



health ministry and US-based consultant Abt Associates Inc, showed that 90% do not have a consistent water supply and 50% do not have electrical generators.

“We never have a day without the electricity cutting off for 12 hours or longer, and half of these centers have no generator,” said Alwan.

The same survey showed that 95% of those centers do not have gynecologic tables or electrocardiogram machines. “When we say there’s a scarcity of equipment, we’re not talking about MRI or CT scans,” Alwan explained. “We’re talking about stethoscopes, sphygmomanometers—central equipment is missing.”

Even though the health ministry has developed a new formulary, Alwan said the country’s pharmaceutical sector is

“totally inorganized . . . we do not have a national drug policy.” In June, he added, a task force charged with investigating medication shortages found that of 900 essential medications that should be available in Iraq, supplies of 400 were down to zero.

#### MATERNAL AND CHILD HEALTH

In Alwan’s list of health care priorities, nearly all seem urgent. Some of the most pressing, however, concern maternal and child health. Iraq’s maternal mortality rate is 294 per 100 000 live births compared with 40 per 100 000 in nearby Jordan, he said.

According to Alwan, it appears that death rates in infants and children younger than 5 years from acute respiratory diseases and diarrheal diseases have risen since 1990, but that

surveillance data and death certification information are unreliable. However, the country has a goal to cut the infant mortality rate by 50% by the end of next year.

In early August, the health ministry was working to complete an analysis of health needs and priorities for a conference at the end of the month. Over the next 4 years, Iraq will need \$1 billion per year just to rebuild the physical infrastructure, Alwan estimated. Beyond the country’s immediate needs, which also include nutrition programs, training for health professionals, and strengthening emergency health services, long-term goals must address improving management and health information systems and combating pervasive corruption, he said. □

## Scientists Probe Role of Vitamin D Deficiency a Significant Problem, Experts Say

Catherine Meyer, MD

**V**ITAMIN D HAS RECEIVED INCREASING attention over the past few years—with good reason. A surprising number of people of all ages worldwide have suboptimal levels of this vitamin. Low levels may lead to unexplained diffuse body pains and a variety of other symptoms and may also contribute to serious health problems that only become apparent years later.

Vitamin D deficiency often goes undetected. But if considered as a possibility, it can be easily diagnosed and remedied.

The condition is more prevalent than most physicians suspect and the incidence may be increasing over time. Past studies have demonstrated that people who immigrate to the north from equatorial countries, patients with chronic illnesses, and undernourished or homebound individuals are at risk.

More surprising, however, are recent reports of vitamin D deficiency in people who would seem to be less vulnerable. A 2002 study of healthy young



Sunlight exposure and oily fish such as mackerel, sardines, and salmon are the significant natural sources of vitamin D.

adults in Boston found that of 165 men and women aged 18 to 29 years screened at the end of the winter, 36% were vitamin D deficient (*Am J Med*.2002;112:659-662). Another study of 150 otherwise healthy adults from

Minneapolis aged 10 to 65 years who had persistent, nonspecific musculoskeletal pain syndromes found that 93% had some deficiency and 28% had severe deficiency of vitamin D (*Mayo Clin Proc*. 2003;78:1463-1470). Earlier this year, a study of 307 healthy urban adolescents screened during their annual physical examination found that 24% were vitamin D deficient and 4.6% were severely deficient (*Arch Pediatr Adolesc Med*. 2004;158:531-537).

The term *vitamin D* is used to refer to a number of related molecules. Vitamin D<sub>2</sub> (ergocalciferol) or vitamin D<sub>3</sub> (cholecalciferol) are the forms of the molecule that can be ingested. Cholecalciferol can also be formed by the body when 7-dehydrocholesterol, its precursor in the skin, is exposed to ultraviolet B sunlight.

Cholecalciferol is converted by the liver into 25-hydroxyvitamin D (calcidiol), the circulating storage form of the molecule, which is further con-



verted by the kidney into the active metabolite, 1,25-dihydroxyvitamin D (calcitriol). Vitamin D deficiency can affect bone, breast, colon, prostate, brain, muscle, cells of the immune system, and other tissues in the body that have receptors for calcitriol.

**CONSEQUENCES OF DEFICIENCY**

Because vitamin D is necessary for calcium absorption and transport of calcium into bone, a deficiency can lead to osteoporosis. A less appreciated consequence of vitamin D deficiency is osteomalacia, the adult counterpart of childhood rickets, which can cause diffuse, dull, aching body pain affecting many areas of the body, including the ribs and sternum.

Vitamin D deficiency is associated with weakness and with falls in the elderly. In a meta-analysis of 5 randomized controlled trials involving 1237 participants, vitamin D supplementation reduced the risk of falls among ambulatory or institutionalized older individuals by more than 20% (*JAMA*. 2004;291:1999-2006).

