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JAMA Review: 'Good' Bacteria Can Help Protect Against Many Infections

Using "good" bacteria and other microorganisms to fight "bad" ones does have medical value, according to a recent article in the *Journal of the American Medical Association*.

"Crude mixtures of microorganisms (e.g., fermented milk products or poultices of moldy bread) have been used since antiquity," wrote Gary W. Elmer, PhD, in *JAMA* (March 20, 1996;275:870-6). "With the advent of antimicrobials, the use of this approach diminished. Research conducted mainly in Europe and more recently in the United States provides evidence for the therapeutic use of whole microorganisms with antagonistic activities against troublesome pathogens."

In a review article, Elmer and his colleagues at the University of Washington, Seattle, acknowledged that new approaches to treating infectious diseases are needed. One reason is that increasing numbers of bacteria are resistant to antibiotics.

They surveyed medical journal articles published between 1966 and 1995. The so-called "probiotics" or "biotherapeutic agents," seem to work most effectively in preventing or treating gastrointestinal and vaginal infections. Large numbers of beneficial bacteria normally populate both organs and discourage the growth of disease-causing microorganisms.

Elmer noted that, overall, 29 percent of hospitalized patients receiving antibiotics develop diarrhea. He described one study in which 180 such patients were also given either lyophilized (freeze-dried) *Saccharomyces boulardii* or a placebo. Only 9.5 percent of the patients getting *S. boulardii* developed diarrhea, compared with 22 percent of those taking the placebo. *S. boulardii* is a non-pathogenic yeast.

Among the most promising beneficial bacteria are certain *Lactobacillus* and *Bifidobacteria* species. All three species have been shown of value in preventing diarrhea caused by antibiotics. Elmer also pointed out that

- antibiotic-associated diarrhea has been successfully treated with *L. casei* GG, *B. longum*, *L. acidophilus*, and *S. boulardii*;
- acute infant diarrhea has been successfully treated with a combination of *B. bifidum* and *Streptococcus thermophilus*;
- recurrent *Clostridium difficile* intestinal infections have been treated with *S. boulardii*;
- other diarrheal diseases have been treated with *Enterococcus faecium* SF68, *L. casei GG*, and *S. boulardii*;
- and candidal vaginitis has been treated with *L. acidophilus*.

Although probiotics are sometimes used to treat diarrhea, they may also serve as an alternative to antibiotics in intestinal and vaginal infections. "Biotherapeutic agents may offer an alternative to conventional antimicrobials to which many pathogenic microorganisms eventually develop resistance," Elmer wrote. "Based on experience with existing biotherapeutic agents, their advantages may include low risk, presumed low cost, and likely existence of multiple mechanisms of action for a single agent."

Probiotics can be obtained in supplemental form at most natural food stores. They are also found in cultured foods, including "live culture" yogurt, kefir, tempeh, sauerkraut, and kimchi. □

Soy Genistein Promotes Antioxidant Activity

Genistein, one of the principal flavonoids found in soybeans, appears to lower the risk of breast and prostate cancers. Its benefits have largely been attributed to it being a very weak estrogen, blocking the effect of more potent estrogens.

However, a recent study suggests that genistein also stimulates the body's production of its own antioxidant enzymes, including glutathione peroxidase, catalase, and superoxide dismutase. These antioxidants would also reduce the risk of cancer.

"Accumulating evidence suggests that reactive oxygen species (ROS) and their subsequent modification of macromolecules (such as DNA, lipids, and proteins) play an important role in cytotoxicity, genotoxicity, and carcinogenic processes," wrote Qiuyin Cai, PhD, and Huachen Wei, PhD, in *Nutrition and Cancer* (1996;25:1-7). "Antioxidant enzymes are capable of eliminating ROS and products of lipid peroxidation, thereby protecting cells and tissues from oxidative damage."

Cai and Wei fed mice diets containing either 50 or

Continues on next page

250 parts per million of genistein for 30 days. The amounts were comparable to a human diet containing 5 or 20 percent soy, respectively. Glutathione peroxidase, catalase, and superoxide dismutase levels increased in response to genistein consumption, though levels of the antioxidants varied in different organs. □

Micronutrients May Limit Down's Syndrome Damage

It's almost too strange to be true. In the 1940s and 1950s, the late Henry Turkel, MD, developed and refined a therapeutic regimen that dramatically improved the physical and mental functioning of children with Down's syndrome (DS). Turkel's controversial "U Series" program was based on supplemental vitamins, minerals, and drugs intended to enhance brain chemistry.

