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INSIDE

Policosanol: A Natural Alternative for Lipid Management?

By Howell Sasser, PhD, and Thomas Barringer, MD

LOWERING LOW-DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) HAS become the cornerstone in reducing the risk of coronary heart disease (CHD). The most popular drugs used for this purpose include statins, niacin preparations, and fibrates. All of these drugs have certain drawbacks: Most require a prescription and are generally expensive; there is a small risk of muscle or liver toxicity, especially with treatment with combinations of drugs; and the list of drug interactions is a growing challenge. Also, for various reasons, more than half of those patients prescribed these medications discontinue them within two years.[1] Thus, for patients who cannot or will not use these prescription medications, or who need additional cholesterol lowering, phytochemical alternative therapies may play an important role.

Policosanol is one of several "natural" products that have been studied as potential lipid-lowering agents. In studies conducted almost exclusively by researchers working for the Cuban company Dalmer Laboratory, where the compound was first developed, policosanol has been shown to lower total cholesterol (TC) by 15% to 25% and low-density lipoprotein cholesterol (LDL-C) by 20% to 30%, and to raise high-density lipoprotein cholesterol (HDL-C) by 5% to 15%.[2] It also has demonstrated effects on other physiological variables generally assumed to be protective in atherothrombotic disease states, such as platelet aggregation, LDL peroxidation, and smooth muscle cell proliferation.[3] Other clinical effects that have been reported include blood pressure lowering and improvement in claudication symptoms in patients with peripheral vascular disease.[4]

Commercial Availability

Policosanol has been in common use in Cuba since 1991 and currently is available in the United States without a prescription from various sources including health food stores and Internet web sites. It is isolated and purified from sugar cane wax, and composed of a natural mixture of higher aliphatic primary alcohols, of which 1-octacosanol is the major constituent. Notably, the proportion of each alcohol is highly reproducible from batch to batch and stable under

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storage conditions. A similar compound, produced from beeswax, is widely sold in health food stores. However, all of the published clinical literature to date refers to the sugar cane wax-derived product.

Pharmacology and Mechanism of Action

Policosanol is orally administered, reaching peak levels from 30 to 120 minutes after ingestion in different animal species and humans. After absorption there is a liver first-pass effect. Radioactivity studies reveal predominant distribution into the liver, with much smaller uptake noted in the heart, aorta, fat, and plasma. Excretion is primarily fecal.[2]

The precise mechanism of action is uncertain. Evidence from in vitro studies suggests that policosanol may inhibit hepatic cholesterol synthesis at a step before mevalonate generation.[5] There is a decrease in cellular expression of hydroxy-methylglutaryl-coenzymeA (HMG-CoA) reductase, but no direct inhibition of this enzyme.[6] A study in cultured human fibroblasts showed that LDL binding, uptake, and degradation were enhanced at concentrations that did not significantly decrease cholesterol synthesis.[5] Because the overall absorption of policosanol is low, but its effects are substantial, an intra-intestinal lipid-lowering effect has not been excluded. It also has been suggested that some of the secondary metabolites, such as the very long chain fatty acids, could play a significant role in the hepatic cholesterol metabolism changes induced by policosanol.[7]

Published Studies

Virtually all of the published medical literature on policosanol has been authored by researchers affiliated with the developer of the product in Cuba. A total of about 60 studies have included approximately 3,000 subjects. To date, there are no published data on Caucasian, African-American, or other non-Hispanic populations.

At policosanol doses from 5 to 20 mg/d, it has been demonstrated in hypercholesterolemic patients that there is a dose-dependent reduction in TC and LDL-C. At 5 mg/d, mean reduction in LDL-C has ranged from 11.3% to 23.7%, and 10 mg/d has induced mean reductions of LDL-C from 21.2% to 27.5%.[8] Studies with 20 mg/d have demonstrated mean reductions of LDL-C of around 30%, with one study revealing no further reduction at 40 mg/d.[9,10] Long-term maintenance of these lipid effects has been demonstrated in several studies with follow-up from one to five years.[11]

Generally, only modest (5-15%)—but desirable—increases in HDL cholesterol have been noted. However, this still yields dose-dependent reductions in the ratio of TC to HDL-C, and the ratio of LDL-C to HDL-C. A dose of 20 mg/d produces reductions of 20% to 25% for TC/HDL-C and 25% to 30% for LDL-C/HDL-C.[8] Only minimal reductions in triglycerides have been observed. No studies have evaluated non-lipid biochemical markers of CHD risk, such as C-reactive protein, apoB, or total LDL particle concentration as endpoints.

Comparisons with Other Lipid-Lowering Agents. Published clinical studies have included short- and long-term, placebo-controlled and comparative studies vs. statins (lovastatin, pravastatin, and simvastatin), fibrates (bezafibrate and gemfibrozil), acipimox, and probucol.

Policosanol administered at 10 mg/d has demonstrated similar lipid-lowering efficacy to lovastatin administered at 20 mg/d.[12] Lovastatin was slightly more effective in lowering TC, but policosanol was slightly more effective in increasing HDL-C. In addition, policosanol did not result in the mildly elevated transaminases and creatine phosphokinase values noted in the lovastatin group, and clinical adverse experiences were more frequent in the lovastatin-treated patients. Similar results

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have been obtained in comparative studies with other statins, specifically simvastatin and pravastatin.[13,14]

A few studies have compared policosanol with the fibrates, specifically gemfibrozil and bezafibrate. Unfortunately, most of these trials have been published only in Spanish, or exist as "data on file" in the manufacturer's laboratory. In summary, they apparently demonstrate greater reductions with policosanol than with fibrate therapy in TC, LDL-C, apoB, and the ratios of TC/HDL-C and LDL-C/HDL-C. There were comparable increases in HDL-C, but greater reductions in triglycerides with the fibrates.

One study of combined therapy with policosanol and bezafibrate revealed that the combination was well tolerated, while policosanol augmented the HDL-C-raising and LDL-C-lowering effects of fibrate monotherapy.[15]

Trials in Specific Populations. The cholesterol-lowering efficacy of policosanol is similar among men and women. Maximal effects on LDL-C are observed after 6-8 weeks of treatment. Interestingly, the increase in HDL-C seems to develop much more slowly than the reduction in LDL-C.[11]

Two trials have demonstrated similar lipid-lowering effects of policosanol among hypercholesterolemic patients with and without Type 2 diabetes mellitus.[16,17] In addition, there was no apparent impairment of glycemic control as assessed through effects on glucose and HbA1c values. However, no studies have evaluated the effect of policosanol on more sensitive indicators of impaired glucose tolerance, such as measurements of insulin resistance.

