Boron—An Overlooked Element of Potential Nutritional Importance

by FORREST H. NIELSEN, Ph.D.

Evidence is presented which shows that boron has a role in major mineral metabolism and thus may be important in osteoporosis.

About 1980, a fortuitous happening, which was very frustrating at the time, directed me and collaborators toward the study of boron, an element which probably is of major importance in nutrition. In studies designed to examine the importance of arsenic in nutrition, the experimental animals, chicks, exhibited poor growth and leg abnormalities even though all known essential nutrients were added to the diet in sufficient quantity. As a result, a study was then carried out to ascertain whether the lack of some unrecognized essential nutrient was the cause of the problem. To the pleasure of those involved, the study showed that boron stimulated growth and partially prevented the leg abnormalities. Further study revealed that the diet contained inadequate cholecalciferol (vitamin D$_3$) because the indicated potency of the cholecalciferol supplement was apparently not true. After correcting for the impotent cholecalciferol, the stimulation of growth by boron supplementation was less marked; this suggested an interaction between boron and cholecalciferol, and a possible role for boron in calcium and phosphorus metabolism. The findings showing a relationship between boron and cholecalciferol were first presented$^1$ in 1981 at a meeting in Australia. Surprisingly, at the same meeting there was another presentation$^2$ touting boron as a cure for arthritis. Both presentations on boron were received somewhat skeptically. Nonetheless, Dr. Curtiss Hunt and I felt we had made an important discovery and doggedly continued in the study of the element. Our efforts yielded extensive data that has proven difficult to interpret; for example, diet variation gave marked changes in the response of experimental animals to dietary boron. Nonetheless, a clear picture seems to be emerging. The findings strongly suggest that boron is an essential nutrient with an important

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and apparently unrecognized role in mineral metabolism making it important for maintaining healthy bones. It seems likely that boron will be found to be a significant nutritional factor in the incidence of osteoporosis.

WHAT IS BORON?

Boron (atomic number 5) is the only nonmetal of the Group IIIA elements in the periodic table. Boron exhibits binding and structural characteristics intermediate to both metals and nonmetals. Like carbon, boron has a tendency to form double bonds and macromolecules. Like elements such as aluminum and germanium, boron complexes with organic compounds containing hydroxyl groups. Because of this ability, boron complexes with many substances of biological interest. These substances include numerous sugars and polysaccharides, adenosine 5-phosphate, pyridoxine, riboflavin, dehydroascorbic acid and pyridine nucleotides. To date, two biologically synthesized compounds containing boron have been identified. These compounds are aplasmomycin, a novel ionophoric macrolide antibiotic which was isolated from strain SS-20 of *Streptomyces griseus*, and boromycin, an antibiotic produced by *Streptomyces antibioticus*.

HISTORY OF BORON IN BIOLOGY

In 1857, the presence of boron was detected in *Maesa picta* seeds. Boron toxicity was first described in the late 1800's-early 1900's. However, it was not until after 1910 that boron was recognized as an element of physiological importance. In that year findings were reported indicating that boron was essential for higher plants. Conclusive evidence and acceptance of the essentiality of boron for plants dates from studies reported in 1923. A recent review indicated that between 1939 and 1944, several attempts to induce a boron deficiency in rats were unsuccessful, although the diets used apparently contained only 155 to 163 ng of boron/g. In 1945, there was a report that supplemental boron in the diet enhanced survival and maintenance of body fat and elevated liver glycogen in potassium-deficient rats. Those findings were not confirmed in a subsequent study in which rats were fed a different diet with an unknown boron content and different levels of boron supplementation. After those reports, boron was generally accepted as being essential for plants, but not for animals. However, since 1981 evidence that boron is an essential nutrient for animals including humans has been accumulating.

