Silicon

Ample evidence exists to indicate that silicon is essential for forming or maintaining normal healthy bones, brains and blood vessels, and thus may be a factor in the occurrence of some human diseases involving these tissues.

Silicon has been long suspected to be important in maintaining health in humans.[3] Before much was known about silicon in biology, one of the luminaries of medical science, Louis Pasteur, predicted that silicon would be found to be an important therapeutic substance for many diseases. At the beginning of this century, numerous French and German reports suggested that the prediction of Pasteur would become fact. These reports described therapeutic successes in treating numerous diseases, including atherosclerosis, hypertension and dermatitis with sodium silicate, with simple organic silicon compounds and with tea made from the silicon-rich horsetail plant. However, by 1930, silicon in medicine faded into obscurity as a consequence of therapeutic failures and inadequate evidence for silicon being biologically active. For the next 40 years, silicon, as consumed in the diet, was generally considered a biologically inert, harmless, nonessential element for living organisms except for some lower forms of life (diatoms, radiolarians and sponges) in which silica serves a structural role.

In 1972, it was reported that silicon was essential for bone formation.[5] About the same time, other reports appeared suggesting, like earlier reports, that inadequate dietary silicon may contribute to some cases of atherosclerosis and hypertension, in addition to some bone disorders and the aging process.[6] Since then, reports have periodically appeared that give further support for silicon being nutritionally important in preventing some chronic diseases associated with aging. Surprisingly, these reports seem to have been generally ignored or considered inconsequential by clinical and nutritional professionals, media personnel or the general public. For 20 years, the battle of bringing attention to the nutritional importance of silicon has been essentially fought by Dr. Edith Carlisle.[5-10] Recently, we decided to join the fray. Based upon our findings during the past 2 years, we believe the possibility that silicon is needed for healthy bones, blood vessels and brain deserves more attention by the research and clinical communities.

SILICON BIOCHEMISTRY

Organosilicon compounds are analogues of organocarbon compounds[19]; thus, the possibility of a silicon-based life analogous to a carbon-based life has been a seductive idea for science fiction writers. Support for this possibility could be the finding that silicon can partially replace carbon in the biosynthetic processes of nocardioform chemo-autotrophic bacteria from leprosy tissues.[11] However, the biochemistry of silicon makes it unlikely that silicon-based life exists anywhere in the universe. Silicon is larger and less electronegative than carbon. Silicon forms very rigid bonds; they do not bend, nor does silicon undergo

stereochemical conversions as easily as carbon.[19] Nonetheless, silicon has some properties that make it a possible structural or bonding agent in living organisms. Silicon forms Si - O - C bonds with a strong ionic component that can be transferred from an oxygen atom to another with only small changes in energy, and thus the Si - O bridge could act as a "switch" mechanism.[19] Also, hydrogen bonding via silanol groups could occur in vivo. For example, hydrogen-bonded complexes between silicic acid and compounds containing hydroxy groups can be sufficiently stable to be important in the secondary structure of biopolymers such as collagen.

In animals and humans, silicon is found both in the free and bound forms. Silicic acid probably is the free form. The bound form of silicon never has been rigorously identified.

SILICON AND BONE

Silicon deprivation results in abnormal skeletal development in animals.[5-8,19] In silicon-deficient chicks, the leg bones have a reduced circumference, thinner cortex and reduced flexibility. In both silicon-deficient chicks and rats, skulls are abnormally shaped with the cranial bones appearing flatter, or more "serpent-like," than normal. Bone matrix of skulls from silicon-deficient chicks lacks the normal striated trabecular pattern of normal chick skulls. The deficient chick skull shows a nodular pattern of bone arrangement indicative of an immature or primitive type of bone.

The distribution of silicon and the biochemical changes caused by silicon deprivation in bone indicate that silicon influences bone formation by affecting cartilage composition and ultimately cartilage calcification. Carlisle found that silicon is localized in the active growth areas, or the osteoid layer and within the osteoblasts, in young bone of mice and rats.[6-8] Carlisle also found that the more mature the bone mineral, the smaller the amount of measurable silicon.[6-8] In the process of bone mineralization, initially silicon and calcium contents rise congruently in osteoid tissue. In the more advanced stages of mineralization, the silicon concentration falls markedly while the calcium concentration approaches proportions in bone apatite. These findings suggest that silicon is involved in the initiation of calcification through some effect on the preosseous matrix.

Further support of the concept that the primary role of silicon in bone formation involves the organic matrix is that hexosamine (glycosaminoglycans) and collagen concentrations are depressed while macromineral composition of bone mineral is not markedly affected in bone of silicon-deficient animals. Extraction and purification procedures have shown silicon to be chemically combined with the glycosaminoglycan fraction of several types of connective tissue.[6-8] In addition, findings have been obtained which suggest that silicon is involved with phosphorus in the organic phase in the series of events leading to calcification.[7] Although these findings do not define the specific role of silicon in calcification, they strongly suggest that silicon is involved in allowing an association between phosphoprotein-

mucopolysaccharide macromolecules and collagen, which play a role in the initiation of calcification and the regulation of crystal growth.

In the last few years, a large number of extracellular matrix macromolecules containing glycosaminoglycans and saccharide, and for which functions are beginning to be defined, have been described.[14] Some of these macromolecules provide an association between cells and their surrounding matrix; this association allows cells to monitor the composition and properties of the matrix and to respond to matrix alterations by changing their synthetic activity. Silicon may be necessary for the association between one or more of these macromolecules and cells, and in this way affects cartilage composition and ultimately cartilage calcification.

We recently found further evidence that silicon status affects a circulating or local macromolecular mediator of bone metabolism. Mediators extracted from bones can stimulate bone cell proliferation, collagen synthesis and bone formation of embryonic chick tibia in culture and ectopic bone formation in rats. We implanted subcutaneously in the thoracic region of rats gelatin capsules containing powdered bone from silicon-deprived or silicon-adequate rats. Compared to those implanted with the silicon-deficient bone, animals implanted with silicon-adequate bone exhibited decreased calcium and increased copper concentrations in their tibias (Table 1) and had a higher uptake of a [Ca.sup.45] tracer in femur. This suggests that silicona-adequate bone powder contained a substance that affected bone composition elsewhere and that was present in lower quantity in silicon-low bone powder. In addition, the [Ca.sup.45] uptake by ectopic bone (implanted bone powder) was higher in silicon-adequate than silicon-deprived rats (Figure 1).

[TABULAR DATA OMITTED]

Based upon the substantial evidence accumulated to date, there is little doubt that silicon deprivation affects bone health. Because silicon apparently affects the initiation and rate of calcification of bone, silicon may be an important factor in disorders characterized by an imbalance between bone formation and resorption. Furthermore, because silicon affects cartilage composition, including articular cartilage, inadequate silicon nutriture may be of consequence in some joint disorders such as osteoarthritis.

