

HIP FRACTURES AND FLUORIDE REVISITED: A CRITIQUE

See abstract page 39 (S Hillier, *et al*, Fluoride in drinking water and risk of hip fracture in the UK: a case-control study. *Lancet* 2000 Jan 22;355(9200):265-9.)

In the continuing debate concerning water fluoridation, the question of its role in hip fracture is still unresolved. A number of studies found that hip fracture incidence rises with increased fluoride concentration in drinking water. A fewer number of studies found no detrimental bone effect of fluoridated water compared to unfluoridated water. In a previous report,¹ I have pointed out that the few studies that found no increase of hip fracture relative to fluoride concentration in drinking water are all faulty due to the short duration of exposure to fluoridated water (6 years or less), the small number of subjects, or the advanced age of the subjects.

In 1993, for example, the National Research Council reviewed 10 studies comparing fracture incidence with fluoridation status. *Seven* of these reported a positive correlation, while three did not. Of the latter three, the elderly women in the Cauley *et al* study² had drunk fluoridated water for a mean duration of only 6 years. This obviously can not compare to life long fluoridation. A 1993 study by Jacobsen *et al*³ of hip fracture and fluoridated water found remarkable variation in the year-to-year incidence of fracture, and Jacobsen himself declared that the study could not be used to prove whether or not fluoridation had a deleterious effect on fracture incidence. This study, too, must be discarded. The third study, by Goggin *et al*,⁴ looked at hip fracture incidence in women over 60 years of age for the 5 years before and after fluoridation of Elmira, NY, in 1960. The women in this study had all passed through menopause prior to fluoridation, and the number of women with hip fracture in the study was too small for the purpose of the study. It should be pointed out that, since bone loss in women of industrialized countries generally starts at age 35, it should be obvious that any study that does not compare the fluoridation status of women during the early bone-forming years of life is useless and must be discarded.

The seven studies⁵⁻¹¹ that reported a positive correlation of fluoridated water with fracture incidence did not suffer from these same deficiencies. Since my 1993 report, a large 1995 study in France found the same positive correlation between water fluoride exposure and hip fracture incidence.¹² The available evidence thus greatly supports the fluoridation/fracture hypothesis.

The authors of the present study by Hillier *et al* are apparently aware of the deficiencies that invalidate the studies used to support the hypothesis that fluoridation is safe for bones. They argue, instead, that ecological studies that compare one population with another might fail to adjust for the effects of potential confounding variables such as physical activity, body build, cigarette smoking, dietary calcium intake, and reproductive variables between the two populations. It is of no small importance that the present study found no clear association between hip fracture incidence and the suspect variables such as

age at menopause, alcohol consumption, cigarette smoking, or dietary calcium intake. Thus, criticism of previous ecological studies has no basis.

This present study of hip fractures in Cleveland County in northeast England included 169 cases from Hartlepool and 745 from elsewhere in the county. This is of interest since Hartlepool residents use naturally fluoridated water that is high in calcium. In this study, Hartlepool is the only source of hip fracture cases using water with a fluoride content over 1 ppm. The rest of the county uses water with low fluoride content. None of the subjects lived in artificially fluoridated communities. Technically, this is not a study of the bone effects of artificially fluoridated water.

There is a difference between natural and artificially fluoridated water. Natural fluoride in northeast England occurs as mineral/fluoride salts such as calcium fluoride, magnesium fluoride, etc., whereas artificial fluoridation uses industrial waste fluoride complexed with silica or sodium. Fluoride complexed with silica or sodium is readily ionized to free fluoride ions that are quickly absorbed in the gastrointestinal tract, whereas, when chemically bound to calcium, less of it ionizes and less is absorbed. Calcium inhibits fluoride absorption and is, in fact, the treatment of choice for fluoride ingestion overdoses. Note that fluoride concentrations in trabecular bone from Hartlepool patients were no different than that from "elsewhere" patients. (hip and lumbar fractures are fractures of trabecular bone.) This is clear indication that fluoride absorption is essentially equal between the "high" fluoride Hartlepool water and the "low" fluoride water elsewhere in Cleveland County. Furthermore, industrial waste fluoride is not pure fluoride: the industrial waste "fluoride" includes several other toxic compounds that act synergistically with fluoride to increase overall toxicity.

More simply put, the Hartlepool water contains more beneficial minerals than surface water. These minerals not only inhibit fluoride absorption but also are themselves beneficial to bones and to general health. Adding industrial waste fluoride to mineral-poor surface water is not the same. Again, this study says nothing about the bone effects of artificially fluoridated water.

Fluoride concentration of drinking water does not necessarily indicate fluoride exposure: it depends on how much water is drunk. Manual work leads to more water drinking than sedentary occupations. Many people drink little water from the tap; they may use bottled water or watery beverages such as beer. Beer drinking is not unheard of in the pubs of England. Therefore, without knowing the amount of tap water consumed each day, little is known about water-borne fluoride exposure. Furthermore, fluoride absorption from fluoridated toothpaste can be a major factor of total fluoride intake. The study did not take this in to consideration.

The study population included only people aged 50 years or over. I have no difficulty with this since most non-traumatic hip fractures occur in people over age 50. The collection of hip fracture data involved only a 17-month period. Was there a reason for this? Why not a 24-month period? It would not be diffi-

cult to determine yearly incidence of hip fracture over a number of years to measure annual or seasonal variations that might be different in different parts of Cleveland County.

The study found no significant difference in hip fracture incidence between naturally fluoridated Hartlepool and unfluoridated communities elsewhere in Cleveland County. Given the considerations discussed above, this is not surprising. It found a positive correlation of low body-mass index and low physical activity with increased risk of hip fracture. This, too, is no surprise. However, the study also found no clear association with age at menopause, alcohol consumption, cigarette smoking, or dietary calcium intake.

