THE REQUEST

From: Christine Massey <XXX>
Date: Wed, May 29, 2019 at 2:57 PM
Subject: peer-reviewed papers on fluoride exposure during pregnancy
To: <foip@calgary.ca>

Dear FOIP Coordinator,

This is a request for General Information, made under Alberta's *Freedom of Information and Protection of Privacy Act.*

The $25 application fee will be mailed to you.

Background

Two important studies examining total exposure to fluoride during pregnancy and neurodevelopmental effects in offspring, by Bashash et al., were published in late 2017 and late 2018. Both were funded by the U.S. National Institutes of Health and conducted by an international team that included researchers from the Harvard School of Public Health, the Dalla Lana School of Public Health at the University of Toronto and various other universities and institutions.

Both studies used data collected from mother-child pairs followed in Mexico City, with measurements of total fluoride exposure at various time points obtained from urine samples starting in pregnancy. Both studies found that higher total fluoride exposure in pregnancy is related to worse outcomes in children. Specifically, the researchers found lower IQs and increased ADHD symptoms in the children whose mothers had the higher total fluoride exposures.

A third study by Till et al. published in late 2018, also funded by the U.S. government, found that the total fluoride exposures of Canadian pregnant women in fluoridated cities are very similar to those of the mothers in the Bashash et al. studies. It also found that pregnant women in Canadian fluoridated cities have double the fluoride exposure as compared those in unfluoridated cities and that drinking water is the major source of fluoride exposure for pregnant women in Canada.

Public Health Ontario's review of the 2017 Bashash el al IQ study entitled *Article Review on "Prenatal Fluoride Exposure and Cognitive Outcomes in Children at 4 and 6–12 Years of Age in Mexico"* (https://www.publichealthontario.ca/-/media/documents/fluroide-iq-mexico.pdf?la=en) stated that:

- *"Previous research in the area of fluoride exposure and neurological outcomes during childhood has often been limited by small sample sizes and/or ecological study designs. The study by Bashash et al. is a considerable improvement over previous research given the large*

population size and the availability of individual level data to assess both exposure and outcome."

- *"…a 0.5mg/L increase in maternal urinary fluoride was associated with a decrease in GCI of 3.15 points (95% CI: -5.42,-0.87), and a decrease in IQ of 2.50 points (95%CI: -4.12, -0.59)."*

- *"The authors used linear regression, adjusting for a number of potential confounders…"*

- *"Another strength of the study design is that exposure was measured during what is perhaps the most vulnerable window of neurological development in children, the prenatal period...."*

Description of Requested Items:

Primary, peer-reviewed scientific research studies on fluoride exposure during pregnancy, showing that fluoride exposure during pregnancy is safe with respect to IQ and ADHD symptoms in human offspring, in the City's possession (for example: downloaded to a computer, printed in hard copy, contained in an email attachment, etc.).

[If any records match the above description and are currently available to the public elsewhere, please provide enough information about each record so that the public may identify and access each record with certainty (i.e. title, author(s), date, journal, where the public may access it).]

Format:
Pdf documents sent to me via email; I do not want anything shipped to me.

Contact Information:
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Phone: XX
Email: XX

Relevant Keywords to Assist with the Search:

fluoride
fluoridation
pregnancy
fetal
prenatal
neurological
development
IQ
intelligence
children
offspring
brain

ADHD
behaviour
science
controlled
study

Best wishes,
Christine Massey, M.Sc.

ISC: Confidential

July 26, 2019

Our file #: 2019-G-0187

Christine Massey
#221 – 93 George St. S.
Brampton, Ontario L6Y 1P4

Subject: Final Response to FOIP Request

This is in response to your request for access to information to The City of Calgary, in accordance with the *Freedom of Information and Protection of Privacy Act* (FOIP Act).

Please find enclosed records responsive to your request. This office will not provide additional copies of these records.

The enclosed records are released under your access to information request, without exception to disclosure.

Section 65 of the FOIP Act provides that an applicant may make a written request to the *Office of Information and Privacy Commissioner* (OIPC) of Alberta to review this decision. You have 60 days from the date of this notice to request a review. A request for review is sent to:

Office of the Information & Privacy Commissioner
#410, 9925 – 109 Street
Edmonton, Alberta T5K 2J8

The *Request for Review* form is available under the Resources tab on the Commissioner's website www.oipc.ab.ca or you can call 1-888-878-4044 to request a copy.

Section 67(1) of the FOIP Act requires the OIPC to provide a copy of a request for review to The City of Calgary and other parties who may be affected by the review. Please ensure that the request for review does not contain information that you do not wish to share.

For all future correspondence or inquiries, I may be reached at 403-476-4117 or by email at eugene.mcgarrigle@calgary.ca.

Sincerely,

Eugene McGarrigle,
Analyst, Access and Privacy
City Clerk's
City of Calgary

The city's non-responsive enclosure begins on the next page. It is 39 pages in length, and every single page is marked "*Non-Responsive*" in the bottom left-hand corner.

The enclosure consists of a narrow and biased Evidence Review published by Public Health Ontario (PHO) in 2018, and PHO's review of the 2017 Bashash et al. IQ study (which indicates lowered IQs), and the 2015 Newsweek article by Douglas Main *("Fluoridation May Not Prevent Cavities, Scientific Review Shows*"). None of these documents cite a single responsive study.

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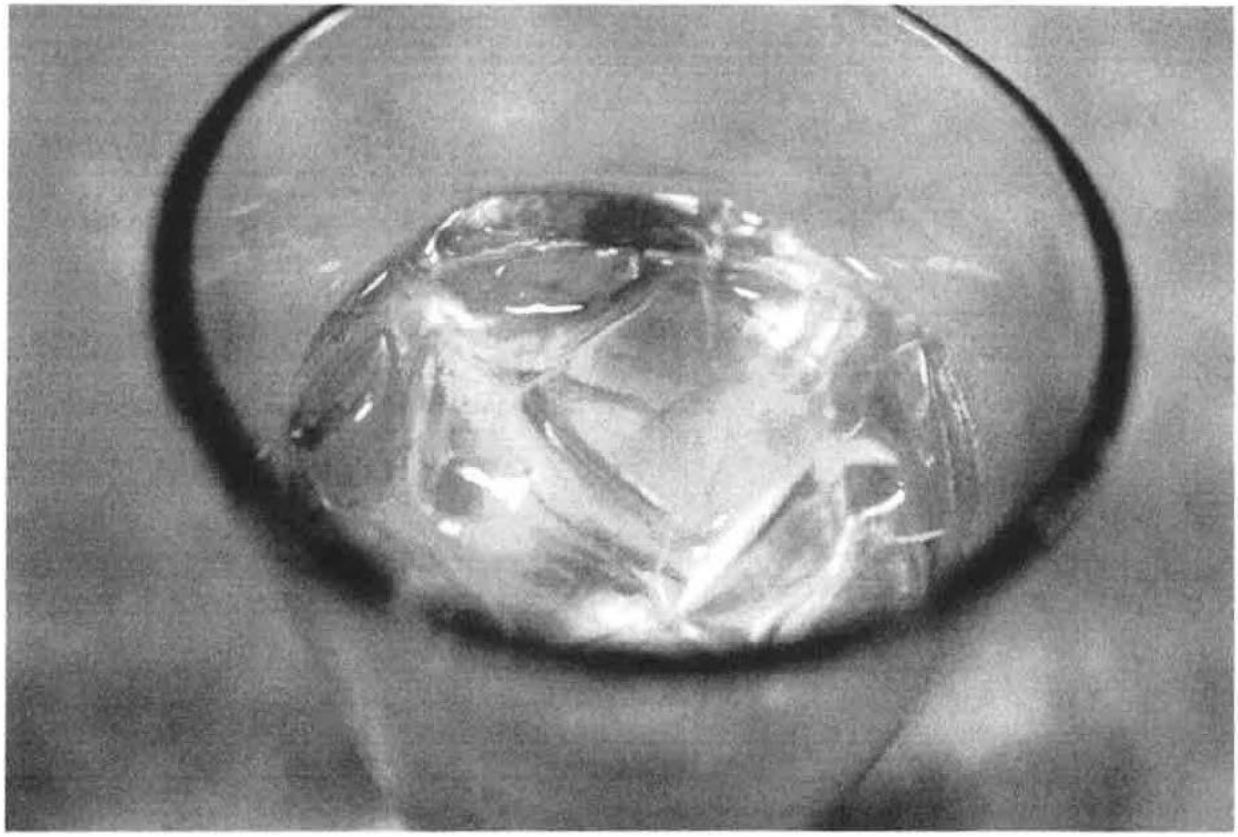
TECH & SCIENCE

FLUORIDATION MAY NOT PREVENT CAVITIES, SCIENTIFIC REVIEW SHOWS

BY DOUGLAS MAIN ON 6/29/15 AT 2:57 PM



There is little recent or high-quality evidence that fluoridation reduces tooth decay, according to a review.