Two trials in hypercholesterolemic patients with hypertension not only resulted in favorable lipid changes, but also after six and 12 months of therapy showed a significant reduction in systolic blood pressure.[4,18] Other studies have seen no impact on blood pressure. Therefore, this potential benefit has not yet been settled.

Multiple studies of policosanol in elderly populations have demonstrated efficacy, safety, and tolerability similar to that observed in younger populations.[18,19] Several studies have specifically included high-risk coronary artery disease patients with the same outcomes as already noted. One study in patients with concomitant liver function test abnormalities revealed no further deterioration in hepatic function; another study in patients with nephrotic syndrome did not reveal an impact of policosanol on renal function parameters.[20,21]

Interactions, Safety, and Tolerability

Formal drug interaction studies in humans have not been published. However, data from long-term studies in humans have revealed no clinically apparent problems resulting from the concomitant administration of policosanol with the following drugs and drug classes: calcium antagonists, angiotensin-converting enzyme inhibitors, beta blockers, diuretics, nitrates, nonsteroidal anti-inflammatory drugs, anxiolytics, antidepressants, neuroleptics, oral hypoglycemic drugs, digoxin, thyroid hormones, and anti-ulcer drugs.[22]

According to the Cuban manufacturer's product monograph, single oral doses of 1,000 mg administered to healthy volunteers were tolerated without adverse effects. In most of the published short- and long-term studies, adverse effects and tolerability were assessed, and policosanol consistently was found to be equal to or better than placebo. Furthermore, there have been no serious adverse clinical or biochemical effects reported in published studies. Withdrawal rates from policosanol therapy have been the same as placebo.

A postmarketing surveillance study of 27,879 patients from the six major Cuban medical centers supports the findings obtained in randomized, controlled trials.[23] A total of 17,225 patients were followed for two years and 10,654 for four years. Most patients received policosanol 5 mg/d. The duration of therapy ranged from one month to four years, with a mean of 2.7 years. During the study only 0.31% (86 participants) reported adverse effects felt to be related to the drug, and only 0.08% (22 participants) discontinued treatment because of adverse effects. The most frequently reported side effects were (incidence): weight loss (0.08%), polyuria (0.07%), polyphagia (0.05%), insomnia (0.05%), headache (0.03%), and dizziness (0.02%).

In another postmarketing surveillance study of 6,611 patients, which included an age-matched control group, a similar side effect profile was reported: weight loss (1.75%), polyuria (0.68%), headache (0.61%), dizziness (0.44%), and polyphagia (0.36%).[24] There was no significant difference between the groups in the frequency of any side effect. Over a mean follow-up of 3.1 years, 10.3% of the control group required hospitalization for any cause compared with 7.5% of the policosanol group. All vascular events and death were less frequent in the policosanol group, although this was not a randomized trial.

Conclusion

Policosanol appears to have potent cholesterol-lowering properties, comparable to the effects of various statins. It appears to have few side effects, and a therapeutic effect over a range of doses, permitting its use either alone or in combination with other agents. Also of note, it is much less expensive than the statin drugs

($1.71 per dose vs. $4.51 per dose, average wholesale price). However, a lingering concern is that a single group with a commercial interest in the product has performed all of the published studies. Their findings are therefore open to question until corroborated by other independent research groups, with study participants drawn from other ethnic populations. If the encouraging findings to date are borne out, policosanol has great promise as an addition to the lipid-lowering armamentarium.

Recommendation

What advice should the clinician offer his or her patients about the use of policosanol? First, clinicians must recognize that because it is inexpensive and readily available over the counter, policosanol already is being used by some patients in need of lipid-lowering therapy.

As with most herbs and supplements, a key piece of advice should be, "Know what you are taking." The scientific evidence for the benefit of policosanol is based on the sugar cane-derived version. Although the beeswax version may work as well, when presented with both, the well-tested form is probably the better choice.

Consider all options, including use of policosanol in combination with other lipid-lowering therapies. Statins have the most evidence for reducing the risk of death from CHD, yet when used alone, they often do not lower cholesterol to target levels. This may be especially important in patients who cannot tolerate or afford a treatment regimen including additional prescription medications. However, one caveat is that there are no published studies on the statin-policosanol combination, so we do not know how much more effective it is than either agent used alone.

Continue to follow the literature: As interest in policosanol increases in the United States and elsewhere, additional studies will be published. If the opportunity exists, recommend that patients wanting to use policosanol participate in some of these trials. ❖

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References

1. Benner JS, et al. Long-term persistence in use of statin therapy in elderly patients. *JAMA* 2002;288: 455-461.
2. Policosanol Product Monograph. Dalmer Laboratory. Havana, Cuba.
3. Castano G, et al. Effects of policosanol and pravastatin on lipid profile, platelet aggregation and endothelemia in older hypercholesterolemic patients. *Int J Clin Pharm Res* 1999;19:105-116.
4. Castano G, et al. Effects of policosanol in hypertensive patients with type II hypercholesterolemia. *Curr Ther Res* 1996;57:691-699.
5. Menendez R, et al. Policosanol inhibits cholesterol biosynthesis and enhances low density lipoprotein processing in cultured human fibroblasts. *Biol Res* 1994; 27:199-203.
6. Menendez R, et al. Effect of policosanol on the hepatic cholesterol biosynthesis of normocholesterolemic rats. *Biol Res* 1996;29:253-257.
7. Menendez R, et al. Cholesterol-lowering effect of policosanol on rabbits with hypercholesterolaemia induced by a wheat starch-casein diet. *Br J Nutr* 1997;77: 923-932.
8. Pons P, et al. Effects of successive dose increases of policosanol on the lipid profile of patients with type II hypercholesterolaemia and tolerability to treatment. *Int J Clin Pharmacol Res* 1994;14:27-33.
9. Aneiros E, et al. Effect of successive dose increases of policosanol on the lipid profile and tolerability of treatment. *Curr Ther Res* 1993;54:304-312.
10. Castano G, et al. Effects of policosanol 20 versus 40 mg/day in the treatment of patients with type II hypercholesterolemia: A 6-month double-blind study. *Int J Clin Pharmacol Res* 2001;21:43-57.
11. Castano G, et al. A long-term open label study of the efficacy and tolerability of policosanol in patients with high global coronary risk. *Curr Ther Res* 1999; 60:379-391.
12. Crespo N, et al. Comparative study of the efficacy and tolerability of policosanol and lovastatin in patients with hypercholesterolemia and noninsulin dependent diabetes mellitus. *Int J Clin Pharmacol Res* 1999;19:117-127.
13. Ortensi G, et al. A comparative study of policosanol versus simvastatin in elderly patients with hypercholesterolemia. *Curr Ther Res* 1997;58:390-401.
14. Benitez M, et al. A comparative study of policosanol versus pravastatin in patients with type II hypercholesterolemia. *Curr Ther Res* 1997;58:859-867.
15. Marcello S, et al. Effects of bezafibrate plus policosanol or placebo in patients with combined dyslipidemia: A pilot study. *Curr Ther Res* 2000;61:346-357.
16. Torres O, et al. Treatment of hypercholesterolemia in NIDDM with policosanol. *Diabetes Care* 1995;18: 393-397.
17. Crespo N, et al. Effect of policosanol on patients with non-insulin dependent diabetes mellitus and