SILICON AND THE BRAIN

Recently, signs of silicon deprivation in rats have been described that seem unrelated to connective tissue and bone. Rats fed a low-calcium diet accumulated high amounts of aluminum in all brain regions examined when dietary aluminum was high and silicon was low; aluminum content was increased 14-, 5- and 4-fold in the caudate, thalamus and hippocampus, respectively, over that found in those areas of similarly treated, but calcium-adequate, rats.[9] No increase in brain aluminum occurred with a low-

calcium, high-aluminum diet supplemented with silicon. Also, brain aluminum increased in calcium-adequate mature rats (aged 10 months upon initiation of deprivation) fed a silicon-deficient diet for 18 months. The aluminum contents in the hippocampus, posterior cortex and cerebellum were 26, 24 and 126% higher, respectively, in silicon-deprived than in silicon-supplemented rats. In thyroidectomized rats, aluminum supplementation markedly decreased brain zinc content if the diet was low in silicon; no decrease occurred when silicon was supplemented to the diet.[10]

Further evidence that silicon performs a vital function in the brain is the pattern of distribution of silicon in the brain. The concentration of silicon is higher in brain than in plasma. Furthermore, silicon concentrations vary widely among the different brain regions, with much higher concentrations in the hippocampus, caudate and lentiform nucleus than in the spinal cord and brain stem.[9]

Electron probe analysis has associated silicon with calcium and phosphorus in the brain.[15] The relationship between calcium and silicon is discussed above. A possible biochemical relationship between phosphorus and silicon may involve protein phosphorylation. This suggestion is supported by the finding that the addition of silicate to silicon-starved diatoms resulted in three proteins showing a significant and rapid change in phosphorylation.[18] In other words, silicon apparently affected the phosphorylation and dephosphorylation of specific proteins.

Alzheimer's disease has been associated with an increased concentration of aluminum in the brain. In this disease, calcium homeostasis, protein phosphorylation and membrane iron metabolism of certain target neurons are disturbed. Perhaps because silicon is associated with calcium and phosphorus in the brain, silicon deprivation, especially when dietary calcium is low, has an effect similar to the Alzheimer's disease process. That is, it changes the blood-brain barrier, which allows aluminum to enter and accumulate in nerve cells when dietary aluminum is high.

Although the mechanism through which silicon affects brain biochemistry is unknown, accumulating evidence clearly indicates that silicon is needed to prevent detrimental changes in the brain, especially under stress conditions of low dietary calcium, high dietary aluminum and/or inadequate thyroid function. Thus, silicon nutriture may be of consequence in some aging and disease processes that affect the brain.

SILICON AND BLOOD VESSELS

Because blood vessels contain glycosaminoglycans and collagen, which are affected by silicon deprivation, it is not surprising that silicon has been implicated in maintaining normal blood vessels and in preventing atherosclerosis.[2,16,20] The first suggestion that silicon may be beneficial in preventing atheromas and arteriosclerosis appeared in 1911. Since 1965, numerous findings have been obtained to support this suggestion.

French investigators have reported that the silicon content of normal human aorta decreases markedly with age and that the concentration of silicon in the arterial wall decreases with the development of atherosclerosis.[16] The changes in the aortic silicon content were found to occur mainly in the elastin and mucopolysaccharide fractions. Also, in rabbits, the induction of atheroma by an excess of cholesterol resulted in a rapid fall in the silicon concentration of aorta; silicon supplementation ameliorated this fall and decreased or delayed the appearance of atheromas. Other observations supporting the concept that silicon nutriture is important for healthy blood vessels is that of an inverse relationship between the concentration of silicic acid in drinking water and the prevalence of cardiovascular disease in Finland [20] and that blood vessels of old rats with chronic hypertension contain relatively low amounts of silicon and have a shortage of collagen fibers, which require silicon-rich hyaluronic acid for their development.[2]

The beneficial role of silicon in preventing atheroma formation has been suggested to involve assuring the integrity of elastic fibers and thus impermeability of the arterial wall to fatty infiltration and calcium deposition [16] This suggestion is supported by the finding that silicon inhibits the diffusion of dye into rabbit derma.[16]

A major piece of evidence is lacking to make a strong case for silicon being nutritionally important for blood vessel integrity; that is, abnormalities in blood vessels have not been described as a sign of silicon deprivation in experimental animals. This lack, plus the fact that relatively high amounts of silicon were used to induce the beneficial effects described, allows for the possibility that silicon may have been acting pharmacologically instead of physiologically in the animal experiments done to date involving blood vessel integrity. Here, pharmacologically is defined as "the ability of a relatively high dietary intake of a substance to either alleviate an abnormality caused by something other than a nutritional deficiency of that substance or alter some biochemical function or biologic structure in a manner that can be construed as beneficial."

The possibility that silicon can act pharmacologically is indicated by the finding that, while a silicon supplement of 5 mg/kg of diet had no effect, 135, 270 and 540 mg/kg supplements increased aortic elastin in copper-adequate rats.[13] Moreover, the 540 mg/kg supplement, but not the other supplements, increased aortic elastin in copper-deficient rats; these rats have defective elastin formation.

Much remains to be learned about the nature of the beneficial effects of silicon on blood vessel health and whether a decline in aortic silicon content enhances the atherosclerotic process. Nonetheless, the findings to date indicate that further studies are warranted in determining whether inadequate dietary silicon may contribute to cardiovascular diseases such as ischemic heart disease and hypertension.

SILICON METABOLISM

Little is known about the metabolism of silicon. Apparently, the form of dietary silicon determines whether it is well absorbed. In one study, humans absorbed only about 1 % of a large single dose of an

aluminosilicate compound but absorbed over 70% of a single dose of methylsilanetriol salicylate, a drug developed for the treatment of circulatory ischemias and osteoporosis.[1] Further evidence that some forms of silicon are well absorbed is that daily urinary silicon excretion apparently is over 50% of daily silicon intake.

Average daily intakes of silicon have been suggested to range from about 20 to 50 mg/day.[17] This suggestion was based on limited, perhaps somewhat questionable food analyses, and the composition of the Food and Drug Administration's (FDA) Total Diet, which contains substantial amounts of grains and cereals. The calculated silicon content of the FDA Total Diet was 19 mg/day for women and 40 mg/ day for men. These values seem reasonable because one report of a study involving 23 individuals indicated that normal urine contains about 21 mg/L, and that about 33 mg of silicon is excreted daily in urine.[4] However, this report stated that others had found much lower, in addition to similar, amounts in urine. These values indicate that the elimination of absorbed silicon is mainly through the urine where it probably exists as magnesium orthosilicate.[4]

DIETARY CONSIDERATIONS OF

SILICON

Impairment in the Elderly

Hélène Jacqmin-Gadda, Daniel Commenges, Luc Letenneur, and Jean-François Dartigues

