

Parathyroid

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PTH

- Instant hormone signaler
- Not just calcium dynamics
- But it's instantaneous as directs **electrical system** of the body
- Through its combined actions with boron in parathyroid tissue

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Hyperparathyroidism

- Primary hyperparathyroidism – due to adenoma on any of 4 or more parathyroid glands Calcium levels in 10's
- Secondary hyperparathyroidism – Calcium level in 10's - due to vitamin D deficiency
- Normocalcemic primary hyperparathyroidism – Normal Calcium levels but elevated PTH

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Normocalcemic

- This condition is not well understood in the medical literature.
- This is simply because normal individuals do not have their parathyroid hormone levels checked.
- Normocalcemic primary hyperparathyroidism (nPHPT) is hypothesized to be an "early" type of primary hyperparathyroidism.

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Primary hyperparathyroidism

- Primary hyperparathyroidism is when one or more of the parathyroid glands makes too much parathyroid hormone, which draws calcium from the bones into the blood, weakening bone density and raising blood calcium level.
- In normocalcemic PHPT, the parathyroid glands are releasing too much hormone, but the blood calcium level has not risen yet.

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Normal primary hyperparathyroid

- Primary hyperparathyroidism is typically diagnosed when patients are found to have high blood calcium during routine checkups.
- However, nPHPT cannot be detected through high blood calcium lab results, because these patients have normal calcium levels.
- Patients with nPHPT are often uncovered during work up for osteoporosis or low bone mineral density.
- Proper diagnosis of normocalcemic primary hyperparathyroidism is challenging, because there are several other causes of high parathyroid hormone levels and normal calcium levels.

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Diagnosis

- Old dx: “bones, moans, groans”
- But often it is low bone density, GERD, fatigue, inability to think as extra Calcium is sticky which induces brain fog.
- Change in personality.
- Ionized calcium above 6
- Regular calcium above 10 consecutive while off calcium supplements for two months
- Sestamibi scan - many diagnostic centers don't do often so don't get great imaging

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GERD

- **GERD (Gastro-Esophageal-Reflux Disease) occurs in 65% of patients with primary hyperparathyroidism and high calcium. Removing the parathyroid tumor cures the GERD in the majority of patients.**
- A 51 year old male school teacher presented with fatigue, tiredness, memory loss, and GERD—typical signs and symptoms of primary hyperparathyroidism. His primary care provider was “monitoring” his blood calcium levels for over four years, and treating his low Vitamin D with high dose Vitamin D in order to “fix his calcium level.” He had nearly a dozen calcium levels checked over the period of “monitoring” and they all ranged from 10.1 to 10.9 mg/dl (note: adults over 35 should have all or almost all calcium levels “in the 9's”, not the 10's. And remember that it is not appropriate to “monitor” high blood calcium!).
- Prescribed PPIs but not getting better.

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GERD + Bone Loss

- He went to see a psychiatrist for depression, who checked some blood work (chemistry panel, thyroid function, parathyroid hormone level) to see if he had a 'metabolic problem' causing him to lose focus, lose interest in things he used to enjoy doing and be depressed. His blood tests proved he had primary hyperparathyroidism. Blood calcium was now even higher than before (11.4 mg/dl) and his parathyroid hormone level was too high (104 pg/ml where the normal range is between 14 and 65 pg/ml).
- He was referred to an endocrinologist who sent the patient for bone DEXA scan.
- The bone scan showed that he had osteoporosis.
- A parathyroid tumor(s) was causing loss of calcium from his bones and that his bones were thinning and that's why his bones were aching.