While the "U Series" treatment could not cure DS, which is caused by an extra copy of chromosome 21, it did improve children with the genetic disorder. The nutrients, which included generous amounts of the B vitamins, may have leapfrogged defective metabolic pathways.

While not supporting Turkel's specific treatment, a recent article in the journal *Nature* (Dec 21, 1995;378:776-9) suggests that he might have been on the right track.

Bruce A. Yankner, MD, of the Harvard Medical School, reported that neurons from children with DS appear to have a defect resulting in levels of free radicals three to four times higher than normal. These free radicals lead to apoptosis, also known as programmed cell death. "This defect may contribute to mental retardation early in life and predispose to Alzheimer's disease in adults," Yanker wrote.

In experiments, Yankner found that the death of neurons in DS could be inhibited by a variety of natural and synthetic antioxidants. The natural antioxidants included vitamin E and N-acetyl-L-cysteine.

"These experiments demonstrate that fetal DS neurons generate increased levels of reactive oxygen species [free radicals] leading to neuronal apoptosis," Yankner wrote. "Increased generation of reactive oxygen species may contribute to abnormal brain development and mental retardation in DS...These observations also raise the possibility that a neuronal oxidative defect may predispose to the early onset of Alzheimer's disease in DS individuals, consistent with increased oxidative damage in the brains of patients with Alzheimer's disease. If these findings in cell culture are confirmed *in vivo*, then the neuroprotective effects of antioxidants may provide an important therapeutic approach to mental retardation and the prevention of Alzheimer's disease in DS individuals."

Editor's note: To order a copy of *Medical Treatment of Down Syndrome and Genetic Diseases*, by Dr. Turkel, send $12 to the Autism Research Institute, 4182 Adams Ave., San Diego, CA 92116. The institute also sells a tape ($17) describing recent research on DS. □

Flavonoids in Tea Protect Against Stroke

Drinking black tea, naturally rich in antioxidant nutrients called flavonoids, can dramatically reduce the risk of stroke. Beta-carotene, maligned by recent studies, can also reduce stroke risk, though not as dramatically.

Sirving O. Keli, MD, PhD, of the National Institute of Public Health and Environmental Protection, the Netherlands, tracked the dietary habits and health of a group of men in Zutphen for 15 years. Black tea contributed 70 percent of their dietary flavonoids, and the rest came from fruit and vegetables.

The lowest risk of stroke occurred in men who drank about 5 cups of tea daily. "Men with a high intake of flavonoids had a 73 percent lower risk of stroke during 15 years of follow-up examinations compared with those with a low intake of flavonoids, Keli wrote in *Archives of Internal Medicine* (March 25, 1996;156:637-42). "The intake of beta-carotene, independent from flavonoid intake, was associated with a 46 percent lower stroke risk, although this was not statistically significant."

Of the flavonoids in tea, quercetin appeared to be the most protective. However, Keli noted that tea contains other antioxidants, such as epicatechingallate and epigallocatechingallate.

These antioxidants likely prevent the oxidation of polyunsaturated fatty acids found in the low-density lipoprotein (LDL) form of cholesterol, according to Keli. □

Vitamin C: It's Time to Finally Change the RDA

A new study argues that the Recommended Dietary Allowance (RDA) should be increased to 200 mg from the current 60 mg. The study also questions the value of mega-doses of vitamin C, though all of the findings are based on a very small group of subjects.

Mark Levine, MD, PhD, of the National Institutes of Health, Bethesda, Md., hospitalized seven young male volunteers, then fed them a diet almost devoid in vitamin C. Next, he gave them progressively higher daily doses of vitamin C, ranging from 30 mg to 2,500 mg.

Based on blood-level measurements, Levine determined that 100 percent bioavailability of vitamin C was achieved after a single dose of 200 mg. After intake of 500 mg, bioavailability of the vitamin declined and a higher percentage was excreted in the urine. Only about half of an oral 1,250 mg dose of vitamin C was absorbed.

Levine cautioned that after 1,000 mg of vitamin C, urinary oxalate levels increased. Oxalate is considered a risk factor for kidney stones, although a recent study found no strong relationship between vitamin C and kidney stones. (See Wandzilak T, *Journal of Urology*. April 1994;151:834-7.)