hyper-cholesterolemia: A pilot study. *Curr Ther Res* 1997;58:44-51.
18. Castano G, et al. Effects of policosanol on older patients with hypertension and type II hypercholesterolaemia. *Drugs R D* 2002;3:159-172.
19. Pons P, et al. Effects of policosanol in elderly hypercholesterolemic patients. *Curr Ther Res* 1993;53:265-269.
20. Zardoya R, et al. Effects of policosanol on hypercholesterolemic patients with abnormal serum biochemical indicators of hepatic function. *Curr Ther Res* 1996;57: 568-577.
21. Davalos JM, et al. Effect of policosanol in hypercholesterolemia due to nephrotic syndrome. X Latinoamerican Congress of Nephrology and Hypertension, 1-4 September, Santiago de Chile, Chile (as reported in Reference 1).
22. Gouni-Berthold I, Berthold HK. Policosanol: Clinical pharmacology and therapeutic significance of a new lipid-lowering agent. *Am Heart J* 2002;143:356-365.
23. Fernandez L, et al. Policosanol: Results of a postmarketing surveillance study of 27,879 patients. *Curr Ther Res* 1998;59:717-722.
24. Mas R, et al. Pharmacoepidemiologic study of policosanol. *Curr Ther Res* 1999;60:458-467.

Echinacea: An Update on the Popular Cold Cure

By David Kiefer, MD

ECHINACEA PRODUCTS CONTINUE TO REPRESENT BOTH the popular use of herbal remedies by the general public and the uncertainty and even controversy in the scientific and medical communities about proper and proven indications. Recent clinical trials and review articles have shed some light on these issues, expanding on the information provided in past reviews published in this newsletter by Udani and Ofman,[1] and Kattapong.[2] It is important for physicians to know what to tell patients taking echinacea as a "cure" for the common cold or for its other popular uses.

Traditional Uses

The name echinacea comes from a genus (Echinacea) of plants in the daisy family (Asteraceae, also includes chamomile and milk thistle); these plants are native to North America and commonly are referred to as purple coneflower, a name immediately obvious given the shape and color of the flowering parts. There are many species and varieties of echinacea, though three of them are the ones primarily used medicinally. Until recently, the medicinally used species were called *Echinacea angustifolia*, *Echinacea pallida*, and *Echinacea purpurea*; these are also the names that show up in the medical literature as detailed below.

Recent taxonomic work has clarified the correct naming of these species. According to this analysis, *E. purpurea* remains its own species, as does *E. pallida*.[3] However, *E. pallida* includes many different varieties, including *Echinacea pallida var. angustifolia*, the new name for *Echinacea angustifolia*. Of these, *E. purpurea* is the most widely cultivated and used species.[4]

Native Americans were the first to use echinacea for medicinal purposes, the specifics of which were continued and expanded upon by a variety of practitioners who prescribed herbal medicines (including the Eclectic physicians, homeopaths, and naturopaths) in the late 1800s and early 1900s in the United States.[4,5] At that time, echinacea was recommended for a variety of ailments, including snakebite, syphilis, cancer, dysentery, scarlet fever, and other infectious diseases.[4,5]

Contemporary Uses

Modern times have seen a resurgence in interest and use of echinacea. In Germany, the largest market for echinacea in Europe, general acceptance of herbal medicines and popularity of echinacea follow a long tradition of research in botanical medicine. However, the United States has begun to catch up in research and market sales.[5]

Mechanism of Action

There are numerous in vitro and animal studies showing the effect of echinacea on various immune system parameters.[5] Most of these studies demonstrate that echinacea increases macrophage phagocytosis, and stimulates other monocytes, natural killer cells, and polymorphonuclear cells. In addition, echinacea may enhance antibody responses and increase levels of certain interleukins, tumor necrosis factor, and interferon.

The specific effects on the immune system have been found to be variable, a function of the plant part, extraction process, and species used.[5] Of the many phytochemicals present in echinacea, most of the immune system effects derive from the polysaccharides, glycoproteins, and alkylamides.[4,5] Of note, it is the alkylamides that account for the tingling sensation in the mouth caused by some echinacea tinctures, though these compounds are absent in *E. pallida*.

In vitro and animal studies have also demonstrated anti-inflammatory effects; echinacea inhibits

hyaluronidase, cyclooxygenase, and 5-lipoxygenase via its cichoric acid, and alkylamide compounds.[4,5] *E. purpurea* may act as an inhibitor of COX-I and COX-II enzymes, or the nitric oxide synthase system.[6]

Other studies have demonstrated antifungal effects (such as against *Candida albicans*); there is disagreement about the quality of evidence for direct anti-viral effects.[4,5]

Clinical Trials

The latest review on echinacea in this newsletter[2] described some of the clinical trials investigating the use of echinacea for colds, citing overall a lack of evidence, some possible benefit in treating colds, and no demonstrated efficacy in preventing colds.[2] Since then, there has been further research defining the role of echinacea in the common cold.

A recent trial investigated the safety and efficacy of echinacea in treating upper respiratory infections (URI) in children.[7] Healthy children ages 2-11 were randomized to receive echinacea or placebo for up to three URIs over a four-month period. The treatment product was dried pressed *E. purpurea* juice of the above-ground plant parts combined with syrup dosed at 50-67% of the adult dose twice a day; the placebo was only syrup. The researchers analyzed 707 URIs in 407 children focusing on duration and severity of URIs and adverse events.

There was no significant difference between the two groups with respect to duration of symptoms, severity of symptoms, days of fever, peak severity of symptoms, and number of days of peak severity. There also was no significant difference in rates of adverse events between the two groups, except for a slightly higher rate of rash in the echinacea group (7.1%) as compared to the placebo group (2.7%, $P = 0.008$). The results of this study do not support the use of this product and this dosing regimen in children as an URI treatment.