We studied the relation between silica and aluminum levels in drinking water and the risk of cognitive impairment using data from a population-based survey of 3,777 French subjects age 65 years and older. We also studied the effect of pH and the concentrations of calcium, magnesium, fluorine, zinc, copper, and iron. We used a mixed effects logistic regression adjusting for age, sex, educational level, and occupation of the subjects.
We confirmed the inverse relation previously found between calcium level and cognitive impairment. We found no important association between cognitive impairment and fluorine, magnesium, iron, copper, or zinc. The association between cognitive impairment and aluminum depended on the pH and the concentration of silica: high levels of aluminum appeared to have a deleterious effect when the silica concentration was low, hut there was a protective effect when the pH and the silica level were high. The threshold for an aluminum effect, however, was very low (3.5 ug per liter) and did not support the hypothesis of a deleterious effect for only high levels of aluminum. (Epidemiology 1 996;7:28 1—285).
The etiology of Alzheimer’s disease is not well known. Genetic findings have drawn major attention, but among environmental factors, aluminum has been the most studied. Aluminum has been found in cerebral lesions of patients 2, 3 and aluminum toxicity for the

brain has been evident from dialysis encephalopathy 4 and experimental studies. Several epidemiologic studies have reported a geographical association of aluminum concentration in drinking water and rates of Alzheimer's disease 6-8 or cognitive impairment. 9-11.
The hypothesis relating aluminum intoxication from drinking water to Alzheimer's disease raises a paradox: the intake of aluminum from drinking water is only about 10% of the total daily intake from food. This **I** paradox might he explained by higher bioavailability of aluminum in water than in solid nutrients. Alternatively, some authors have suggested that the observed.

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effect of aluminum from drinking water was due **to** silicon.'2"3 Birchall et al14 showed that silicon could reduce the toxicity of aluminum for fish, because hydroxyalumino silicate compounds prevent the absorption of aluminum. In old rats on a low-silicon diet, aluminum supplementation induced an increase in the brain aluminum level, but no increase was observed in rats on a silicon-supplemented diet.15 In a study of five men, Ed Wardson *et* al.6 showed that gastrointestinal absorption of aluminum from orange juice is reduced if sodium silicate is added to the beverage. Moreover, some authors have suggested that silicon could counteract the adverse effects of aluminum after absorption, 7 particularly in the formation of neurofibrillary tangles, one of the two cerebral lesions of Alzheimer's disease patients.[18]
From these experimental studies, two hypotheses may be proposed. The first was suggested by Birchall and Chappell, 2 who pointed out that the aluminum and silicon concentrations in drinking water generally are negatively correlated; thus, silicon may be a confounding factor in the statistical association observed between aluminum in drinking water and Alzheimer's disease. Moreover, silicon from drinking water would be an important part of daily silicon intake, and in a form particularly available for reaction with aluminum. 7 Finally, the authors noted that "the ingestion of aluminum is probably fairly constant within the population." 2 Thus, Birchall and Chappell12 suggested that the association between aluminum level in drinking water and Alzheimer's disease might be a consequence of the protective effect of silicon in water: silicon in water would protect against the effect of dietary aluminum intake, and not only from aluminum in water.

Keywords:
Aluminum, Alzheimer's disease, cognitive impairment, dementia, drinking water, elderly, silicon.

The second hypothesis is simpler: a high level of silicon in drinking water protects against a deleterious effect only from aluminum in drinking water. The single epidemiologic study on this subject found
little relation between silicon in drinking water and Alzheimer's disease19 In this article, we study the relation between cognitive impairment in elderly people and silica concentration in drinking water, using the data of the Paquid cohort. Previously, we reported an association of cognitive impairment with aluminum, pH, and calcium, 1 but some of these results were difficult to explain: we found a negative association between aluminum concentration and cognitive impairment for high pH (above 7.3) and a positive association for low pH. If the first hypothesis is true and if there is a correlation between silica level and aluminum level, calcium level, and pH, 27 our previous results could he explained by a confounding effect of silica level.

TABLE 1. Spearman Rank Correlation Coefficients between pH, concentrations of Aluminum, Fluorine, Calcium, Magnesium, and Silica in Samples from Water Supplies

	pH	Aluminum	Fluorine	Calcium	Magnesium	Silica
pH Aluminum	1.00 -0.22	1.00				
Fluorine	0.40	-0.42	1.00			
Calcium	-0.58	0.13	-0.28	1.00		
Magnesium Silica	0.33 0.01	-0.50 -0.18	0.80 0.04	-0.07 0.21	1.00 0.06	1.00

The major objective of this study was to assess the effect of
silica in water on cognitive impairment and to test the two hypotheses about the specific mechanism mediating the effect of silica. Our secondary objective was to study a possible role of magnesium, fluorine, zinc, iron, and copper.

Subjects and Methods

The Paquid study comprises 3,777 subjects age 65 years and older living at home in 75 civil parishes of Gironde and Dordogne in southwestern France. The sample was randomly selected from the electoral rolls by a three-step procedure with stratification by age, sex, and size of the urban unit. Methodological details are given elsewhere.11,20

MEASURE OF COGNITIVE IMPAIRMENT

Cognitive status was measured by the Mini-Mental State Examination (MMSE), which evaluates orientation to time and place, simple arithmetic, registration and recall of three objects, simple language tasks, and visuoconstructional abilities. The score ranges from 0 to 30. We defined cognitive impairment as a score of less than 24, following the recommendations of Foistein *et al. 21*

MEASURE OF EXPOSURE

On the basis of information given by the sanitary administration, we divided the sample into 78 drinking water areas. Two surveys were carried out in 1991 to measure pH and concentrations of aluminum, calcium, and fluorine in each water supply. These data were used for the previous study and are described in detail by Jacqmin *et al.11*

For the present study, we collected all of the results of chemical analyses of drinking water carried out by the sanitary administration since 1991. The protocol for measurement of aluminum was identical to that of the previous surveys, using electro thermal atomic absorption. The pH was measured at the laboratory. Silica was measured by colorimetry. Between 0 and 9 new analyses were collected (mean: 2.0) according to the importance of the water supply. Thus, this study is based on 71 areas for which measurements of water were available and includes 3,450 subjects who have completed the MMSE and 3,430 subjects for whom the covariates were also collected.

For each drinking water area, we computed a weighted mean of the measures of each component of drinking water available from the water supplies used in the area:
the weighting took into account the length of the period of use of each water supply over the previous 10 years and the hourly flow or the relative contribution of each water supply. This weighted mean was used as a measure of exposure to each component of drinking water.

STATISTICAL ANALYSIS

We used a mixed effects logistic regression[22] to take into account the grouping of the subjects in parishes and to adjust for the major individual risk factors:[23] age, sex, educational level, and principal lifetime occupation. This regression model accounts for the residual correlation of the observations in the parishes that could be due to some characteristics of the parishes not included in the model.