SHANNON STAPLETON / REUTERS

Non-Responsive

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TECH & SCIENCE WATER FLUORIDATION PUBLIC HEALTH

If you're like two-thirds of Americans, fluoride is added to your tap water for the purpose of reducing cavities. But the scientific rationale for putting it there may be outdated, and no longer as clear-cut as was once thought.

Water fluoridation, which first began in 1945 in Grand Rapids, Michigan, and expanded nationwide over the years, has always been controversial. Those opposed to the process have argued—and a growing number of studies have suggested—that the chemical may present a number of health risks, for example interfering with the endocrine system and increasing the risk of impaired brain function; two studies in the last few months, for example, have linked fluoridation to ADHD and underactive thyroid. Others argue against water fluoridation on ethical grounds, saying the process forces people to consume a substance they may not know is there—or that they'd rather avoid.

Despite concerns about safety and ethics, many are content to continue fluoridation because of its purported benefit: that it reduces tooth decay. The Centers for Disease Control and Prevention's Division of Oral Health, the main government body responsible for the process, says it's "safe and effective."

You might think, then, that fluoridated water's efficacy as a cavity preventer would be proven beyond a reasonable doubt. But new research suggests that assumption is dramatically misguided; while using fluoridated toothpaste has been proven to be good for oral health, consuming fluoridated water may have no positive impact.

The Cochrane Collaboration, a group of doctors and researchers known for their comprehensive reviews—which are widely regarded as the gold standard of scientific rigor in assessing effectiveness of public health policies—recently set out to find out if fluoridation reduces cavities. They reviewed every study done on fluoridation that they could find, and then winnowed down the collection to only the most comprehensive, well-designed and reliable papers. Then they analyzed these studies' results, and published their conclusion in a review earlier this month.

The review identified only three studies since 1975—of sufficient quality to be included—that addressed the effectiveness of fluoridation on tooth decay in the population at large. These

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papers determined that fluoridation does not reduce cavities to a statistically significant degree in permanent teeth, says study co-author Anne-Marie Glenny, a health science researcher at Manchester University in the United Kingdom. The authors found only seven other studies worthy of inclusion dating prior to 1975.

The authors also found only two studies since 1975 that looked at the effectiveness of reducing cavities in baby teeth, and found fluoridation to have no statistically significant impact here, either.

The scientists also found "insufficient evidence" that fluoridation reduces tooth decay in adults (children excluded).

"From the review, we're unable to determine whether water fluoridation has an impact on caries levels in adults," Glenny says. ("Tooth decay," "cavities" and "caries" all mean the same thing: breakdown of enamel by mouth-dwelling microbes.)

"Frankly, this is pretty shocking," says Thomas Zoeller, a scientist at UMass-Amherst uninvolved in the work. "This study does not support the use of fluoride in drinking water." Trevor Sheldon concurred. Sheldon is the dean of the Hull York Medical School in the United Kingdom who led the advisory board that conducted a systematic review of water fluoridation in 2000, that came to similar conclusions as the Cochrane review. The lack of good evidence of effectiveness has shocked him. "I had assumed because of everything I'd heard that water fluoridation reduces cavities but I was completely amazed by the lack of evidence," he says. "My prior view was completely reversed."

"There's really hardly any evidence" the practice works, Sheldon adds. "And if anything there may be some evidence the other way." One 2001 study covered in the Cochrane review of two neighboring British Columbia communities found that when fluoridation was stopped in one city, cavity prevalence actually went down slightly amongst schoolchildren, while cavity rates in the fluoridated community remained stable.

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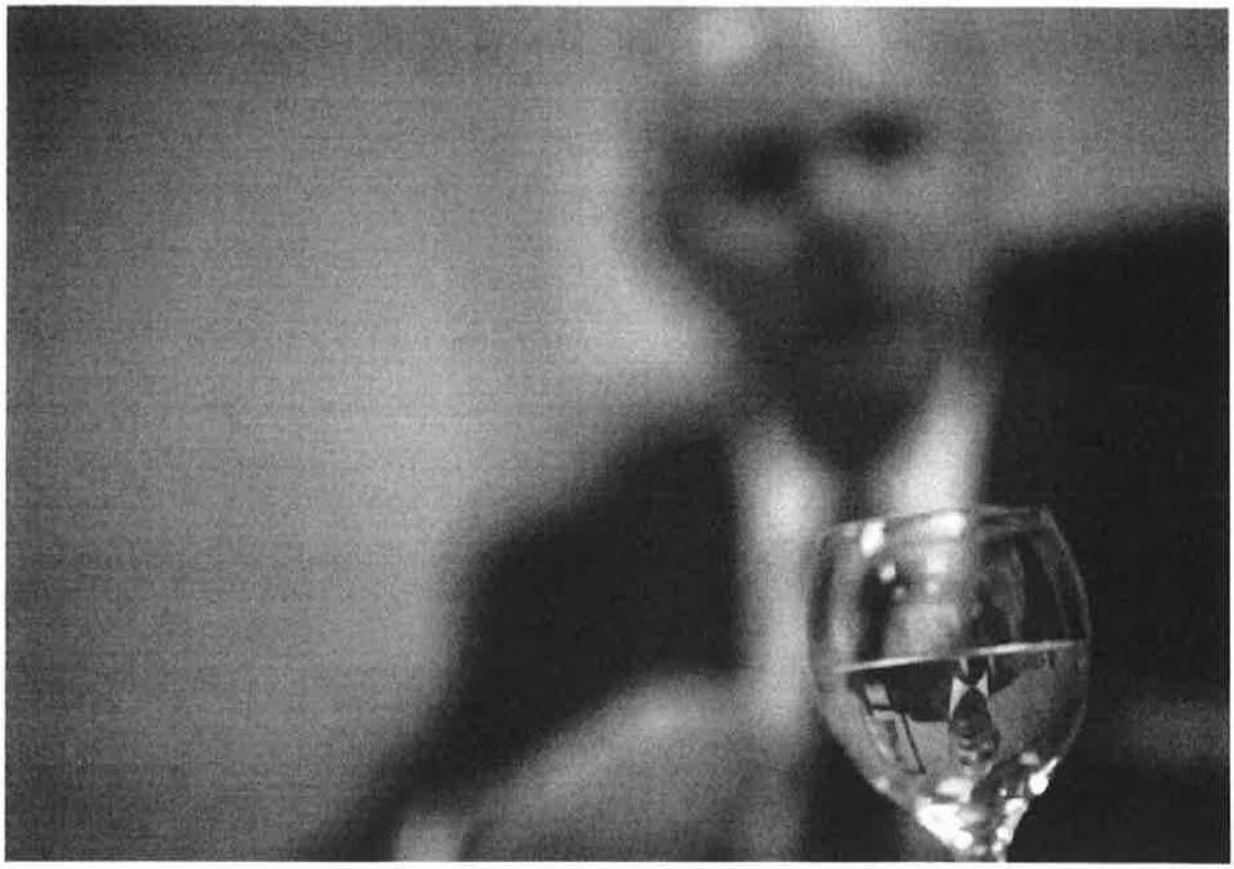

NACHO DOCE / REUTERS

Overall the review suggests that stopping fluoridation would be unlikely to increase the risk of tooth decay, says Kathleen Thiessen, a senior scientist at the Oak Ridge Center for Risk Analysis, which does human health risk assessments of environmental contaminants.

"The sad story is that very little has been done in recent years to ensure that fluoridation is still needed [or] to ensure that adverse effects do not happen," says Dr. Philippe Grandjean, an environmental health researcher and physician at Harvard University.

The scientists also couldn't find enough evidence to support the oft-repeated notion that fluoridation reduces dental health disparities among different socioeconomic groups, which the CDC and others use as a rationale for fluoridating water.

"The fact that there is insufficient information to determine whether fluoridation reduces social inequalities in dental health is troublesome given that this is often cited as a reason for fluoridating water," say Christine Till and Ashley Malin, researchers at Toronto's York University.

Non-Responsive

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Studies that attest to the effectiveness of fluoridation were generally done before the widespread usage of fluoride-containing dental products like rinses and toothpastes in the 1970s and later, according to the recent Cochrane study. So while it may have once made sense to add fluoride to water, it no longer appears to be necessary or useful, Thiessen says.