He also acknowledged that his findings were for "seven healthy men under age 27," but that the implications for women, sick people, smokers, and the elderly were less clear. These seven "healthy" subjects consumed only 50 to 95 percent of the RDA for vitamins A, B6, D, folic acid, pantothenic acid, calcium, magnesium, and zinc. Furthermore, four of the subjects dropped out of the study before its completion.

One of the most notable—and generally unreported—findings was that six of the seven subjects became fatigued and irritable when fed vitamin C-deficient diets. "Since fatigue and irritability are common symptoms and were so easily reversible, physicians should ask patients with these symptoms about vitamin C ingestion from foods or supplements," Levine wrote in the *Proceedings of the National Academy of Sciences* (April 15, 1996;93:3704-9).

Comment: In news reports, Levine was quoted as saying he had "proved Linus Pauling wrong" about the need for multi-gram daily intake of vitamin C. An independent researcher who knows Levine told THE NUTRITION REPORTER that the comment was "political" and made with the intent of placating NIH researchers hostile to vitamin C. □

Vitamin C Lowers Risk of Stomach Cancer

Helicobacter pylori, the bacterium that causes ulcers, is a known risk factor for stomach cancer. As an infectious microorganism, it triggers an inflammatory immune response in which white blood cells (neutrophils) release large numbers of free radicals. The body uses these free radicals to destroy the bacteria, but unless quenched by antioxidants, they can damage the deoxyribonucleic acid (DNA) of nearby cells and set the stage for cancer.

"Epidemiological studies have demonstrated that dietary ascorbic acid appears to protect against gastric cancer, and it has been suggested that this may be due to the action of this molecule as a highly effective scavenger of reactive oxygen species," wrote Ian M. Drake, MD, and his colleagues in *Carcinogenesis* (Jan 1996;17:559-62).

In a study of 82 patients with dyspepsia at the University of York, Drake identified 37 with *H. pylori*-associated gastritis. All 37 patients had higher numbers of vitamin C free radicals, "believed to be due to a higher level of oxidative stress." The oxidative stress occurred because insufficient vitamin C was present to quench free radicals produced by the immune system.

According to the researchers, higher levels of vitamin C (and other antioxidants) help convert oxidized vitamin C back into "reduced" vitamin C, which can continue quenching free radicals. □

Studies Find Antioxidant Skin Creams Do Work

Antioxidant creams can control free radical damage and promote healing of the skin, according to Alain Martin, PhD, a researcher at the Warner-Lambert Co. Martin reviewed the evidence and described experiments conducted on a proprietary cream in *Dermatologic Surgery* (Feb 1996;22:156-60).

Martin's paper focused on sodium pyruvate, vitamin E, and essential fatty acids. These compounds are the active ingredients in Warner-Lambert's Lubriderm® Recovery Gel Cream, a patented product. The cream was identified as "CRT" in the paper.

"Sodium pyruvate is an intracellular antioxidant that protects DNA and enhances cellular growth and repair," Martin wrote. "Vitamin E protects cell membranes from oxygen radical damage. The fatty acids used in CRT provide a replacement source for damaged membrane fatty acids."

In the body's inflammatory response to infection, white blood cells use free radicals to destroy bacteria. However, some of these free radicals attack nearby tissues and break down collagen. Vitamin E, the major fat-soluble antioxidant, slows this destruction of collagen.

Pyruvate, involved in cellular energy production, was only recently discovered to have antioxidant properties. And fatty acids similar to those found in skin cells encourage the replacement of dead cells.

The cream "inhibited the production and damage produced by oxygen radicals in skin cells and white blood cells after exposure to toxic chemicals and UV light," according to Martin. The combination of sodium pyruvate, vitamin E, and fatty acids reduced free radical production better than any of the ingredients by itself or in pairs. As a group, these ingredients promoted faster wound healing and less scarring than other creams. □

Diet, Rheumatoid Arthritis

Dietary changes can help some people with rheumatoid arthritis. Jens Kjeldsen-Kraugh, MD, PhD, of the University of Oslo, reports that patients with the disease may benefit from a 7-10 day fast followed by a vegetarian diet. The changes appear to reduce the levels of *Proteus mirabilis*, a species of bacteria normal to the gastrointestinal tract but one that overgrows in rheumatoid arthritis, according to Kjeldsen-Kraugh in the *Scandinvanian Journal of Rheumatology* (1996;25:63).□