We entered age into the model as a continuous variable. Educational level was in three classes: no education, grade school level, and high school or university level. We included principal lifetime occupation with eight categories: homemakers, farm workers, farm managers, domestic service employees, blue-collar workers, craftsmen and shopkeepers, other employees, and intellectual occupations. As in the previous study, [11]calcium was entered as a binary variable, with 75 mg per liter (the median) as the cut point. We included aluminum, pH, and silica as binary variables. We present analyses based on three cut points for the pH and the concentrations of aluminum and silica (first quartile, median, or third quartile) because they led to different results.

Results

Table 1 shows the Spearman rank correlation coefficients between the concentrations of aluminum, fluorine, calcium, silica, and magnesium and the pH measured in the water supplies. The associations hypothesized

between silica and aluminum, calcium and magnesium concentrations, and pH are low in our sample.
The correlations between silica and pH and between silica and magnesium are close to zero, and the correlate between silica and calcium is negative. Thus, in these drinking waters, a high silica level is not associated with hard or acid water. Finally, the negative correlation between aluminum and silica levels, essential to Birchall's hypothesis of a confounding effect of silicon, is very low in our data. Table 2 presents the distributions for pH and the elements we measured in drinking water.

COGNITIVE IMPAIRMENT AND SILICA
For three categories (low, medium, high) defined by the first and last quartiles of the distribution of the connections of silica, the crude prevalence of cognitive impairment was 24.0% (N = 775), 21.8% (N = 1,828), and 28.3% (N = 847), respectively. The prevalence did not decrease when the silica concentration increased, but rather, it exhibited a U-shape.
Table 3 gives results of six regression models: in Model 1A and 1B, the cut points for the variables aluminum, silica and pH were the first quartiles; in Models 2A and 2B,the cut points were the medians; and in Models 3A and 3B, the cut points were the third quartiles. Models 1B, 2B, and 3B included the interaction between aluminum and silica.
Persons exposed to water with a high calcium concentration *(>=75* mg per liter) are less likely to be cognitively impaired when compared with persons exposed to a low calcium concentration [odds ratio (OR) 0.8 in the six models]. For the other variables, only one model, Model 1 B, which uses the first quartiles as cut points, presents odds ratios appreciably different from one. This model exhibited an interaction between aluminum and silica in addition to the interaction between aluminum and pH: when the level of silica and the pH were both low, subjects exposed to an aluminum concentration above 3.5 pg per liter appeared more likely to have cognitive impairment when compared with subjects not exposed to aluminum (OR = *3.94),* the level of silica and the pH were both high, subjects exposed to aluminum appeared less likely to be cognitively impaired than subjects not exposed (OR = 3.94 x 0.58 x 0.31 = 0.71).
Table 4 presents ORs for the eight categories defined h the first quartiles of the distributions of aluminum, pH, and silica. We estimated these ORs from a saturated model that included seven binary variables to describe the eight categories. We chose "low aluminum, high silica, and high pH" as the reference category because, according to our hypotheses, this category was expected to have low risk, and the number of areas in this category was substantial.
As hypothesized, we found a greater OR for high aluminum, low silica, and low pH, but this category included only four regions, and thus the estimate has a large confidence interval. As indicated by Model 1 B, the areas with high aluminum had a higher risk of cognitive impairment when the level of silica was low (OR = 0.89/0.42 = 2.1, and OR = 1.30/0.25 5.2), but these results are based on only a few areas. On the other hand, the category "high aluminum, high silica, and high pH" had a lower risk of cognitive impairment than the class "low aluminum, high silica, and high pH" (OR = 0.75), and this result relies on a larger number of regions. This finding indicates a paradoxical protective effect of aluminum for some levels of silica and pH. When pH was low and the concentration of silica was high, the OR for the effect of aluminum was close to one (OR = 0.74/ 0.64 = 1.16).

RESULTS FOR OTHER MINERAL COMPONENTS
We replaced silica with magnesium, fluorine, iron, zinc, and copper successively in these models. We found no remarkable association between the risk of cognitive impairment and the concentration of magnesium, iron, zinc, or copper in drinking water.

Discussion
Our findings indicate that if an association exists between cognitive impairment and aluminum, pH, and silica, the thresholds for these effects are low *(3.5* µg per liter for aluminum, 10.4 mg per liter for silica, and 7.35 for pH). Using higher thresholds, we found little or no association between these mineral elements and cognitive impairment.
Our results support the hypothesis of a protective effect of silica against the aluminum from drinking water, as opposed to protection against all sources of dietary aluminum. Indeed, a high concentration of aluminum in drinking water appeared to increase the risk of cognitive impairment only when the silica level was low. This finding could be explained by a change in the bioavailability of aluminum from drinking water when silica is present, as has been suggested from experimental studies.'5"6 It is difficult, however, to explain why aluminum may be protective when pH and silica levels are both high.

As in the case-control study of Taylor *et al*[19], our work did not support the hypothesis of a protective effect of
Silica against all sources of dietary aluminum; we found that the effect of silica was small and U-shaped in the three analyses (Models 1A, 2A, 3A). Our study has two important limitations, however. The first is shared by the study of Taylor *et at:* if dietary aluminum intake is highly variable, contrary to the assumption of Birchall and Chappell,[12] our finding might be biased because we did not adjust for the total daily aluminum intake, which is difficult to measure. Second, the concentrations of silica in our sample were high: all except one were higher than the threshold of 100 µmol per liter suggested by Birchall[13] to protect against the absorption of aluminum; in the study of Taylor *et* at,[19] these concentrations were low.
This study shows that the relations found previously between cognitive impairment and aluminum, calcium, and pH° are not explained by a confounding effect of the silica content in drinking water. As the correlations between the level of silica and the levels of aluminum, calcium, and pH are very low in our sample, silica concentration could not be a strong confounding factor. Edwardson *et al*[16] suggested that the negative correlation between the concentrations of aluminum and silicon in drinking water could be due to aluminum sulfate treatment used in surface water. In our sample, only seven areas had had this treatment during the previous 10 years, which may explain why we did not find a strong negative correlation as in the study of Taylor *et al*[19].
A shortcoming of this study, as in most studies or drinking water, is that exposure is measured only at the community level.
We found a complex association between components of drinking water and cognitive impairment. Among nine elements of drinking water studied, only pH and the concentrations of aluminum, calcium, and silica were found to he associated with cognitive impairment. A high aluminum content in drinking water may be associated with a high risk of cognitive impairment only when the concentration of silica is low.

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We thank the referees for their stimulating comments

TABLE 2. Distributions of pH and Concentrations calcium, Magnesium, Silica, Iron, Copper, and Zinc.

