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Rickets: Once Believed Eradicated, This Nutritional Deficiency Disease Reemerges

Nutritional rickets, at one time referred to as rachitis, was a common childhood disease during the industrial revolution through the 1940s in the United States. It results in delayed closure on the fontanelles in infants, slow physical development, "bow-legged" appearance, and other skeletal and metabolic disorders. Rickets is caused by a lack of vitamin D in the infant or the mother's diet (if she breast feeds) or inadequate sunlight exposure. Sunlight converts cholesterol in the skin to vitamin D.

Between 1910 and 1961, some 14,000 infant and childhood deaths were attributed to rickets. Perhaps not entirely surprising, in the early part of the 20th century, medical controversies raged on the role of diet and environment in rickets. A 1924 booklet published by the Metropolitan Life Insurance Co. recommended that infants and children be given pure cod liver oil or egg yolk or be exposed to direct sunlight to cure rickets. Later, cow's milk was fortified with vitamin D, and by the 1960s rickets became rare in the United States.

But, according to a number of medical papers published in the 1990s, nutritional rickets—i.e., severe vitamin D deficiency—is reemerging. The latest report, by Shelley R. Kreiter, MD, of the Wake Forest University School of Medicine, Winston-Salem, N.C., focused on 30 infants and toddlers. More than half of the children were diagnosed with rickets in the past two years. All of them were African-American and were breast fed without vitamin D supplementation. The infants also had relatively little sunlight exposure.

"Maternal vitamin D status is a major factor regulating the vitamin D content of human milk, and dark-skinned mothers are at higher risk for being vitamin D deficient than those who are light-skinned," wrote Kreiter in the *Journal of Pediatrics*. He added that the large amount of melanin, a skin pigment, reduces the vitamin D-producing effect of sunlight in dark-skinned individuals. Longer periods of sunlight are needed to compensate.

In a related editorial, Thomas R. Welch, MD, of the Children's Hospital Research Foundation, Cincinnati, noted that rickets began reemerging in the late 1970s. One hospital survey identified "several hundred children with nutritional rickets," he wrote.

In advocating vitamin D supplementation for infants, Welch pointedly wrote, "We do not believe that additional research is required to support a practice that nearly a century of experience has been shown to be safe, cheap, and effective."

In adults, vitamin D deficiency may also be more common than thought, according to two studies. In one, Harvard University researchers reported that, of 290 hospitalized patients, 57 percent were judged deficient and 22 percent were considered "severely" deficient. Another study, conducted at the Brigham and Women's Hospital, Boston, found that women with hip fractures had relatively low vitamin D levels, with half of them being seriously deficient.

References: Kreiter SR, Schwartz RP, Kirkman HN, et al. Nutritional rickets in African American breast-fed infants. *Journal of Pediatrics*, 2000;137:153-157. Thomas MK, Lloyd-Jones DM, Thadhani RI, et al. Hypovitaminosis D in medical inpatients. *New England Journal of Medicine*, 1998;338:777-783. LeBoff MS, Koklmeier L, Hurwitz S, et al. Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *JAMA*, 1999;281:1505-1511. □

Blood Sugar, Baldness and Antioxidants: Could They All Be Related?

Reducing your intake of refined sugars could slash the number of free radicals produced by your body, lowering your risk of diabetes and diabetic complications. Doing so might also – if it's not too much of a stretch – help keep you from getting bald.

The background: High levels of free-radical activity and free-radical damaged tissues are common among people with diabetes or obesity. Obesity is the major risk factor for adult-onset diabetes.

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In a recent study, Paresh Dandona, PhD, of the State University of New York, Buffalo, and his colleagues asked 14 healthy men and women to take either a glucose-tolerance test (75 grams of glucose) or to consume a noncalorically sweetened drink.

Dandona found that the number of free radicals generated by two types of lymphocytes (immune cells) in the subjects more than doubled two hours after drinking the glucose solution. In addition, the subjects' vitamin E levels dropped by 4 percent, suggesting increased free-radical production. There was no change in the subjects consuming the artificially sweetened water.

