levels of maternal urinary fluoride during pregnancy ... in the range of levels of exposure in other general populations ... were associated with lower scores on tests of cognitive function ... in offspring”. The phrase “in the range of levels of exposure in other general populations” is important, because it means this study in Mexico had fluoride exposures in the same range that women experience in the USA from artificially fluoridated drinking water. There is no artificial water fluoridation in Mexico, and instead salt is fluoridated, but the total intake of fluoride covers the same range as in the USA.
This study, Cui 2018, is noteworthy because it is the second to examine gene-fluoride interactions. Just as the first such study by Zhang 2015, it found a much greater loss of IQ in those children with a particular gene variant, although in this study they looked at a different gene. For the genetically susceptible children, this study found a 10 IQ point loss for each 1 mg/L increase in urine fluoride. This was a 4-fold greater loss than in all children combined. 14% of the children had this susceptible TT gene variant. The graph shows that this large loss of IQ was found even below 1.5 mg/L urine fluoride.
The Green 2019 paper is the highly cited study in *JAMA Pediatrics*, which the editors commented about in their Podcast that I gave excerpts from earlier. This study was also NIH funded, and is important not just because of its very high quality, but because it was done in Canada. Canada is about as similar to the USA in socioeconomic and fluoride exposure conditions as anywhere. Fluoride exposure in both countries comes mainly from artificial water fluoridation, with the average level in Canada being about 0.6 mg/L and in the USA, somewhat higher, at 0.7 mg/L. Although no study of fluoride and IQ has yet been done in the USA, this study in Canada can be considered very applicable to the USA.

It found large statistically significant effects on IQ. For boys, the average IQ loss was 4.5 points for each 1 mg/L increase in mother’s urine. The study also estimated total daily fluoride intake in the mothers and found an average 3.7 IQ points loss for both boys and girls for each 1 mg/day increase in mother’s fluoride ingestion.

Defenders of water fluoridation have tried to criticize this Green 2019 study. I won’t get into a detailed discussion of this, other than to point out that the authors themselves have rebutted virtually all the criticisms in a letter published in *JAMA Pediatrics* in December 2019. If you are interested in the discussions about the validity and relevance of the Green 2019 study that response letter is a good place to start.
The NTP review of fluoride neurotoxicity studies only included studies published up until August 2019. There have been 3 more high quality studies published in just the last 6 months, and they both reinforce and extend the evidence compiled in the NTP review. This study, Malin 2019, was the first to ever examine sleep patterns in relationship to fluoride exposure. Furthermore, it used data from the USA in the nationally representative sample of the NHANES survey conducted by the CDC. It found altered sleep patterns in adolescents with higher drinking water fluoride levels. Altered sleep patterns can be considered a neurologic effect. Animal studies suggest fluoride may impair melatonin production in the pineal gland, so that might be the mechanism for altering sleep patterns.
This is the most recently published study, and in my opinion, is the most concerning study yet. It was done in the same Canadian cohort as the Green 2019 paper in *JAMA Pediatrics*. But, instead of estimating prenatal exposure to fluoride it measured exposure to the infants between birth and age 6 months, with comes largely through infant formula when it is made up with fluoridated water.
The study found that 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.
Children given formula as infants lost 9 IQ points for each 1 mg/L increase in tap water fluoride. For the so-called Performance Scale IQ score, also known as “non-verbal IQ score”, the children lost 19 points for each 1 mg/L increase in tap water fluoride. These are dramatic and very concerning reductions in IQ that are even larger than the losses from prenatal exposure.

Two possible factors may explain this greater loss from infant period exposure than from prenatal. First: Brain development is actually more rapid during early infancy than prenatally, so may be more sensitive to disruption by neurotoxic agents. Second: Infant exposures to fluoride are much simpler and are less subject to random error than are maternal urine fluoride measurements. Maternal urine fluoride can vary by whether the mother ingested any fluoride in the hour or so before the urine sample was taken. Random error in estimating the prenatal exposures can lead to what is called “bias toward the null” which is an underestimate of the true effect. Therefore, the studies of prenatal fluoride exposure may be underestimating the size of the effect. In contrast, this study of fluoride from infant formula is not underestimating the effect, so this larger effect may be closer to the true effect.
The authors conclude that for infants: “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” to make formula.
While most studies of fluoride neurotoxicity have looked at IQ loss, there have also been several that have looked at the association with ADHD, or Attention Deficit Hyperactivity Disorder. I’ll discuss three such studies.
The first study to ever look at fluoride and ADHD was by Malin in 2015. It found a dramatic increase of ADHD prevalence with increasing percent of state-level fluoridation. States with high proportions of their population fluoridated had significantly higher rates of ADHD than states with less fluoridation. The effect is large, with the most fluoridated states having about 50% higher rates of ADHD than the least fluoridated states.