	Minimum	1st Quartile	Median	3rd Quartile	Maximum
pH	6.31	7.35	7.48	7.62	8.44
Aluminum (µg/liter)	1.0	3.5	9.0	16.0	459
Fluorine (mg/liter)	0. 05	0.08	0.19	0.24	1.83
Calcium (mg/liter)	8. 9	52.5	75.0	93.9	146.2
Magnesium (mg/liter)	1.1	4.8	7.0	12.1	34.0
Silica (mg/liter)	4.2	10.4	11.2	12.4	22.4
Iron (mg/Iiter)*	0.00	0.00	0.00	0.05	0.71
Copper (mg/liter)*	0.00	0.00	0.00	0.00	0.17
Zinc (mg/liter)*	0.00	0.00	0.0.0	0.07	0.60

TABLE 3. Odds Ratios (OR) for the Association between Cognitive Impairment and pH and Concentrations of Aluminum, calcium, and Silica Estimated Using Mixed Effects Logistic Models Adjusted for Age, Sex, Educational Level, and Occupation

Variable	Model 1A* OR	95% CI	Model IB* OR	95% CI	Model 2A + OR	95% CI	Model 2B+ OR	95% CI	Model 3A++ OR	95% CI	Model 3B++ OR	95% CI
Calcium	0.78	0.60—1.01	0.79	0.61—1.02	0.82	0.62—1.08	0.83	0.63—1.10	0.80	0.62—1.04	0.81	0.63—1.05
Aluminum	1.65	0.80—3.39	3.94	1.39—11.2	1.08	0.79—1.48	1.15	0.80—1.66	1.14	0.86—1.51	1.17	0.86—1.59
PH	1.96	0.93—4.15	1.57	0.73—3.35	1.27	0.90—1.79	1.24	0.88—1.75	1.18	0.89—1.56	1.18	0.89—1.57
Alx pH Silica	0.47 0.84	0.22—1.02 0.63—1.10	0.58 2.45	0.27—1.27 0.97—6.18	0.77 1.00	0.48—1.22 0.77—1.30	0.77 1.07	0.49—1.22 0.77—1.50	0.71 1.17	0.34—1.50 0.90—1.53	0.70 1.21	0.33—1.48 0.90—1.63
Silica x Al	–	–	0.31	0.12—0.80	–	–	0.87	0.54—1.38	–	–	0.86	0.47—1.58

TABLE 4. Odds Ratios (and 95% Confidence Intervals) for the Association between Cognitive Impairment and Levels of Aluminum, Silica, and pH Estimated by the "Saturated" Mixed Effects Logistic Model with Adjustment on Personal Characteristics and Concentrations of Calcium (r = number of regions)

	Aluminum Level			
	High		Low	
pH Level	*Silica Level High*	Silica Level Low	Silica Level High	Silica Level Low
High	0.75 (0.59—0.96)	0.89 (0.64—1.22)	1 (Referent)	0.42 (0.15—1.21)
OR	1,085	609	710	34
N	21	14	15	1
r				
Low	0.74 (0.53—1.02)	1.30 (0.75—2.24)	0.64 (0.29—1.43)	0.25 (0.05—1.15)
OR	810	102	55	25
N	13	4	2	1
r				

The effect of aluminum was close to 1(OR = 0.74/0.64 = 1.16)

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Dietary Silicon Affects Acid and Alkaline Phosphatase and ^{45}Calcium Uptake in Bone of Rats

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Silicon (Si) apparently is involved in bone calcification; however, its exact role is unclear. Thus, the effect of Si on bone turnover and bone formation was investigated by utilizing a 2 x 2 factorially arranged experiment. Groups of 12 animals were fed Si- deficient (0.6 µg/g) or Si-adequate (35 µg/g) casein/ground corn diets for 9 wk. At 7 wk, six animals from each group were implanted subcutaneously in the thoracic region with a gelatin capsule containing 30 mg of demineralized bone (DB) and another capsule containing 70 mg mineralized bone (MB) obtained from rats fed Si-low (1.2 µg/g) diets; the remaining animals were implanted similarly but the source of DB and MB was rats fed Si-supplemented *(50 µ*g/g) diets. The animals were intraperitoneally injected with 0.1 µCi ^{45}Ca/g body weight 14 h before the end of the experiment which was 14 d after the capsules were implanted. Marker enzyme activities (alkaline-formation and acid- resorption phosphatases) and the uptake of ^{45}Ca by femur and bone implants were measured. Both bone turnover and bone formation as indicated by acid phosphatase and alkaline phosphatase were higher in femurs of Si-adequate than Si-deficient rats. Neither dietary Si nor source of bone for the MB or DB implants affected ectopic bone formation; however, an interaction between Si and implant bone source affected acid phosphatase in both MB and DB implants. Silicon did not affect ^{45}Ca uptake by femur, but uptake by both MB and DB implants was increased by dietary Si supplementation. The bone implants significantly decreased calcium and increased copper concentrations in the tibia when the source of bone was animals fed Si-adequate diets. The decreased activity of alkaline and acid phosphatase in femur bone, the decreased uptake of ^{45}Ca in ectopic bone, and decreased copper concentration in tibia of Si- deprived rats is new evidence confirming that Si affects bone metabolism.
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Key words: silicon, ^{45}calcium, bone, ectopic bone, calcium, copper, acid phosphatase, alkaline phosphatase

INTRODUCTION

Early studies describing signs of silicon (Si) deprivation in chicks and rats have been summarized [1,21. Most of the described signs indicate aberrant connective tissue and bone metabolism. Silicon apparently is involved in bone and cartilage mineralization; however, its exact involvement is unclear. The marked influence of Si on collagen and mucopolysaccharide formation and structure [3] suggests

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That Si influences calcification indirectly by changing these matrix components. Support for this view is that, in Si-deficient animals, the formation of organic matrix, whether in cartilage or bone, is apparently affected more severely than the mineralization process [4].
However, in bone formation, apatite crystallization in matrices apparently occurs on sites that form specific nucleation centers at which calcium (Ca) binding is probably the most important and first event. Silicon may be associated with Ca in this early stage of bone calcification because, as mineralization progresses, the Si and Ca contents rise congruently in osteoid tissue. In the advanced stages of mineralization Si concentrations fall markedly, whereas Ca concentrations approach proportions found in bone apatite [5].
The early studies of Si essentiality first described about 20 yr ago[6,7] have not been confirmed by any other laboratory using strenuously controlled experiments with the Si-adequate diets providing non-pharmacological amounts of Si. Thus, in the present study the objectives were to confirm early findings of Si deficiency in addition to further defining the locale and mechanisms through which Si affects bone turnover and bone formation. Demineralized (DB) and mineralized (MB) bone powders were implanted subcutaneously in the thorax region of Sprague-Dawley rats.' Bone formation as indicated by alkaline phosphatase activity, and bone resorption as evidenced by acid phosphatase activity, were measured in femur homogenates. In this short-term in vivo model [8], the implants developed in a nutritional and hormonal environment similar to that of the bones of the skeletal tissue.