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Adenoma

- We found a single large (3.6 x 2.2 x 1.5 cm) parathyroid tumor located deep in the right neck next to the esophagus and removed it.
- The other three parathyroid glands were normal (must always check the other three parathyroid glands or the patient may not be cured and their symptoms will not go away).
- The patient went home a few hours after the operation. I saw the patient back in follow up 6 weeks later and he was down to 2 pills per day and his blood calcium level was 9.8 mg/dl, and parathyroid hormone level was normal – 22 pg/ml.
- The patient said that he felt great and that he previously thought that feeling tired, irritable, disinterested, and aching as well as having difficulty concentrating was just the aging process. All of symptoms he had prior to surgery resolved. What's more he was able to reduce his blood pressure medication in half, and he no longer needed to take his PPI because the GERD symptoms were gone.

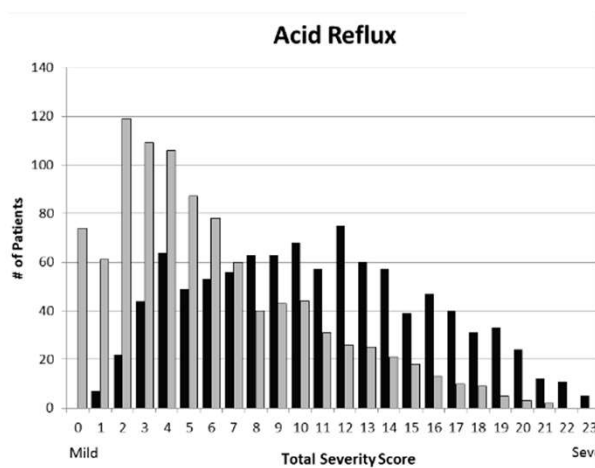


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GERD / Parathyroidectomy. A Prospective Study in 3000 Patients

- Almost 60% of the 3,000 patients treated for primary hyperparathyroidism had GERD symptoms and 81% of them were taking prescription reflux medications every day for two or more years prior to enrolling in the study.
- We used a standardized questionnaire to evaluate GERD symptoms before and for up to two years after surgery – the Standardized Frequency Scale for Symptoms of GERD (FSSG) questionnaire.
- **Our Findings: GERD symptoms were much improved or completely resolved for 62% of patients one year after they were cured by parathyroid surgery.** This dramatic improvement in GERD symptoms can be seen in the dramatic decrease in GERD medications. Prescription medications for GERD decreased from 81% of the patients in the study down to 26% one year after removal of the parathyroid tumor(s). Nearly 40% of patients had complete relief of GERD symptoms and no longer needed to take medications for GERD. The graph below is one of 7 important graphs in our upcoming publication. The black bars shows the severity of GERD Acid Reflux in patients prior to their parathyroid surgery, and the grey bars shows the severity of GERD and acid reflux 1 year later. Note that the vast majority of people got a lot better—as indicated by the grey bars which are shifted to the left (less severe GERD symptoms).

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What was learned from the largest study done on GERD in primary hyperparathyroidism?

- GERD symptoms are common in patients with primary hyperparathyroidism
- Surgical cure of the primary hyperparathyroidism [removal of parathyroid tumor(s)] provides significant, durable relief of GERD symptoms in most people.
- Curing the primary hyperparathyroidism enables most patients who were on prescription drugs for GERD prior to operation, to stop taking these prescription drugs after the operation
- .
- So, surgical cure of primary hyperparathyroidism is effective in reducing GERD symptoms, making this yet another reason to remove parathyroid tumor(s) in patients with primary hyperparathyroidism.

1. Surgical cure of primary hyperparathyroidism ameliorates gastroesophageal reflux symptoms. World J Surg. 2015 Mar;39(3):706-12. doi: 10.1007/s00268-014-2876-5. PMID: 25409840.

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GERD

- **Conclusion:** Symptomatic GERD is common in pHPT. Parathyroidectomy provides significant, durable relief of both motility and acid reflux symptoms allowing discontinuation of prescription drug use for GERD in most (74%) patients providing yet another indication for parathyroidectomy in pHPT.
- Surgical cure of primary hyperparathyroidism ameliorates gastroesophageal reflux symptoms. World J Surg. 2015 Mar;39(3):706-12. doi: 10.1007/s00268-014-2876-5. PMID: 25409840.