In a separate study of 305 men, researchers at the University of Oulu, Finland, reported a strong association between Syndrome X and premature, male-hormone-dependent baldness. Syndrome X is a prediabetic condition characterized by insulin resistance (the result of elevated glucose and insulin levels), elevated blood fats, high blood pressure, and abdominal obesity.

"Our observations raise the question whether insulin resistance could be a pathophysiological mechanism or promoting factor in early androgenic alopecia [baldness], which could, in turn, be an early marker of insulin resistance," wrote Veikko Matilainen, MD, and his colleagues.

Numerous studies have noted that people with diabetes, Syndrome X, and insulin resistance experience above-normal levels of free radicals and below-normal levels of radical-quenching antioxidants. The same pattern also appears to be true in bald men, though it's not clear whether a cause-and-effect relationship exists.

Adding to the picture, a recent study of 71 men by Turkish researchers found that bald men had relatively low levels of several antioxidants, including beta-carotene, glutathione, and glutathione peroxidase. These men also had high levels chemicals indicating elevated free radical activity.

References: Mohanty P, Hamouda W, Garg R, et al. Glucose challenge stimulates reactive oxygen species (ROS) generation by lymphocytes. *Journal of Clinical Endocrinology & Metabolism*, 2000;85:2970-2973. Matilainen V, Koskela P, Keinanen-Kiukaanniemi S. Early androgenic alopecia as a marker of insulin resistance. *Lancet*, 2000;356:1165-1166. Kokcam I. Antioxidants and lipid peroxidation status in the blood of patients with alopecia. *Cell Biochemistry and Function*, 2000;18:169-173. □

Ginkgo Supplements Improve Memory, Reaction Times in Healthy Subjects

The herb *Ginkgo biloba* may do more than just help fuzzy minded boomers and seniors. Researchers

have reported that, in a small study, *Ginkgo* supplements sharpened the minds of college students.

Andrew B. Scholey, PhD, of the University of Northumbria, Newcastle upon Tyne, England, tested several key cognitive characteristics of 20 college students ages 19-24 years. In a crossover study, the students were given 120 mg, 240 mg, or 360 mg of a standardized *Ginkgo* extract or a placebo.

"Compared with the placebo, administration of *Ginkgo* produced a number of significant changes...The most striking of these was a dose-dependent improvement of the 'speed of attention' factor following both 240 mg and 360 mg of the extract..." wrote Scholey. Speed of attention essentially referred to the subjects' reaction times, and the improvements were evident two and one-half hours after taking the supplement and were still present at six hours.

In addition, the subjects' quality of memory and speed of memory also improved, with the improvements generally being more noticeable after the higher dosages of *Ginkgo*.

Reference: Kennedy DO, Scholey AB, Wesnes KA. The dose-dependent cognitive effects of acute administration of *Ginkgo biloba* in healthy young volunteers. *Psychopharmacology*, 2000;151:416-423. □

Two Studies Link Dietary Sources of Vitamins C and E to Low Stroke Risk

Two new studies show that high dietary intake of vitamins C and E – not necessarily supplements – can substantially reduce the risk of stroke.

In the first study, Tetsuji Yokoyama, MD, of the Osaka City University Medical School, Japan, and his colleagues tracked the health of 2,100 men and women in a rural community for 20 years. None of the subjects had a stroke before entering the study.

Overall, subjects with the highest blood levels of vitamin C at the beginning of the study – suggestive of long-term vitamin C consumption – had the lowest risk of stroke from age 40 onward. People over age 64 with high vitamin C levels were 41 percent less likely to suffer a stroke compared with those who had the lowest vitamin levels.

People with the highest vitamin C levels also had a lower risk of cerebral infarction, a stroke in which blood flow to the brain is blocked. Elderly people with high vitamin C levels were 49 percent less likely to suffer this type of stroke. Also, people with high vitamin C levels were 55 percent less likely to experience a hemorrhagic stroke, characterized by a rupture of a blood vessel in the brain.

It's very possible that the blood levels of vitamin C were only a marker of overall fruit and vegetable intake. Yokoyama reported that people who ate

vegetables six or seven times weekly were 58 percent less likely to have a stroke. Even consumption of just three to five vegetables weekly was associated with a 44 percent reduced risk of stroke.