Another study examined the use of echinacea in treating the common cold in a college student population.[8] One hundred forty-eight students were randomized to receive either a dried, whole-plant, unrefined echinacea capsule (50% *E. purpurea*, 50% *E. angustifolia*) or placebo (a capsule containing alfalfa) on the first day of a URI. No statistically significant differences were noted in any of the parameters measured, including self-reported severity and duration of symptoms. Also, there were no statistical differences between the two groups in reports of adverse effects. Although clearly a negative trial, the authors mention that it may be a result of an ineffective or bio-unavailable formulation, the use of self-reported symptoms, or the healthy college population studied.

In one study, 80 adult employees of a German company were randomly allocated at the first signs of a common cold to receive either a placebo or a specific echinacea extract (EC31J0, the juice expressed from the fresh, above-ground parts of *E. purpurea*) for 10 days.[9] This double-blind trial then used the number of days of illness as the primary endpoint. The echinacea-treated group had a mean number of illness days of six, as compared to nine in the placebo group, a statistically significant finding. There were no relevant differences between the two groups with respect to adverse events, and there were no serious reactions. One researcher pointed out some of the weaknesses of this trial, including a lack of evidence of blinding, unclear data analysis, and the use of unvalidated measures.[5]

Another study looked at the use of an echinacea tea product.[10] The researchers in this double-blind, placebo-controlled study randomized 95 people (81 women, 14 men) with early symptoms of a cold to drink 5-6 cups of a proprietary echinacea tea (made out of leaves, flowers, and stems of *E. angustifolia* and *E. purpurea*, as well as a small amount of lemongrass and spearmint) daily for five days or a placebo drink (made out of ginger, peppermint, and cinnamon). A self-scoring, three-part questionnaire revealed that the group assigned to echinacea tea had significantly fewer days of cold symptoms, more effective symptom relief, and more days of noticeable symptom change. Some problems with this study include no evidence of blinding and a poor outcome measure (a retrospective assessment).[5]

Other Literature

In addition to the individual clinical trials mentioned above, readers should be aware of literature reviews examining the topic of echinacea in the treatment or prevention of the common cold.[11,12] In general, these authors underscore the inability to make specific recommendations regarding the use of echinacea given the significant heterogeneity in research trials, including the form and species of plant used, as well as the large variation in the methodological quality of the research conducted. However, the authors note that most of the studies report positive results in the treatment of the common cold early in its course.

Furthermore, in an effort to translate some of the in vitro and animal research results of echinacea's effect on the immune system to humans, researchers examined the effect of orally administered juice from fresh *E. purpurea* on various immune system parameters of 40 healthy men in a double-blind, placebo-controlled crossover trial.[13] Two treatment periods of 14 days separated by a washout period of one month failed to show

any differences between the echinacea group and placebo group on phagocytic activity of polymorphonuclear leukocytes or monocytes, or on the production of TNF-alpha or IL-1beta. This study conflicts with past research showing that echinacea does modulate several different immunological parameters;[5] there is still debate about the exact mechanism of action as well as which forms of the herb might be most active and for which people.

As mentioned above, there are methodological flaws in some of the research evaluating the therapeutic actions of echinacea that make practical application of the data problematic. For example, studies may not mention the species of echinacea used,[14] or use a variety of forms and preparations that complicate the final assessment.

Adverse Effects and Contraindications

Adverse reactions to echinacea are rare and mild, most often involving gastrointestinal distress or dizziness.[15,16] Allergic reactions, including anaphylaxis, angioedema, and exacerbation of asthma, have been documented especially in people with atopic conditions or a history of allergies to plants in the daisy family (which includes ragweed, sagebrush, marigolds, and sunflowers).[16,17]

Some authors advise against the long-term use of echinacea due to the possibility for immunosuppression[18,19] and because of the lack of evidence for efficacy in prevention of URIs. Others note that due to this possibility for immunosuppression, as well as the above-mentioned immune system stimulation, echinacea is contraindicated for long-term use in patients for whom immune system depression (i.e., AIDS) or enhancement (i.e., autoimmune disorders, tuberculosis, multiple sclerosis, during immunosuppressive therapy, etc.) would have serious consequences.[18-20] These are, however, theoretical possibilities that have yet to be documented in humans.[16]

Recommendations for the oral use of echinacea in pregnant or lactating women vary, from avoidance due to a lack of information[21] to no effects or warnings listed.[19] One recent cohort study compared 206 women who had used echinacea during pregnancy to 206 women in a control group; there were no significant differences in the rates of major malformations, minor malformations, miscarriages, or neonatal complications between the two groups.[22]

Echinacea Preparations

There are a wide variety of echinacea formulations available in the current dietary supplement market, including variable combinations of the three medicinally active species, the plant parts used, the extraction process, and the final form of the plant. Another compounding factor is the frequent lack of correlation between listed label contents and the actual amount of echinacea in a given product;[22] there is, however, difficulty in arriving at consensus about correct assay protocols for the phytochemicals listed in a standardized product.

Dosage

Recommended dosage of echinacea depends on the form, the product, and the source consulted. The usual range is 900-1,000 mg three times a day, 6-9 mL of pressed juice daily, or 0.75-1.5 mL of tincture daily;[15] some authors recommend higher doses in the early stages of a cold, tapering off over the course of 7-10 days.[16] Echinacea tea is ingested 6-8 oz four times daily for days 1-2 of a cold, down to once or twice daily for the remainder of a week.[16]

Conclusion

Evidence continues to accumulate about the use of echinacea in treating and preventing the common cold. As noted, there is still a problem in arriving at specific recommendations on the use of echinacea given the heterogeneity in form and species of plant used, as well as the large variation in methodological quality of the research conducted.

A review of some recent trials, however, suggests that echinacea is not useful in treating URIs in healthy children or college students. Two other trials did, however, show some benefit in treating the common cold in adults. Any conclusions that are drawn from these results, or attempts to extrapolate the data, must take into consideration the different types of extracts used, the plant species involved, and the populations being studied.

There are some groups of people for whom echinacea is not appropriate, including atopic individuals who might be at a greater risk for an allergic reaction to these plants.