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Case Report

- Forced in to retirement psychotherapist, severe brain fog severe fatigue, personality changes, inability to work, osteoporosis, GERD
- Calcium levels 16+
- Parathyroidectomy
- Normal calcium within 3 months
- Back to full time work within 6 months

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Case for Boron Repletion

- Ultrastructural shifts in parathyrocytes and atrial cardiomyocytes induced by long-term treatment with boron-containing water (250 mg/liter) were found against the background of boron accumulation. These changes are indicative of enhanced secretory activity of these cells. It is hypothesized that boron modulates the effect of parathyroid hormone and atrial natriuretic factor and the rate calcium-sodium exchange
- Boron affects the functioning of the parathyroid gland and production of parathyroid hormone (PTH) which regulates blood calcium level and reduces blood pressure
- [Effect of boron on the ultrastructure of parathyrocytes and atrial cardiomyocytes]. Biull Eksp Biol Med. 1997 Jul;124(7):111-4. Russian. PMID: 9303718.

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Boron

- High dose in healthy renal patients up to 30 mg
- For several years
- Monitor ionized calcium, PTH and bones.
- In renal patients use 3 mg and 2 days a week increase to 6 mg/

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Boron helps keep calcium out of solution in renal tissue

- **OBJECTIVE:**
- Stone disease is an increasingly common form of renal disease. Diet plays an important role in expression of the tendency to stone formation. Renal epithelial cell injury by reactive oxygen species is a pre-requisite step and the administration of natural antioxidants has been used to protect against nephrolithiasis. Considering the nutrients, boron as an ultra-trace element is revealing to enhance the antioxidant defense mechanism and along vitamin status seems to have an impact on the stone removal.
- **METHODS:**
- A male patient with urolithiasis received daily boron plus antioxidants supplement and asked to consume enough of the dairy serving products plus adequate liquids.
- **RESULT:**
- Ultrasonography assessment revealed continuous stone removal or disposal without hydronephrosis with significant pain alleviation and reduction in hematuria. The lithiasic residues were collected. The 9*20 mm size of the one eliminated stone is of noteworthy.
- **CONCLUSION:**
- Successful and comfortable kidney stone repulsion with a minor pain and bleeding indicates that this impact of boron plus antioxidants deserves further study and clarification.
- [Endocr Regul](#). 2014 Jul;48(3):120-5. n**Boron and antioxidants complex: a new concept for the treatment of kidney stones without rigorous pain.**

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Boron – anti-oxidant in kidney

- **OBJECTIVES:**

- Kidney stone disease is a common form of renal disease. Antioxidants, such as vitamin E (Vit E) and boron, are substances that reduce the damage caused by oxidation.

- **METHODS:**

- Adult male rats were divided into 5 groups (n=6). In group 1, rats received standard food and water for 28 days (control group); in group 2, standard rodent food and water with 0.75% ethylene glycol/d (dissolved in drinking water) (EG Group); in group 3, similar to group 2, with 3 mg of boron/d (dissolved in water) (EG+B Group); in group 4, similar to group 2, with 200 IU of vitamin E injected intraperitoneally on the first day and the 14th day, (EG+Vit E Group); in group 5, mix of groups 3 and 4, respectively (EG+B+Vit E Group).

- **RESULTS:**

- Kidney sections showed that crystals in the EG group increased significantly in comparison with the control group. Crystal calcium deposition score in groups of EG+B (160), EG+Vit E, and EG+B+Vit E showed a significant decrease compared to EG group. Measurement of the renal tubules area and renal tubular epithelial histological score showed the highest significant dilation in the EG group. Tubular dilation in the EG+B+Vit E group decreased compared to the EG+B and EG+Vit E groups.

- **CONCLUSIONS:**

- Efficient effect of boron and Vit E supplements, separately and in combination, has a complimentary effect in protection against the formation of kidney stones, probably by decreasing oxidative stress.

