

Fluoridation and Cancer

Does water fluoridation have negative side effects?

A critique of the York Review

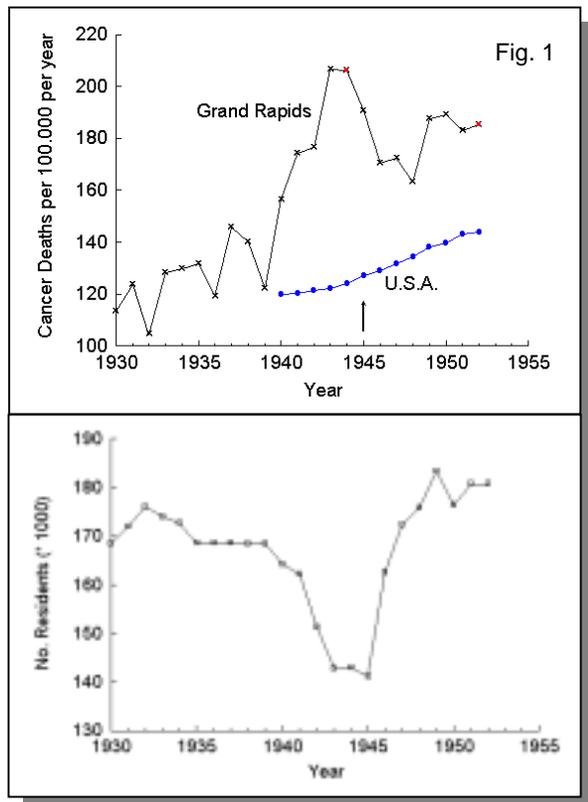
Objective 4, Sections 9.1 – 9.6 : CANCER STUDIES

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(Note by Dr. Andrew Saul: *Fluoridation of water owes its continued existence more to politics than to science. If safety and effectiveness are truly considered, fluoride would be questionable even as a prescription drug. But to freely add it to public water supplies, often without any public vote whatsoever, is far beyond questionable. Mr. Meiers' discussion of the dangers of fluoride is important reading.*)

The National Health Service (NHS) Centre for Reviews and Dissemination at the University of York recently released a review perceived to be "the final word on fluoridation" [McDonagh et al. 2000]. To judge from the course of a discussion about the layout of this York review [Schuld 2000], the result was to be expected: benefits (though smaller than previously claimed) with regard to caries prophylaxis, at the cost of some "cosmetic defects" (dental fluorosis), no harm to general health. This report is just one of many made in the past apparently aimed at giving support to preoccupied views of the proponents of fluoridation. Like other sections, the evaluation of the fluoridation-cancer link in this report is far from presenting "a summary of the best available and most reliable evidence on the safety and efficacy of water fluoridation". Not only did the York team disregard all relevant experimental data (a prerequisite to decide what effects of fluoride should be looked for), it also, quite obvious to anyone knowing the relevant literature, distorted facts to make its point.

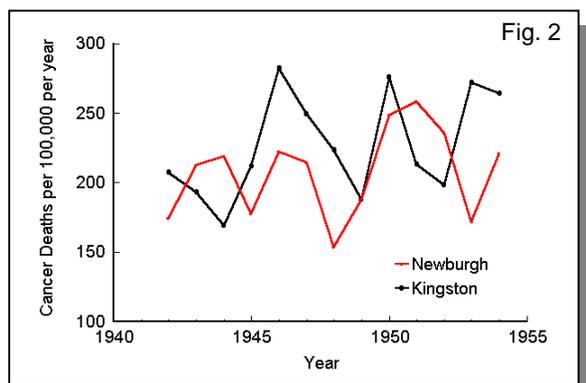


This is not a new experience. Fears of undesired effects of the controversial "public health measure" have never been taken serious by its promoters. Even though animal experimentation on fluoride and cancer, performed long before any fluoridation experiment was started in the United States [Meiers 1984, 1986], could have given reason for concern, investigations into possible fluoride effects on human cancer victims were not initiated by promoters of the measure prior to any fluoridation efforts nor in the course of the first experimental trials, but by opponents whose charges posed a threat to the continuing supply of public funds and thus necessitated appropriate replies [American Dental Association 1952]. For example, at government hearings in 1952, Taylor [1952] presented evidence that fluoride shortens the lifespan of cancer-prone mice. Perkins [1952] speculated on this basis that people in fluoridated cities might die of cancer at an earlier age because of their fluoride exposure: If a person would die of cancer at the age of 80, 70, 60, 50, or 40 on a water intake free from fluorine, the same person would die at the age of 65.6, 57.4, 49.2, 41, or 32.8 years, respectively, on a water intake containing approximately 1 ppm of sodium fluoride.