This last factor should be of interest since conventional wisdom emphasizes calcium intake for the prevention of osteoporosis. The truth is that osteoporosis is not a disease of calcium deficiency; it is a metabolic disease in which the rate of new bone formation lags behind the rate of bone loss. In this matter, many factors are important, particularly the sex hormones. Estrogen inhibits bone loss while progesterone and testosterone both stimulate new bone formation. The study totally neglected these important bone factors. Diet, exercise, exposure to xenobiotics (pesticides of all sorts), and genetic factors all affect sex hormone production.

In testing sex hormone levels, it is important to keep in mind that circulating sex hormones exist in two different forms, protein-bound, relatively non-bioavailable form and the non-protein-bound, "free" form that is bio-available. Blood tests, as shown by Cummings *et al.*,¹³ fail to distinguish between protein-bound and "free" hormones. In fact, their study found that the serum concentration of sex hormone binding globulin (SHBG), the binding protein of estradiol, is a far stronger correlate of hip fracture risk than estradiol serum concentrations are. The higher the SHBG level (i.e., less bioavailable estradiol), the greater is the rate of bone loss. Saliva hormone assay is far more relevant since it accurately reflects blood-borne "free" sex hormone.

Progesterone not only stimulates new bone formation but also increases the sensitivity of estrogen receptors. Thus, progesterone supplementation often prevents and/or reverses osteoporosis, thus preventing hip fractures without estrogen supplementation.

Finally, it is important to understand the bone effects of fluoride. It may increase bone quantity (osteofluorosis, osteosclerosis) but also decrease bone quality and bone strength. It is well known that pharmacological doses of fluoride increase the risk of torsion-type fractures (such as hip fractures) despite the appearance of greater bone density. Conventional medicine interprets the observed fluoride-induced increase of serum alkaline phosphatase concentration as a sign of osteoblast activity. Actually, it is a reflection of increased mortality of osteocytes within bone. Osteocytes are rich in alkaline phosphatase, which is released when the cells are killed by fluoride.¹⁴ It is unlikely, therefore, that a window of fluoride-induced bone benefit exists.

The editorial by Clifford J Rosen that accompanies the study reminds me of book reviews done by friends of the author. Entitled *Fluoride and fractures: an ecological fallacy*, it attempts to denigrate previous unfavorable (to him) ecological studies and praises the present study. Even though the study included no subjects using fluoridated drinking water, he claims that it presents “compelling evidence that lifelong exposure to fluoridated water does not increase the risk of hip fracture.” Read it if you like but it offers no insight into the fluoridation/hip fracture problem.

Sensible conclusions from the Cleveland County, England, study:

- Calcium-rich drinking water protects against absorption of the fluoride from the mineral/fluoride complexes it might also contain.
- Calcium intake did not affect the incidence of hip fracture.
- People with low body-mass index and low physical activity are more likely than huskier, more physically active people to experience a hip fracture.
- Since the study did not include any subjects drinking artificially fluoridated water, no conclusion can be made about the bone effects of artificial fluoridation.

John R Lee

REFERENCES:

- 1 Lee, JR. Fluoridation and hip fracture. *Fluoride* 1993;26:274-277.
- 2 Cauley JA, Murphy PA, Riley T, Black D. Public health bonus of water fluoridation: Does fluoridation prevent osteoporosis and its related fractures? (Abstract) *Am J Epidemiol* 1991;133:768.
- 3 Jacobsen SJ, O’Fallon WM, Melton III IJ. Hip fracture incidence before and after fluoridation of public water supply, Rochester, MN. *Am J Public Health* 1993;83:743-745.
- 4 Goggin JE, Haddon W, Hambley GS, Hoveland JR. Incidence of femoral fractures in post-menopausal women. *Public Health Rep* 1965, 80:1005-11.
- 5 Sowers MFR, Clark MK, Jannausch ML, Wallace RB. A prospective study of bone mineral content and fracture in communities with differential fluoride exposure. *Am J Epidemiol* 1991;133:649-660.
- 6 Keller C. Fluorides in drinking water. Paper presented at the Workshop on Drinking Water Fluoride Influence on Hip Fractures and Bone Health. Bethesda MD April 10 1991.
- 7 May DS, Wilson MG. Hip fractures in relation to water fluoridation: an ecologic analysis. Paper presented at the workshop on “Drinking Water Fluoride Influence on Hip Fractures and Bone Health.” Bethesda MD April 10 1991.
- 8 Jacobsen SJ, Goldberg J, Miles TP et al. Regional variation in the incidence of hip fracture among white women aged 65 years and older. *JAMA* 1990; 264:500-502.

- 9 Jacobsen SJ, Goldberg J, Cooper C, Lockwood SA. The association between water fluoridation and hip fracture among white women and men aged 65 years and older. A national ecologic study. *Annals of Epidemiology* 1992; 2:617-626.
- 10 Danielson C, Lyon JL, Egger M, Goodenough GK. Hip fractures and fluoridation in Utah's elderly population. *JAMA* 1993;268:746-774.
- 11 Cooper C, Wickham CAC, Barker DJR, Jacobsen SJ. Water fluoridation and hip fracture. (Letter) *JAMA* 1991;266:513-514.
- 12 Jacqmin-Gadda H, Cummenges D, Dartigues J-F. Fluorine concentration in drinking water and fractures in the elderly. *JAMA* 1995;275-276.
- 13 Cummings SR, Browner WS, Bauer D, Stone K, et al. Endogenous hormones and the risk of hip and vertebral fracture among older women. *N Engl J Med* 1998;339:733-738.
- 14 Krook L, Minor RR. Fluoride and Alkaline Phosphatase. *Fluoride* 1998;31:177-82. Cornell University, 1998.