



PERSPECTIVE

Controversy: The evolving science of fluoride: when new evidence doesn't conform with existing beliefs

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Over the past 75 years, health authorities have declared that community water fluoridation—a practice that reaches over 400 million worldwide—is safe. Yet, studies conducted in North America examining the safety of fluoride exposure in pregnancy were nonexistent. When a Canadian study reported that higher fluoride exposure in pregnant women was associated with lower IQ scores in young children, critics attacked the methodology of the study and discounted the significance of the results. Health authorities continued to conclude that fluoride is unequivocally safe, despite four well-conducted studies over the last 3 years consistently linking fluoride exposure in pregnancy with adverse neurodevelopmental effects in offspring. We describe the challenges of conducting fluoride research and the overt cognitive biases we have witnessed in the polarized fluoride debate. The tendency to ignore new evidence that does not conform to widespread beliefs impedes the response to early warnings about fluoride as a potential developmental neurotoxin. Evolving evidence should inspire scientists and health authorities to re-evaluate claims about the safety of fluoride, especially for the fetus and infant for whom there is no benefit.

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Do not avoid difficult areas of investigation. Take risks. If scientists exclusively choose the safe routes, avoid controversial research problems and play only minor variations of someone else's themes, they voluntarily turn themselves into technicians. Our craft will indeed be in peril.¹ Herbert Needleman, MD

Most people assume that community water fluoridation (CWF)—adding fluoride to public drinking water supplies—is a safe and effective way to prevent cavities. After all, it has been endorsed by public health, dental and medical organizations since it was introduced 75 years ago.^{2,3} Today, about three-fourths of people in the United States and one-third of Canadians have fluoride added to their drinking water.

After reviewing the scientific literature, it became clear that there were growing concerns about fluoride as a developmental neurotoxin.^{4,5} In 2006, a report by the National Research Council (NRC)⁶ acknowledged that fluoride exposure may be associated with adverse cognitive and endocrine outcomes, and recommended further study, especially for vulnerable populations. One NRC panel member, Dr. Isaacson, said the report “should be a wake-up call”. Yet, nearly 10 years later, not a single study had directly examined fetal exposure to fluoride in humans.

In many academic circles, it is a taboo to study fluoride. Dr. Phyllis Mullenix,⁷ former Head of the Toxicology Department at the Forsyth Dental Centre in Boston, was heavily criticized for publishing her study showing that sodium fluoride was neurotoxic to developing rats. People who questioned the safety of water fluoridation are quickly dismissed as zealots or anti-science fanatics. Indeed, some scientists dismissed our funding application with comments such as, “This study is not needed. We know that

fluoride is safe”. But we forged ahead; shouldn't claims about safety be based on evidence?

In 2015, we sought funding to investigate the safety of fluoride exposure in pregnancy. We assembled an interdisciplinary team of scientists from complementary fields including epidemiology, environmental health, neuropsychology, and dentistry—knowing that diverse perspectives would be critical for minimizing conscious or unconscious biases in our investigative process. We naively expected that the public health and medical community would trust the scientific process.

THE SCIENTIFIC PROCESS

We studied 512 mother–child pairs enrolled in the MIREC (Maternal Infant Research on Environmental Contaminants) study. The families lived in six Canadian cities; 40% lived in cities with CWF. To our astonishment, we found that higher levels of fluoride in pregnant women and water concentrations were associated with a 3- to 5-point lower IQ score in their 3- to 4-year-old children.⁸ We thought there may be other factors at play, but this association held up after accounting for important characteristics of the study population and looking at the relationship in many different ways.

In August 2018, we presented our findings at an international meeting held in Ottawa. We were nervous how the results would be received by the audience, which included members from Health Canada and other public health agencies. Afterwards, someone approached me and said, “Congratulations – you have just sabotaged your career before it even started”. Rivka Green

As part of our agreement, our manuscript required approval by the MIREC Biobank before we submitted it for publication.

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Considering the sensitive nature of the topic, the manuscript was sent to reviewers from various divisions of public health. In over 60 pages, we responded to over 200 specific critiques. The upshot of addressing each critique was that we were able to do better science by refining our methods.

We submitted the manuscript to three top medical journals; two did not send it for peer review because it was “of low research relevance”. As we waited, we hired an independent data analyst to rerun all of the analyses for the third time. In April 2019, *JAMA Pediatrics* accepted our paper. We responded to several additional rounds of review by the *JAMA* editors until we eventually reached a compromise that reflected the strength of the evidence, as well as their implications for public health.

One year after that conference in Ottawa, our article was published on August 19, 2019. In only 2 months, it was viewed over 100,000 times and ranked among the top 0.0005% of research output scored by Altmetric. We expected our study would reignite the debate about the safety of fluoridation, but we didn't expect we would be at the crossfire of this political and polarized debate.

THE BACKLASH

Outside of our colleagues in environmental epidemiology, who were initially skeptical, the results were met with resistance. Attempts to debunk the data were especially apparent from “experts” who held strong beliefs about the benefits and safety of fluoridation.