Relative to the city of Grand Rapids, fluoridated since January 1945, Perkins wrote: *"The vital statistics provided by the health authorities of that city to the United States Public Health Service and published in 'Vital Statistics of the United States', Part II, Table 14, for the year 1945 (the year fluoridation was installed in Grand Rapids) show that 252 persons died of cancer. Four years later, the same sources showed that the deaths in that city from cancer totaled 349. This is an increase of approximately 39 percent in cancer deaths during the first five years of fluoridation in Grand Rapids. It is significant that the*

records for the five years previous to the adoption of fluoridation showed an actual decrease in the cancer death rate of approximately 6 percent."

It was these claims that prompted Swanberg [1953] to evaluate the cancer data of Grand Rapids and to compare them with cancer mortality data for the United States as a whole. The York Committee describes this study [Section 9.4] as showing that "The death rate from cancer in the study area decreased during the study period whereas the death rate from cancer in the whole of the US (the control area) increased over the same period" and excludes it from the main analysis because the "whole of the US includes areas with fluoride in the water supplies and so [is] not a suitable control area". While this was a wise decision [see Ziegelbecker 1987] the team did not realize, apparently, that the Swanberg study actually revealed something quite different from the author's conclusion: the number of cancer deaths per 100,000 residents per year increased in Grand Rapids as it did in the U.S.A. (Fig.1, upper graph). As to the large rise during the years of World War II and the decrease afterwards, Swanberg explains that "it is known that in the early forties there was a migration away from Grand Rapids toward the center of war industries. After 1945 there was a migration back" which fact is illustrated in the lower graph of Fig.1 (data taken from Swanberg's publication). If this migration involved just the younger residents it led to a relative increase of the fraction of older people "per 100,000 residents" during the years of war, thus increasing the crude cancer death rate. Though Swanberg, editor of the journal that published his study, gave the full set of data, he selected for his conclusion those data points appropriate to show a decrease in cancer death rate after the start of fluoridation:



"The death rate from cancer in Grand Rapids in 1944, the year before fluoridation was adopted, is given as 206.2 per 100,000 population. In 1952, after 8 years of fluoridation, the cancer death rate was 185.3 per 100,000, a decrease of 10 per cent. In the 9-year period between 1944 and 1952 in the United States as a whole, the cancer death rate rose from 124 per 100,000 population in 1944 to 143.9 per 100,000 in 1952, an increase of 16 per cent."

The York review committee either did not realize this fraud or it chose to mention the unjustified conclusions of the author to put some undeserved

weight to other studies which apparently found a decrease in cancer death rates after fluoridation started.

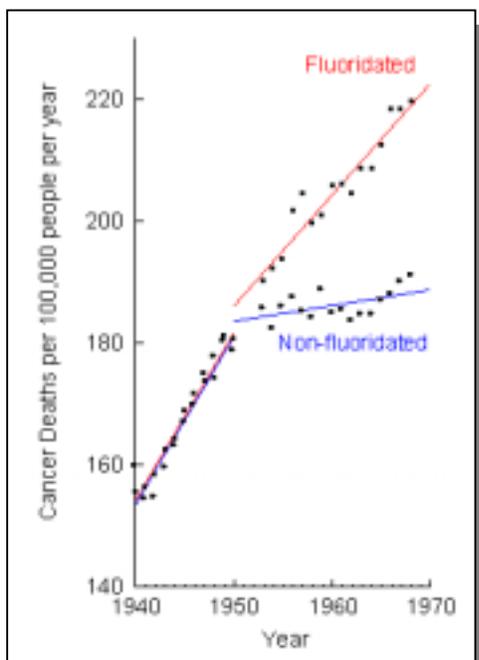
Likewise, the York team used a very special approach to evaluate data from the Newburgh-Kingston study by Schlesinger et al. [1956]. Table 12 in the Schlesinger et al. publication lists the number of cancer deaths per 100,000 people in fluoridated Newburgh and the non-fluoridated control city of Kingston for 1942 to 1954, an up and down so that hardly any difference can be ascertained between the two cities (Fig. 2). Yet, the York review team [see App. C10, p. 196] excerpted from this list data for 1944 (219.0 for Newburgh vs. 169.0 for Kingston) and the last year reported (221.2 for Newburgh, 264.4 for Kingston) when the number of cancer deaths was in favor of fluoridated Newburgh (while in 1952, for example, it was lower in Kingston). With this data selection the York team created the picture that cancer mortality went way up in non-fluoridated Kingston, while it remained nearly unchanged in fluoridated Newburgh. Several studies published after the 1956 Newburgh-Kingston "final report" focused on possible effects of natural fluoride waters on the incidence or mortality of cancer and revealed some major shortcomings. They were essentially static (comparing data of just one year) as opposed to the time-trend analyses quoted above. Further-more, the concentration of natural fluoride varies (even in one and the same water supply), and so does the number of registered water supplies within each municipality [Heasman and Martin 1962; Glattre and Wiese 1979]. Therefore, it seems to make no sense to compare areas with a water fluoride level of 0.06-0.10 mg/l to areas with 0.11-0.5 mg/l, as Glattre and Wiese do, nor to arrange fluoride cities into groups based on a difference of one hundredth mg/l (i.e. 0.5-0.99 vs. 1 mg/l and more) as Kinlen [1974, 1975] does. Where more than one water source supplies a local authority some authors calculated "weighted means" [Chilvers and Conway 1985]. On this basis, the latter authors found some of the areas used by Kinlen [1974, 1975] to be misclassified (see also Heasman and Martin 1962; Nixon and Carpenter 1974). While these facts should have been reason enough to exclude the Kinlen paper from