It has also become clear in the last 15 years that fluoride primarily acts topically, according to the CDC. It reacts with the surface of the tooth enamel, making it more resistant to acids excreted by bacteria. Thus, there's no good reason to swallow fluoride and subject every tissue of your body to it, Thiessen says.

Another 2009 review by the Cochrane group clearly shows that fluoride toothpaste prevents cavities, serving as a useful counterpoint to fluoridation's uncertain benefits. Another study that year which tracked the fluoride consumption of more than 600 schoolchildren in Iowa showed there was no significant link between fluoride ingestion and tooth decay.

Across all nine studies included in the review looking at caries reductions in children's permanent choppers, there was evidence linking fluoridation to 26 percent decline in the prevalence of decayed, missing or filled permanent teeth. But the researchers say they have serious doubts about the validity of this number. They write: "We have limited confidence in the size of this effect due to the high risk of bias within the studies and the lack of contemporary evidence." Six of the nine studies were from before 1975, before fluoride toothpaste was widely available.

The review also found fluoridation was associated with a 14 percent increase in the number of children without any cavities. But more than two-thirds percent of the studies showing this took place more than 40 years ago, and are not of high quality.

Nearly all these papers were flawed in significant ways. For example, 70 percent of the cavity-reducing studies made no effort to control for important confounding factors such as dietary sources of fluoride other than tap water, diet in general (like how much sugar they consumed) or ethnicity.

When it comes to fluoridation research, even the best studies are not high quality. Although this was already well-established, it doesn't seem to be well-known.

"I couldn't believe the low quality of the research" on fluoridation, Sheldon says.

The data suggest that toothpaste, besides other preventative measures like dental sealants, flossing and avoiding sugar, are the real drivers in the decline of tooth decay in the past few

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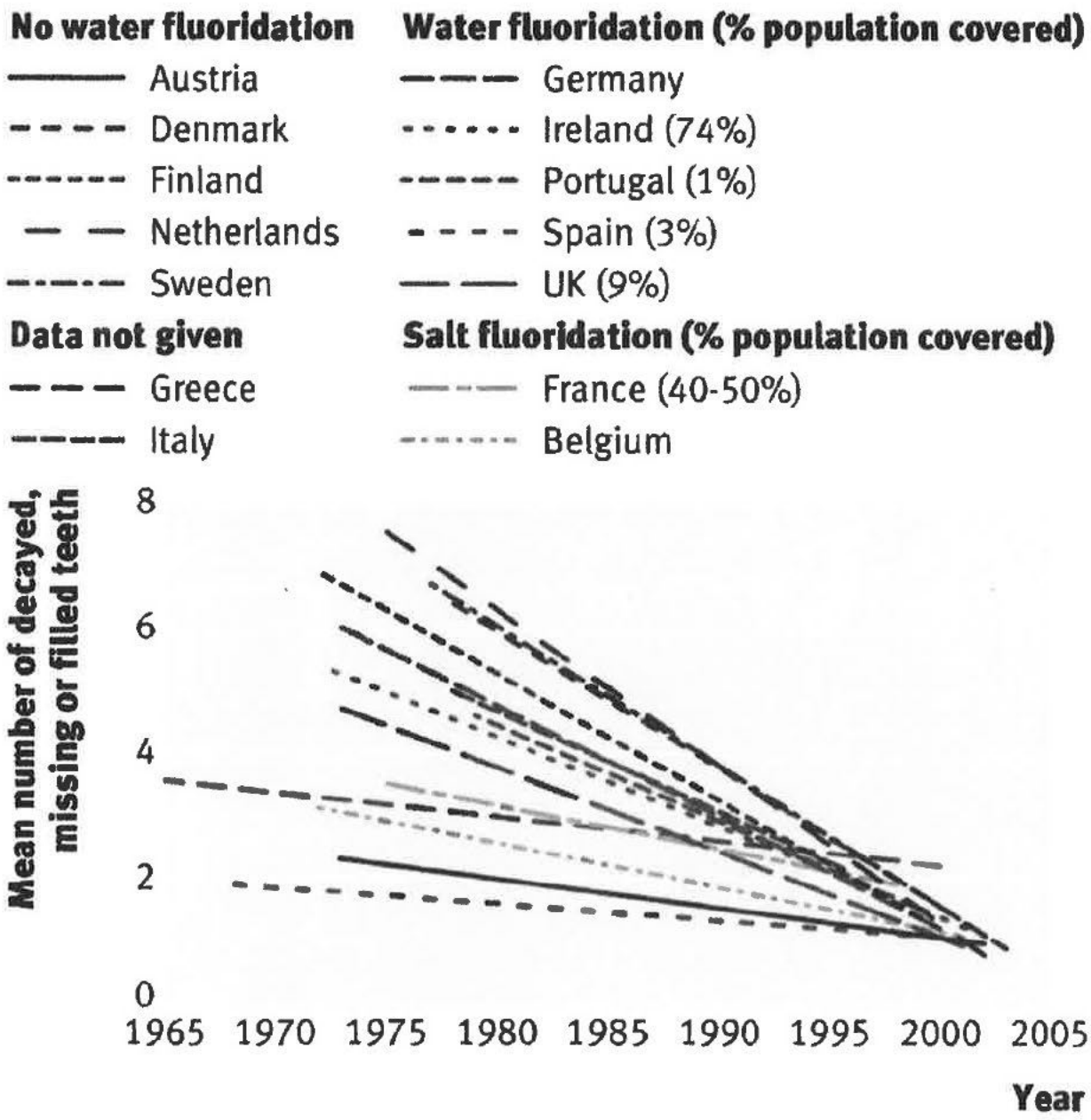
decades, Thiessen says. Indeed, cavity rates have declined by similar amounts in countries with and without fluoridation.



Rates of cavities have declined by similar amounts in countries with and without fluoridation.

KK CHENG ET AL / BMJ

Meanwhile, dental health leaves much to be desired in widely fluoridated America: About 60 percent of American teenagers have had cavities, and 15 percent have untreated tooth decay.

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One thing the review definitively concluded: Fluoridation causes fluorosis.

This condition occurs when fluoride interferes with the cells that produce enamel, creating white flecks on the teeth. On average, about 12 percent of people in fluoridated areas have fluorosis bad enough that it qualifies as an "aesthetic concern," according to the review. According to Sheldon, that's a "huge number." A total of 40 percent of people in fluoridated areas have some level of fluorosis, though the majority of these cases are likely unnoticeable to the average person.

In a smaller percentage of cases, fluorosis can be severe enough to cause structural damage, brown stains and mottling to the tooth.

Sheldon says that if fluoridation were to be submitted anew for approval today, "nobody would even think about it" due to the shoddy evidence of effectiveness and obvious downside of fluorosis.

There is also a definite issue of inequality when it comes to fluorosis. Blacks and Mexican-Americans have higher rates of both moderate and severe forms of the condition. Blacks also have higher levels. As of 2004, 58 percent of African-Americans had fluorosis, compared to 36 percent of whites, and the condition is becoming more common.

The Cochrane review concerned itself only with oral health. It didn't address other health problems associated with fluoride, which Grandjean says need to be researched.

Many of the Cochrane study's conclusions conflict with statements by the CDC, the American Dental Association and others that maintain fluoridation is safe and effective. The ADA, for example, maintains on its website that "thousands of studies" support fluoridation's effectiveness—which is directly contradicted by the Cochrane findings. The ADA didn't immediately respond to requests for comment.

The CDC remains undeterred. "Nothing in the Cochrane review" reduces the government's "confidence in water fluoridation as a valuable tool to prevent tooth decay in children as well as adults," says Barbara Gooch, a dental researcher with CDC's Division of Oral Health.

The CDC and others "are somehow suspending disbelief," Sheldon says. They are "all in the mindset that this is a really good thing, and just not accepting that they might be wrong." Sheldon and others suggest pro-fluoridation beliefs are entrenched and will not easily change, despite the poor data quality and lack of evidence from the past 40 years.

Derek Richards, the editor of the journal *Evidence-Based Dentistry* (published by the prestigious Nature group) concedes that "we haven't got any current evidence" that fluoridation

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reduces cavities, "so we don't know how much it's reducing tooth decay at the moment," he says. "But I have no qualms about that." Richards reasons that because fluoridation may help reduce cavities in those who don't use toothpaste or take other preventative measures, including many in lower socioeconomic groups, it's likely still useful. He also argues that there's no conclusive evidence of harm from fluoridation (other than fluorosis), so he doesn't see a large downside.