- Protective effects of boron and vitamin E on ethylene glycol-induced renal crystal calcium deposition in rat. *Endocr Regul.* 2016 Oct 1;50(4):194-206. doi: 10.1515/enr-2016-0021. PMID: 27941176.

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Boron protects kidneys

- **Methods:** We determined 24 h urinary boron excretion using inductively coupled plasma mass spectrometry as a measure of boron exposure in 693 stable KTR (57% male, mean age 53y), enrolled in the TransplantLines Food and Nutrition Biobank and Cohort Study. Dietary intake was assessed using validated food-frequency questionnaires.

- **Results:** Linear regression analyses showed that dietary intake of fruit, wine and nuts were key determinants of boron excretion. **In addition, boron excretion was negatively correlated with homocysteine and inflammatory parameters.** In total, 73 (32%), 47 (20%) and 30 (13%) KTR died among the lowest, middle and highest tertiles of 24 h urinary boron excretion, respectively ($P_{\text{log-rank}} < 0.001$). Cox regression analyses showed that **high boron excretion was strongly associated with lower risk of mortality**, independent of age, sex, estimated glomerular filtration rate and history of cardiovascular disease (HR per doubling: 0.51, 95% CI: 0.40 to 0.66, $P < 0.001$).

- **Conclusion:** Boron may be an overlooked target to improve long-term survival among KTR and potentially other patients, likely through pathways other than inflammation or the methionine-homocysteine cycle that were previously suggested. Interventional trials are warranted to confirm the potential of dietary boron supplementation in KTR and other patient population

- Boron Intake and decreased risk of mortality in kidney transplant recipients. *Eur J Nutr.* 2022 Mar;61(2):973-984. doi: 10.1007/s00394-021-02702-0. Epub 2021 Oct 22. PMID: 34677681; PMCID: PMC8854244.

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HRT – Lung Cancer

- Lung cancer incidence and mortality rates are higher in men than women in the United States.
- Cigarette smoking is the major exposure associated with lung cancer, but other factors such as diet and genetics may also contribute to causation. For example, evidence based on five prospective cohort studies demonstrated that lung cancer incidence is higher among women than men who have never smoked.
- We and others have previously suggested a protective role of hormone replacement therapy (HRT).
- Hormone replacement therapy and lung cancer risk: a case-control analysis. *Clin Cancer Res.* 2004;10:113–123.
- Reproductive factors, hormone use, estrogen receptor expression and risk of non small-cell lung cancer in women. *J Clin Oncol.* 2007;25:5785–5792.

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Boron – Lung Cancer Protection

- Hormone replacement therapy (HRT) may reduce lung cancer risk.
- Dietary boron may have actions similar to those of HRT; however, no previous study has reported the associations between dietary boron intake and lung cancer risk or the joint effects of boron intake and HRT use on lung cancer risk.
- The authors examined the associations between boron intake and the joint effects of boron intake and HRT on lung cancer risk in women.
- In an ongoing case-control study in Houston, Texas (July 1995 through April 2005, end date for this analysis), 763 women were diagnosed with lung cancer, and 838 were matched healthy controls with data on both diet and HRT. Multiple logistic regression analyses were conducted to assess the associations between dietary boron and HRT with lung cancer risk.
- In joint-effects analyses, compared with women with high dietary boron intake who used HRT, the odds ratio for lung cancer for low dietary boron intake and no HRT use was 2.07 (95% CI: 1.53, 2.81).
- Boron intake was inversely associated with lung cancer in women, whereas women who consumed low boron and did not use HRT were at substantial increased odds.
- Dietary boron and hormone replacement therapy as risk factors for lung cancer in women. *Am J Epidemiol.* 2008 May 1;167(9):1070-80. doi: 10.1093/aje/kwn021. Epub 2008 Mar 14. PMID: 18343880; PMCID: PMC3390773.