the main analysis in the York review, his method of standardization should have given it the final blow. But as to the Standard population used by Kinlen the York team claims: "Not stated" (Appendix C10, p. 191). The Kinlen paper has appendices, among them Appendix B which reads:

"The method for obtaining the ratios shown in table I was to calculate for each sex and each age group the number of cases that would be expected in the population in question in each fluoride category if the total number of cases in all areas combined was distributed uniformly." That means, he pooled the groups to calculate his "expected" cancer deaths and thus used a reference population partly exposed to the variable to be tested! While the York team excluded the Swanberg study on this basis, it did ignore the same mistake made by Kinlen.

In case fluoride increases the number of deaths, inclusion of exposed people in the reference population would raise the number of (speculative) "expected" deaths in the groups to be examined (depending on population structure). As Standardized Mortality Ratios (SMR's) are calculated by dividing the number of observed cancer deaths per 100,000 people (O) by the number of "expected" cancer deaths per 100,000 people (E), the SMR (O:E) becomes the lower the higher the "expected" (E) rate. This kind of SMR calculation applied in time-trend studies to populations of different size and structure (fluoridated vs. non-fluoridated cities) using a shifting refer-ence population (USA 1950, 1960, 1970 as the standard for the corresponding census years) creates the artifact of decreasing cancer death rates in fluoridated cities.

An example: In a hypothetical population with no change both in population structure and the number of cancer deaths during 1950 to 1970, applying U. S. data in 1950 by age, gender and race to calculate the number of deaths expected for 1950 in that population, and likewise U.S. data in 1960 and 1970 for those respective years, will result in an increasing number of expected deaths in the time span 1950 to 1970, since cancer death rates rose in the U.S. during that time. As the number of deaths expected in the hypothetical population will increase, i.e. "E" becomes higher, the O:E ratio (SMR) becomes lower. Thus one will be able to show that the cancer death rates decreased in that population (while, as presupposed above, nothing happened at all with the actual rates). What a large increase in cancer death rates would be required just to balance the misleading SMR calculations for the hypothetical population if it were exposed to a carcinogen to be evaluated!