But most scientists interviewed for this article don't necessarily think fluoridation's uncertain benefits justify its continuation without more stringent evidence, and argue for more research into the matter.

"When you have a public health intervention that's applied to everybody, the burden of evidence to know that people are likely to benefit and not to be harmed is much higher, since people can't choose," Sheldon says. Everybody drinks water, after all, mostly from the tap. "Public health bodies need to have the courage to look at this review," says Sheldon, "and be honest enough to say that this needs to be reconsidered."

Public Health Ontario | Santé publique Ontario

ARTICLE REVIEW

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

Article Summary

The article by Bashash et al.,[1] published in *Environmental Health Perspectives* on September 19, 2017, describes a longitudinal birth cohort study that followed children from the prenatal period through to school age to assess the relationship between environmental fluoride exposures prenatally and in early life with cognitive outcomes during childhood. Fluoride exposure was assessed through urine taken from the mother during pregnancy (prenatal exposure) and from the child. Cognitive performance was assessed through standardized testing at preschool (4 years) and school age (6-12 years).

The study was conducted in Mexico City and used stored samples from cohorts set up as part of previous research studies. The environmental sources of fluoride for this population include fluoridated salt (250 ppm) and naturally occurring fluoride in drinking water (estimated range: 0.15-1.38 mg/L). Mexico City does not fluoridate their drinking water. Mothers were recruited during the first trimester of pregnancy across two birth cohort studies during the periods 1997-2001 (cohort '2A') and 2001-2006 (cohort '3'). Cohort 3 was a randomized double-blind placebo-controlled trial in which approximately half (334 out of 670 participants) of the study population received calcium supplements during pregnancy. Cohort 2A was an observational birth cohort designed to examine the influence of lead during pregnancy (327 participants).

Urine was collected from mothers up to three times during the study (once during each trimester of pregnancy) and from children at the time of their final cognitive performance assessment at 6-12 years. Many of the mothers did not provide a urinary fluoride for all trimesters. Creatinine-adjusted urinary fluoride concentrations and urinary fluoride values corrected for specific gravity were calculated for mothers and children, respectively. The authors found no correlation (p-value < 0.44) between maternal and childhood urinary fluoride concentrations. Creatinine-adjusted urinary fluoride concentrations were available for 512 mothers.

The authors measured cognitive performance at 4 years using the McCarthy Scales of Children's Abilities (measuring General Cognitive Index, GCI). Complete GCI and covariate data were available for 287 children. The authors measured cognitive performance at 6-12 years using the Wechsler Abbreviated Scale of Intelligence (measuring IQ). Complete IQ and covariate data were available for 211 children. The authors found a significant correlation (p-value < 0.01) between standardized testing scores at preschool and school age.

The authors used linear regression, adjusting for a number of potential confounders, to examine the relationship between fluoride exposure and cognitive performance. The authors found that a 0.5mg/L

increase in maternal urinary fluoride was associated with a decrease in GCI of 3.15 points (95% CI: -5.42,-0.87), and a decrease in IQ of 2.50 points (95%CI: -4.12, -0.59). The association with GCI appeared linear across the complete range of maternal exposures while there was no clear association with IQ below maternal urinary fluoride concentrations of 0.8 mg/L. The authors found that a 0.5mg/L increase in child urinary fluoride was associated with a decrease in IQ of 0.77 (95%CI: -2.53, 0.99).

The authors conclude this study by stating:

"Our findings must be confirmed in other study populations, and additional research is needed to determine how the urine fluoride concentrations measured in our study populations are related to fluoride exposures resulting from both intentional supplementation and environmental contamination."

Public Health Ontario Assessment

STRENGTHS

Previous research in the area of fluoride exposure and neurological outcomes during childhood has often been limited by small sample sizes and/or ecological study designs. The study by Bashash et al. is a considerable improvement over previous research given the large population size and the availability of individual level data to assess both exposure and outcome.

Another strength of the study design is that exposure was measured during what is perhaps the most vulnerable window of neurological development in children, the prenatal period.

This study measured fluoride exposure through a well established method that was first published in 2011.[2] The study also measured cognitive performance through well established methods.

LIMITATIONS

The study population was comprised of two cohorts (referred to as "Cohort 2A" and "Cohort 3") that were both recruited from hospitals in Mexico City that *serve low-to-moderate income populations*. This recruitment strategy has the potential to result in selection bias.

This study did not measure, or try to identify, environmental sources contributing to total fluoride exposure. There is no information on the contribution of drinking water and fluoridated salt to total fluoride intake, and there is also no information on other potential dietary sources of fluoride (e.g. consumption of foods high in fluoride or swallowing of toothpaste).

The study used two labs for urine analysis, and for one of these labs there was substantial data loss based on quality control criteria (305 out of 1,484 samples). This is unusually high but it is difficult to understand how this might have impacted the study results without additional details.

It is unclear why data outliers were excluded from the analysis. The authors also do not report the proportion of data that was excluded for this reason.

There was an attempt to adjust for maternal lead in this study, by measuring and adjusting for maternal bone lead levels. Bone lead is an excellent measure of long-term exposure to lead, but for a study such as this it would be preferable to have measured blood lead given that the interest is in circulating lead that would have the potential to cross the placenta and negatively affect neurological development in utero. Given the environmental levels of lead that would be present during the study period, and the well established link between lead and neurological outcomes in children, there is potential for

unmeasured confounding. The study is also lacking data on other environmental exposures that could potentially confound the association between fluoride and cognitive performance, such as iodine and arsenic.

There were differences in the distribution of covariates between the two study cohorts, and the authors note that this might have resulted in potential biases. For example, participants in cohort 2A had higher mean bone lead levels (p-value 0.001) than participants in cohort 3. There were also differences between participants with and without missing data. For example, mean levels of maternal blood mercury for those included in the cognitive performance assessments were 28.5% (at age 4) and 24.9% (at age 6-12) higher compared with those who were excluded from cognitive assessments due to missing data.

Finally, the external validity (or generalizability) beyond the cohort to areas with markedly different socio-economic, cultural and environmental circumstances (e.g. Ontario) is limited.

Biological Plausibility

As an observational study, the article is not able to provide insight into possible mechanisms behind the association observed. There is good evidence that low doses of non-essential elements may have adverse effects on health. A large body of evidence links relatively low level exposure to lead and methyl mercury to neurotoxicity and adverse effects on neurocognitive development at the population level. A similar body of evidence does not exist for fluoride.

The US National Academy of Sciences (NAS), in a 2006 review on fluoride in drinking water, made reference to Chinese studies reporting IQ deficits in children exposed to fluoride at 2.5 to 4 mg/L in drinking water and concluded they lacked sufficient detail to assess their quality and relevance to the US population.[3] Reference was also made to animal studies reporting behavioural changes after administration of fluoride, although the changes were not large in magnitude. The NAS found studies on molecular, cellular and anatomical changes in the nervous system after fluoride exposure more compelling. The NAS review called for more research on the effects of fluoride on intelligence, brain chemistry and function. The current article can viewed as a part of the research effort recommended by the NAS.

Key Messages from the Article

- This is an important area for research given the level of public concern around the use of fluoride as a public health intervention to improve dental health. This article adds to our growing knowledge in this area.
- The study is methodologically better than many others in the literature and incorporates individual level, rather than ecological, exposure assessment. However, not all potential confounders were fully addressed and this remains a possible explanation for the association found.
- The study population in Mexico City does not receive fluoridated drinking water although fluoride is added to salt in Mexico. Although we do not have urinary fluoride levels specifically for pregnant women in Canada, the urinary fluoride levels found in the study are within the range that may be found in some individuals in Canadian communities with fluoridated water supplies (or in some individuals without fluoridated water but with other sources of fluoride exposure).

- The study did not find any clear relationship between IQ and urinary fluoride levels less than 0.8 mg/L. Whether or not this reflects a threshold for effect is unclear.
- Given the socio-economic, cultural and environmental differences between the study population in Mexico City and residents of Ontario communities, caution should be exercised in generalizing the results beyond cohort studied.
- This study should be viewed in the context of a growing body of literature which investigates possible relationships between low dose fluoride exposure and possible effects on neurocognitive development. While many published studies have reported an association, considered individually, there are at present, no methodologically strong studies of direct relevance to Ontario.

