

Key points

- Epidemiological studies and independent reviews of the relevant medical and scientific literature have consistently failed to find evidence that fluoride in water at or around one part per million has any effect on the health of the body other than reducing tooth decay.
- Water fluoridation has been practised for almost 60 years, and, in addition, people

have drunk naturally fluoridated water for generations. Worldwide, over 400 million people consume fluoridated water, including the residents of 46 of the 50 largest US cities.

- Neither the York review, nor the Medical Research Council and other expert panels, found any evidence of adverse health effects.

Improvements to health

Oral health and general health are strongly linked. Eating, speaking and most social activities are dependent to some extent on good oral health. Fluoridation improves a population's oral health, and as a consequence its general health [1].

Tooth decay and its treatment are, at best, unpleasant for otherwise healthy individuals. However, for certain groups tooth decay or its treatment can present far more serious risks. Individuals suffering certain physical or mental disabilities are particularly vulnerable, and the cardiac status of children and adults with heart problems may be seriously affected by dental disease. Fluoridation of water supplies in socially deprived areas where tooth decay rates are generally high would significantly reduce decay rates and hence reduce the general health risks that the most vulnerable youngsters in those communities face.

No evidence of harmful effects

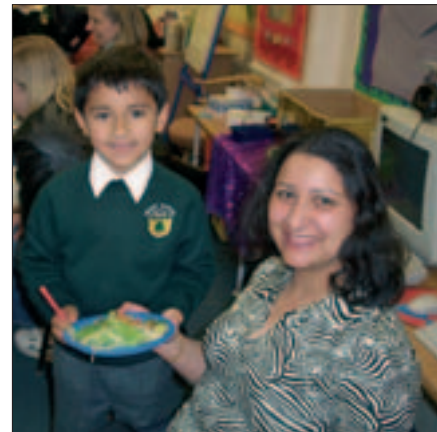
The main purpose of fluoridation is to reduce tooth decay which it does very effectively and, from all the available evidence, very safely. However, opponents of fluoridation claim that it might cause serious general health problems. It is important therefore for health agencies advocating fluoridation for the purpose of improving dental health to satisfy themselves that it is safe.

How nature showed the way

Fluoride is not a 'new' chemical in drinking water. It is naturally present at varying concentrations in all water supplies. In the United Kingdom natural concentrations are typically

lower than the 1 part per million (1ppm) which is recommended for dental health. However, some water supplies - for example in Hartlepool in the North East of England - have always had a natural fluoride concentration at about 1ppm - and supplies in parts of Essex used to contain even higher concentrations - up to nearly 6ppm - until the switch was made to different water sources.

In the early 1900s scientists were trying to find out why people living in certain areas had a particular type of mottling of the teeth. Eventually the link between the mottling and very high concentrations of fluoride in drinking water was made, and they called the mottling *dental fluorosis*. However, they also noticed that the people affected had remarkably low levels of tooth decay. Soon, they were able to establish that at one part per million, fluoride in water caused mottling of only minor cosmetic significance but did bring with it the benefit of improved dental health. This early work led to the suggestion that it might be possible to reproduce the benefits of nature by artificially adjusting the natural fluoride levels in drinking water to around 1ppm. So, starting with Grand Rapids in Michigan in 1945, a series of studies of artificial fluoridation in the United States and Canada were set up, and quickly provided evidence that this was indeed the case. The key question to ask, of course, is whether fluoride at this level could or does cause harm to other parts of the body. Again, the early research suggested that there was not a problem.



Good oral health is important for eating, speaking, and smiling

As described above, some communities have had more than a lifetime's exposure to naturally fluoridated water. Because the laws of chemistry dictate that fluoride ions in solution in water are identical whether they occur naturally in the water or are added artificially, it has long been believed that there is no difference in absorption of fluoride from naturally and artificially fluoridated water. However, to establish conclusively whether there was any difference, the UK Government asked the University of Newcastle to undertake a study. The results confirmed that there is no significant difference in the absorption of fluoride from naturally and artificially fluoridated water [2]. This confirmation is important because it means that evidence from populations such as Hartlepool, where water supplies have been naturally fluoridated at the right level for dental health (1 part of fluoride per million parts of water) for hundreds of years, and which have shown no increased risk of any adverse health effects, can be applied to populations receiving artificially fluoridated supplies.