MATERIALS AND METHODS

Twenty-four male weanling Sprague-Dawley rats (Sasco, Omaha, NE) were weighed individually upon arrival and housed three per all-plastic cage measuring 50 x 24 x 16 cm and located inside a laminar air flow rack (Lab Products, Carfield, NJ). The rats had access to deionized water (Super 0 System, Millipore Corp., Bedford, MA) in plastic cups. Fresh food also in plastic cups was provided each day. Room temperature was maintained at 23°C, relative humidity at *45—55%,* and lighting controlled to provide 12 h of light and 12 h of darkness.
Groups of 12 animals were fed Si-deficient (0.6 µg Si/g diet) or Si-adequate casein ground corn diets *(35* pg Si as sodium metasilicate/g diet) (Table I) for 9 wk. The rationale behind supplementing the adequate diet with silicon at 35 pµg/g (or 50 µg/g in the experiment from which bone implant material was obtained) was that this amount was high enough to assure adequacy, but low enough to not evoke pharmacologic or toxic actions. This tenet was based upon findings from a response surface designed experiment [9]; in this experiment, 870 µg/g diet seemed to have pharmacologic or toxicologic actions. Diets were mixed 1 wk before the start of the experiment and stored daily at — 16°C in tightly-capped plastic containers. Mineral concentrations were determined by inductively Coupled argon plasma atomic emission spectrometry [10].

Effect of Si on Bone Metabolism

TABLE I. Composition of Basal Diet

Ingredient	**g/kg** diet
Casein, low trace element[a,b]	120.00
Ground corn, acid washed[a,c]	*765.00*
Corn oil[d]	*75($)*
dl α tocopherol[a]	0.20
Choline chloride[e]	0.75

Calcium phosphate[e]	500
Potassium chloride	700
Methionine[f]	2.50
Vitamin mix[g]	4.55
Mineral mix[h]	20.00

[a]ICN Pharmaceutical, Cleveland, OH.
[b]Deionized water was vacuum filtered through the casein and then the casein was freeze-dried. This procedure decreased Si content of the casein tenfold.
[c]Corn was acid washed by a described procedure [12].
[d]Best Foods, Englewood Cliffs, NJ.
[e]JT Baker, Phillipsburg, NJ.
[f]Ajinomoto, Teaneck, NJ.
[g]Composition of vitamin mix, ingredient (g/kg diet): Vitamin A palmitate (1,000,000 IU/g), 0.008; cholecalciferol mix (Vitamin D^3 powder in corn endosperm carrier, 400,000 IU/g), 0.0038; biotin, 0.001; di-pantothenic acid, 0.048; thiamine HCl, 0.01; pyridoxine HCI, 0.015; vitamin B-12 (0.1% triturate), *0.05;* glucose, 4.2992 (ICN, Cleveland, OH); menadione, 0.001 g; folic acid, 0.002; i-inositol, 0.050; niacin, 0.03; riboflavin, 0.027; p-aminobenzoic acid, 0.005 (GIBCO, Grand Island, NY).
[h]Composition of mineral mix, ingredient (g/kg diet): NaH_2PO_4• H_2O, 9.0; Mg $(C_2H_3O_2)2.4H_2O$, *3.5;* Na_2HAsO_4•$7H_2O$, 0.005; ("Reagent" grade, JT Baker, Phillipsburg, NJ), Mn $(C2H_3O_2)$. 4H2O, 0.225; (EM Industries, Inc., Cherry Hill, NJ), Zn $(C_2H_3O_2)2.2H_2O$, 0.05; Cr $(C_2H_3O_2)$•$3H_2O$, 0.002; ("Purified" grade, Fisher Scientific, Fair Lawn, NJ), iron powder dissolved in HC1, 0.04 g; CuSO4•$5H_2O$, 0.03 g; NaF, 0.002; $(NH4)_6$ Mo_70_{24}'$4H_2O$, 0.0004; H_3BO_3, 0.006; NH_4VO_3, 0.0003; ("Puratronic" grade, Johnson Matthey Chemicals, Limited, England), KI, 0.004; Na_2SeO_3, 0.0003; $NICl_2$*$3H_2O$, 0.002; (Alfa, Danvers, MA) and corn, acid washed, 7.1366.

Diet samples and tibias were ashed in platinum crucibles by a lithium-boron fusion technique [ii]. Fourteen days before the end of the experiment, animals were anesthetized with ether and their thoracic area shaved of hair. Two 1-cm incisions were made at base of the thorax over the pectoral muscle under sterile conditions and pockets were prepared by blunt dissection. In six animals from each dietary group, a *#5* gelatin capsule containing 30 mg of demineralized bone and another *#5* capsule containing 70 mg mineralized bone both obtained from 9-wk-old rats fed Si-low (1.2 µg/g) diets were inserted in the surgically prepared pockets. The remaining animals were implanted similarly, but the source of demineralized and mineralized bone was 9-wk-old rats fed Si-supplemented *(50 µg/*g) diets.

The demineralized and mineralized powders were prepared as described by Sinha et al. f8] with some modification. Bone marrow from the tibias and femurs was removed by flushing with deionized water. After freeze drying, tibias and femurs were immersed in liquid nitrogen and pulverized. The powder was sieved so that it contained only particles 70—240 pm in diameter. A portion of mineralized bone was retained and the remainder demineralized in *0.5* M HCl for 3 h. The demineralized bone in HC1 was centrifuged at *4,500* g for 15 mm and the precipitate washed in deionized H_2O for 2 h, in ethanol for 1 h, in diethyl ether for 0.5 h, then dried at room temperature.
Fourteen hours before the end of the experiment, the animals were injected intraperitoneally with 0.1 µCi/g body weight with $^{45}CaCI_2$ (New England Nuclear, Boston, MA) (specific

activity 0.7489 GBq/mg). At autopsy, implants were removed and weighed. Implants were homogenized in 10 mM Tris buffer with an OMNI 2000 homogenizer (OMNI International, Waterbury, CT) followed by sonication (Sonicator Ultrasonic Liquid Processor, Heat Systems-Ultrasonics, Inc., Farmingdale, NY). The homogenate was centrifuged for 15 mm at 4,500g at 4°C. The supernatant was used for determining alkaline and acid phosphatase activities (Sigma 104-LL and 104-AL, Sigma Chemical, St. Louis, MO). Protein was determined by Sigma Procedure TPRO-562 (Sigma Chemical, St. Louis, MO) and enzyme activities were expressed as units/mg protein.

The insoluble precipitate was equilibrated in *5* ml of 0.1 M $CaCI_2$ in 0.02 M Tris HCl, pH 7.4 at 20°C for 20 mm. The equilibration mixture was centrifuged at 4,500 g for 15 mm. The precipitate was washed twice in 10 ml of *5* mM Tris HCl, pH 7.4 and centrifuged at 4,500 g for 15 mm. The precipitate was demineralized in 10 ml of *0.5* M HC1 for 2 h at *25°C.* One hundred microliters of the demineralized supernatant was mixed with Aquasol-2 (Dupont, Boston, MA) and counted to determine ^{45}Ca incorporation. ^{45}Ca incorporation into implanted bone matrix was expressed as CPM/g tissue. The right femur was also homogenized and centrifuged as outlined for the implants. Alkaline and acid phosphatase enzyme activities and ^{45}Ca uptake were determined. Data were analyzed by a two-way ANOVA followed by Scheffé contrasts when appropriate.