References

1. Bashash M, Thomas D, Hu H, Martinez-Mier EA, Sanchez BN, Basu N, et al. Prenatal fluoride exposure and cognitive outcomes in children at 4 and 6-12 years of age in Mexico. Environ Health Perspect. 2017;125(9):097017. Available from: https://ehp.niehs.nih.gov/wp-content/uploads/2017/09/EHP655.alt_.pdf

2. Martínez-Mier EA, Cury JA, Heilman JR, Katz BP, Levy SM, Li Y, et al. Development of gold standard ion-selective electrode-based methods for fluoride analysis. Caries Res. 2011;45(1):3-12. Available from: https://www.karger.com/Article/FullText/321657

3. National Research Council. Fluoride in drinking water: a scientific review of EPA's standards. Washington, DC: The National Academies Press; 2006. Available from: https://www.nap.edu/read/11571/chapter/1

Non-Responsive

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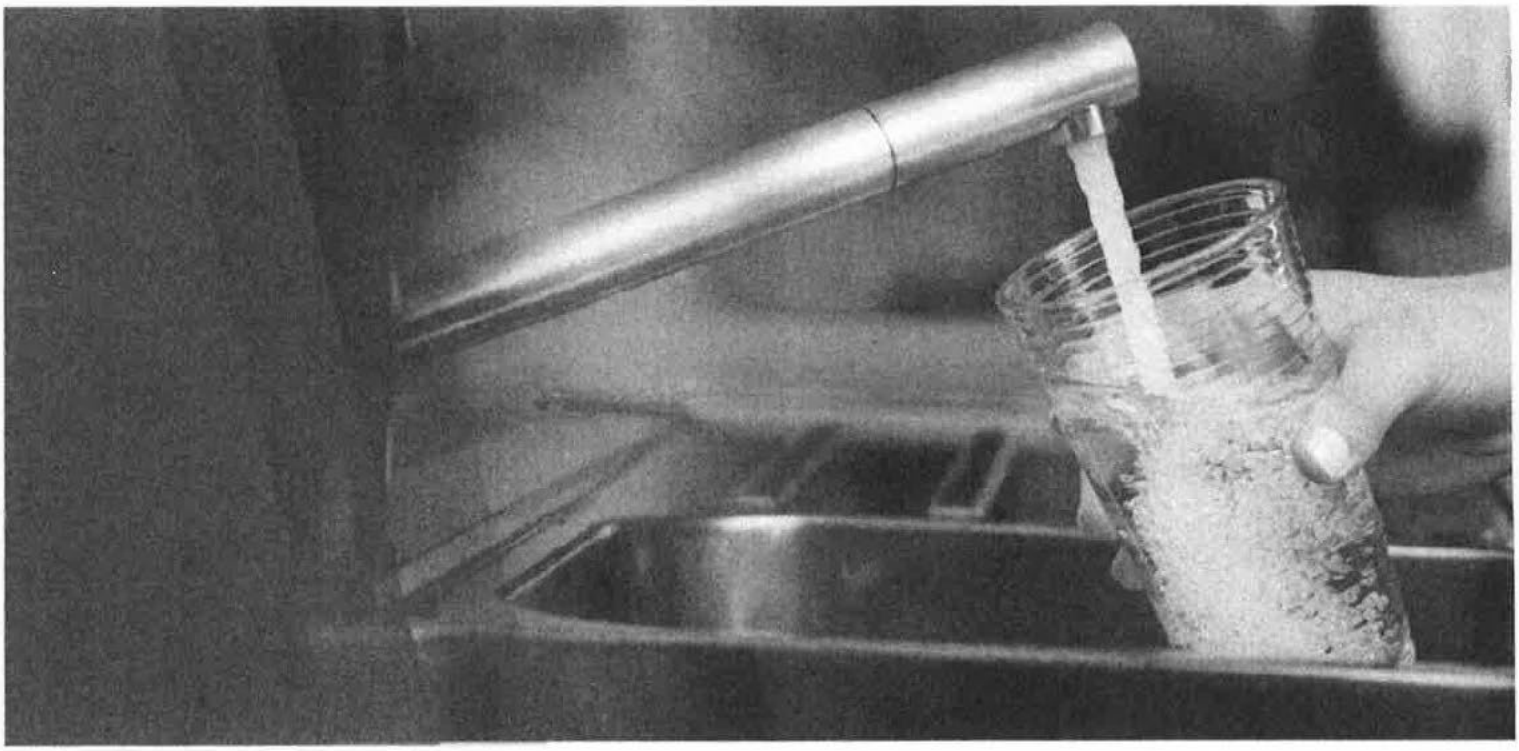
Public Health Ontario acknowledges the financial support of the Ontario Government.

Ontario
Agency for Health Protection and Promotion
Agence de protection et de promotion de la santé

Public Health Ontario | Santé publique Ontario

Evidence Review for Adverse Health Effects of Drinking Optimally Fluoridated Water (2010-2017)



October 2018

Public Health Ontario

Public Health Ontario is a Crown corporation dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, frontline health workers and researchers to the best scientific intelligence and knowledge from around the world.

Public Health Ontario provides expert scientific and technical support to government, local public health units and health care providers relating to the following:

- communicable and infectious diseases
- infection prevention and control
- environmental and occupational health
- emergency preparedness
- health promotion, chronic disease and injury prevention
- public health laboratory services

Public Health Ontario's work also includes surveillance, epidemiology, research, professional development and knowledge services. For more information, visit publichealthontario.ca.

How to cite this document:

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Evidence review for adverse health effects of drinking optimally fluoridated water: evidence since the 2010 Health Canada fluoride document. Toronto, ON: Queen's Printer for Ontario; 2018.

ISBN: 978-1-4868-2722-0

Public Health Ontario acknowledges the financial support of the Ontario Government.

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The application and use of this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.

Contents

Key Messages

- The existing literature (to May 10, 2017) indicates that mild dental fluorosis (generally unnoticeable white specks on teeth) is the only adverse effect experienced from the consumption of optimally fluoridated water (Health Canada recommends the optimal level of fluoride in water at 0.7 mg/L).
- Infant formulas mixed with optimally fluoridated water may increase the chance of the mild form of dental fluorosis if they are the child's main food source. If prevention of the mild form of fluorosis is desired then infant formula can be occasionally mixed with low-fluoridated bottled water.
- If prevention of the mild form of fluorosis is desired, early exposure to other forms of fluoride including fluoride toothpaste, fluoride rinse, and fluoride supplements should be monitored.
- Considering the dose-response relationship between the fluoride exposure and health effects, as a practice consideration it is important to fluoridate water at the optimal concentration, where a suitable trade-off is achieved (benefits are maximized and adverse effects are minimized).

Background

To reduce the burden of dental decay, community water has been fluoridated in parts of North America for more than 70 years.[1] According to the US Centers for Disease Control, community water fluoridation (CWF) is considered one of the top 10 public health achievements of the 20th century.[2] According to a position statement released by the Public Health Agency of Canada (PHAC), the advantage of CWF is that it benefits all residents of a community, irrespective of their age, oral health behaviours, socioeconomic status, education, employment, or access to dental care, making it a truly equitable public health practice.[3]

Fluoride occurs naturally in water and its concentration can vary widely. In the United States (US), the natural level of fluoride in ground water varies from very low levels of less than 0.1 mg/L to over 4 mg/L.[4] Water fluoridation is a process of optimally adjusting the concentration of fluoride in community drinking water to help reduce tooth decay in the populations served. Health Canada recommends an optimal level of 0.7 mg/L and a maximum acceptable concentration of 1.5 mg/L. While the benefits of CWF in caries prevention are well documented,[5] there is ongoing public debate regarding the continuation of CWF, given the availability of fluoride from other sources and concerns about adverse health effects.[6]

In 2010, Health Canada developed the "Guidelines for Canadian Drinking Water Quality: Guideline Technical Document – Fluoride", to provide a better understanding about the different aspects related to fluoride including any adverse health effects.[7] This technical document from this point onward is referred to as the 2010 Health Canada fluoride document. The 2010 Health Canada fluoride document summarized findings from reports and studies published in or before 2010, focusing on both effectiveness and adverse health effects related to consumption of fluoridated water. The main adverse effects examined in the 2010 Health Canada fluoride document included dental fluorosis, skeletal effects, cancers, reproductive/developmental effects, mutagenicity/genotoxicity, neurobehavioral effects, and urolithiasis (kidney stones).[7]

The full-text 2010 Health Canada fluoride document is available from the Health Canada website.

Following the release of the 2010 Health Canada fluoride document, research has continued looking for any relationship between fluoridated community drinking water and adverse health effects.

Purpose

Based on a request from public health units in Ontario, the purpose of this report is to provide a summary of the 2010 Health Canada fluoride document findings (Appendix A) and new evidence on adverse health effects of optimally controlled fluoridated community drinking water on humans, published since then.