Recommendation

Uncertainties remain about which form of echinacea to recommend and for which populations. However, with a paucity of effective cold treatments in the conventional medical armamentarium, for most people echinacea is safe, well-tolerated, and potentially effective. Echinacea may be a reasonable treatment choice for adults if used early in the course of an upper respiratory infection. The most favorable studies used an extract of

the juice of fresh *E. purpurea*; dried forms of the herb in the few studies available seem to be less effective. Caution is advised in atopic individuals and in people for whom any immunomodulatory effects might be detrimental. ❖

Dr. Kiefer recently completed a fellowship at the Program in Integrative Medicine, College of Medicine, University of Arizona, Tucson.

References

1. Udani JK, Ofman JJ. Echinacea for the common cold. *Altern Med Alert* 1998;1:16-18.
2. Kattapong VJ. Echinacea for colds. *Altern Med Alert* 2000;3:128-130.
3. Binns SE, et al. A taxonomic revision of echinacea (Asteraceae: Heliantheae). *Systematic Botany* 2002;27:610-632.
4. Mills S, Bone K. *Principles and Practice of Phytotherapy: Modern Herbal Medicine.* Edinburgh, England: Churchill Livingstone; 2000.
5. Barrett B. Medicinal properties of echinacea: A critical review. *Phytomedicine* 2003;10:66-86.
6. Clifford LJ, et al. Bioactivity of alkamides isolated from *Echinacea purpurea* (L.) Moench. *Phytomedicine* 2002;9:249-253.
7. Taylor JA, et al. Efficacy and safety of echinacea in treating upper respiratory tract infections in children: A randomized controlled trial. *JAMA* 2003;290: 2824-2830.
8. Barrett BP, et al. Treatment of the common cold with unrefined echinacea. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 2002;137: 939-946.
9. Schulten B, et al. Efficacy of *Echinacea purpurea* in patients with a common cold: A placebo-controlled, randomised, double-blind clinical trial. *Arzneimittelforschung* 2001;51:563-568.
10. Lindenmuth GF, Lindenmuth EB. The efficacy of echinacea compound herbal tea preparation on the severity and duration of upper respiratory and flu symptoms: A randomized, double-blind placebo-controlled study. *J Altern Complement Med* 2000;6:327-334.
11. Barrett B, et al. Echinacea for upper respiratory infection. *J Fam Pract* 1999;48:628-635.
12. Melchart D, et al. Echinacea for preventing and treating the common cold (Cochrane Review). In: *The Cochrane Library*. Issue 1. Chichester, UK: John Wiley & Sons, Ltd.; 2004.
13. Schwarz E, et al. Oral administration of freshly expressed juice of *Echinacea purpurea* herbs fail to stimulate the nonspecific immune response in healthy young men: Results of a double-blind, placebo-controlled crossover study. *J Immunother* 2002;25: 413-420.
14. Turner RB, et al. Ineffectiveness of echinacea for prevention of experimental rhinovirus colds. *Antimicrob Agents Chemother* 2000;44:1708-1709.
15. Ernst E. The risk-benefit profile of commonly used herbal therapies: Ginkgo, St. John's wort, ginseng, echinacea, saw palmetto, and kava. *Ann Intern Med* 2002;136:42-53.
16. Kligler B. Echinacea. *Am Fam Phys* 2003;67:77-80.
17. Mullins RJ, Heddle R. Adverse reactions associated with echinacea: The Australian experience. *Ann Allergy Asthma Immunol* 2002;88:42-51.
18. Kemp DE, Franco KN. Possible leukopenia associated with long-term use of echinacea. *J Am Board Fam Pract* 2002;15:417-419.
19. Blumenthal M, et al, eds. *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines.* Austin, TX: American Botanical Council; 1998.
20. Brinker F. *Herb Contraindications and Drug Interactions*. 3rd ed. Sandy, OR: Eclectic Medical Publications; 2001.
21. Gallo M, et al. Pregnancy outcome following gestational exposure to echinacea: A prospective controlled study. *Arch Intern Med* 2000;160:3141-3143.
22. Gilroy CM, et al. Echinacea and truth in labeling. *Arch Intern Med* 2003;163:699-704.

Melatonin for Jet Lag

By Dónal P. O'Mathúna, PhD

GLOBALIZATION AND MULTINATIONAL BUSINESS HAVE made it more common for people to fly across several time zones. Those flying on vacation or to visit family expect it will take a few days to get over the jet lag. However, those on business, diplomatic, sports, or military trips often are expected to perform as normal almost as soon as they get off the plane. Many strategies are proposed to avoid the symptoms of jet lag, including dietary and exercise adjustments and carefully regulating one's exposure to bright light.[1] However, much interest recently has been given to the use of melatonin, a hormone involved in the natural sleep-wake cycle. This review examines whether studies support the use of melatonin in combating jet lag. These results may also have wider implications for those regularly switching between shifts at work.

Background

Jet lag has been regarded as a nuisance that had to be accepted as part of long-haul air travel. However, the symptoms mitigate against the purpose of sending people long distances for business. These include fatigue, irritability, loss of concentration, and reduced productivity during daytime, as well as difficulties getting to sleep and staying asleep.[2] Jet lag can be distinguished from travel fatigue because of the differing effects of flying east-west as opposed to north-south. The severity of the symptoms depends on the number of time zones crossed, and the direction of travel (eastward travel is usually more difficult than westward).[3] It typically takes 4-6 days to re-establish normal sleep patterns after flying through six or more time zones.

The body operates on circadian rhythms that influence hormone levels, core body temperature, and the autonomic nervous system.[1] These rhythms are under the influence of exogenous factors (lifestyle and environment) and endogenous factors (body clocks). The body clock is adjusted daily to keep in phase with solar time via a process called entrainment.[1] Factors affecting entrainment are the daily cycles of light-dark, physical activity-inactivity, and feeding-fasting. The symptoms of jet lag arise when exogenous and endogenous factors are not entrained.

Things that speed up re-synchronization will alleviate or prevent jet lag. Some studies have found that light, activity, and food can impact jet lag;[1] however, the effects are relatively small and hence the focus of research has been directed toward pharmacological influences, and melatonin in particular.

Mechanism of Action

Melatonin is synthesized in the pineal gland under the control of a circadian clock. This clock is located in the base of the hypothalamus in an area called the suprachiasmatic nucleus.[4] The clock is impacted by light, with darkness stimulating the production of melatonin and light inhibiting its production. How melatonin exerts its effects is unclear.