RESULTS

At wk 9 the average body weights, ranging from *316—335* g, were not significantly affected by dietary Si. Both alkaline and acid phosphatase activities were decreased *(P* <= 0.0001 and *P* <= 0.005, respectively) in the femurs of rats fed the Si-deficient diet (Fig. 1). However, uptake of ^{45}Ca as measured by CPM/g bone was not affected by dietary Si (Table II) but bone implant source tended *(P* = 0.06) to affect ^{45}Ca of the rat femur. Implant source significantly affected ^{45}Ca retention by both the mineralized and demineralized implants. Less ^{45}Ca was found in the mineralized and demineralized implants harvested from animals fed the Si-deficient diets.

The source of the implant affected the Ca and Cu concentrations of tibias (Table II). The two groups of animals with implants obtained from bones of animals fed Si-supplemented diets had lower Ca and higher Cu concentrations in the tibias than the two groups of animals implanted with bone from animals fed Si-deficient diets. Although dietary Si did not affect Ca concentrations, the Cu concentration in the tibia was higher in Si-adequate than Si-deficient rats.

Alkaline phosphatase activity of the mineralized and demineralized implants was not affected by either dietary Si or source of bone for implants (Table III). Acid phosphatase enzyme activity of both mineralized and demineralized implants was affected by an interaction between the source of implant and dietary Si, which can be described as follows. When the rats were fed adequate Si, the acid phosphatase activity of the mineralized implants from bone of animals fed

Fig. 1. Means ± SEM of acid and alkaline phosphatase activities of femurs from rats fed a Si-low (0.6 µg/g) diet or a Si-supplemented (35 µg/g) diet. Silicon effect is significant at *P* «= 0.0001 for alkaline phosphatase and at *P* «= 0.005 for acid phosphatase. Implant (+) indicates source of implant bone was rats fed a Si-supplemented (50 µg/g) diet. Implant (—) indicates source of implant bone was rats fed a Si-low (1.2 µg/g) diet. Silicon (+) identifies animals fed a Si-adequate (35 µg/g) diet; silicon (—) identifies animals fed a Si-deficient (0.6 µg/g) diet.

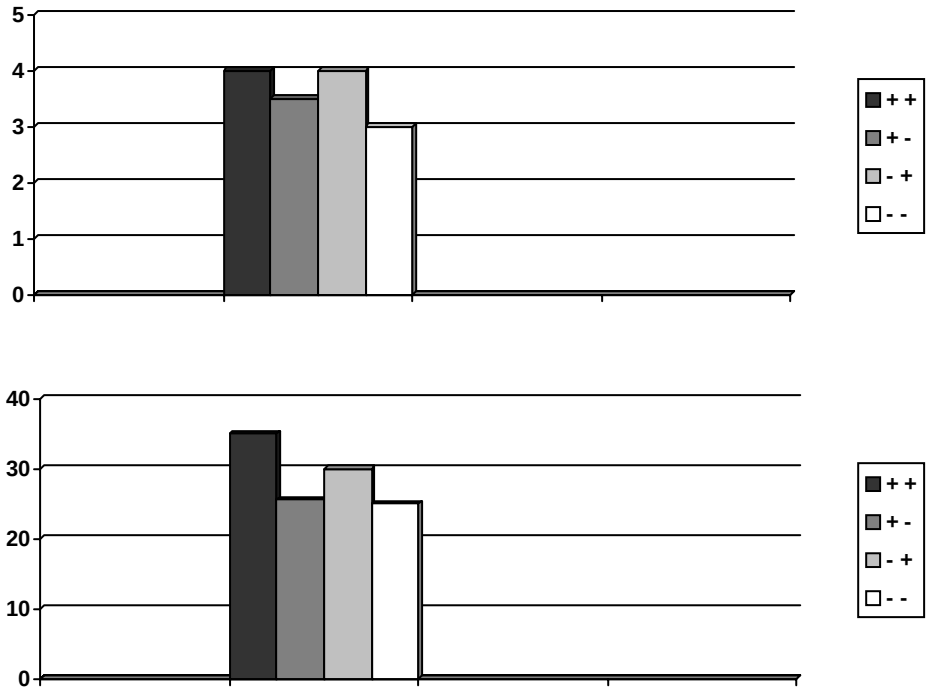

TABLE II. Effect of Dietary Si and Implant Source on Calcium and Copper Concentrations of Tibia and ^{45}Ca Uptake of Femur and Mineralized Bone (MB) and Demineralized Bone (DB) in plants in rats.

Treatment[a]		^{45}Ca				
Implant	Silicon	Femur CPM x 10^5/g	MB implant CPM x 10^5/g	DB implant CPM x 10^5/g	Tibia Ca mg/g dry wt	Tibia Cu µg/g dry wt
÷	+	15.26 ± **0•50Lt**	*15.49 ± 1.76*	0.66 ± 0.06	194 ± 2	4.98 ± 0.07
+	—	*15.58 ± 0.50*	9.28 ± 1.60	0.40 ± 0.05	198 ± 2	4.89 ± 0.08
—	+	**14.67** *±0.50*	14.98± 1.75	0.55 ±0.04	207 ±2	4.25 ±0.07
—	—	14.13 ± *0.54*	8.89 ± *1.75*	0.38 ± 0.04	207 ± 2	4.01 ± 0.07
Source of variation						
Implant		0.0600	NS	NS	0.0002	0.0001
Silicon		NS	0.0023	0.0004	NS	0.0300
Implant x silicon		NS	NS	NS	NS	NS
Error mean square		1.4771	*15.4020*	0.0121	30.2400	0.0322

[a]Implant (+) indicates that implant bone was taken from rats fed a Si-supplemented (50 µg/g) diet. Implant (—) indicates that implant bone was taken from rats fed a Si-low (1.2 µg/g) diet. Silicon (+) identifies animals fed a Si-adequate (35 µg/g) diet; silicon (—) identifies animals fed a Si-deficient (0.6 µg/g) diet.
[b]Mean ± SEM.