Recent studies suggest that low vitamin D levels may also contribute to the development of a number of common and serious diseases. Interest in vitamin D deficiency, says Robert P. Heaney, MD, of Creighton University in Omaha, has become “greater virtually every week, in part because of the increasing number of publications implicating vitamin D [deficiency] in so many disorders.”

Vitamin D plays a part in regulating cell proliferation, differentiation, and removal (apoptosis). Calcitriol is a powerful inhibitor of cancer cell growth, and studies have shown that inadequate stores of this molecule contribute to development of some of the most common cancers including breast, colon, prostate, and ovarian.

Small clinical trials have shown that calcitriol can slow rising rates of prostate-specific antigen levels in men with prostate cancer. Phase 1 and 2 studies of vitamin D as a treatment for prostate cancer, alone or combined with traditional cancer drugs, are currently in progress.

Selected Food Sources of Vitamin D		
Food	International Units	Daily Value, %*
Cod liver oil, 1 tablespoon	1360	340
Salmon, cooked, 3 1/2 ounces	360	90
Mackerel, cooked, 3 1/2 ounces	345	90
Sardines, canned in oil, drained, 3 1/2 ounces	270	70
Eel, cooked, 3 1/2 ounces	200	50
Milk, nonfat, reduced fat, and whole, vitamin D fortified, 1 cup	98	25
Margarine, fortified, 1 tablespoon	60	15
Cereal grain bars, fortified with 10% of the DV, 1 each	50	10
Pudding, 1/2 cup prepared from mix and made with vitamin D fortified milk	50	10
Dry cereal, vitamin D fortified with 10% of DV, 3/4 cup (other cereals may be fortified with more or less vitamin D)	40-50	10
Liver, beef, cooked, 3 1/2 ounces	30	8
Egg, 1 whole (vitamin D is present in the yolk)	25	6

\*DV indicates daily value. DVs are reference numbers based on the recommended dietary allowance. They were developed to help consumers determine if a food contains very much of a specific nutrient. The DV for vitamin D is 400 IU. The percent DV listed on the nutrition facts panel of food labels tells adults what percentage of the DV is provided by one serving. Percent DVs are based on a 2000-calorie diet. Your DVs may be higher or lower depending on your calorie needs. Foods that provide lower percentages of the DV will contribute to a healthful diet. Source: Clinical Nutrition Service. *Facts About Dietary Supplements: Vitamin D*. Bethesda, Md: National Institutes of Health; 2002.

Studies in animal models have demonstrated that vitamin D may also prevent or arrest such autoimmune diseases as type 1 diabetes, rheumatoid arthritis, inflammatory bowel disease, and multiple sclerosis, and some clinical studies are supporting these findings. Earlier this year, researchers found, in a long-term study of 180 000 women, that those who took 400 IU/d of supplemental vitamin D (the amount in an ordinary multivitamin) were 40% less likely than those who did not to develop multiple sclerosis (*Neurology*. 2004;62:60-65).

Another study found that of 10366 children studied at 1 year of age, those who took a recommended dose of vitamin D during infancy were only one fifth as likely to develop type 1 diabetes as those who did not (*Lancet*. 2001;358:1500-1503). Scientists believe that suboptimal levels of vitamin D may also play a part in the development or worsening of other medical conditions including osteoarthritis, hypertension, and cardiovascular disease.

**SUNLIGHT AND OTHER SOURCES**

The best way to obtain vitamin D is through direct exposure of the skin to ultraviolet B rays in sunlight. Milk, the main dietary source, is fortified with modest amounts of vitamin D, as are some orange juices and a few breads and cereals. Unfortunately, the amount of vitamin D added to fortified foods is notoriously unreliable, and the only significant natural food sources are oily fish (such as salmon, mackerel, and sardines) and fish oils.

Concerns over the contribution of sun exposure to skin cancers have led the American Academy of Dermatology to recommend strict measures for minimizing this risk. Vitamin D experts, on the other hand, suggest that the modest amount of sunlight required to prevent vitamin D deficiency is probably safe for most individuals—but they also note that for many individuals, sunlight exposure is too limited to obtain adequate vitamin D by this route.

Almost no ultraviolet B sun rays reach those living in latitudes greater than 35°



to 40° from the equator during the winter months. Heavy air pollution filters out ultraviolet B light; so does glass, with the consequence that sun exposure may be absent or severely limited in institutionalized or homebound individuals. Sun exposure is also decreased for people whose clothing covers most of their bodies, such as traditionally dressed women in the Middle East and for those who use sunscreen or have dark skin. Vitamin D levels also can be low in the elderly because they have decreased amounts of the precursor to cholecalciferol in their skin. This means that for many populations, the only way to obtain adequate vitamin D is through ingestion of vitamin D-rich foods or supplements.