Normally, body temperature reaches a minimum between 4 a.m. and 5 a.m., when melatonin levels are highest. Exogenous melatonin given 8-13 hours before this time will advance the phase of the rhythm in the desired direction during eastward travel.[5] If the melatonin is taken between 11 p.m. and 4 a.m., the phase can be moved in the opposite direction. Bright light has the opposite effect.[1] However, these trends are complicated by the finding that after eastward flights some people adjust by phase advance and others by phase delay.[6]

Clinical Studies

A Cochrane review examined all randomized controlled trials (RCT) of melatonin for jet lag that were published up until 2000.[3] A total of 10 trials met the inclusion criteria for the review. The primary outcomes in all trials were subjective ratings of jet lag measured using various instruments. Two trials also measured endogenous cortisol and melatonin serum levels, and another measured core body temperature. The studies varied extensively in design. The melatonin daily dose ranged from 0.5 mg to 8 mg. Melatonin usually was taken at bedtime in the destination time zone on the day of the flight and for 2-7 days afterwards. Eight of the 10 trials found melatonin significantly better than placebo at reducing jet lag symptoms after journeys crossing five or more time zones. The optimal dose appeared to be 5 mg daily, with higher doses being no more effective and lower doses failing to improve sleep quality.

For the five trials that reported global jet lag scores, the mean score after placebo was 48 and after melatonin it was 25.[2] The scores for eastward flights were 51 with placebo and 31 with melatonin, while for westward flights the scores were 41 with placebo and 22 with melatonin. Thus, the effect size was similar flying in either direction, although the jet lag symptoms themselves were less severe going westward.

A search of Medline revealed two additional studies published after the review was completed. One trial studied the rate at which the melatonin levels in eight men became entrained after flying eastward through 11 time zones.[7] Baseline readings were obtained when the men flew without taking any substances. At a later occasion, the men flew again and took 3 mg melatonin daily and were exposed to bright light at the time in their destination that corresponded to midnight in their place of origin. Plasma melatonin levels were re-entrained 15 minutes per day faster when the subjects took melatonin.

The most recent study was a double-blind RCT involving three groups with nine subjects in each.[8] The subjects were given either 300 mg sustained-release caffeine, 5 mg melatonin, or placebo. The subjects spent six days in a controlled environment and then flew eastward through seven time zones. Nighttime sleep was measured using polysomnography and daytime drowsiness by subjective reports and wrist actigraphy (which records wrist activity as a measure of overall sleep and wake patterns). The results found that those taking melatonin slept longer and better than those taking placebo or caffeine ($P < 0.05$). During the daytime, there were no significant differences between the groups for the first two days, but after that those taking caffeine were less drowsy than either those taking melatonin or placebo.

Oral temperatures were taken as an objective measure of re-entrainment. Temperature and plasma melatonin levels were re-synchronized two days after arrival in those taking melatonin, but only started to re-synchronize on day 3 in those taking caffeine or placebo.

Table

Recommendations for re-synchronizing sleep patterns after travel

After Westward Flight	After Eastward Flight
• Stay awake during daylight	• Stay awake, but avoid bright light, in the morning
• Go to bed as soon as it gets dark	• Get outside in the sunlight as much as possible in the afternoon
• Eat modestly at the times that correspond to usual mealtimes	• Eat modestly at the times that correspond to usual mealtimes
• Take comfortable, usual exercise	• Take comfortable, usual exercise
• Take 2-5 mg melatonin when going to bed in destination for 2-4 days	• Take 2-5 mg melatonin early evening when commencing travel and when going to bed in destination for 2-4 days

Adverse Effects

The Cochrane reviewers also searched for reports of adverse effects among those taking melatonin.[3] About 10% of the research subjects experienced hypnotic effects that were relatively mild and subsided quickly. Other adverse effects included headaches, disorientation, nausea, and gastrointestinal problems. The reviewers found 25 other adverse event reports, leading them to conclude that melatonin should not be taken by people with epilepsy.[3]

Drug Interactions

Six cases have been reported of bleeding problems in people taking warfarin who then took melatonin, resulting in the precaution that melatonin should not be taken by people also using anticoagulants.[3] The antidepressant fluvoxamine increases endogenous melatonin levels by inhibiting its elimination.[4] Endogenous melatonin release can be suppressed by relatively common drugs such as aspirin, ibuprofen, and beta blockers.[9]

Formulation

Melatonin is available in the United States as a dietary supplement and has been formulated in many different ways. A study of nine U.S. melatonin products found ample evidence of poor quality.[10] Immediate-release tablets should disintegrate within 30 minutes. In this study, two products failed to disintegrate within four hours and two more failed to disintegrate within 20 hours. One of the controlled-release products had released 90% of its melatonin within four hours.

Conclusion

Melatonin has demonstrated itself to be effective in relieving jet lag symptoms in several RCTs. Although most studies have been relatively small, and were conducted with a variety of designs, the results are clearly in favor of melatonin's effectiveness. Few adverse effects were reported, and those noted were short-lived and reversible. All of the studies were conducted over relatively short periods of time. No information is available on the effects of repeated use of melatonin or of its long-term effects.

Recommendation

For extended flights, 5 mg melatonin daily can be recommended to alleviate symptoms of jet lag *(see Table)*. Best results have been reported with westward flying when melatonin is taken in the evening of departure to start phase delay and then at bedtime at the destination for a few days. Eastward flying is less predictable with the usual recommendation being to initiate melatonin at local bedtime after arriving at the destination. There is no evidence that starting melatonin in the days before departure brings additional benefit. Those experiencing excessive drowsiness should reduce the dosage and be cautious driving or operating machinery. Practitioners should work with patients to identify supplements of proven quality. The data reviewed here are specific for jet lag and cannot be directly applied to the use of melatonin for treating insomnia or for those engaged in variable shift work. Research on the use of melatonin for insomnia will be reviewed in a later issue. ❖

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References

1. Waterhouse J. Jet-lag and shift work: (1) Circadian rhythms. *J R Soc Med* 1999;92:398-401.
2. Herxheimer A, Waterhouse J. The prevention and treatment of jet lag. *BMJ* 2003;326:296-297.
3. Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag (Cochrane Review). In: *The Cochrane Library.* Issue 1. Chichester, UK: John Wiley & Sons, Ltd.; 2004.

4. *PDR for Nutritional Supplements.* 1st ed. Montvale, NJ: Medical Economics; 2001:302-306.
5. Arendt J. Jet-lag and shift work: (2) Therapeutic use of melatonin. *J R Soc Med* 1999;92:402-405.
6. Edwards BJ, et al. Use of melatonin in recovery from jet-lag following an eastward flight across 10 time-zones. *Ergonomics* 2000;43:1501-1513.
7. Takahashi T, et al. Melatonin alleviates jet lag symptoms caused by an 11-hour eastward flight. *Psychiatry Clin Neurosci* 2002;56:301-302.
8. Beaumont M, et al. Caffeine or melatonin effects on sleep and sleepiness after rapid eastward transmeridian travel. *J Appl Physiol* 2004;96:50-58.
9. Zeitzer JM, et al. Do plasma melatonin concentrations decline with age? *Am J Med* 1999;107:432-436.
10. Hahm H, et al. Comparison of melatonin products against USP's nutritional supplements standards and other criteria. *J Am Pharm Assoc* 1999;39:27-31.

