Antioxidants do not prevent heart disease in high-risk individuals

MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomized placebo-controlled trial. Lancet 2002; 360:23–33.

■ BACKGROUND Several nonrandomized, observational studies have suggested that antioxidant vitamins decrease vascular disease, cancer, and mortality. However, large randomized trials are needed to counter biases such as the "healthy user effect" often seen in observational studies.

■ POPULATION STUDIED The investigators studied 20,536 adults (mostly men from the United Kingdom) aged 40 to 80 years with diabetes, peripheral artery disease, or coronary artery disease. Patients were included if their total cholesterol concentration was above 3.5 mmol/L (135 mg/dL) and they were at a "substantial risk" for more than 5 years of death from coronary disease due to the presence of known cardiovascular disease (coronary artery disease, peripheral artery disease, cerebrovascular disease), diabetes, or hypertension. Patients were excluded if they had other life-threatening illnesses, diagnosed cancer, or were already taking high-dose vitamin E supplements.

■ STUDY DESIGN AND VALIDITY Patients in this impressive placebo-controlled, double-blind randomized (masked allocation via central telephone system) trial received antioxidant supplementation (vitamin E 600 mg, vitamin C 250 mg, and beta-carotene 20 mg daily) or matching placebo. This study was part of the MRC/BHF study on simvastatin. All patients in the vitamin treatment group also received simvastatin. In an 8- to 10-week "prerandomization run-in" phase eligibility and compliance with the 5-year study protocol was assessed. Patients were seen at 4, 8, and 12 months, and then every 6 months during a 5-year period.

The intervention and placebo groups were similar in baseline characteristics. Subjects were analyzed according to the groups to which they were assigned ("intention-to-treat" analysis). Follow-up was available for 77% of subjects in both groups. The design allowed assessment of the separate effects of simvastatin and of the antioxidant vitamins, and enabled information about their combined effects to be obtained.

■ OUTCOMES MEASURED The primary outcomes measured were "major coronary events" (nonfatal myocardial infarction or death from coronary disease) and fatal coronary heart disease. Secondary outcomes measured were effects on major coronary events and major vascular events and nonfatal or fatal stroke. Other outcomes included site-specific cancer, cerebral hemorrhage, vascular procedures, and hospitalization for various causes.

■ RESULTS Patients taking vitamins had significantly higher levels of these vitamins in their blood. Despite this increase no difference was noted in all-cause mortality or deaths due to vascular or nonvascular causes. There were no differences in nonfatal myocardial infarctions, coronary death, nonfatal or fatal stroke, or coronary or noncoronary revascularization. No differences were noted in cancer incidence or hospitalization for any other nonvascular cause.

RECOMMENDATIONS FOR CLINICAL PRACTICE

This impressive placebo-controlled, double-blind randomized trial clearly shows that antioxidants, specifically vitamin E and C and beta-carotene, should not be recommended for secondary prevention of heart disease in high-risk patients. Site-specific cancers were not affected in this study. However, the study was too short (5 years) to be able to conclusively comment about the antioxidants' effects on cancer.

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Arthroscopic surgery ineffective for osteoarthritis of the knee

Moseley JB, O'Malley K, Petersen NJ, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med 2002; 347:81–8.

■ BACKGROUND More than 650,000 arthroscopic procedures are performed each year when medical therapy fails in the treatment of osteoarthritis (OA) of the knee. Uncontrolled studies have shown that up to half of patients receive pain relief from this procedure; however, the exact reason is unclear. There is no evidence that arthroscopic surgery contributes to the cure or arrest in the natural course of OA.

■ POPULATION STUDIED The investigators enrolled patients (mean age 52.3 ± 11.3 years) recruited from the Houston Veterans Administration Medical Center who had OA of the knee, as defined by the American College of Rheumatology. The patients reported at least moderate knee pain on average (at least a 4 on a 10-point visual analogue scale) despite at least 6 months of medical treatment. These patients had not undergone arthroscopy in the past 2 years. Patients were excluded for severe pain, severe deformity, and serious medical problems.