In addition, artificial fluoridation has now been practised throughout the world for almost 60 years. Around 400 million people in at least 53 countries drink optimally fluoridated water - including two-thirds of the population of the United States. There is therefore a wealth of experience and evidence about the health effects of drinking fluoridated water.

How the facts have refuted allegations of harm

Despite a lack of scientific evidence, opponents of fluoridation have blamed it for a seemingly almost endless list of diseases. Numerous searching reviews of the safety of fluoridation have been unable to find any adequate grounds for these allegations of harm.

The most recent UK reviews of the evidence have been undertaken by the University of York's NHS Centre for Reviews and Dissemination (CRD) [3], and the Medical Research Council [4]. The York CRD review, published in September 2000, included 33 studies of a possible link between water fluoridation and possible adverse health effects. No evidence of a link with *any* adverse health effect - including cancer, bone fractures and Down's Syndrome - was found. However, York identified the need for more good quality research, so the Government asked the Medical Research Council to suggest where it might be possible to strengthen the evidence base.

The Medical Research Council (MRC) Water Fluoridation Working Group sought to move the debate forward and concentrated its efforts on those areas where there might be plausible scientific grounds for an association with ill health - bone health and cancer.

Bone health

Approximately half of the fluoride we take in is rapidly excreted in the urine; however almost all of the fluoride retained in our bodies is deposited in the bones and teeth. It is plausible therefore that any adverse effects from fluoride intake might occur in our bones and teeth. We have noted that too much fluoride ingested at the time that the tooth enamel is forming might result in cosmetically unsightly dental fluorosis. Only one condition - skeletal fluorosis - is known to result from long-term ingestion of exceptionally high concentrations of fluoride in water.

Skeletal fluorosis

Skeletal fluorosis is a bone disease characterised by failure of the bone to mineralise properly. The bones tend to be weaker than normal bones, and, typically, the bones of the legs become deformed due to weight bearing. Calcification extends into tendons and ligaments, making them stiff, and less mobile. The condition is very different from the forms of arthritis common in the UK. Indeed, there are no reports of skeletal fluorosis in the UK or the US associated with fluoride concentrations at 1ppm in drinking water. The condition is very rare in both countries, and only one indigenous case has ever been reported in the UK [5].

Skeletal fluorosis is a widespread problem in several developing countries such as India and Pakistan, and has also been reported sporadically in other parts of the world. These areas tend to have high fluoride exposures, mainly from high fluoride levels in drinking water (up to 18 mg/L in 15 states of India), and hot climates (resulting in increased water consumption). In these developing countries dietary deficiencies and lack of safe water supplies also contribute to the much higher occurrence of crippling bones diseases than is seen in developed countries.

Other possible effects on bone health

There is a large body of evidence from populations drinking *naturally fluoridated* water that it has no adverse effect on our bones [6-8]. However, as hip fracture is the most important of the potential effects of fluoride on bone in developed countries, a number of studies have

investigated fluoride exposure and hip fracture risk. Results vary: some studies have shown a slight protective effect, others have shown a slight increase in fracture rates, while still others found no effect. The York review [3] conducted a meta-analysis (analysing the pooled results) of several studies on bone fracture and water fluoridation. They found no effects, except for studies of 10 years or longer, in which case a protective effect of water fluoridation on fracture risk was shown.

Gaps in the evidence

The laws of chemistry dictate that fluoride ions in solution in water are identical whether they occur naturally in the water or are added artificially. It has therefore long been believed that absorption of fluoride is similar from naturally and artificially fluoridated water [9, 10]. That being the case, the health impact on residents of areas in which fluoride occurs naturally has been applied to those of areas in which drinking water is artificially fluoridated. However, this reasoning has been strongly disputed by opponents of fluoridation, and the Medical Research Council Review therefore recommended new research to investigate the bioavailability and absorption of fluoride from naturally fluoridated and artificially fluoridated drinking water, looking at the impact of water hardness [4]. Consequently, the UK Government commissioned the study of the absorption by humans of fluoride in water described briefly earlier in this chapter [2]. The study carried out by the University of Newcastle, and reviewed by internationally recognised experts, confirms that there is no significant difference in the absorption of fluoride from naturally and artificially fluoridated water. It confirms that evidence from the many studies of populations such as Hartlepool where water fluoride levels have always been naturally at the right level for dental health (1 part of fluoride per million parts of water), and which have shown no increased risk of hip fracture or other adverse health effects, can be applied to populations receiving artificially fluoridated supplies. These results therefore give further reassurance that water fluoridation has no adverse effects on bone health.