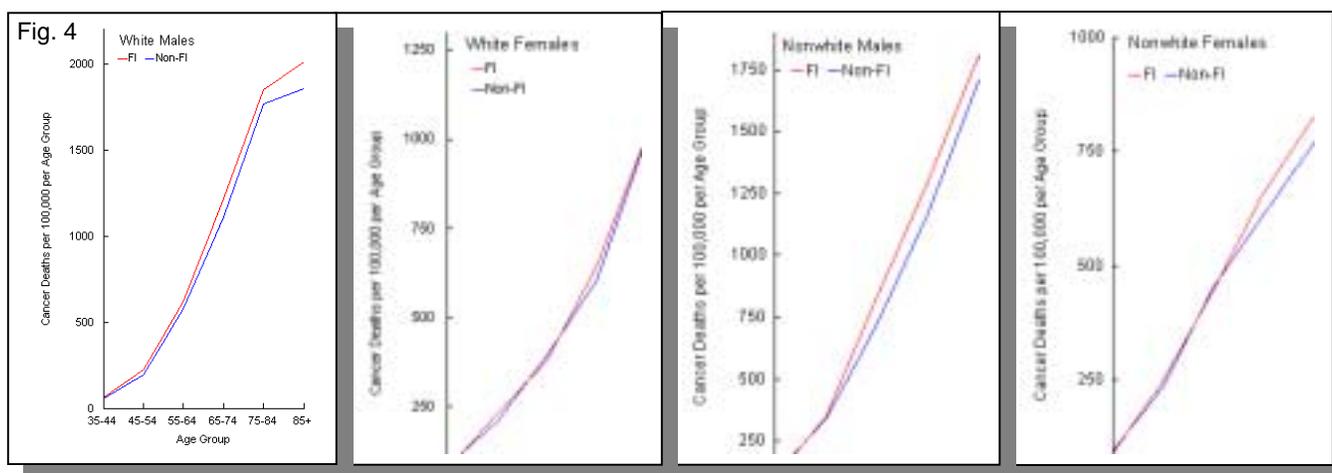


This is why the re-analyses by Smith [1980] as well as Kinlen and Doll [1981] of the Yiamouyiannis and Burk [1977] study on the fluoridation-cancer link are useless. Of these, the Smith paper got a high ranking according to the York validity checklist for it "did not include the error in the NCI data" (Section 9.1.1) – which isn't true, of course. After all, how can one expect the York committee members to know the details of that year-long discussion of the 20-cities study to evaluate properly the relevance of Smith's re-analysis?

As the Grand Rapids and Newburgh/Kingston data show, there are large fluctuations of cancer death rates over time in individual cities so that it isn't appropriate to select just two data points for statistical evaluation, but the best approach would be to make a linear regression analysis to compare rates before and after fluoridation started. As differences might be small it seems to be a good idea to pool the data of several fluoridated cities and to compare them to a set of non-fluoridated ones.

In 1975, Yiamouyiannis and Burk reported to the U.S. Congress that a set of 20 U.S. central cities had almost identical cancer mortality rates (cancer deaths per 100,000 people per year) between 1940 and 1950, but that since fluoridation started (in 1952-1956) in a group of ten of these cities their cancer death rate increased faster than that of the ten cities remaining non-fluoridated (Fig. 3). The study was later published in the Journal "Fluoride" [Yiamouyiannis and Burk 1977] and caused quite a stir.

Early in 1976, a representative of the National Cancer Institute (NCI) claimed in a letter to Congressman Delaney that the NCI's re-analysis showed that the increase was entirely due to changes in the age, race and sex structure of the population in question [Fredrickson 1976]. While refusing congressional requests for detailed data (weighted or unweighted rates used? Which reference population? etc.), the NCI clandestinely has passed this data on to other scientists [Yiamouyiannis 1977] who reported them as their "independent analysis" [Doll and Kinlen 1977; Oldham and Newell 1977]. However, the NCI data submitted contained two characteristic errors reproduced in both papers: (A) The non-white females, age 65-74 in 1970, in the non-fluoridated population should be 46.1 (not 51.1; thousands) so that the total population becomes 7342.7 (thousands) instead of 7347.7. As a result the expected number of cancer deaths in non-fluoridated cities in 1970 is 12,384 (instead of 12,407). (B) Total cancer deaths in the non-fluoridated cities in 1970 should be 14,272 (and not 14,487) [Kinlen and Doll, 1977; Oldham and Newell 1979]. The Smith [1980] paper eliminated error (B) of the NCI data, but still contains error (A).



However, the main point of disagreement between the statisticians is that whereas Burk and his group derived putative "observed Cancer Death Rates" (CDRo) by linear regression analysis of all available and pertinent data, i.e. the crude CDR's characterizing the observation period of 1953 to 1968, and extrapolation to 1950 and 1970, other investigators have taken reported or pericentral CDRo figures for 1950 and 1970. "If, as they say, only the censal or pericentral data for 1950 or 1970 ought to be taken into account, the association between fluoridation and cancer is wiped away by adjustment. If instead, as we insist, the intermediate data for 1953 through 1968 must be used, a large association remains, notwithstanding adjustment" [Graham et al. 1987]. Neither regression analysis of cancer death rates [Mahoney et al. 1991] nor calculation of intercensal population by interpolation of data acquired in census years [Cohn 1992] seem to be unacceptable methods. Furthermore, a look at age-specific cancer mortality data for the twenty cities, unfortunately only available for 1970, indicates a higher cancer mortality at an earlier age in the fluoridated group (Fig. 4). The difference is obvious in these large populations even though people in non-fluoridated cities are exposed to fluoride from sources other than drinking water (tablets, drops, mouthwashes, topical applications, canned foods prepared in fluoridated cities, etc.).