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Boron – Hormone Balance & Protect for Young Males with low T

- Boron possesses widespread properties in biochemistry and nutrition. Acute supplementation with 11.6 mg of boron resulted in a significant increase in plasma boron concentration. Given such a fast bioavailability, the objective was to determine whether acute (hourly or daily), and weekly supplementation could have any significant biological effects on the steroid hormones and further on some inflammatory biomarkers.
- Eight healthy male volunteers attended the laboratory on three occasions (days 0, 1 and 7).
- On the first day (day 0), a blood sample collection at 8.00 A.M. was followed by ingestion of placebo with the breakfast. On the next day (supplementation-day 1), similar procedure was followed by ingestion of a capsule containing 10mg of boron. On both occasions blood was collected every 2h for the next 6h. Subjects were requested to consume a capsule of 10mg boron every day with their breakfast, and on the day 7, the blood collection was carried out at 8.00 A.M., again.
- Boron in plasma increased significantly following hours and weekly consumption.
- Six hours supplementation showed a significant decrease on sex hormone binding globulin (SHBG), high sensitive CRP (hsCRP) and TNF- α level.
- After one week (in samples taken at 8.00 A.M., only), the mean plasma free testosterone increased.
- Also, concentrations of all three inflammatory biomarkers decreased after supplementation. Of note, despite decreased proinflammatory cytokines, based on recent clinical data, this must be the first human study report to show an increase level of free testosterone after boron consumption.
- Comparative effects of daily and weekly boron supplementation on plasma steroid hormones and proinflammatory cytokines. J Trace Elem Med Biol. 2011 Jan;25(1):54-8. doi: 10.1016/j.jtemb.2010.10.001. Epub 2010 Dec 3. PMID: 21129941.

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Boron enhances bone

- Need with pHPT
- Need with bone loss
- Need to lower SHBG as age
- Dietary boron supplementation enhanced the action of estrogen, but not that of parathyroid hormone, to improve trabecular bone quality in ovariectomized rats. Biol Trace Elem Res. 2001 Summer;82(1-3):109-23. doi: 10.1385/bter:82:1-3:109. PMID: 11697760.

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Nothing Boring About Boron

- (3) beneficially impacts the body's use of estrogen, testosterone, and vitamin D; (4) boosts magnesium absorption; (5) reduces levels of inflammatory biomarkers, such as high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor α (TNF- α); (6) raises levels of antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase; (7) protects against pesticide-induced oxidative stress and heavy-metal toxicity; (8) improves the brains electrical activity, cognitive performance, and short-term memory for elders; (9) influences the formation and activity of key biomolecules, such as S-adenosyl methionine (SAM-e) and nicotinamide adenine dinucleotide (NAD(+)); (10) has demonstrated preventive and therapeutic effects in a number of cancers, such as prostate, cervical, and lung cancers, and multiple and non-Hodgkin's lymphoma; and (11) may help ameliorate the adverse effects of traditional chemotherapeutic agents.
- In none of the numerous studies conducted to date, however, do boron's beneficial effects appear at intakes > 3 mg/d. Dose in Hormone Balance and Protect.
- No estimated average requirements (EARs) or dietary reference intakes (DRIs) have been set for boron-only an upper intake level (UL) of 20 mg/d for individuals aged ≥ 18 y.
- The absence of studies showing harm in conjunction with the substantial number of articles showing benefits support the consideration of boron supplementation of 3 mg/d for any individual who is consuming a diet lacking in fruits and vegetables or who is at risk for or has osteopenia; osteoporosis; osteoarthritis (OA); or breast, prostate, or lung cancer.
- Nothing Boring About Boron. Integr Med (Encinitas). 2015 Aug;14(4):35-48. PMID: 26770156; PMCID: PMC4712861.