Cancer

There have been many epidemiological studies examining whether or not there could be any link between fluoride in water and cancer. Probably the earliest, published over fifty years ago, was conducted in the UK [11]. It was a simple comparison of death rates, for 1930-39,

in South Shields (fluoride naturally present in water at 1.4ppm) and Tynemouth (fluoride less than 0.25ppm). The author concluded that the death rates from '*malignant disease*' in the two communities were '*approximately the same*'.

Nowadays however little weight can be placed on Weaver's analysis as it did not take into account other relevant differences between the communities, such as the proportions of males and females and the proportions of people in different age groups. These factors have important effects on cancer rates, and, because of the public health implications of cancer, many further investigations of the possibility of any link with fluoridation have been carried out over the years.

The early studies looked at the possible association of fluoride with cancers of all types and these are discussed later in this chapter. However, because fluoride accumulates in bone and has an effect on bone formation, particular attention has been given to bone cancer - especially osteosarcoma.

Osteosarcoma

Osteosarcoma - primary bone cancer - is very rare; not all bone cancers are osteosarcoma, most are secondary from cancer in other organs. There are only about 125 new cases of osteosarcoma per year in England and Wales [4].

In 1990, the independent Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) - which assesses and gives advice to the Government on carcinogenic risk to humans - concluded that there was no evidence that fluoride causes bone cancer in humans, even in people in whom long term exposure to excessive levels of fluoride had caused skeletal fluorosis. In 2000 the York review could find no clear association between osteosarcoma and fluoridation, and in 2002 the Medical Research Council agreed with York that, overall, the evidence does not suggest that artificially fluoridated water increases the risk of cancer. However, because osteosarcoma, is a difficult cancer to study, and because its causes are poorly understood, the Medical Research Council review suggested that *if new studies are undertaken*, exposure to fluoride should be included along with the other possible risk factors.

The Medical Research Council report commented, '*further data are expected from an extension of the preliminary report of McGuire et al*

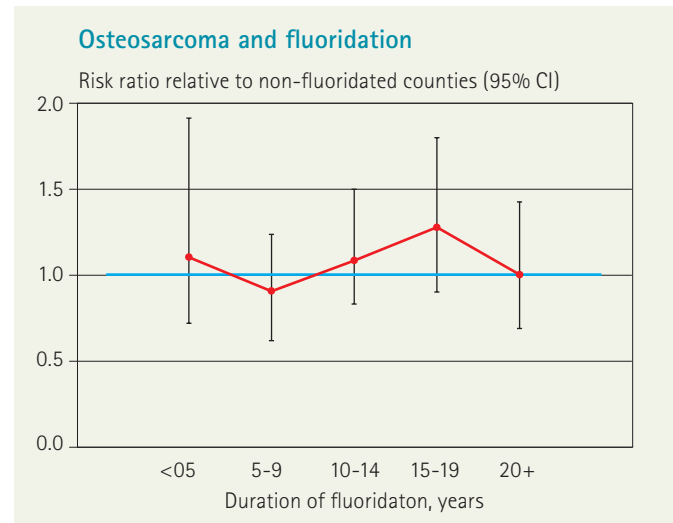
[osteosarcoma case control study]' [12]. Professor Chester Douglass of Harvard University presented preliminary results, as yet unpublished, from that and a separate National Cancer Institute study by Hoover et al, at a symposium held at the Royal College of Physicians, London, in November 2002. These two large case-control studies showed no association between fluoride exposure and osteosarcoma.

Population studies of cancer

Analyses of cancer statistics in the US, the UK and elsewhere have not shown any differences in total cancer rates between fluoridated and non-fluoridated populations, or between populations with water supplies naturally high or low in fluoride. Some studies have looked specifically at bone cancer or at osteosarcoma, and have not observed any association with water fluoridation [13, 14].