It is important to note that the 2010 Health Canada fluoride document included all studies irrespective of the fluoridation level and source, and included human as well as animal studies.

The scope of the present report is *optimally* controlled fluoridated community drinking water and *humans*. Therefore, content from the 2010 Health Canada fluoride document that is beyond the present scope is not described here.

Methods

Public Health Ontario (PHO) Library Services completed a database search on May 10, 2017. Four electronic databases were searched (Ovid MEDLINE, Embase, CINAHL, and Dentistry) for literature from January 1, 2009 to May 10, 2017. Key search terms included, but were not limited to: fluoridation, community water, infant formula, risk, fluorosis, bone and cancer. Duplicate references were removed. In addition, a grey literature search was conducted to identify organizational guidelines, reports and position statements published after the 2010 Health Canada fluoride document.

Peer reviewed published articles were eligible if they represented primary findings from any study design, or syntheses of existing literature. Articles evaluating the effect of naturally fluoridated water (where the fluoride concentrations vary significantly) were not considered, as the intent was to assess the effect of optimally controlled fluoridated water. Also, no studies assessing the effect of fluoridated salt or milk were included in this review. In addition, with the focus on adverse health effects, any study assessing the benefits or effectiveness of fluoride in terms of reducing dental decay, was excluded.

Nine hundred articles were identified and 29 were included: two systematic reviews,[5,8] 20 cross-sectional studies,[9-28] five prospective cohort studies,[29-33] and two case control studies.[34,35] All the included studies were observational in nature. The two included systematic reviews were appraised using the Health Evidence Quality Assessment Tool (HE).[36] The Newcastle-Ottawa Scale (NOS)[37] was used to assess the methodological quality of the observational studies (n=27).

The grey literature search for organizational guidelines, position statements, and reports yielded six documents; one each from the Public Health Agency of Canada (PHAC),[3] Health Services Ireland,[38] Public Health England (PHE),[39] American Dental Association,[40] the Centers for Disease Control and Prevention (CDC),[41] and the EU Scientific Committee on Health and Environmental Risks (EUSCHER).[42] The grey literature was not appraised.

Main Findings

Quality appraisal of included articles

All included articles from the peer review literature were appraised according to the criteria of the relevant quality appraisal tools used. Additional published critiques,[43,44] were considered to augment the quality assessment of two included articles.[18,20] No studies were removed based on their quality appraisal score. In general, the included studies accounted for key methodological parameters such as representativeness and size of the study sample, relevant confounders (such as age, gender etc.), assessment of outcome, and reported adequate follow up periods. However, due to the observational nature of the included studies and the risk factor being fluoride exposure exclusively through community water, it may be difficult to control for other forms of fluoride exposure in respective studies' participants. This is not a reporting issue, but a general limitation for such studies. Similarly, blinding was not possible due to the nature of exposure under consideration i.e., difficult to blind participants to fluoride exposure. Exposure in included studies was assessed either by record linkage or was self-reported. Self-report has the potential to introduce bias. Details about article screening and the quality appraisal scores are available upon request.

Organization of Findings

The evidence in this report is organized by adverse health outcomes that include: dental fluorosis, enamel opacities, hypo-mineralization, and bone health, cancers including bone cancers, reproductive, neurobehavioral effects, mutagenicity, hypothyroidism, and urolithiasis. Broadly, these outcomes align with the 2010 Health Canada fluoride document. For the purpose of comparison, this report includes the relevant background information from the 2010 Health Canada fluoride document for each outcome (see Appendix A).

Developmental defects of teeth

One Cochrane systematic review,[5] 12 primary studies, and two grey literature reports[3,39] assessed the effect of water fluoridation on developmental defects of teeth. Of the 12 primary studies, three each were conducted in Brazil[13,23,35] and England;[11,15,22] two each in Australia[10,26] and the US[16,24] and one each in Hong Kong[12], and Switzerland.[14]

DENTAL FLUOROSIS

Consistent with the 2010 Health Canada fluoride document, the prevalence of mild or worse forms of fluorosis continued to vary across recent studies.[13-15,22-24,26,35] Fluorosis presents as white specks on teeth and is generally unnoticeable.[3] Assessed by the Thylstrup Fejerskov (TF) index (the levels range from TF0 to TF5; Public Health England considers a level of TF3 as mild or mild to moderate), the two communities in Brazil, starting fluoridation (0.7 mg/L) in different years (in 1971 and 1997), observed the fluorosis prevalence among 12-year-olds (in 2007) at TF3 level as 0.67% and 1.51%, respectively. [13] In a study

done in Switzerland, 2.7% of 12-year-old children in a fluoridated community (0.8-1.0 mg/L) scored fluorosis level of TF3. [14] An Australian study showed approximately 9.9% of 8 to 12-year-old children who were exposed to fluoridated water during at least the first three years of life having a fluorosis level of TF2 or more. [26] Pretty et al. found that the prevalence of fluorosis at levels TF3 or greater was 10% in fluoridated communities of England. [15] The 2014 Public Health England's report (based on monitoring the effects of water fluoridation schemes on the health of people living in the areas covered) concluded that among 12-year-olds in fluoridated (1.0 mg/L) communities, the prevalence of TF2 was 9%; TF3 was 6%; and TF4 was 1%. [39]

Assessing fluorosis by the Dean's index (the levels are: normal, questionable, very mild, mild, moderate and severe), a Brazilian study reported 2.6% of 12-year-old children have a mild or moderate form of fluorosis in a fluoridated community.[35] Another Brazilian study reported approximately 10% having mild and 1.5% with moderate form of fluorosis among 12-year-old children regularly exposed to fluoridated water.[23] In a US study, 3.5% children had mild and 1.1% had moderate forms of fluorosis in a fluoridated community.[24] Bal et al. reported that in Australia, a water fluoridation concentration of 1.0 mg/L was associated with 6% mild and 1.5% moderate or severe forms of fluorosis among 7 to 11-year-old children.[10] Bal et al indicated that the relatively higher prevalence of fluorosis was related to the higher-than-optimal level of fluoride in drinking water and fluoridated toothpaste swallowing during early childhood. [10]According to the Cochrane systematic review, with a fluoride level of 0.7 mg/L in water, approximately 12% of people can have mild or worse dental fluorosis.[5]

Similar to the 2010 Health Canada fluoride document, a position statement from the Public Health Agency of Canada (2016) reported that the most likely adverse effect of CWF is mild dental fluorosis, which causes white specks on teeth and is generally unnoticeable.[3] In terms of levels, Health Canada (2010) concluded that a moderate level of dental fluorosis was the end-point of concern, and that the prevalence of very mild and mild dental fluorosis is of no concern. However, the Cochrane systematic review reported that mild or worse fluorosis might be an aesthetic concern.[5] Of note, the various sources of evidence are not consistent in defining the endpoint of concern when it comes to aesthetics (i.e. mild vs. moderate fluorosis).

In terms of self-perception about the aesthetic impact of dental fluorosis, a Swiss study by Buchel et al. reported that fluorosis in communities with fluoridated water did not represent an aesthetic problem nor a public health concern.[14] Interestingly, McGrady et al., in a UK study, found that teeth with a fluorosis level of TF1 and TF2 are ranked more favourably than TF0.[22] Fluorosis, not as an outcome but as an attribute, was studied by Joaloso et al., who found that the milder forms of fluorosis do not affect the eruption time of teeth. [16]

ENAMEL OPACITIES AND HYPO-MINERALIZATION

In regard to the developmental defects of enamel, enamel opacities and hypo-mineralization have been reported as adverse health effects.

A repeated cross-sectional study in Hong Kong assessed diffused enamel opacities on maxillary incisors using data from 1983, 1991, 2001 and 2010, when fluoridation levels were 1.0, 0.7, 0.5 and 0.5 mg/L,

respectively.[12] The prevalence of opacities for the four observed years was 89.3%, 48.5%, 32.4% and 42.1%. The prevalence decreased from 1983 to 2001, but increased again in 2010, although fluoridation levels remained the same. The authors concluded that this change did not fully correspond to the concentration of fluoride in the drinking water during the time of enamel development, but could be due to exposure to other forms of fluoride.[12]

A study conducted in Northern England reported an 11% prevalence of molar and incisor hypo-mineralization in the fluoridated community, and 17.5% in the non-fluoridated community.[11] A higher prevalence of developmental defects including hypo-mineralization in the non-fluoridated community could be the effect of both fluoride and/or non-fluoride factors. Fluoride exposure could be because of the "Halo effect", which is fluoride consumption in a non-fluoridated community from other sources such as foods and beverages manufactured using fluoridated water. Consumption of fluoridated toothpaste or fluoride supplements could also increase levels of systemic fluoride. Non-fluoride reasons could include physical injuries, systemic illnesses (for example, some neurological or endocrine disorders) or certain medications taken during childhood during the formative stage of tooth development, which can also result in such oral manifestations.[12]

Infant formula with fluoridated water and fluorosis

One systematic review from Australia,[8] two primary studies (Australia, the U.S.),[27,31] and two grey literature reports,[40,41] assessed the effect of fluoridated water used to reconstitute infant formula on dental fluorosis.

