FLUORIDE CONCENTRATION IN DRINKING WATER
AND FRACTURES IN THE ELDERLY

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We report the results of a population-based study of the relationship between concentrations of fluorine and calcium in drinking water and risk of hip fractures or fractures at any site. Results reported herein are based on the sample of the Paquid study of normal and pathological aging, which comprised 3777 subjects aged 65 years or older, living at home in 75 civil parishes of southwestern France. The mean time that individuals in the sample had remained in the same parishes was 41 years. Data about fractures were available for 3578 subjects; 503 (14.1%) indicated they had at least one fracture at any site during the previous 10 years and 70 (1.95%) had at least one hip fracture. Calcium and fluorine concentrations were measured in water from each parish; data from two measurement surveys performed in 1991 and data collected routinely since 1991 were used.

All analyses were performed using a multiple logistic regression. Five personal characteristics were studied: age, sex, Quetelet index (weight in kilograms divided by the square of height in meters), smoking status, and sport activity.

Only age (odds ratio, [OR], 2.5 for 10 years; 95% confidence interval [CI], 1.7 to 3.6), sex (OR, 2.3 for women vs. men; 95% CI, 1.2 to 4.3), and Quetelet index (OR, 0.90; 95% CI, 0.84 to 0.97) were significantly associated with the risk of hip fractures, and only age (OR, 1.2; 95% CI, 1.1 to 1.4) and sex (OR, 2.0; 95% CI, 1.6 to 2.4) were significantly associated with the risk of any fractures. These variables were used as adjustment variables in the subsequent analyses.

Two classes of fluorine (0.05-0.11 mg/L and 0.11-1.83 mg/L) and calcium (8.90-75 mg/L and 75-146 mg/L) concentration were defined, using the median of the distribution among parishes as the cut-off point.

The risk of hip fractures was significantly higher when water fluorine concentration was higher than 0.11 mg/L (OR, 1.86; 95% CI, 1.02-3.36; P = 0.04), and this result persisted when using a mixed-effect logistic regression for taking into account the grouping of the subjects in parishes. No association was found between hip fractures and water calcium (OR, 1.32; 95% CI, 0.78-2.22; P = 0.30) and between fractures at any site and water fluorine (OR, 0.98; 95% CI, 0.80-1.21; P = 0.88) or water calcium (OR, 1.07; 95% CI, 0.88-1.30; P = 0.50). Thus adjusting for major individual risk factors, this study suggests a deleterious effect of fluorine in drinking water on the risk of hip fractures, even for moderate concentrations of fluorine, and no effect on other kinds of fractures.

Key words: Bone; Fractures; France; Hip fractures; Water fluoride.
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FLUORIDE INCREASES NET $^{45}$Ca UPTAKE BY HUMAN OSTEOSARCOMA CELLS: THE EFFECT IS PHOSPHATE DEPENDENT

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Previous in vitro studies have shown that the effect of fluoride to increase avian osteoblast-like cell proliferation was dependent on the phosphate concentration. In vitro studies have further revealed that fluoride could also have direct effects on osteoblast-like cells to increase phosphate uptake and transiently increase cytosolic calcium. The current studies were intended to determine whether fluoride could increase net $^{45}$Ca uptake by human osteosarcoma (SaOS-2) cells and, if so, whether those effects would also be phosphate dependent. The results of these studies indicate that fluoride increased net $^{45}$Ca uptake by SaOS-2 cells, with biphasic dose and time dependencies. After 30 minutes of exposure, net $^{45}$Ca uptake was increased to a greater extent by 50 microM fluoride (217 ± 16% of control, $P < 0.001$) than by 200 microM fluoride; and the stimulatory effect of 100 microM fluoride on net $^{45}$Ca uptake was greater after 20 minutes (187 ± 22% of control, $P < 0.001$) than after 60 minutes (122 ± 7% of control, $P < 0.05$). These effects of fluoride to increase net $^{45}$Ca uptake were dependent on the phosphate concentration in the medium. Fluoride had no effect on net $^{45}$Ca uptake in medium containing 0.4 mM phosphate, but increased net $^{45}$Ca uptake in medium containing 1.2 or 2.0 mM phosphate ($P < 0.005$). As the phosphate concentration was increased, the biphasic fluoride dose-response curve was shifted to a lower range of fluoride concentrations.

Key words: Bone; Calcium; Fluoride; Osteoblasts; Osteosarcoma; Phosphates.
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CONFOUNDED CARCINOGENICITY STUDY OF SODIUM FLUORIDE IN CD-1 MICE

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To determine its carcinogenic potential, sodium fluoride (NaF) was fed to CD-1 mice for up to 97 weeks. Mice given NaF at a dose of 4, 10, or 25 mg/kg of body weight per day added to a low-fluoride diet were compared to controls given either an unsupplemented low-fluoride diet or laboratory chow. Non-neoplastic changes consistent with those previously recognized from fluoride toxicity were observed in teeth, bones, and joints. Unexpectedly, osteomas occurred in all groups. The incidence of osteomas was similar in groups given the low-fluoride control diet, laboratory chow, or NaF doses of 4 or 10 mg/kg per day. The incidence of osteomas in these groups was increased over that historically experienced at the laboratory