An important study by Hoover et al [13], which included 2.3 million cancer deaths, was not included in the York Review's main analysis because it grouped non-fluoridated areas together with areas fluoridated within the most recent five years. However, the MRC working group considered that, since cancers take many years to develop, this grouping was appropriate, and that the results of the Hoover study are very important for the evaluation of the effects of fluoridation because the large numbers involved made it possible to detect small effects. The Hoover study singled out osteosarcomas for detailed analysis and found no relationship with fluoridation. Figure 1 shows the risk of osteosarcoma in fluoridated compared with non-fluoridated US counties. The horizontal line at 1.0 is the theoretical line of identical risk. As can be seen, the actual risk over a 20+ year period hovers above and below the line of identical risk. The bar lines indicate that, statistically, the risk of osteosarcoma is no different in fluoridated compared with non-fluoridated for any of the 5-year periods. The Hoover study did find some evidence suggestive of a relationship with fluoridation and the occurrence of renal cancer. However, in contrast, the data for renal cancer deaths showed evidence of an opposite relationship. Overall, the Hoover study identified no trends in cancer cases or deaths that could be attributed to the consumption of fluoridated drinking water.

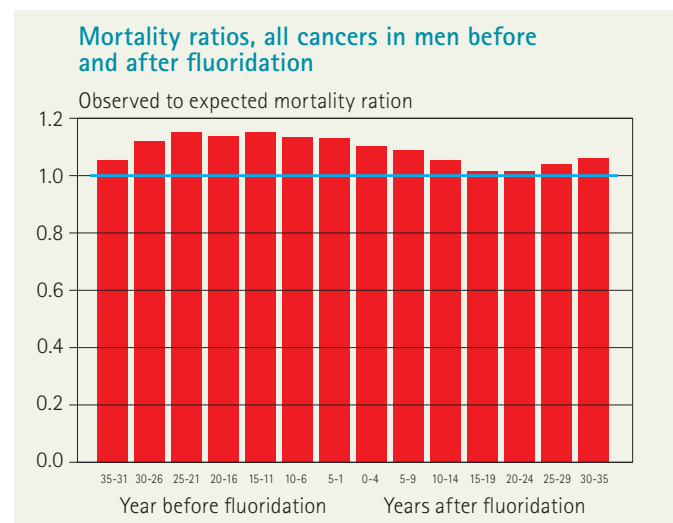
Figure 1 NCI study, Hoover et al 1991



Osteosarcoma and fluoridation. 91 incident osteosarcomas in fluoridated counties. Risk ratios relative to non-fluoridated counties, adjusted for age, calendar time, geographic area, and sex. (Adapted from Hoover et al 1991.)

Figures 2 and 3 show the pattern of cancers deaths in 1.2 million men (Figure 2) and 1.1 million women (Figure 3) for a period 35 years before and 35 years after fluoridation compared with cancer deaths in similar, but non-fluoridated, populations. Again, the horizontal line at 1.0 is the theoretical line of no difference. As can be seen, up to 35 years of fluoridation did not increase the risk of death from cancer for either men or women compared with the risk before fluoridation, or compared with non-fluoridated populations.

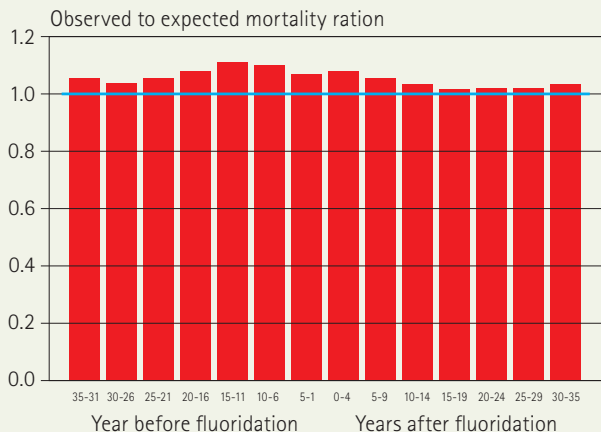
Figure 2 NCI study, Hoover et al 1991



Mortality ratios, all cancers in men before and after fluoridation. Mortality relative to non-fluoridated counties, adjusted for age, calendar-time, and geographic region. (1.2 m deaths.) (Adapted from Hoover et al 1991.)

Figure 3 NCI study, Hoover et al 1991

Mortality ratios, all cancers in women before and after fluoridation



Mortality ratios, all cancers in women before and after fluoridation. Mortality relative to non-fluoridated counties, adjusted for age, calendar-time, and geographic region. (1.1 m deaths.) (Adapted from Hoover et al 1991.)