While epidemiologists hitherto essentially looked for evidence in human populations of a per se carcinogenic effect of fluoride, substantiated by more recent in-vitro experiments [Tsutsui et al. 1984; Jones et al. 1988; Lasne et al. 1988], the question raised by Perkins in 1952 relative to the promoter effects of fluorides has still not been addressed, neither by health officials in general nor by the York team. Humans today are exposed to not one but many different carcinogenic agents (including chemicals, viruses, ionizing radiation) which interact in very intricate ways. Fluoride is known to inhibit some enzymes and to activate others. Fluoride inhibits the enzymatic deacetylation of N-Hydroxy-Acetylaminofluorene [Irving 1966] and thus leaves more of the substrate for a sulfotransferase enzyme that builds the ultimate carcinogen from that compound. Fluoride activation of dimethyl-nitrosamine demethylase in liver microsomes [Dophuoc et al. 1981, 1983] increases the carcinogenic potential of dimethylnitrosamine. It has no obvious influence on the oxidative activation of the ubiquitous carcinogenic hydrocarbon benzo(a)pyrene in vitro [Dophuoc et al. 1981, 1983], yet addition of fluoride to the food of

experimental animals injected with this compound leads to increased incidence of malignant tumors [Tannenbaum and Silversone 1949]. Likewise, skin cancer induced in animals by skin painting with benzo(a)pyrene becomes earlier visible and leads to earlier death if the painting solution contains 1 ppm fluoride (as sodium fluoride) in addition to the hydrocarbon [Wagner 1981]. Beryllium compounds are carcinogenic, but exposure of animals to beryllium fluoride enhances the growth of lung tumors induced by the beryllium [Schepers 1961]. Fluoride and fluorophosphate promote tumor growth induced in vitro by benzo(a)pyrene and many other compounds [Jones et al. 1988]. In this assay the promoter effect came to a halt as soon as the fluoride was omitted from the culture medium. Thus the early experiments of Taylor [1952, 1954, 1965] are fully supported by more recent evidence.

According to a WHO scientific group "the occurrence of tumors earlier than in the controls, without increased incidence" is among the types of responses "used to classify chemicals as carcinogens" [WHO 1969].

Enhancing effects are also apparent from some life table data published in the National Toxicology Program carcinogenicity test of sodium fluoride [NTP 1990]. This test had been requested by the U.S. Congress during hearings in 1977. Back then, NCI representative Kraybill [1977] presented a list of publications which, he alleged, had already shown that sodium fluoride has no carcinogenic activity. However, not a single one of the publications on his list had anything to do with fluoride and cancer. Anyway, the start of the carcinogenicity test requested by Congress was announced four years later [Whitmire 1981]. After another four years, a first result was declared inadequate because the low fluoride semisynthetic diet "was deficient in several vitamins and minerals" [NTP 1985]. Another two-year study was scheduled to begin in October 1985. The report, released in 1990, focused on the occurrence of a rare form of cancer, osteosarcoma, in several of the male (but not the female) dosed rats used in the study [NTP 1990]. This evidence of carcinogenicity was downgraded to be "equivocal".

Nevertheless, a few epidemiological studies addressed a possible influence of water fluoridation on the incidence of osteosarcoma in humans. It occurs in less than one in 100,000 people or about 0.1 percent of all reported cancers, and therefore it would be hard to detect small increases in risk (on the order of five to ten percent) [USPHS 1991]. Examinations in a very limited number of afflicted people led to conflicting results. The study designs (e.g. exclusion of people formerly exposed to some radiation) reveal that still the search for a per se carcinogenic effect of fluoride was in the foreground. There seems to be agreement that osteosarcoma incidence in the U. S. increased in people below age 30 with some decrease at later age. A contribution by water fluoridation could not be ascertained by these limited studies, but obvious difficulties in classification of exposure to fluoridated drinking water and examination of exposure from other sources need to be more carefully addressed in more thorough future investigations. The York team apparently was not aware of these shortcomings.

In summary, the York review fits well in a history of attempts to downgrade possible risks associated with exposure to fluoride. Selection of data, inconsistent use of exclusion criteria, disregard of experimental studies which could have offered a clue to proper evaluation of epidemiological investigations render the York review useless. Either the York team was not really interested (to say the least), aimed at supporting proponents' views, or was hopelessly lost in its task.

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