ANIMAL EXPERIMENTS—1981 TO PRESENT

In 1981, Hunt and Nielsen reported that boron deprivation depressed growth and elevated plasma alkaline phosphatase activity in chicks fed inadequate cholecalciferol. Through a series of experiments with both chicks and rats it was found that the response to changes in dietary boron was markedly influenced by the amino acid methionine, potassium, magnesium, cholecalciferol, manganese and calcium status of the animal. For example, in weanling rats fed a casein-based diet not supplemented with methionine, but containing luxuriant amounts of arginine (probably methionine-deficient) and marginal potassium, the interaction between magnesium and boron was different from that in rats fed optimal amounts of methionine, arginine and potassium. In the former instance, the interaction was characterized by the deprivation of one of the elements making deficiency signs of the other more marked. In the latter case, magnesium deprivation seemed to affect boron-deprived rats less markedly than boron-supplemented rats. Generally, the studies by Hunt and Nielsen have shown that when the diet is manipulated to possibly cause changes in cellular membrane integrity (potassium or magnesium deficiency) or in hormone responsiveness (magnesium or cholecalciferol deficiency; aluminum toxicity), a large number of responses to dietary boron occur. For example, in rats fed marginal methionine and potassium, growth and bone magnesium concentration were lower and spleen weight/body weight and kidney weight/body weight ratio were higher in boron-deprived than in boron-supplemented rats. Magnesium deprivation accentuated these differences.

Just recently, a shortcoming was identified in the diet used for all the boron studies with rats. Initial formulation of the diet was based on a 1972 report on the nutrient requirements of laboratory animals. As a result, all the diets contained about 1.8 mg of potassium/g which is one-half of the present suggested requirement for the rat. Experiments are in progress to define the signs of boron deficiency in rats fed all nutrients except boron in apparent optimal amounts. To date, the only sign of boron deficiency identified under these conditions is depressed growth.

THE HUMAN EXPERIMENT OF 1986

In 1986, a study to examine the effects of aluminum, magnesium and boron on major mineral metabolism in postmenopausal women between the ages of 48 and 82 involved subjects housed in a metabolic unit. In this study, a boron supplement of 3 mg/day markedly affected several indices of mineral metabolism of seven women consuming a magnesium-low diet and five women consuming a magnesium-adequate diet; the women had consumed a conventional diet supplying about 0.25 mg of boron/day for 119 days. Some of the findings are shown in Table 1. Boron supplementation markedly reduced the urinary excretion of calcium and magnesium; the depression seemed more marked when dietary magnesium was low. Boron supplementation depressed the urinary excretion of phosphorus by the magnesium-low, but not by the magnesium-adequate, women. Boron supplementation also markedly elevated the serum concentrations...
Table 1
Effect in Postmenopausal Women of Boron and Aluminum on Serum Concentrations of Estradiol-17β and Testosterone and on Urinary Excretion of Calcium

<table>
<thead>
<tr>
<th>Dietary Treatment (mg/day)</th>
<th>Mg-Low Diet</th>
<th>Mg-Adequate Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serum Estradiol-17β* (pg/ml)</td>
<td>Serum Testosterone (ng/ml)*</td>
</tr>
<tr>
<td>B</td>
<td>0.25 21.1 ± 6.5</td>
<td>0.31 ± 0.06</td>
</tr>
<tr>
<td>A</td>
<td>0 17.8 ± 4.2</td>
<td>0.34 ± 0.06</td>
</tr>
<tr>
<td></td>
<td>3.25 41.4 ± 12.1</td>
<td>0.83 ± 0.09</td>
</tr>
<tr>
<td></td>
<td>3.25 38.5 ± 5.9</td>
<td>0.66 ± 0.10</td>
</tr>
</tbody>
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Analysis of Variance—p Values

| Boron                 | 0.01  | 0.0008  | 0.0004  | 0.03  | 0.02  | 0.0001  |
| Aluminum             | NS    | NS      | NS      | NS    | NS    | NS      |
| Boron × aluminum     | NS    | NS      | NS      | NS    | NS    | NS      |

* Average serum concentration of six women ± SEM on days 16 and 24 of each dietary period of 24 days.
† Average excretion of seven women ± SEM during the last 20 days of each dietary period of 24 days.
‡ Average serum concentration of five women ± SEM on days 16 and 24 of each dietary period of 24 days.
§ Average excretion of five women ± SEM during the last 20 days of each dietary period of 24 days.

of estradiol-17β and testosterone. Similar to the changes in the urinary excretion of minerals, the elevation in serum steroids seemed more marked in the magnesium-low women. Although it was not significant, aluminum supplementation tended to reduce the steroid response of the magnesium-adequate women to boron supplementation. The changes in the steroid concentrations are particularly noteworthy because estradiol-17β is the most biologically active form of native human estrogen, and estrogen administration is the only known effective means to slow the loss of calcium from bone which occurs after menopause. Testosterone is a precursor of estradiol-17β. During this study, two women were on estrogen therapy; their serum estradiol-17β levels were the same as the women fed supplemental boron without estrogen therapy. Like the animal studies, the findings indicate that boron deprivation leads to suboptimal mineral metabolism.