Cancer studies with data for fluoride exposure in individuals

There are few cancer studies where data on fluoride exposure were estimated for individuals rather than populations. However, three small case control studies of osteosarcoma have been reviewed by the Australian National Health and Medical Research Council [12, 15-17]. None of these studies found any evidence of fluoride increasing the risk of cancer.

Evaluation of existing information

Overall, the available evidence suggests there is no association between artificially fluoridated water and cancer in humans. The results of studies to date rule out more than a very small effect of fluoridation on cancer risk for up to about 35 years of exposure. Furthermore, studies of cancer rates in populations drinking naturally fluoridated water, which provide information on lifetime exposure, provide a high level of reassurance concerning safety. (See the section on the Knox report below.)

The Knox report

A Working Party convened by the UK Department of Health and Social Security and led by Professor George Knox reported in 1985 on its evaluation of analyses of cancer data available at that time, including some commissioned for the Working Party itself [18]. The team concluded that:

'We have found nothing in any of the major classes of epidemiological evidence which could lead us to conclude that either fluoride occurring naturally in water, or fluoride added

to water supplies, is capable of inducing cancer, or of increasing the mortality from cancer. This statement applies both to cancer as a whole and to cancer at a large number of specific sites. In this we concur with the great majority of scientific investigators and commentators in this field. The only contrary conclusions are in our view attributable to errors in data, errors in analytical technique, and errors in scientific logic.

The evidence permits us to comment positively on the safety of fluoridated water in this respect. The absence of demonstrable effects on cancer rates in the face of long-term exposures to naturally elevated levels of fluoride in water: the absence of any demonstrable effect on cancer rates following the artificial fluoridation of water supplies: the large human populations observed: the consistency of the findings from many different sources of data in many different countries: lead us to conclude that in this respect the fluoridation of drinking water is safe.

The routine monitoring of public health has been an important feature of many fluoridation programmes, and has contributed to the confidence with which we can assert the safety of fluoridation with respect to cancer. We recommend that such monitoring should continue.'

Conclusion

Public health authorities around the world have taken seriously the suggestion that fluoridation might increase cancer rates. In 1990 the independent Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) which assesses carcinogenic risk to humans, and gives advice to the UK Government, examined the available evidence and concluded that there was no evidence of carcinogenic to humans from fluoride.

The MRC review used material included in the York Review, and 'other significant reviews' to assess the risk of cancer from fluoridation. As has been noted above, the MRC agreed with York that, overall, the evidence does not suggest a link between artificially fluoridated water and the risk of any cancer. The Working Group commented that there is no evidence on the effects on cancer risk from artificial fluoridation for more than 40 years, and recommended an updated analysis of UK population data on artificial fluoridation and cancer rates that would detect any effect after long exposure. However, as stated earlier,

the recent Government-commissioned study of the absorption by humans of fluoride in water confirms that there is no significant difference in the absorption of fluoride from naturally and artificially fluoridated water; therefore, evidence from studies of populations drinking naturally fluoridated water which have shown no increased risk of cancer or any other adverse health effects, can be applied to populations receiving artificially fluoridated supplies. These studies give further reassurance that water fluoridation does not increase the risk of cancer. The results of the absorption study are expected to be published in full in due course.

Other health concerns

It has been suggested that water fluoridation causes a variety of unwanted health effects other than those mentioned above. Many of these claims have not been substantiated. Below is a brief summary of what is known about the most important of these possible effects.

Allergy and immunological effects

It has been claimed that many allergic reactions are caused by fluoride in drinking water. However these claims have been investigated and reviewed by experts and all concluded that there is no credible evidence to support claims that fluoride is allergenic [4, 19-21].

Effects on reproduction

On the question of whether fluoridation affects reproduction, the Medical Research Council's 2002 review said:

'Adverse effects of fluoride intake on reproductive performance, such as reduced lactation, have been demonstrated in many species. However, these studies have used dietary concentrations very much higher than those in the fluoridated drinking water of humans (National Research Council, 1993).

Fluoride has also been implicated in a number of adverse outcomes relating to fertility and pregnancy, but there is insufficient evidence to establish a link between decreased fertility and fluoride exposure (National Health and Medical Research Council, 1999). The York Review found no evidence of reproductive toxicity in humans (McDonagh et al, 2000).

The plausibility of fluoride affecting the reproductive capacity of humans at the intakes experienced from fluoridated drinking water is low.'