Higher fluoride intakes from reconstituted powdered formulas and other water-added beverages at the age of 3-9 months increased the risk of mild fluorosis.[27,31] Each 0.1 mg/L increase in fluoride level in the water that is mixed with infant formula was associated with a 5% increase in enamel fluorosis of any level.[8] The authors concluded that infant formula mixed with fluoridated water is potentially associated with an increased risk of developing enamel fluorosis.[8]

According to an expert panel convened in 2011 by the American Dental Association (ADA), dentists can continue to advise parents and/or caregivers to reconstitute infant formulas with optimally fluoridated water while being cognizant of the potential risks of enamel fluorosis development.[40] According to the CDC, if a child is consuming only infant formula mixed with fluoridated water, the chances of developing faint white markings of very mild or mild dental fluorosis on teeth may be increased.[41] The CDC advises the use of bottled water (low-fluoridated) sometimes instead of tap water (optimally fluoridated) to mix infant formula; it is important to note, "these bottled waters are labeled as de-ionized, purified, demineralized, or distilled, and without any fluoride added after purification treatment." [41] The Ontario Dental Association (ODA), citing both the ADA and the CDC, also states that if a "child is exclusively consuming infant formula reconstituted with fluoridated water, there may be an increased chance for mild enamel fluorosis, but enamel fluorosis does not affect the health of the child or the health of the child's teeth." [45]

Bone Health including skeletal fluorosis, bone mineral density, and fractures

Four primary studies, two from the US;[30,32] and one each from Canada[9] and Ireland,[19] and two grey literature reports[38,39] assessed the impact of water fluoridation on physical and structural properties of bone. One additional study conducted in Sweden[33] assessed the impact of fluoride in drinking water on hip fractures. We did not identify any studies released since the 2010 Health Canada fluoride document to comment on the association with skeletal fluorosis.

The Canadian study compared the fluoride content and structural or mechanical properties of bone between adults from Toronto (fluoridated community) and Montreal (never fluoridated), and found a weak relationship among fluoride exposure, accumulated fluoride, and the physical characteristics (density and compressive mechanical property) of bone.[9] The fluoride content of bone of Toronto residents was significantly higher ($p < 0.001$) than residents of Montreal; however, the range for the Toronto specimens fully included the range of the Montreal ones. Although, the mean density of cancellous cores of Toronto specimens (0.90 ± 0.04 g/cm^3) was significantly greater than Montreal (0.75 ± 0.05 g/cm^3), the density of cancellous cores in the study did not correlate closely with the fluoride content. Interestingly, a prospective US cohort study observed children from birth to adolescence, and performed gender-stratified analysis for 11-year-olds and found no associations between average daily fluoride intake and bone outcomes for girls (Spearman association between daily fluoride intake and DXA bone measures were $r = -0.01$ to 0.24), but found a non-significant positive association for boys (Spearman correlation of $r = 0.04$ to 0.24).[32] In addition, when observing the same cohort at 15 years of age, the same study found fluoride exposures do not have significant effects on bone mineral measures.[30] The authors noted the need for additional research to better understand the potential gender and age-specific effects of fluoride intake on bone development.[32]

A study in Ireland found no significant relationship between the proportion of households with a fluoridated water supply and bone health (index of bone stiffness calculated as a measure of bone mineral density).[19] The Ireland Health Services report also found no association between fluoridation of drinking water at the recommended levels and risk of bone fracture.[38] According to the report from Public Health England, "there was no evidence of a difference in the rate of hip fractures between fluoridated and non-fluoridated areas."[39] In the Swedish study, Nasman et al., found no association between chronic fluoride exposure from drinking water and the occurrence of hip fracture.[33]

Cancers including osteosarcoma

Five primary studies, two from England,[21,25] two from the US[28,34] and one in Ireland,[17] as well as two grey literature reports[39,42] assessed the effect of water fluoridation on bone cancers.

Findings from the primary studies were consistent with the 2010 Health Canada fluoride document. None of the recent studies found a relationship between fluoridation and incidence rates of osteosarcoma at any age.[17,21,25,28,34] Furthermore, Public Health England stated there was no evidence that osteosarcoma rates differed between fluoridated and non-fluoridated communities.[39] Also, Public

Health England stated there was no evidence for an association of fluoridated water consumption with bladder cancer and all cancers, in general. The EUSCHER report also concludes, "epidemiological studies do not indicate a clear link between fluoride in drinking water, and osteosarcoma and cancer in general".[42]

Reproductive/developmental effects

No peer-reviewed articles assessing the reproductive or developmental effects of fluoride in water were identified. Two grey literature reports discussed reproductive and developmental effects.[39,42]

The Public Health England report stated there was no evidence of a difference in the rate of Down's syndrome between fluoridated and non-fluoridated communities.[39] The EUSCHER concludes that fluoride at concentrations in drinking water permitted in the EU did not influence the reproductive capacity of males or females.[42]

Neurobehavioral effects

Two primary studies, one in New Zealand[29] and another in the US,[18] as well as one grey literature report[42] assessed the neurobehavioral effects of fluoridated water.

The recent New Zealand prospective cohort study detected no clear differences in IQs between the fluoride-exposed (mean (SD): 100.0 (15.1)) and non-exposed group (mean (SD): 99.8 (14.5)), suggesting that community fluoridated water is not neurotoxic. [29]

The US ecological study assessed the relationship between water fluoridation and Attention Deficit Hyperactivity Disorder (ADHD) among 4-17 year olds using administrative data.[18] The authors concluded that states with a greater proportion of people receiving fluoridated water from public water supplies had higher proportions of parents reporting medically-diagnosed ADHD among their children, which warrants future studies to explore this relationship further.[18] This study was critiqued by other researchers for methodological limitations including measurement error and no consideration for other potential explanatory variables (such as pre-term birth or exposure to tobacco, alcohol, arsenic or lead) apart from SES.[43] The results are advised to be interpreted with great caution due to high risk of ecological fallacy (water fluoridation measured at state level) and confounding bias.[43]
The EUSCHR report concluded that based on available human studies, fluoride in drinking water at levels permitted in the EU does not impair children's neurodevelopment.[42]

Mutagenicity/genotoxicity

No studies assessing the impact of community-fluoridated water on mutagenicity/genotoxicity were identified. Future studies may be helpful to understand any potential relationship.

Hypothyroidism

One study, conducted in England, assessed the association of fluoridated water and hypothyroidism. [20]

This study found that clinical practices located in fully-fluoridated areas are nearly twice as likely to

report high hypothyroidism prevalence in comparison to non-fluoridated areas.[20] This study was highly critiqued by scientists; Newton et al stated that the authors did not establish a clear prior hypothesis for the association, misrepresented the conclusions of the existing literature, did not adequately control for potential confounding variables, and categorised variables with arbitrary cut-offs that deviated from normal practice.[44]

Current literature does not provide enough evidence to assess the relationship between the consumption of fluoridated water and hypothyroidism. Future studies with greater methodological rigour will be helpful in this regard.

Kidney Stones/Urolithiasis

One grey literature report assessed the impact of optimally fluoridated water on kidney stones.[39] No peer-reviewed studies were identified.

According to the Public Health England report, there was strong evidence that the rate of kidney stones was lower in fluoridated communities than in non-fluoridated areas following adjustment for age, gender, deprivation and ethnicity.[39] Future studies may be helpful to further understand any potential association.

Discussion and Conclusion

This report is a summary of the evidence published since the 2010 Health Canada fluoride document to May 10, 2017 about the adverse health effects of optimally controlled fluoridated water, including the effects when mixed with infant formula.

Overall, the existing literature suggests that at an optimal concentration of water fluoridation, the only adverse health consequence observed is a mild form of dental fluorosis. As the timing and dosage of fluoride exposure is critical in attributing the severity of dental fluorosis, the results of such studies further emphasize that early exposure to other forms of fluoride, including fluoride toothpaste, should be monitored to reduce cumulative fluoride exposure. For example, fluorosis was observed in some non-fluoridated communities as well.