There are thousands of articles pointing to the safety of community water fluoridation ... this study doesn't change the benefits of optimally fluoridated water and exposure to fluoride.⁹ Dr. Braun, chair of the AAP Section on Oral Health Executive Committee

Yet, there are no other prospective studies with biomarkers of fluoride in pregnant women living in regions with CWF. Canada's national newspaper rang with the headline, “Fluoride won't make you dumber, but the ‘debate’ about its safety might”.¹⁰ Didn't the NRC deliberately call for more studies to address this “debate”?⁶

Vitriolic comments and claims with little scientific basis, such as the results are driven by outliers, were made by the American Council on Science and Health¹¹ and the UK-based Science Media Centre,¹² both heavily funded by the pharmaceutical and food and beverage industries. In reality, we presented our models with and without outliers and the effect remained. These types of vacuous claims exemplify attempts to manipulate the scientific evidence and manufacture doubt.

So what this study found was just an association. And we know from other areas ... they are inherently problematic and inherently complex.¹³ Timothy Caulfield, University of Alberta

This was not a scholarly debate on the neurotoxicity of fluoride; it was an attack on IQ scores, statistical methodology, and observational studies. Ironically, the evidence showing that CWF protects against tooth decay was largely based on observational or “association” studies, most of which were conducted prior to the introduction of fluoridated toothpaste in the early 1970s.¹⁴ Moreover, most landmark studies in public health—including those linking smoking with lung cancer, air pollution with coronary heart disease, and asbestos with mesothelioma—were observational. Indeed, this design is optimal to study many important public health problems, usually in conjunction with toxicological studies.

There is no sensible biochemical reason why fluoride would harm the brains of boys but not those of girls. So, are the authors wrong? Probably.¹⁵ Alex Berezow, Ph.D., Vice President of Scientific Affairs, American Council on Science and Health

Our paper continued to be attacked in scientific and public arenas, many of them drawing upon critiques made by the industry-funded groups. Accusations that our data did not support our conclusions spread quickly and were propagated by social media. “Experts” wrote that the association between maternal urinary fluoride and lower IQ in males, but not females, defied plausibility. However, as we noted in our original proposal, males are often more susceptible to toxicants and failure to examine sex-specific effects of fluoride exposure may result in missing a potentially vulnerable group. Further, the NTP in 2016 specifically called for more studies on fluoride exposure with an emphasis on sex-specific associations.¹⁶

I'm confused as to why the authors would want to withhold the data.¹⁷ Stuart Ritchey, Ph.D.

On October 23, 2019, a letter signed by 30 health-care professionals and scientists from six countries was sent to the Acting Director and Acting Deputy Director of the NIEHS. The letter cited concerns about the replicability of scientific research in general and the need for transparency. Our research team was accused of “refusing to release data”, but we had not refused to release the data. The policies that govern access to the MIREC Biobank and procedures to access it are sent to anyone who requests the data.

RISK AND BENEFITS

Some critics maintained that our conclusion—that pregnant women should reduce their fluoride intake—overstated the implication of the findings and was “dangerous”. Other critics said that we should not change our actions based on “one study”. We agree that no one study is definitive; we should carefully evaluate the collective evidence from multiple studies, as well as the risks and benefits of fluoridation.

Four high-quality, prospective birth cohort studies^{5,8,18,19} show that fetal exposure to fluoride is associated with diminished cognitive abilities. In November 2019, the National Toxicology Program released a draft report on fluoride concluding that fluoride is presumed to be a cognitive neurodevelopmental hazard. This report was largely ignored by the critics of our study.^{17,20}

Fluoride offers no benefits to the fetus. The beneficial effects of fluoride predominantly occur at the tooth surface, after the teeth have erupted.^{21–23} Accordingly, the Canadian Pediatric Society and the American Academy of Pediatrics advise against fluoride supplements during the first 6 months of life.²⁴

Exposure to fluoride comes from a variety of sources, but for people who live in cities with fluoridated water, the main source of ingestion is drinking water. Importantly, pregnant women and formula-fed babies may not be able to access nonfluoridated water.

CONCLUSION

Did our article shift the needle? Perhaps for those who are willing to integrate new knowledge with their existing beliefs. To understand why many questions about the safety of CWF are still not settled after 75 years, we need to recognize how entrenched beliefs can lead to biases and blind spots, even among highly trained clinicians and scientists. Science advances by continuously challenging old ideas and adjusting our beliefs as new knowledge emerges, even if this new evidence conflicts with conventional wisdom or is inconvenient.

Dr. Lanphear, a senior scientist on our team who conducted many of the pivotal lead toxicity studies that helped confirm Dr. Needleman's work, reminded us that it took two decades of research before the CDC declared, “there is no safe level of lead in children's blood”. Dr. Lanphear wrote, “The critics—who were often paid by industry or simply ignorant about lead toxicity but

still willing to offer their 'expert' opinion—delayed efforts to prevent lead poisoning by decades”.

We typically fret about subtle biases, like recall bias and unmeasured confounding, but confirmation bias, the tendency to ignore or debunk data that does not conform to what we believe, is arguably a much larger problem. Failure to act on consistent evidence that indicates safety risks could amount to enormous costs at the population level.

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