Birth defects

Fluoride reaches the unborn baby and is incorporated into its tissues; it could therefore plausibly cause birth defects. However, studies in areas of India and Africa that have high levels of naturally fluoridated water have not shown an increase in birth defects [7]. In 1957, an investigator linked an excess of Down's Syndrome to fluoridation. However, later studies by other investigators provided strong evidence against this suggestion [3, 7].

On this question, the Medical Research Council's 2002 review concluded:

'Human and experimental animal data suggest that drinking even high levels of fluoride in water does not cause birth defects.... Further work on this aspect is not considered to be of high priority.'

One recent study has concluded *'that there is no evidence that fluoridation has had any influence on the rate of congenital abnormalities or stillbirths in the North East of England'* [22]. Another which looked at all pregnancies that were recognized to be affected by Down Syndrome in England and Wales over a five year period found no convincing evidence of an association between water fluoridation and Down Syndrome [23].

Renal effects

The kidney is exposed to relatively high fluoride concentrations and therefore the potential for it to be harmed by fluoride exists. However, several large community-based studies have found no increase in kidney disease associated with long-term exposure to drinking water with fluoride concentrations of up to eight times the optimal for dental health [7, 20]. The Medical Research Council's 2002 review concluded that further research of this question is not high priority.

Gastrointestinal tract

High concentrations of fluoride can be irritating to the stomach. However, at optimal drinking water fluoride concentrations (1 part per million) this is not a problem [7, 20]. Again, the Medical Research Council's 2002 review concluded that further research of this question is not high priority.

Intelligence

Two Chinese studies have found a positive association between *high levels* of fluoride in drinking water and reduced children's intelligence/IQ. However at fluoride

concentrations that are more comparable to the levels in fluoridated water in the UK, the Chinese studies found no reduction in children's IQ [24, 25]. The Medical Research Council's 2002 review concluded that further investigation of this aspect was of low priority.

Thyroid disease

The York Review found two studies which found no significant association between water fluoride level and goitre [26, 27], and one, unpublished, study that found an association between combined high fluoride/low iodine levels and goitre [28]. Again, the Medical Research Council's 2002 review concluded that further investigation of this aspect was of low priority.

Miscellaneous effects

The Medical Research Council's 2002 review concluded that further targeted research on several other possible health outcomes such as effects on the pineal gland, dementia, and Sudden Infant Death Syndrome, was of low priority 'unless and until critical literature reviews are undertaken that demonstrate specific research needs'.

Conclusion

Water fluoridation has been practised for almost 60 years, and, in addition, people have drunk naturally fluoridated water for generations. Worldwide, over 400 million people consume fluoridated water, including the residents of 46 of the 50 largest US cities. Given the number of research reports reviewed by York, the Medical Research Council and other expert panels, it seems to us inconceivable that any adverse health effects would not by now have been uncovered. As previously mentioned, the recent University of Newcastle study of the absorption of fluoride from naturally and artificially fluoridated water confirms that there is no significant difference in the absorption of fluoride from naturally and artificially fluoridated water. The study confirms that evidence from the many studies of populations throughout the world where water fluoride levels have always been naturally at the right level for dental health (1 part of fluoride per million parts of water), and which have shown no increased risk of any adverse health effects, can be applied to populations receiving artificially fluoridated supplies. These results therefore give further reassurance as to the safety of water fluoridation.