TABLE III. Alkaline Phosphatase and Acid Phosphatase Activities in Mineralized Bone (MB) and Demineralized Bone (DB) Implants From Rats Fed Si-Deficient or Si-Adequate Diets

Treatment[a]	Alkaline phosphatase		Acid phosphatase	

Source of	Dietary	MB units/mg	DB units/mg	MB units/mg	DB units/mg
implant	silicon	protein	protein	protein	protein
+	+	0.68 ± 016b	*3.25 ± 0.34*	8.20 ± 0.52~	7.18 ± *0.45*
+	–	*0.45 ± 0.15*	2.86 ± 0.34	10.18 ± 0.47~	*5.47 ± 0.45*
–	+	0.26 ± *0.15*	2.40 ± 0.31	10.78 ± *0.52w*	*5.55 ± 0.41*
–	–	0.47 ± 0.16	2.67 ± 0.31	8.34 ± 0.52~	*5.95 ± 0.41*
Source of variation					
Implant		NS	NS	NS	NS
Silicon		NS	NS	NS	NS
Implant x silicon		NS	NS	0.0004	0.0300
Error mean square		0.1336	*0.5675*	1.3347	1.0207

[a]Implant (+) indicates source of implant bone was rats fed a Si-supplemented (50 µg/g) diet. Implant (—) indicates source of implant bone was rats fed a Si-low (1.2 µg/g) diet. Silicon (÷) identifies animals fed a Si-adequate *(35 µ*g/g) diet; silicon (—) identifies animals fed a Si-deficient (0.6 µg/g) diet.
[b]Mean ± SEM.
[c]Means not sharing a common superscript letter (x,y) are significantly different *(P < 0.05).*

supplemental Si was lower than that of implants whose source was animals fed Si- low diets; just the opposite tended to occur when the rats were deficient in dietary Si. When rats were fed adequate Si, the acid phosphatase activity of the demineralized implants obtained from bone of rats fed supplemental Si was elevated in comparison to the activity in demineralized implants from rats fed low Si diets. When the rats were fed the Si-deficient diet, implant source of demineralized bone did not affect acid phosphatase activity.

DISCUSSION

Bone turnover as evidenced by elevated acid and alkaline phosphatase activities in femurs was higher in Si-adequate than Si-deficient animals. Osteoblasts and osteoclasts can alter the enzymatic activity [14] of each other. With increased osteoclastic activity, a factor from osteoclasts is released that stimulates osteoblastic activity [15]. Thus, dietary Si apparently impacts bone mineralization by affecting osteoclast and osteoblast enzyme activities.
Bone volume is regulated by circulating and local mediators. Mediators extracted from bones have been found to stimulate bone cell proliferation, collagen synthesis and bone formation of embryonic chick tibia in culture [14], and ectopic bone in rats [16]. The decreased ^{45}Ca uptake by ectopic bone in rats deficient in Si in this study supports the concept that a mediator of bone metabolism exists that is affected by the Si status of an animal. Decreased Cu (which usually is associated with matrix or the organic portion of bone) [17] in tibia of Si-deficient animals may be additional evidence that a mediator involved in bone metabolism is lacking when dietary Si is low.

Further evidence that Si might be affecting a mediator involved in bone metabolism is that the implantation in the thoracic area of bone material from animals fed supplemental Si decreased Ca and increased Cu concentrations in tibia. This finding also suggests that the mediator can emanate from sites distant from bones affected, or be transported through the body. Examples of mediators or substances that are transported in the blood and affect bone metabolism are growth factors, cytokines, and non-collagenous bone proteins . The fact that rats with ectopic bone implants derived from animals fed Si-supplemented diets tended to have greater ^{45}Ca uptake in the femur while having a lower Ca concentration in the tibia than rats with implants from rats fed Si-low diets also is further support for the concept that a mediator affected by Si is involved in bone mineral turnover. The increased alkaline and acid phosphatase enzyme

activities of the femurs of rats fed silicon suggest that this mediator induces changes in the enzymatic activity of osteoblasts and osteoclasts.

The difference between mineralized and demineralized implants in the alkaline and acid phosphatase activities responses to the experimental treatments seems discordant. These differences may have been caused by different rates of calcification occurring in the two different types of implants. Mineralized or undecalcified implanted bone mineral exhibits only limited osteogenic activity; this is indicated by low alkaline phosphatase activity as was found in the present study. As an implant, demineralized bone has a much higher osteogenic activity than mineralized bone; this is indicated by elevated alkaline phosphatase activity as was found in demineralized implants in the present study.
The integrity of the helical and nonhelical domains of implanted collagenous matrix is essential for the mineralization of ectopic bone. Moreover, a molecule covalently linked to the collagenous matrix as a mediator apparently is necessary for mineralization. For example, bone morphogenic protein is a necessary factor in inducing bone formation, but it is not necessarily the only factor . Silicon may affect ectopic bone turnover or formation by affecting the covalent linkage of a molecule to the collagenous matrix, or may be involved in assuring the presence of morphogenetically crucial molecules immobilized in the collagen molecule. Silicon may affect bone proteoglycans which are necessary for collagen fibril assembly and which also contain glycosaminoglycans. Both glycosaminoglycans and collagen of bone are decreased in Si deficiency.

In conclusion, the findings of this study confirm that Si affects bone formation and in physiological amounts is involved in bone turnover, and that this involvement might involve a mediator that may be transported through the body. Further studies are needed to establish whether Si influences bone calcification by changing a matrix component directly, altering the activity or amount of a circulating bone morphogenetic macromolecule, or affecting Ca binding at specific nucleation centers.

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New Studies Support Silicon's Role in Bone Formation

1. Reffitt DM, Ogston N, Jugdaohsingh R, et al. Orthosilicic acid stimulates collagen type 1 synthesis and osteoblastic differentiation in human osteoblast-like cells in vitro. Bone. 2003 Feb; 32(2):127-35.
2. Jugdaohsingh R, et al. Silicone intake is a major dietary determinant of bone mineral density in men and premenopausal women of the Framingham offspring cohort. Bone. 2003 May; 32(5):S192.

Two recent studies in the medical journal Bone support the theory that silicon, the second most abundant element in the Earth's crust, plays an important role in bone formation.

In the first study, researchers found that silicon (as orthosilicic acid) may have a stimulatory effect on bone formation in the human body.1 "Orthosilicic acid at physiologic concentrations stimulates collagen type 1 synthesis in human osteoblast-like cells and enhances osteoblastic differentiation," the researchers reported.

In another study, scientists found that dietary silicon was associated with greater bone mineral density in approximately 3,000 American men and pre-menopausal women, but not in post-menopausal women.2 Acc-ording to the researchers, these findings are "consistent with [silicon's] role in bone formation rather than in preventing bone resorption. Orthosilicic acid app-ears to be an important nutrient with anabolic effects on bone."

In an interview with Life Extension, researcher Dr. Ravin Jugdaohsingh of St. Thomas' Hospital in London said, "silicon is a major component of the human diet, the intake of which has greatly been reduced due to modern food processing and refining, water treatment and purification, and the growth of vegetables under hydroponic conditions. Animal studies have shown that silicon is important for normal growth and development, specifically with skeletal growth.

"Currently, nearly all treatments for osteoporosis (or low bone mass) work by reducing the breakdown of bone, but none, with the exception of parathyroid hormone, actually increase bone formation (i.e., make new bone). Silicon could thus provide a new type of therapy for low bone mass or osteoporosis by increasing bone formation. Silicon has also been linked to atherosclerosis, having anti-atherosclerotic properties, and with connective tissue (i.e., skin, hair, and nails), and thus may have a wider beneficial role in human health."

References

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