In a separate study, Aaron R. Folsom, PhD, of the University of Minnesota, reported that high vitamin E consumption from food reduced the risk of death from stroke by 60 percent in a group of more than 34,000 postmenopausal women. This particular study did not find a protective effect from either vitamin C or vitamin E supplements.

References: Yokoyama T, Date C, Kokubo Y, et al. Serum vitamin C concentration was inversely associated with subsequent 20-year incidence of stroke in a Japanese rural community: the Shibata study. *Stroke*, 2000;31:2287-2294. Yochum LA, Folsom AR, Kushi LH. Intake of antioxidant vitamins and risk of death from stroke in postmenopausal women. *American Journal of Clinical Nutrition*, 2000;72:476-483. □

Eating a Lot of Fish, Rich in Good Fats, Lowers the Risk of Heart Disease

Eating a diet rich in fatty fish, compared with lean fish, reduces the risk of dying from heart disease by one-third, according to European researchers.

Claudia M. Oomen, PhD, of the National Institute of Public Health and the Environment, Netherlands, and her colleagues tracked the health and dietary habits of more than 2,700 Finnish, Italian, and Dutch men for 20 years, beginning in 1970.

Oomen found no relationship between overall fish consumption and the risk of death from heart disease. However, men eating fatty fish were 34 percent less likely to die from heart disease.

Fatty fish include salmon, mackerel, and hering, whereas nonfatty fish include codfish, perch, and pike. Fatty fish are particularly high in omega-3 fatty acids, eicosapentanoic acid and docosahexaenoic acid, which other studies have found to reduce arrhythmias and blood pressure.

Reference: Oomen CM, Feskens EJM, Rasanen L, et al. Fish consumption and coronary heart disease mortality in Finland, Italy, and the Netherlands. *American Journal of Epidemiology*, 2000;151:999-1006. □

N-Acetylcysteine May Help Preserve Cartilage, Protect Against Osteoarthritis

N-acetylcysteine (NAC), a sulfur-containing antioxidant, has been shown to significantly reduce flu symptoms and may also reduce the risk of cancer. A new study has found that it may also help prevent osteoporosis.

Osteoporosis entails the breakdown of cartilage pads that cushion physical stresses on joints, such as

knees and knuckles. Cartilage and chondrocytes – the cells that form cartilage – are very sensitive to free radical damage, and the wear and tear of joints generates large amounts of free radicals.

Recent research has shown that NAC can inhibit inflammatory activity in joints as well as block cartilage damage. So Muhammad Zafarullah, PhD, of the University of Montreal, Canada, tested how human and cow chondrocytes responded to NAC.

In his experiment, Zafarullah found that NAC and other sulfur-containing antioxidants (e.g., glutathione) rapidly activated specific enzymes involved in promoting chondrocyte survival.

“In view of these results, benefits of nutritional antioxidants to prevent chondrocytes apoptosis [cell death] and maintain cartilage integrity in arthritis clearly merit additional investigation,” Zafarullah wrote.

Reference: Li WQ, Dehnade F, Zafarullah M. Thiol antioxidant, N-acetylcysteine, activates extracellular signal-regulated kinase signaling pathway in articular chondrocytes. *Biochemical and Biophysical Research Communications*, 2000;275:789-794. □

Yet Another Study Finds that St. John's Wort is Better than Rx Antidepressant

This year, several well-designed studies have shown the herb St. John's wort (*Hypericum perforatum*) to be as good as, if not better than, Prozac and Zoloft, the two leading antidepressant drugs. Now, researchers report that St. John's wort is at least as effective as imipramine – if not a little better – and also results in far fewer side effects.

Helmut Woelk, MD, of the University of Giessen, Germany, led a study of 324 outpatients with mild to moderate depression. The patients were given either 500 mg of a St. John's wort extract or a therapeutic dose of imipramine daily for six weeks.

Using a battery of standard psychiatric tests, both the herb and drug were equally effective in reducing signs of depression by almost half. However, St. John's wort was a little better than the drug in relieving anxiety.

Overall, subjects taking St. John's wort had about half of the side effects of those taking imipramine. Only 3 percent of those taking the herb withdrew from the study because of side effects, compared with 16 percent of those taking the drug.