■ STUDY DESIGN AND VALIDITY This double-blind, randomized controlled trial evaluated 3 treatments: arthroscopic lavage alone, arthroscopic debridement along with lavage, or placebo ("sham") procedure. Allocation to these groups was appropriately concealed. One orthopedist performed all the operations. The lavage-only group had the joint lavaged with 10 L of fluid and no general debridement was performed. "Bucket-handle" tears to a meniscus or mechanically important deficits were repaired as in the debridement group. The debridement group underwent arthroscopy and joint lavage with 10 L of fluid, shaving of any rough articular surface, removal of debris, and repair of any torn menisci to form a smooth, firm, and fixed rim. Patients in these 2 groups received general anesthesia and were intubated. The placebo procedure simulated debridement by placing three 1-cm incisions in the skin and the surgeon asking for all of the instruments and manipulating the knee as if arthroscopy was being performed. These patients received a short-acting intravenous tranquilizer and an opioid and spontaneously breathed oxygen-enriched air but were not fully anesthetized.

The study was well done. Patients were followed for 2 years with properly blinded study personnel. Intention to treat was not stated in the analysis. Patients were not able to guess their treatment assignments. The trial was designed to have 90% power and to detect a moderate effect size on pain (0.55) between placebo and the 2 treatment groups. No "watchful waiting" group was used in this study; thus this study could not assess the strength of the placebo effect.

■ OUTCOMES MEASURED The primary end point was pain in the study knee 2 years after the intervention, as assessed by a 12-item self-reported Knee-Specific Pain Scale created for this study. The scale ranged from 0 to 100 with higher scores indicating more pain. Five secondary end points were assessed using 2 measures of pain and 3 measures of function.

■ RESULTS Mean pain scores for all groups did not differ at any of the recorded time intervals (mean Knee-Specific Pain Scale scores in all 3 groups were 51–54 out of 100). The improvement in pain occurred within the first 2 weeks for all groups (6- to 12-point improvement) and then increased slightly for the remaining 2 years.

Furthermore, no significant improvement in function was noted for the arthroscopic intervention groups vs placebo groups. For example, a test of physical functioning (timing how long patients took to walk 100 feet and then climb up and down a flight of stairs as quickly as possible) found a slight worsening immediately after arthroscopy but no difference after 2 years.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Arthroscopy does not provide any benefit over "sham surgery" in reducing pain symptoms or physical functioning. Both, probably, had a placebo effect, although the combination of surgery and anesthesia is an expensive and potentially dangerous placebo.

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POEMS

β-Blocker survival benefit outweighs side-effect risks

Ko DT, Hebert PR, Coffey CS, Sedrakyan A, Curtis JP, Krumholz HM. β-Blocker therapy and symptoms of depression, fatigue and sexual dysfunction. JAMA 2002; 288:351–7.

■ BACKGROUND Despite mortality benefits, β-blockers are often underused, possibly because of concerns of developing side effects. The authors systematically reviewed trials with patients receiving β-blockers for myocardial infarction, heart failure, or hypertension that assessed for symptoms of depression, fatigue, and sexual dysfunction.

■ POPULATION STUDIED Researchers identified controlled trials completed before December 2001 using a MEDLINE search. Reference lists of published trials were reviewed for additional studies. The authors identified 475 articles that matched keyword searches and found 15 randomized placebo-controlled trials meeting inclusion criteria of enrollment of at least 100 patients with a minimum 6-month follow-up. This evaluation included 6 post-myocardial infarction, 3 heart failure, and 6 hypertension trials totaling more than 35,000 patients.