Always mixing infant formula with fluoridated water has been recognized to increase the potential for mild dental fluorosis. Both Canadian and American organizations including ODA, ADA, and the CDC recommend occasional use of low-fluoridated bottled water as an alternative instead of always using optimally fluoridated tap water.[45]

Attaining an optimal concentration of fluoride in community drinking water is considered crucial in establishing a trade-off between dental caries and dental fluorosis. A 2011 study by Frazão et al. analyzed the fluoride concentration in drinking water, taking into account the balance between the benefits and risks to health.[46] The authors concluded that fluoride levels should be between 0.6 and 0.9 mg/L in order to prevent dental caries, and that concentration > 0.9 mg/L presents a risk to the dentition among children under the age of 8 years.[46] The authors also concluded that, to reduce the proportion of children and adolescents with fluorosis levels of aesthetic significance, the water fluoridation levels should be in the range of 0.5 to 0.7 mg/L.

The 2010 Health Canada fluoride document states that there is no evidence to support a link between exposure to fluoride in drinking water at or below 1.5 mg/L and any adverse health effects such as any types of cancer, developmental defects, neurobehavioral effects, or genotoxicity.[7] The studies conducted and the organizational reports published after the 2010 Health Canada fluoride document and until May 10, 2017 corroborate these findings.

Considering that the studies included in this report assessed the impact of optimally fluoridated water and most of them were from countries that have similar demographic and socio-political environments, their findings can be generalized to the Canadian context. Health Canada recommends water fluoridation at 0.7 mg/L, which is much lower than the maximum acceptable concentration of 1.5mg/L; therefore, the likelihood of any adverse health consequences at this concentration is low.

Limitations

This report is based on a review of recent studies conducted across a range of jurisdictions. Not all

findings may be directly comparable to the Ontario context because of variations in exposures to other forms of fluoride, general oral health behaviours or access to the healthcare system, for example. In addition, our search focused on studies reported in the English language, which means some relevant literature could have been missed.

Implications for Practice

The fluoridation of community drinking water has been considered a safe and cost effective population-based approach to reduce dental decay. The current literature (to May 2017) has identified the mild form of dental fluorosis, which is not of health concern, as the only inadvertent effect of consuming drinking water fluoridated at optimal levels.

There is a dose-response relationship between fluoride exposure and health effects. Therefore, as a practice consideration, fluoridating water at an optimal concentration, where a suitable trade-off is achieved (benefits are maximized and adverse effects are minimized), is important.

The age of fluoride exposure is also an important consideration. Exposure during the first three to four years of life, during the formative stage of tooth development, is associated with increased fluorosis risk. As such, if a child is solely consuming infant formula, mixing it with low-fluoridated water on an occasional basis can reduce the risk of mild fluorosis. In addition, the consumption of fluoridated toothpastes and mouth rinses needs to be monitored.

The studies included in this report are those that were published until May 10, 2017. Evidence updates may be provided as new relevant evidence emerges.

Appendix A: Background from the 2010 Health Canada fluoride document

Developmental defect of teeth including dental fluorosis, enamel opacities, and hypo-mineralization

Dental Fluorosis

According to the literature synthesized in the 2010 Health Canada fluoride document, the "moderate level" of dental fluorosis (as per the Dean's index) is the end-point of concern and the prevalence of "very mild" and "mild" dental fluorosis is of no concern.[7] However, the 2010 Health Canada fluoride document also considers "mild" fluorosis or worse as dental fluorosis of aesthetic concern.

The risk for and severity of fluorosis is related to various aspects including the timing, dose and duration of fluoride intake (irrespective of the source).[7] The period for susceptibility to dental fluorosis is during the first three to four years of life. Prolonged periods of fluoride exposure during the formative stage of tooth development is associated with increased fluorosis risk; however, if higher exposure is limited to the first year of life and the following years have low exposure it may not be as much of a concern. A suitable trade-off between dental caries and dental fluorosis appears to occur around 0.7 mg/L. At this level, both caries experience and fluorosis severity appear to be lower than that seen at 1.0 mg/L.

In regards to the prevalence of mild or worse forms of fluorosis, the Canadian Health Measures Survey (2007 to 2009) from the 2010 Health Canada fluoride document, shows 12.0% dental fluorosis classified as Very Mild, 4.4% as Mild, and only 0.3% had Moderate or Severe fluorosis among children 6-11 years old.[7] As of 2008, 45.1% of Canadians had access to fluoridated water (usually at the level of 0.7 mg/L).

Infant formula with fluoridated water and fluorosis

Powdered infant formula reconstituted with fluoridated drinking water has a higher fluoride concentration than ready-to-use infant formulas. Among 7-12 month olds, if they are breastfed then the daily fluoride intake from food and beverages can be 0.017- 0.021 mg/kg-bw/day in a fluoridated community and 0.011- 0.012 mg/kg-bw/day in a non-fluoridated community.[7] For non-breastfed infants, the intake can be 0.024 - 0.026 mg/kg-bw/day in a fluoridated community, and 0.013 -0.014 mg/kg-bw/day in a non-fluoridated community.[7] Infant formulas with higher levels of fluoride can lead to an increased risk of mild dental fluorosis.

Bone Health including skeletal fluorosis, bone mineral density, and fractures

Skeletal fluorosis is an excessive accumulation of fluoride in bone resulting in increased bone density and outgrowths.[7] Studies in the 2010 Health Canada fluoride document did not show any correlation of water fluoridation and skeletal fluorosis at concentrations of 1.2 and 3.3–6.2 mg/L for 10 years or more.

Regarding fractures, studies showed exposure to fluoride concentrations at 1.0-1.5 mg/L was occasionally associated with a positive effect on bone mineral density; however, it did not significantly increase the risk of fractures.[7] Also, there was inconsistent evidence for an association between water fluoridation and increased risk of hip fracture, primarily because the incidence of hip fractures in several studies was too small to enable definitive conclusions about the risk of such fractures.[7]

Cancers including osteosarcoma

Reviews in the 2010 Health Canada fluoride document suggested no clear association between water fluoridation and overall cancer incidence including osteosarcoma.[7] Some major challenges were recognized in assessing fluoride exposure as a risk factor for osteosarcoma. Firstly, the incidence of osteosarcoma is so low that not many studies are able to capture the new cases in a study population; secondly, it is difficult to estimate precisely the fluoride intake because of multiple sources of fluoride exposure; and lastly, the method of measuring fluoride in bones of studies participants' is too invasive.[7]

Reproductive/developmental effects

Only a few studies in the 2010 Health Canada fluoride document assessed the link between fluoridated drinking water and reproductive or developmental effects. No associations were found between fluoride intake and spontaneous abortions, congenital cardiac disease, or stillbirths.[7] Infants exposed to fluoridated water supplies in utero were not at increased risk for sudden infant death syndrome (SIDS).[7] In addition, there was inconclusive evidence of an association between water fluoride level and Down's syndrome.[7]

Neurobehavioral effects

A number of studies from China in the 2010 Health Canada fluoride document measured the impact of fluoride on children's intelligence quotient (IQ).[7] The significance of these studies is uncertain and concern has been raised about their validity and generalizability, due to lack of methodological rigour and the dose of fluoride exposure (i.e., fluoride concentration of 4.12 mg/L) in those studies.[7]

Mutagenicity/genotoxicity

A study from China in the 2010 Health Canada fluoride document investigated the genotoxic risks of long-term ingestion of drinking water containing fluoride (0.2, 1.0, or 4.8 mg/L) in humans.[7] Results showed numerically small but significant differences; subjects with low fluoride in the water (0.2 mg/L) had higher sister chromatid exchange (SCE) frequencies than those with optimal (1.0 mg/L) or higher (4.8 mg/L) fluoride exposures. Reasons for the reduced SCE frequency in subjects with optimal higher

fluoride exposure were unclear; however, authors concluded that long-term exposure to fluoride in the drinking water, even at an elevated level, does not have genotoxic effects in humans.[7]

Hypothyroidism

As per the 2010 Health Canada fluoride document, fluoride may adversely affect endocrine glands such as the thyroid.[7] The effects of fluoride on thyroid function might depend on the intake of iodine, as there is an association of thyroid dysfunction with low iodine intake; however, in Canada, this is unlikely to occur because iodized salt is mandatory.

Kidney Stones/Urolithiasis

There were no studies in the 2010 Health Canada fluoride document that assessed the impact of optimally fluoridated water on the formation of kidney stones. Only studies from fluoride endemic areas (3.5 to 4.9 mg/L) found the prevalence of kidney stones was 4.6 times higher when compared to non-endemic areas.[7]

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