

that CO could be implicated in any of the health improvements attributable to smoking cigarettes with unventilated filter-tips.

Unfortunately, hopes that tobacco substitutes may be safer to smoke have not as yet been supported, at least so far as CO production is concerned. Planet cigarettes, which were hastily withdrawn just over a year ago, had a CO yield well above the other brands used in this study. It was also higher than has ever been reported for cigarettes. Cigarette X, which contains a mixture of tobacco (70%) and tobacco-substitute (30%), gave a CO yield which was about average for the group of medium and high nicotine brands. The very high CO yield of the cigar tested agrees with previous work⁶ and also with the evidence that cigarette smokers who switch to smoking cigars often have high COHb levels.^{14 15}

Our smoking machine "smoked" with a square-waved rather than bell-shaped puff,¹⁶ and the mean duration of each puff was 1.82 instead of 2.0 s. This is unlikely to have affected the absolute values more than negligibly, and would not affect the comparisons between brands. Our aim was to draw attention to the considerable differences between brands rather than to construct a CO yield table. Since CO may be implicated in some of the adverse consequences of smoking¹⁷ any assessment of the degree of hazard of a particular brand of cigarette seems to be incomplete without knowledge of the CO yield. It is only since the public have been given the information, and can consequently act on it, that the tar and nicotine yields have been dramatically lowered by the manufacturers. Official publication of CO yields might have a similar effect.

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Prophylactic Fluoride Treatment and Aged Bones

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Summary

In a double-blind trial with monofluorophosphate (25 mg fluoride per day) given to 460 aged persons (237 treated, 233 control) for eight months no difference was observed in height, admission to hospital, or mortality. Fractures and exacerbation of arthrosis were more frequent in the fluoride group. Vertebral x-ray films showed no difference. The free ionized fluoride levels in the plasma of the fluoride-treated group were still twice as high two months after treatment ended. Fluoride treatment in the prophylaxis of osteoporosis is not recommended unless there is simultaneous measurement of plasma ionized fluoride levels.

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Introduction

Fluoride has been used to treat metabolic disturbances and malignant diseases of bone ever since Möller and Gudjonson¹ first showed its possible application. It may also considerably alleviate pain in osteoporosis.^{2 3}

Some population surveys have shown that osteoporosis is less frequent in areas with a high water fluorine content.⁴ In contrast, Kornis⁵ noted no such difference. Prophylactic fluoride treatment for osteoporosis has not been tried and this study aimed to investigate whether fluoride prophylaxis slows down the development of osteoporosis in the aged.

Methods and Results

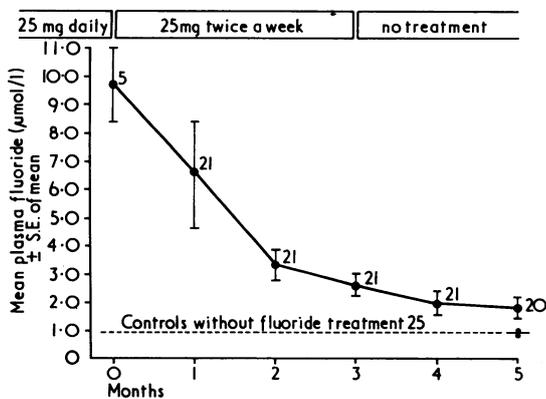
Two groups were chosen among patients over 65 in the Koukkuniemi municipal home for the aged (Tampere, Finland) according to whether the year of birth was an odd or even number, and in double-blind tests these groups were given respectively one capsule of sodiummonofluorophosphate, corresponding to 25 mg fluorine per day (caps. Fluoryl, Leiras, Turku, Finland) or one capsule of 30 mg sodium bicarbonate as a placebo. The capsules were distinguished only by colour and their contents were known to the manufacturer alone. The series started on 1 June 1971. The fluoride group comprised 237 patients (41 men), aged 65-95, average age 78.4. The controls numbered 223 (58 men), aged 65-94, average age 78.4. Patients with high serum creatinine levels were omitted from the experiment. Patients with known osteoporosis were included and their former treatment continued. A random sample was also taken from each group, comprising 10 normally mobile, 10 poorer, and 10 moving only with assistance, and x-ray films of the thoracic and lumbar spine were taken at the start of treatment and after six months. As spontaneous bone

fractures occurred after five months the code was broken and most of the fractures were found to have taken place in the group receiving fluoride. The fluoride dose was then lowered to 25 mg twice a week and the plasma free fluoride content was measured in 21 patients on fluoride who had undergone radiological examination and 25 controls (electrometric technique).⁷ The blood sample was taken while fasting 24 hours after the last dose of fluoride. The data were analysed statistically using Student's *t* test and χ^2 -test.

The total number of patients and the number discontinuing treatment or admitted to hospital during treatment are shown in the table. Treatment was ended in the fluoride group more frequently than in the controls ($P < 0.001$), usually because of abdominal discomfort.