Clinical Briefs

With Comments from Russell H. Greenfield, MD

Antibacterial Soaps and Infectious Disease

Source: Larson EL, et al. Effect of antibacterial home cleaning and handwashing products on infectious disease symptoms. *Ann Intern Med* 2004;140:321-329.

Goal: To evaluate the effect of antibacterial cleaning products and soaps on the household incidence of infectious disease symptoms.

Design: Randomized, double-blind trial.

Subjects: Two hundred thirty-eight primarily Hispanic, inner-city households of three or more inhabitants, of whom at least one was a pre-school age child (224 households completed the entire study).

Methods: Households were randomly assigned to use of handwashing and household cleaning products either with or without antibacterial ingredients for a total of 48 weeks. During an initial home visit, baseline data concerning symptoms of infectious disease and home hygiene practices were collected. Home visits were then made monthly, during which time adherence to protocol was assessed through weight of remaining product, and a search for the presence of other cleaning products. Phone contact was made weekly, and home hygiene was assessed quarterly via completion of a lengthy questionnaire. The development of infectious disease symptoms was to be reported with a phone call by a member of the household to their interviewer, or during the weekly phone follow-up.

Results: No statistically significant difference between treatment groups with respect to rates of infectious disease symptoms was found, even when subgroup analyses were considered (reportable symptoms included runny nose, cough, fever, vomiting, diarrhea, conjunctivitis, or boils). The most commonly encountered symptoms were compatible with upper respiratory tract infections.

Conclusion: Use of antibacterial products in the home does not reduce the risk for development of symptoms of infectious disease among generally healthy people.

Study strengths: Duration of intervention and level of follow-up, including repeated household visits.

Study weaknesses: Strong possibility of differing household cleaning and hygienic practices was dismissed; self-reporting of symptoms; weight of residual product offered as surrogate for adherence to protocol; lack of generalizability.

Of note: The products employed had similar formulation save for the presence or absence of an antibacterial ingredient (for example triclosan in liquid handwashing soap, kitchen spray containing quaternary ammonium compounds, or hypochlorite in laundry detergent); both groups received the same liquid dishwashing detergent and bar soap, neither of which contained antibacterial ingredients; all products were delivered monthly and provided free of charge to study participants; the majority of household members were age 19 years or younger; 12.1% of household members had known chronic illness.

We knew that: The majority of outpatient visits made for symptoms of infectious disease are due to upper respiratory tract infections; 75% of liquid and 29% of bar soaps available in the United States contain antibacterial ingredients; data from developing countries suggest a strong association between risk of infection and low prevalence of handwashing; hospitalized patients and people with atopic dermatitis do appear to benefit from the use of antibacterial soaps; risk of promoting antiseptic or antibacterial resistance through the use of antibacterial products, while concerning, remains theoretical.

Clinical import: Health care practitioners will not be surprised to learn that antibacterial products in the home were shown to have little impact on the development of symptoms of viral infectious disease. Still, the authors are quick to point out that results of their study do not preclude a possible effect of reducing symptoms of bacterial disease. With most U.S. residents possessing antibacterial cleaning products in the home, it seems remarkable that manufacturers' advertised benefits of these agents had, until now, not been put to the test. Acknowledging this study's shortcomings, otherwise healthy consumers should be advised regarding the lack of significant benefit ascribed to the use antibacterial products in the home, and directed toward less costly alternatives.

What to do with this article: Keep a copy on your computer. ❖

Safety of Niacin

Source: Mills E, et al. The safety of over-the-counter niacin. A randomized placebo-controlled trial [ISRCTN18054903]. *BMC Clinical Pharmacol* 2003;3:4.

Goal: To determine the safety of a single dose of 500 mg immediate-release niacin.

Design: Randomized, placebo-controlled trial.

Subjects: Healthy student volunteers (51 female and 17 male with a mean age of 27 years).

Methods: Subjects gathered in the one study location after having fasted for 12 hours and then received either 500 mg of immediate-release niacin or placebo. Self-reported incidence of adverse effects, including flushing, and time of onset and duration were the measured outcomes. Tolerability of the study drug also was judged by the participants using a Likert-like scale.

Results: All subjects receiving niacin, and one subject in the placebo group, experienced flushing. On average, flushing appeared 18 minutes after ingestion and lasted for more than 75 minutes. Other adverse effects were noted and include gastrointestinal upset, chills, generalized pruritis, and cutaneous tingling. The majority of those receiving the active agent found the treatment difficult to tolerate.

Conclusion: Use of over-the-counter agents like immediate-release niacin can result in significant adverse effects that may be underplayed in manufacturers' warning statements.

Study strength: Realistic dosing.

Study weaknesses: Subjects were informed that they would experience unpleasant flushing with niacin, the necessary awareness of which may have heightened their reactions; no explanation of why 10 invited participants were not randomized.

Of note: Three subjects required medical attention for severe gastrointestinal upset (vomiting or cramps); the single subject in the placebo arm who experienced flushing did so 35 minutes after ingestion of the pill.

We knew that: The cutaneous flushing associated with niacin ingestion may be due to prostaglandin D_2 release from dermal macrophages; pre-treatment with aspirin or nonsteroidal anti-inflammatory agents may prevent the flush; niacin in combination with statin drugs has been shown to benefit people with known coronary artery disease.

Clinical import: Niacin, also known as vitamin B_3, is recognized by clinicians and the lay public as a treatment for dyslipidemia. While most practitioners are well aware of the potential for the niacin flush, unsuspecting consumers exploring alternative methods to address their cholesterol problems could be in for a rude awakening. The authors note that manufacturers' statements of warning or precaution regarding flushing or other adverse effects with niacin often emphasize the mild or temporary nature of the symptoms. This study serves to re-emphasize the importance of promoting open discussion of available conventional and complementary approaches to our patients' clinical situations. Only in so doing might we be able to help our patients avoid such unpleasant experiences as the niacin flush, or the more serious consequences associated with the use of other specific therapies.

On a closing note, this editor believes a discussion of the ethics behind recruiting medical students for such a study would make for lively debate.