■ STUDY DESIGN AND VALIDITY The authors compared β-blockers with placebo in relation to patient-reported depression, fatigue, and sexual dysfunction, and withdrawal due to these agents. Propranolol and timolol were classified as early-generation drugs and the remaining tested β-blockers classified as late-generation agents. Bucindolol, carvedilol, and propranolol were categorized as highly lipid soluble agents, with the rest as low-to-moderately lipid soluble.

The evaluation lacked a dose–response assessment and was inconsistent in the methods for assessing symptoms of depression, fatigue, and sexual dysfunction. The criteria used to identify and select trials were appropriate and consistent.

■ OUTCOMES MEASURED The main outcomes measured were number of patient-reported symptoms and withdrawal of therapy related to each of the evaluated side effects—depression, fatigue, or sexual dysfunction—compared with placebo.

■ RESULTS Seven of the 15 trials evaluated the overall frequency of reported depressive symptoms. Combining the result of these 7 trials identified no difference compared with placebo. Withdrawal of medication attributed to depression was assessed in 4 trials (N = 5800) with an average follow-up of 14 months. No difference was noted between b-blocker therapy and placebo for risk of withdrawal due to depression (relative risk [RR] = 0.94; 95% confidence interval [CI], 0.44–2.01). Early-generation and highly lipid soluble b-blockers were studied in 3 and 5 trials, respectively, with an average follow-up of 16 months. The comparisons for generation and solubility revealed no difference in the incidence of depression.

Fatigue was assessed in 10 studies. The combined analysis showed an increase in the number of reported symptoms (32%) versus placebo (28%) (RR = 1.15; 95% CI, 1.05–1.26; number needed to harm [NNH] = 57 per year). However, of 29,400 patients followed for an average of 29 months with fatigue-related symptoms, only 2.4% withdrew from therapy (RR = 3.8; 95% CI, 1.16–5.94; NNH = 225 per year). Five trials studied early-generation β-blockers (N = 24000) over an average of 25 months and found a small but statistically significantly higher risk for fatigue when compared with the 5 trials of late-generation β-blocker use (N = 12,200). No difference was noted in fatigue when agents were assessed by lipid solubility.

In assessing patient-reported sexual dysfunction, 6 trials showed no difference between β-blocker and placebo. Withdrawal of medication due to sexual dysfunction was evaluated in 4 trials (N = 11260) with an average follow-up 33 months. A small significant increase in withdrawal from β-blockers due to sexual dysfunction was found (RR = 4.89; 95% CI, 2.98–8.03; NNH = 438 per year). No significant differences were shown in risk estimates of sexual dysfunction between early- and late-generation β-blockers. No differences were noted between high or low-to-moderate degrees of solubility, although only propranolol and bucindolol were studied.

RECOMMENDATIONS FOR CLINICAL PRACTICE

β-Blockers are not associated with a significant increase in depressive symptoms. They do cause a slightly higher incidence of withdrawal because of fatigue and sexual dysfunction. Propranolol is associated with an increased risk of experiencing fatigue. Later-generation b-blockers (metoprolol, atenolol, pindolol, carvedilol, and sotalol) should be used to minimize the potential for fatigue. Lipid solubility made no difference in the risks of side effects. The fear of these side effects should not deter prescribers from initiating b-blockers where mortality benefit has been documented. Close follow-up observation for the infrequent cases of fatigue and sexual dysfunction is appropriate.

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B-type natriuretic peptide is an accurate predictor of heart failure in the emergency department

Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med 2002; 347:161–7.

■ BACKGROUND B-type natriuretic peptide is released from the cardiac ventricles in response to volume expansion and pressure overload. Levels correlate with severity of congestive heart failure (CHF) and prognosis. A rapid assay for B-type natriuretic peptide might help clinicians' accuracy in distinguishing CHF from other conditions (eg, chronic obstructive pulmonary disease) as the cause of acute dyspnea in an emergency setting.