“Treating patients with mild to moderate depression can be a challenge,” wrote Woelk. “The mild nature of the disorder often precludes the treatments commonly used in severe depression... Patients seen in general practice frequently prefer to bear the symptoms of depression rather than sustain

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Quick Reviews of Recent Research

• Beta-Carotene helps patients with cystic fibrosis

People with cystic fibrosis poorly absorb fat-soluble nutrients, mainly because they do not produce sufficient amounts of pancreatic enzymes. Because of this, they typically lack carotenoids and vitamin E and suffer high levels of "oxidative stress." In a study of 24 children with cystic fibrosis, researchers provided 1 mg of beta-carotene per kilogram (2.2 pounds) of body weight, up to 50 mg daily, plus vitamins A, C, and E. Overall, the supplements reduced free radical levels and, in the younger patients, improved lung function.

Rust P, et al. *Annals of Nutrition and Metabolism*, 2000;44:30-37.

• Lutein esters absorbed, increase macular pigment

Lutein is an antioxidant carotenoid believed to prevent macular degeneration, the leading cause of blindness among the elderly. Two forms of lutein are sold in supplemental form, "free lutein" and "lutein esters." Researchers asked eight men, ages 18-50 to take 10 mg of lutein esters, extracted from marigold flowers, for 12 weeks. During the study, blood levels of lutein increased by five times, and the macular pigment (consisting of lutein) increased in thickness by about 20 percent.

Berendschot TT, et al. *Investigative Ophthalmology and Visual Science*, 2000;41:3322-3326.

• Soy isoflavones lower heart risk, but not cholesterol

Researchers fed rabbits high-cholesterol diets, giving some of the animals soy isoflavones. The isoflavones did not alter blood cholesterol levels in the animals. However, rabbits consuming isoflavones were less susceptible to free-radical oxidation of cholesterol, and they also developed smaller cholesterol deposits in the aorta.

Yamakoshi J, et al. *Journal of Nutrition*, 2000; 130:1887-1893.

• Zinc lozenges ease cold symptoms

Studies on the cold-fighting effect of zinc lozenges have had mixed results. In the latest study, researchers asked 50 patients to start taking zinc acetate lozenges or placebos every two to three hours

within the first 24 hours of developing cold symptoms. Each zinc lozenge contained 12.8 mg of the mineral. People taking about 80 mg of zinc daily reported that their cold symptoms ceased in less than five days, compared with eight days among those taking the placebo.

Prasad AS, et al. *Annals of Internal Medicine*, 2000;133:245-252.

• Green tea compounds may protect skin

Green tea is rich in antioxidants called polyphenols. A review of experiments on green tea and skin disorders found that the tea's extracts have anti-inflammatory and anticancer properties.

Katiyar SK, et al. *Archives of Dermatology*, 2000;136:989-994.

• Centenarians have high vitamin E and A levels

A study of people over age 100 found that they had considerably higher levels of vitamins E and than did younger subjects. This finding suggests that diets high in antioxidants may help predispose people to longer lives.

Mecoci P, et al. *Free Radical Biology & Medicine*, 2000;28:1243-1248.

• Vitamin E may protect the prostate

In a cell-culture study, researchers found that vitamin E inhibited the growth of hormone-dependent prostate cancers, but not nonhormone-dependent prostate cancer. This finding supports a recent Finnish study in which vitamin E supplements reduced the risk of prostate cancer by one-third.

Gunawardena K, et al. *The Prostate*, 2000;44: 287-295.

• Antioxidants benefit cancer patients

Cancer patients often have depressed immune function. Researchers reported that alpha-lipoic acid and N-acetylcysteine increased the activity of immune cells obtained from terminal cancer patients.

Mantovani G, *International Journal of Cancer*, 2000;86:842-847.

St. John's Wort and Depression...

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the side effects of treatment with antidepressants.... Hypericum is therapeutically equivalent to imipramine, but is better tolerated by patients."

Reference: Woelk H, et al. Comparison of St. John's wort and imipramine for treating depression: randomized controlled trial. *British Medical Journal*, 2000;321:536-539. □

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Post Office Box 30246 • Tucson AZ 85751-0246 USA

Editor and Publisher: **Jack ChalleM**
Copy Editor: **Melissa Diane Smith**

Medical and Scientific Advisors:
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