What to do with this article: Remember that you read the abstract. ❖

CME Questions

CME Instructions: Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When an evaluation form is received, a certificate will be mailed to the participant.

16. Policosanol administered at 10 mg/d has demonstrated similar lipid-lowering efficacy to lovastatin administered at 20 mg/d.
a. True
b. False

17. With continued use, policosanol is reported to increase HDL-C as well as decrease LDL-C.
a. True
b. False

18. In recent studies, echinacea showed benefit in treating the common cold in which of the following populations?
a. Children
b. College students
c. Adults
d. All of the above

19. Best results of melatonin use have been reported when traveling in which direction?
a. East
b. West

Answers: 16. a, 17. a, 18. c, 19. b.

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ALTERNATIVE MEDICINE ALERT™

A Clinician's Evidence-Based Guide to Alternative Therapies

Patient Handout: Cholesterol and Coronary Heart Disease

HEART DISEASE IS CAUSED BY NARROWING OF THE CORONARY ARTERIES THAT FEED THE heart. Like any muscle, the heart needs a constant supply of oxygen and nutrients, which are carried to it by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by cholesterol and fat deposits—a process called atherosclerosis—and cannot supply enough blood to the heart, the result is coronary heart disease (CHD). If not enough oxygen-carrying blood reaches the heart, you may experience chest pain called angina. If the blood supply to a portion of the heart is completely cut off by total blockage of a coronary artery, the result is a heart attack. This usually is due to a sudden closure from a blood clot forming on top of a previous narrowing.

Cholesterol's Role in CHD

Cholesterol is a waxy, fat-like substance that occurs naturally in all parts of the body and that your body needs to function normally. It is present in cell walls or membranes everywhere in the body, including the brain, nerves, muscle, skin, liver, intestines, and heart. Your body uses cholesterol to produce many hormones, vitamin D, and the bile acids that help to digest fat. It takes only a small amount of cholesterol in the blood to meet these needs. If you have too much cholesterol in your bloodstream, the excess is deposited in arteries, including the coronary arteries, where it contributes to the narrowing and blockages that cause the signs and symptoms of heart disease.

Your blood cholesterol level is affected not only by what you eat but also by how quickly your body makes LDL-cholesterol (LDL-C), often called the "bad" cholesterol, and disposes of it. In fact, your body makes all the cholesterol it needs, and it is not necessary to take in any additional cholesterol from the foods you eat.

Many factors help determine whether your LDL-C level is high or low. The following factors are the most important:

Heredity. Your genes influence how high your LDL-C is by affecting how fast LDL is made and removed from the blood. One specific form of inherited high cholesterol that affects 1 in 500 people is familial hypercholesterolemia, which often leads to early heart disease. But even if you do not have a specific genetic form of high cholesterol, genes play a role in influencing your LDL-C level.

What you eat. Two main nutrients in the foods you eat make your LDL-C level go up: saturated fat, a type of fat found mostly in foods that come from animals; and cholesterol, which comes only from animal products. Saturated fat raises your LDL-C level more than anything else in the diet. Eating too much saturated fat and cholesterol is the main reason for high levels of cholesterol and a high rate of heart attacks in the United States. Reducing the amount of saturated fat and cholesterol you eat is a very important step in reducing your blood cholesterol levels.

Weight. Excess weight tends to increase your LDL-C level. If you are overweight and have a high LDL-C level, losing weight may help you lower it. Weight loss also helps to

National Cholesterol Education Program Guidelines

Total cholesterol less than 200 mg/dL and HDL-C 40 mg/dL or higher

Unless you have other risk factors for heart disease, your chance of a heart attack is relatively low.

- Eat a low-saturated-fat, low-cholesterol diet and stay physically active to help maintain a desirable cholesterol level.
- Have your cholesterol levels rechecked within five years or at your next physical exam.

Total cholesterol less than 200 mg/dL and HDL-C less than 40 mg/dL

- Have your LDL-C level checked. Your doctor will interpret these numbers for you and tell you when to have your cholesterol levels rechecked.
- Work with your doctor to control any other risk factors you have.
- Take steps to modify your diet and increase your physical activity to reduce your risk.

Total cholesterol 200-239 mg/dL, HDL-C 40 mg/dL or higher, and fewer than 2 risk factors

- You may have twice the risk of coronary heart disease as people whose total cholesterol levels are less than 200 mg/dL.
- Work with your doctor to control any other risk factors you have.
- Have your cholesterol levels rechecked in 1-2 years.
- Take steps to modify your diet and increase your physical activity to reduce your risk.
- Not every person whose total cholesterol level is in the 200-239 mg/dL range is at increased risk. Talk with your health care professional to understand your risks.

Total cholesterol 200-239 mg/dL, HDL-C less than 40 mg/dL or 2 or more risk factors

- You may have twice the risk of coronary heart disease as people whose total cholesterol levels are less than 200 mg/dL.
- Have your LDL-C level checked. Your doctor will interpret these numbers for you and tell you when to have your cholesterol levels rechecked.
- Work with your doctor to control any other risk factors you have.
- Take steps to modify your diet and increase your physical activity to reduce your risk.

Total cholesterol 240 mg/dL and above

- Your risk of coronary heart disease is high. It's even higher if you have other risk factors for heart disease.
- Have your LDL-C level checked. Your doctor will interpret these numbers for you and tell you when to have your cholesterol levels rechecked.
- Have your doctor test you for other risk factors. Ask for advice on how to help reduce your risk.

lower triglycerides and raise HDL-cholesterol (HDL-C) levels.

Physical activity/exercise. Regular physical activity may lower LDL-C and raise HDL-C levels.

Age and sex. Before the age of menopause, women usually have total cholesterol levels that are lower than those of men the same age. As women and men get older, their blood cholesterol levels rise until about 60-65 years of age. After the age of about 50, women often have higher total cholesterol levels than men of the same age.

Alcohol. Alcohol intake increases HDL-C but does not lower LDL-C. Doctors don't know for certain whether alcohol also reduces the risk of heart disease. Drinking too much alcohol can damage the liver and heart muscle, lead to high blood pressure, and raise triglycerides. Because of the risks, alcoholic beverages should not be used as a way to prevent heart disease.

Stress. Stress over the long term has been shown in several studies to raise blood cholesterol levels. One way that stress may do this is by affecting your habits. For example, when some people are under stress, they console themselves by eating fatty foods. The saturated fat and cholesterol in these foods contribute to higher levels of blood cholesterol.

Source: www.nhlbi.nih.gov/about/ncep/.