The study also looked at secular trends in ADHD rates by comparing surveys conducted in three different years: 2003, 2007, and 2011. In the graph, the red is the earliest survey in 2003, the light blue is the middle survey in 2007, and the most recent survey in 2011 is shown in dark blue. ADHD diagnoses have been increasing over time, and the association between fluoridation and ADHD has continued and even grown between 2003 and 2011.
The next study of fluoride and ADHD was the first using a high quality longitudinal mother-child cohort design. It found a statistically significant increase in child ADHD score with increasing prenatal exposure, as estimated by the maternal urine fluoride level.
The latest fluoride ADHD study was published just a few months ago, and found a dramatically higher risk of ADHD in children living in fluoridated areas of Canada compared to those living in unfluoridated areas. The risk of having a diagnosis of ADHD was \textbf{300\% higher} in fluoridated areas. The study used a sample of children from throughout Canada from the CHMS survey or Canadian Health Measures Survey. This survey is conducted by Health Canada and is similar to the NHANES survey in the USA.

The increased risk of ADHD, when stated in terms of a 1 mg/L increase in the tap water fluoride concentration, was \textbf{600\% higher}.

An implication of these findings is that the majority of ADHD cases may be attributable to water fluoridation.
Summarizing the overall body of evidence, with particular focus on the strong studies discussed here, the scientific evidence for Fluoride’s developmental neurotoxicity ... is Overwhelming.
But what are the implications of a few IQ points lost per person, on average? Should we care?
As the *JAMA Pediatrics* editors noted in their Podcast, even a small shift downward in the distribution of IQ scores can represent a large population-wide loss of IQ. In order to compare the total harm to the population of the USA from fluoridation to that from other causes of IQ loss, we have calculated the total IQ points lost per year. Since infant formula made with fluoridated water appears to represent the greatest effect on IQ, we used the results from the Till 2020 study in Canada to estimate the total number of IQ points lost in the USA, assuming the same dose-response and infant feeding practices as in Canada but accounting for the much larger population of the USA with fluoridated water. We estimated that 5.4 million IQ points are lost per year. It is likely that a certain fraction of the population who are genetically more susceptible will bear the majority of the burden, although considering the large magnitude of the effect found in the Till 2020 study amongst all children, it is plausible that even those who are genetically less susceptible will suffer loss of IQ.
A loss of 5.4 million IQ points per year can be put into context by comparing it to the estimated losses from a variety of other risk factors, including the best known developmental neurotoxic chemicals lead, mercury, and organophosphate pesticides. Bellinger 2012 estimated the total USA-wide IQ loss for 16 other well-established risk factors and I have graphed them here. My estimate shows that fluoridated water is responsible for a greater total IQ points loss than any of the other risk factors, including lead, organophosphate pesticides, and preterm birth.
It may seem crass, but there are standard methods for estimating the total economic cost to society from IQ loss. The main economic harm arises from the reduced lifetime earnings which have been found associated with lowered IQ.
We have calculated the annual dollar cost of water fluoridation, from earnings lost due to lower IQ. We have used standard methods of health economists that have been applied to other developmental neurotoxins, like mercury. It is worth noting that the US EPA considers that a population-wide average loss of just 1 IQ point is an adverse effect to be avoided.

A standard estimate for lifetime earnings lost per person for a 1 IQ point lowering is about $20,000. When applied to the population of the USA who are formula-fed as infants and live in fluoridated areas, it works out to a cost of over $100 billion a year. This assumes steady-state exposure and costs. This is a huge economic cost.
So, should we care about the scientific evidence showing water fluoridation lowers IQ by a few points? **Absolutely!** Fluoridation is doing much more economic harm than good.

- The dollar cost of IQ loss far exceeds any dental benefit water fluoridation may provide. Furthermore, there is no dental benefit from fluoride prenatally and in infancy. It is well established that the dominant dental benefit of fluoride comes from topical contact on the teeth and not from swallowing the fluoride.
- Fluoride may be causing more neurocognitive harm than any other risk factor, including lead, mercury, and preterm birth.
- The environmental health harm from fluoridation is easier to solve than any other environmental problem. Simply stop adding fluoridation chemicals to public drinking water. I’m not aware of any other environmental harm that is so easily and inexpensively solved.
- **Pregnant mothers and children should be protected from the risks posed by fluoride.**
So ... Should we care?

I’d be happy to answer any questions about the science and individual studies.