Total Number of Patients and Number Discontinuing Treatment or admitted to Hospital (Including Deaths in Hospital) during Treatment

	Fluorine Group		Control Group	
	No.	Average Age	No.	Average Age
At outset	237	78.4	223	78.4
Discontinued	38	78.7	13	78.7
Hospitalized	53 (24)	80.8	41 (22)	80.0
At conclusion	246	77.4	169	78.0



Average plasma free ionized fluoride levels during and after treatment with fluoride. Numbers of patients are shown.

No appreciable difference was found between the initial average height of the two groups nor in the changes during the observation period. The average initial weight was also the same, but patients in the fluoride group lost 0.9 kg and the control group gained 0.7 kg ($P < 0.01$). The rate of admission to hospital was slightly higher in the fluoride-treated group. Exacerbation of arthrosis was the cause in six cases among the fluoride patients and one of the controls ($P < 0.1$). Fractures occurred during fluoride treatment in 11 cases as against six in the controls. In the fluoride group a further three patients developed fractures within a month of treatment ending, but there was no increase in the control group ($P < 0.1$). In the fluoride group eight fractures were of the femoral neck, two compressions of the vertebrae, and one of the patella. During the month after treatment ended there were three more fractures of the femoral neck. In the control group there were five femur fractures and one rib fracture. Spinal x-ray films showed no differences in changes in the bone calcium content between the two groups, nor was osteosclerosis seen in any case.

The plasma ionized fluoride concentration was measured in five patients on a fluoride dose of 25 mg per day (see fig.). The readings averaged $9.8 \pm 1.6 \mu\text{mol/l}$. When the dose was lowered to 25 mg twice weekly this concentration diminished in 2 months to $3.3 \pm 0.40 \mu\text{mol/l}$ (21 patients). When treatment ended the plasma ionized fluoride content ($1.8 \pm 0.31 \mu\text{mol/l}$) had not, even after two months' observation, reached the level of the controls ($0.80 \pm 0.02 \mu\text{mol/l}$). One spinal fracture occurred in a patient whose plasma fluoride concentration was $5.0 \mu\text{mol/l}$. Two femur fractures also occurred in this group with plasma fluoride values 2.1 and $4.3 \mu\text{mol/l}$, and again there was one case of multiple compressions of the thoracic vertebrae: plasma fluoride $4.3 \mu\text{mol/l}$.

For comparison of absorption and excretion of sodium fluoride and sodium monofluorophosphate a cross-over technique was applied

in studying ionized fluoride in plasma and urine in four patients. No difference was found between the products.

Discussion

The many fractures in the fluoride group, 14 during treatment and the following month as against six among the controls, were surprising. Three or four of the fractures in the fluoride group appeared to be spontaneous hip fractures. In the past fractures have not been regarded as being caused by fluoride but as resulting from prolonged osteoporosis before treatment. We believe that the fluoride treatment here was probably partly responsible for the fractures in our cases.

The number of fractures agrees with the osteomalacia reported as a result of fluoride treatment.^{10 11} Jowsey and his co-workers report that the addition of calcium and vitamin D to fluoride treatment produced morphologically normal bone.⁹ We did not consider the addition of calcium necessary in this group as they were drinking an average of a litre of milk a day and were therefore receiving more calcium than the recommended 600 mg/day. On the other hand it has been suggested that the addition of vitamin D contributes to an osteolytic effect.¹² We confined treatment to one effective substance to begin with to facilitate assessment of results.

Fluoride occurs in the serum as both free and bound fluoride.¹³ Total fluoride is $4.6 \mu\text{mol/l}$, of which $0.7 \mu\text{mol/l}$ is free and the remainder protein-bound. Taves¹⁴ suggested that the therapeutic concentration of free fluoride in the plasma must not exceed $15 \mu\text{mol/l}$. We found that the plasma free fluoride concentration was $1.4 \mu\text{mol/l}$ in fluoridated water areas and $0.8 \mu\text{mol/l}$ in non-fluoridated areas.¹⁵ The amount recorded in the fluoride group was considerably higher, but in only one case was the level ($40 \mu\text{mol/l}$) higher than that recommended by Taves. The plasma fluoride contents fell slowly even when the dose was lowered and treatment discontinued. A check of absorption and excretion in urine did not show that the clinical results resulted from the fluoride product used.

The fluoride dose used here, corresponding to 25 mg fluoride ion a day, would seem too high because of the high fluoride contents recorded in some patients, though according to recommendations it is low and Jowsey *et al.*⁹ reported that the fluoride dose should exceed 45 mg sodium fluoride per day (corresponding to 20.5 mg fluoride).

Plasma fluoride content has not been monitored in earlier studies and in the present series it was checked in only 21 patients. The numerous fractures occurring in the group receiving fluoride do not support the prophylactic administration of fluoride to geriatric patients, at least not unless it is possible to observe the plasma fluoride content and ensure that it does not rise higher than is desirable. We would recommend that at the most this level should be $3 \mu\text{mol/l}$.

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