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Boron – regulation of sex hormones

- Increased levels of sex steroids have been demonstrated in both men and women after boron supplementation.^{1,20} In 1987, Nielsen et al¹ reported that dietary boron repletion in postmenopausal women (n = 13), who were previously on a low-boron diet, significantly increased their serum estradiol (E₂) and testosterone levels, particularly for those women whose dietary intake of magnesium was low. In women on a low-magnesium diet, E₂ almost doubled, increasing from an average of 21.1 pg/mL to 41.4 pg/mL. Testosterone more than doubled, rising from an average of 0.51 ng/mL to 0.83 ng/mL. Similar increases were seen in the women on an adequate-magnesium diet: E₂ rose from an average of 15.3 pg/mL to 38.0 pg/mL, and testosterone increased from 0.38 ng/mL to 0.65 ng/mL. In 1997, Naghii et al²⁰ published findings of a similar increase in serum levels of E₂ in healthy males (n = 18) after 4 weeks of dietary supplementation with boron.
- After only 1 week of boron supplementation of 6 mg/d, a further study by Naghii et al²⁰ of healthy males (n = 8) found (1) a significant increase in free testosterone, which rose from an average of 11.83 pg/mL to 15.18 pg/mL, and (2) significant decreases in E₂, which dropped from 42.33 pg/mL to 25.81 pg/mL. All of the inflammatory biomarkers that were measured also decreased: (1) interleukin (IL) 6, from 1.55 pg/mL to 0.87 pg/mL; (2) high-sensitivity C-reactive protein (hs-CRP) by approximately 50%, a remarkable decrease, from 1460 ng/mL to 795 ng/mL; and (3) tumor necrosis factor α (TNF- α) by approximately 30%, from 12.32 to 9.97 pg/mL. Levels of dihydrotestosterone, cortisol, and vitamin D increased slightly.
- In young males with low testosterone give Hormone Balance and protect two twice a day. Clean up diet. Back to basics. Weight work.
- The significant decrease in the men's plasma E₂ after 1 week of boron supplementation suggests a higher rate of conversion of total testosterone (T) to free testosterone (FT) in the testosterone metabolic pathway. In support, the ratios of FT/T, T/E₂, and FT/E₂, were all significantly increased, indicating boron had androgen amplifier effects: (1) FT/T (pg/mL/ng/mL) increased from 3.62 to 4.66; (2) T/E₂ (ng/mL) rose from 91.68 to 148; and (3) FT/E₂ (ng/mL) from 0.31 to 0.67.
- It is well known that approximately 98% of testosterone molecules are bound to proteins in the blood, principally to sex hormone-binding globulin (SHBG), and are not bioavailable because bound hormones cannot exit capillaries.²¹ Thus, the elevation of unbound free testosterone seen with boron supplementation may have significant beneficial ramifications, particularly in aging men in whom, typically, levels of SHBG increase and levels of FT decrease.²¹

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Boron helps lower SHBG and raise E in young women

- In postmenopausal women consuming a low boron diet (below ¼ mg/day) giving 3 mg boron/d
- Significantly increased estradiol and testosterone.
- Perfect in lower hormone young females.
- The concentration of estradiol in blood in females with boron 3 mg/d without HRT was = to menopausal women with no boron getting HRT.
- Effect of Dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. FASEB J 1987,1:394-397

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Boron – Prevention of D Deficiency

- Boron has been shown to increase serum levels of 25-hydroxyvitamin D₃ (25[OH]D₃) in animal studies^{4,24} and of vitamin D-deficient individuals in human studies.^{25,26} In a clinical trial²⁵ in which middle-aged men and women (n = 15) were placed on a low-boron diet, which was also marginal in magnesium and copper status, for 63 days (0.23 mg B/2000 kcal), 25(OH)D₃ rose significantly after boron supplementation (3 mg/d as sodium borate) for an additional 49 days. Levels of 25(OH)D₃ rose from an average of 44.9 nM after the 63 days of boron deprivation to 62.4 nM after the 49 days of boron repletion, a 39% increase.

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