Recent concerns have arisen that infants who are breastfed and kept out of the sun, especially if they are dark-skinned, will develop rickets. A report of 30 black children from North Carolina with nutritional rickets found that all had been breastfed without receiving supplemental vitamin D and more than half presented in the final 2 years of the 10-year observational period—suggesting that the incidence is on the rise (*J Pediatr.* 2000;137:153-157). Last year the American Academy of Pediatrics officially recommended that all infants have a minimum intake of 200 IU/d of vitamin D beginning in the first 2 months of life (*Pediatrics.* 2003;111:908-910).

Other factors that put persons at risk for vitamin D deficiency are certain drugs, notably anticonvulsants. Patients with kidney disorders and malabsorption syndromes (including those resulting from bariatric surgery) are also at risk. In addition, obesity contributes to deficiency of vitamin D because the vitamin accumulates in fat stores that keep it from circulating in the body.

#### MEASUREMENT OF VITAMIN D

Because many individuals in the United States have suboptimal levels of vitamin D, much of the population should be screened for deficiency, notes Connie Weaver, PhD, a nutrition

scientist at Purdue University, West Lafayette, Ind. Such screening should start with the “elderly, people who cover up or use sunscreen or don’t go outside, and dark-skinned individuals,” she says.

Calcidiol (25-hydroxyvitamin D) serum levels are used as a clinical measure of vitamin D stores. There is some controversy about what serum concentration of calcidiol is optimal, and also about what constitutes an adequate daily intake of vitamin D<sub>3</sub>. The current “normal” minimum value for serum concentration of calcidiol is 20 ng/mL (50 nmol/L) and the recommended daily intake of vitamin D<sub>3</sub> is 200 IU for children, adolescents, and adults up to age 50 years, 400 IU for adults aged 51 to 70 years, and 600 IU for those aged 71 years or older.

But new data suggest these intake guidelines, which were drafted by the National Academies’ Food and Nutrition Board in 1997, do not reflect optimal levels, said Heaney, who was a member of that panel. It is with serum concentrations of calcidiol around this minimum level that some individuals begin to have compensatory increases in parathyroid hormone levels. And research from Heaney’s own laboratory, published last year, shows that the body metabolizes about 4000 IU/d of vitamin D, well above the currently sanctioned 2000 IU/d tolerable upper intake limit, he explained (*Am J Clin Nutr.* 2003;77:204-210).

Based on this and other research findings, most experts agree that the current recommendations for serum vitamin D levels, although adequate for prevention of rickets and osteomalacia, fall far short of levels for optimum health and long-term disease prevention.

“I think if the FNB [Food and Nutrition Board] were to reconvene, there would be a strong push to establish 32 ng/mL (80 nmol/L) as the lower end of normal . . . at least that would be my vote,” said Heaney. Almost all individuals with a calcidiol concentration this high will maintain normal levels of parathyroid hormone.

Reinhold Vieth, PhD, a biochemist specializing in vitamin D research at the University of Toronto, Ontario, predicts that in the future, the adult recommended daily intake of vitamin D will exceed 1000 IU/d (>25 µg/d).

“For now, the evidence of RCTs [randomized controlled trials] points to a need for at least 800 IU (20 µg) per day, and a [calcidiol] blood level of 30 ng/mL (75 nmol/L),” he said.

Many researchers advocate fortification of foods in addition to milk. “It would be beneficial if other forms of dairy food were also fortified,” said Weaver. Another way to help individuals increase their vitamin D levels, suggested Heaney, is fortification of cereal grains.

A concern has been that higher intakes of vitamin D may be toxic, but most researchers say that the current recommendation is extremely conservative and far from levels that might be cause for concern. According to Vieth, 10 times the 400 IU/d dose provided by a multivitamin or even more would be safe for most individuals.

#### TREATING, PREVENTING DEFICIENCY

Serious deficiencies can be corrected using oral or parenterally administered prescribed doses of vitamin D. To obviate the need for such repletion, experts recommend simple measures.

“To meet my vitamin D requirements, I try to drink 3 cups of vitamin D fortified milk each day,” said Weaver. “And when I go out into the sun, I don’t put on sunscreen for the first 10 to 15 minutes.”

And supplements can provide a backstop to ensure adequate intake of vitamin D. Both Heaney and Vieth said that based on recent research findings, they have boosted their own vitamin D intake to levels exceeding the current recommended intake levels (400 IU/d) supplied by an ordinary multivitamin. If the Food and Nutrition Board decides to revise current vitamin D intake guidelines, they are likely to have a lot of company. □