Quick Reviews of Recent Research

• Magnesium and bypass surgery

Doctors gave intravenous magnesium sulfate to 50 of 98 patients during and after coronary artery bypass surgery for unstable angina. Left ventricular function was higher among those receiving magnesium. In addition, the incidence of arrhythmia was significantly lower among patients receiving magnesium. Only one of the patients receiving magnesium developed post-operative arrhythmia, compared with 14 of the control patients. Post-operative hypertension was also less of a problem for patients receiving magnesium—only two developed high blood pressure, compared with 16 of the controls. "These results indicate that perioperative administration of magnesium sulfate may contribute to better myocardial recovery and fewer ventricular tachyarrhythmias after operation."

Caspi J, et al., *Annals of Thoracic Surgery*, 1995;59:942-7.

• Inositol and cancer prevention

Inositol hexaphosphate (phytic acid) is commonly found in cereals and legumes. Inositol compounds, related to the B vitamins, are also found in the body's cells, where they regulate various functions. In laboratory and animal experiments, inositol has demonstrated "striking" properties in the prevention and treatment of cancer. Some research has shown that inositol can increase the differentiation and normalization of cancer cells. "Because inositol hexaphosphate is high in high-fiber diets, our studies also may explain, at least in part, the epidemiological observation showing high-fiber diets are associated with a lower incidence of certain cancers.

Shamsuddin AM, *Journal of Nutrition*, 1995;125 (suppl):725S-32S.

• Vitamin C and diabetes

Doctors investigated the effect of 600 mg/day of magnesium and 2 grams/day of vitamin C on a group of 56 non-insulin-dependent diabetics. The vitamin C improved control of blood sugar and fasting blood-sugar levels. It also lowered cholesterol and triglyceride levels. The magnesium lowered blood pressure in the subjects

Eriksson J and Kohvakka A, *Annals of Nutrition and Metabolism*, July/Aug 1995;39:217-223.

• Soy saponins and cancer

Saponins, one of the compounds found in soybeans, can inhibit the growth of some cancers. They are among the many components in soy that may account for the low incidence of cancer among Japanese compared to Americans. Saponins may work by stimulating the immune system, being toxic to cancer cells, binding bile acid, and normalizing carcinogen-induced cell proliferation.

Rao AV and Sung M-K, *Journal of Nutrition*, 1995;125:717S-24S.

• Asthma and vitamin C

The incidence of asthma has increased, perhaps because of a decrease in antioxidant consumption. Inadequate vitamin C may play a major role because it is the most abundant antioxidant in the lung. Numerous studies show a link between tobacco smoke exposure, infection, and asthma. "Decreased preference for foods containing vitamin C and decreased concentrations of vitamin C in blood plasma are also associated with asthma."

Hatch GE, *American Journal of Clinical Nutrition*, 1995;61:625S-30S.

• CoQ10 and heart surgery

Cardiopulmonary bypass is routinely used to create a bloodless environment during open-heart surgery. When oxygenated blood is restored, large numbers of free radicals are generated, leading to post-operative complications and sometimes death. Large doses of coenzyme Q10, an essential metabolite and antioxidant, can prevent much of the free radical damage. The researchers wrote, that "coenzyme Q10 can be used to surgical advantage..."

Morita K, et al., *Journal of Thoracic and Cardiovascular Surgery*, 1995;110:1221-7.

• Spirulina and oral leukoplakia

Oral leukoplakia, found in tobacco chewers, is often a prelude to cancer of the mouth. In a year-long placebo-controlled study, researchers gave 1 gram of freeze-dried spirulina, a type of blue-green algae, to 60 people with oral leukoplakia. Lesions completely disappeared in 44 percent of the people taking spirulina. Within one year of discontinuing the supplements, 45 percent of these people developed new lesions.

Mathew B, et al., *Nutrition and Cancer*, 1995;24:197-202.

• Green tea prevents lung and skin cancer

Researchers used chemicals to induce lung or skin cancer in mice. Lung cell changes were inhibited when epigallocatechin-3-gallate, a polyphenol extract of green tea, was added to the drinking water of the mice. In the skin cancer part of the study, cell changes were inhibited when epigallocatechin-3-gallate was applied topically one hour before chemical exposure.

Hu G, et al., *Nutrition and Cancer*, 1995;24:203-9.

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