References

1. US Department of Health and Human Services (2000): *Oral Health in America: A Report of the Surgeon General*. National Institute of Dental and Craniofacial Research, National Institutes of Health. Rockville, MD. <http://www.nidcr.nih.gov/sgr/sgrohweb/welcome.htm>
2. Maguire A, Zohouri FV, and Moynihan PJ (2004): *Bioavailability of fluoride in drinking water - a human experimental study*. University of Newcastle.
3. McDonagh M, Whiting P, Bradley M, Cooper J, Sutton A, Chestnut I et al., (2000): *A systematic review of public water fluoridation*. York: The University of York NHS Centre for Reviews and Dissemination. Report 18.
4. Medical Research Council (2002): *Working Group Report: Water fluoridation and health*. MRC. London.
5. Webb-Peploe MM, Bradley WG, (1966): Endemic fluorosis with neurological complications in a Hampshire man. *Journal of Neurology, Neurosurgery, and Psychiatry*, 29: 577-583.
6. Royal College of Physicians (1976): *Fluoride Teeth and Health*. Pitman Medical. London.
7. Ad Hoc Subcommittee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs (1991): *Review of Fluoride Benefits and Risks*. Public Health Service, Department of Health and Human Services, USA. Washington DC.
8. Hillier S, Cooper C, Kellingray S, Russell G, Hughes H, Coggon D, (2000): Fluoride in drinking water and risk of hip fracture in the UK: a case-control study. *The Lancet*, 355: 265-269.
9. Cremer H, Buttner W, (1970): *Absorption of fluorides*, In *Fluorides and human health*. World Health Organisation: Geneva.
10. Jackson P, Harvey P, Young W (2002): *Chemistry and bioavailability aspects of fluoride in drinking water*. WRC-NSF. Marlow, Bucks.
11. Weaver R, (1944): Fluorine and dental caries: further investigations on Tyneside and in Sunderland. *British Dental Journal*, 77: 185-193.
12. McGuire S, Douglass C, DaSilva J, Joshi A, Hunter D, (1995): A national case-control study of osteosarcoma and fluoridation. Phase 1 Analysis of prevalent cases. *Journal of Dental Research - AADR abstracts*, 74: 98.
13. Hoover RN, Devesa SS, Cantor KP, Lubin JH, Fraumeni JF, (1991): *Fluoridation of drinking water and subsequent cancer incidence and mortality*, In *Review of Fluoride Benefits and Risks (Appendix E)*. US Department of Health and Human Services, Public Health Service: Atlanta, GA.
14. Freni SC, Gaylor DW, (1992): International trends in the incidence of bone cancer are not related to drinking water fluoridation. *Cancer*, 70: 611-618.
15. Gelberg KH, Fitzgerald EF, Hwang SA, Dubrow R, (1995): Fluoride exposure and childhood osteosarcoma: a case-control study. *American Journal of Public Health*, 85: 1678-1683.
16. Moss ME, Kanarek MS, Anderson HA, Hanrahan LP, Remington PL, (1995): Osteosarcoma, seasonality, and environmental factors in Wisconsin, 1979-1989. *Archives of Environmental Health*, 50: 235-241.
17. National Health and Medical Research Council (1999): *Review of water fluoridation and fluoride intake from discretionary fluoride supplements*. NHMRC. Melbourne, Australia. <http://www.health.gov.au/nhmrc/advice/pdf/fluoride.pdf>
18. Knox EG (1985): *Fluoridation of water and cancer: a review of the epidemiological evidence*. HMSO. London.
19. National Health and Medical Research Council, (1991): *The effectiveness of water fluoridation*. Canberra: Commonwealth of Australia.
20. National Research Council National Academy of Sciences Committee on Toxicology, (1993): *Health effects of ingested fluoride*. Washington DC: National Academy Press.

21. Challacombe SJ, (1996): Does fluoridation harm immune function? *Community Dental Health*, 13 Suppl 2: 69-71.
22. Lowry RJ, Steen N, Rankin J, (2003): Water fluoridation, stillbirths, and congenital abnormalities. *Journal of Epidemiology and Community Health*, 57: 1-2.
23. Lennon K, (2002): *A study of the association between water fluoridation and Down Syndrome, in School of Health and Related Research*. University of Sheffield: Sheffield.
24. Lu Y, Sun Z, Wu L, Wang X, Lu W, Liu S, (2000): Effect of High-Fluoride Water on Intelligence in Children. *Fluoride*, 33: 74-78.
25. Zhao L, Liang G, Zhang D, Wu X, (1996): Effect of a high fluoride water supply on children's intelligence. *Fluoride*, 29: 190-192.
26. Gedalia I, Brand N, (1963): The relationship of fluoride and iodine in drinking water in the occurrence of goiter. *Arch Int Pharmacodyn*, 142: 312-315.
27. Jooste PL, Weight MJ, Kriek JA, Louw AJ, (1999): Endemic goitre in the absence of iodine deficiency in schoolchildren of the Northern Cape Province of South Africa. *Eur. J. Clin. Nutr.*, 53: 8-12.
28. Lin F-F, Zhao H-X, Jian J-Y (1991): *The relationship of a low iodine and high fluoride environment to subclinical cretinism in Xinjiang*. Xinjiang Institute for Endemic Disease Control and Research. Yutian, Xinjiang.