SIGNIFICANCE OF THE BORON STUDIES

Although the findings need to be confirmed by further experimentation, results of studies on boron strongly suggest that supplementation in amounts commonly found in diets high in fruits and vegetables induces changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization. In other words, boron may be an important nutritional factor determining the incidence of osteoporosis.

Boron may be an important nutritional factor in determining the incidence of osteoporosis.

How boron is acting in the body is unknown. However, the findings to date suggest that boron may be needed for the formation of the active or hydroxylated forms of some specific steroid hormones. Because boron deficiency has been found to exacerbate the signs of cholecalciferol deficiency including abnormal bone formation and poor growth, it was suggested that boron might be needed for a hydroxylation step which forms the active or hydroxylated form of cholecalciferol. The formation of testosterone and estradiol-17β from precursors involves the creation of hydroxyl groups on the steroid structure. As described above, these blood-borne steroids were elevated in serum of women given boron supplementation. Also mentioned above was the fact that boron has chemical properties which gives it the ability to complex with organic compounds containing hydroxyl groups. If boron is found to affect the hydroxylation of biological substances in the body, its possible role in disorders of unknown etiology would extend beyond that in osteoporosis. For example, corticosteroids, which are useful in alleviating rheumatoid arthritis, involve the formation of hydroxyl groups during synthesis. Oxalate formation involves hydroxyl group manipulation; oxalate is thought to be an important factor in urolithiasis. These hints of possible boron involvement in some disorders of unknown etiology that exhibit disturbed major mineral metabolism show the urgent need for further research on the nutritional, biochemical and clinical aspects of boron.

SOURCES AND REQUIREMENT FOR BORON

Based on the finding that rats and chicks exhibit altered mineral metabolism when fed diets containing only 0.3 to 0.4 µg of boron/g, human diets probably should contain more than this level. This extrapolates to something greater than 0.2 mg of boron/day. The women showing a response to boron supplementation were fed 0.25 mg of boron/day for 119 days; this also suggests that human diets should contain more than 0.2 mg of boron/day. Based on animal experiments, it seems possible that the human
Table 2
Average Boron Content in Different Food Groups*

<table>
<thead>
<tr>
<th>Food Group</th>
<th>Boron (µg/g dry weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cereals</td>
<td>0.92</td>
</tr>
<tr>
<td>Meat</td>
<td>0.16</td>
</tr>
<tr>
<td>Fish</td>
<td>0.36</td>
</tr>
<tr>
<td>Dairy products</td>
<td>1.1</td>
</tr>
<tr>
<td>Vegetable foods</td>
<td>13</td>
</tr>
<tr>
<td>Other</td>
<td>2.6</td>
</tr>
</tbody>
</table>

* See Ref. 3 for source of data.

requirement for boron will be found to be near 1 to 2 mg/day. The daily intake of boron by humans can vary widely depending upon the proportions of various food groups in the diet. Foods of plant origin, especially fruits, vegetables and nuts are rich sources of boron. Meat or fish apparently are poor sources of boron. A recent extensive study of the mineral content of over 200 Finnish foods included boron (see Ref. 3 for references). The average boron content found in different food groups is shown in Table 2. Foods that contained the highest levels of boron (µg/g fresh weight) included soy meal, 28; prune, 27; raisin, 25; almond, 23; rosehips, 19; peanut, 18; hazel nut, 16; date, 9.2; and honey, 7.2. Wines contained up to 8.5 µg of boron/g.

CONCLUDING STATEMENT

It seems safe to state that boron is a dynamic trace element that affects major mineral metabolism in higher animals including humans. Thus, boron may have a role in some disorders of unknown etiology that exhibit disturbed major mineral metabolism (e.g., osteoporosis). I expect that much will be heard about boron in the near future and that boron will soon lose its classification as an overlooked or neglected element of potential nutritional importance.

REFERENCES