■ POPULATION STUDIED The investigators enrolled 1586 patients from 7 sites (5 in the United States, 1 in France, 1 in Norway). Eligible subjects (at least 18 years old) presented to the emergency department with shortness of breath for which CHF could not be obviously ruled out (such as in trauma or cardiac tamponade). Patients were not included if they had acute myocardial infarction or renal failure; patients were also not included if they had unstable angina, unless their predominant presenting symptom was dyspnea. Forty-four percent of the subjects were women; 49% were white, 45% were black, and 6% were from other races.

■ STUDY DESIGN AND VALIDITY This study evaluated the role B-type natriuretic peptide determinations might play in the diagnosis of CHF by comparing B-type natriuretic peptide levels with clinical diagnosis as the gold standard. Blood was drawn from all included patients for measurement of B-type natriuretic peptide. Emergency room physicians, who were not given the laboratory results, assessed the probability that the patient had CHF. Patients with a history of CHF were classified as having either an exacerbation of CHF or dyspnea from another cause with underlying left ventricular dysfunction.

To determine the actual diagnosis, 2 cardiologists independently reviewed all medical records pertaining to the patient and classified the diagnosis as dyspnea due to CHF, acute dyspnea due to noncardiac causes in a patient with a history of left ventricular dysfunction, or dyspnea not due to CHF. The cardiologists were blinded to the B-type natriuretic peptide level as well as to the emergency department physicians' diagnoses. The cardiologists also had access to the radiologists' report on the chest x-ray; past medical history from old charts; and subsequent test results such as echocardiography, radionuclide angiography, and left ventricular angiography if performed, and the hospital course for patients admitted to the hospital.

This study was well designed. The population was inclusive and appropriate to practice, although it is unclear if all patients who might be have been eligible were enrolled. The test, a rapid assay of sampled blood, was reasonable and acceptable to patients. The results of the B-type natriuretic peptide blood levels were not known to either the emergency department physicians who made the initial diagnosis of CHF or to the cardiologists who confirmed the diagnosis. Although the study measured the immediate diagnostic value of the test, it did not evaluate patient-oriented outcomes such as cost, or whether the test had an effect on treatment decisions, longevity, or quality of life.

■ OUTCOMES MEASURED Whole blood or plasma levels of B-type natriuretic peptide were measured using a fluorescence immunoassay kit (Triage BNP Test; Biosite Inc, San Diego, CA) and the results were compared with clinical diagnoses to determine the sensitivity, specificity, and accuracy of the test in the diagnosis of CHF. Receiver-operating-characteristic curves were constructed to illustrate various cutoff values of B-type natriuretic peptide. Long-term outcomes of patients with CHF were not measured.

■ RESULTS Congestive heart failure was diagnosed in 744 patients (47%), dyspnea due to noncardiac causes in 72 patients with a history of CHF (5%), and no CHF in 770 (48%). The B-type natriuretic peptide level test performed well for diagnosing CHF; the area under the receiver-operating-characteristic curve was 0.91 (where 1.0 indicates a perfect test). A value of 100 pg/mL or more was the single most accurate predictor of the presence of CHF when compared with clinical predictors such as history, physical examination, or chest x-ray. This B-type natriuretic peptide cutoff value of 100 pg/mL was 90% sensitive, 76% specific, and 83% accurate in differentiating CHF from other causes of dyspnea. As such, this cutoff value outperformed the accuracy of 2 commonly used clinical criteria used for diagnosing CHF, the National Health and Nutrition Examination Survey (NHANES) criteria (67%) and Framingham criteria (73%). At this prevalence of 47%, a level of 50 pg/mL was associated with a negative predictive value of 96%. B-type natriuretic peptide values also correlated with CHF severity as determined by the New York Heart Association functional class.

RECOMMENDATIONS FOR CLINICAL PRACTICE

The B-type natriuretic peptide level assay is a rapid (15-minute) whole blood test that can be done at the bedside or in the emergency department to diagnose congestive heart failure as the cause of acute dyspnea. Using a cutoff of 100 pg/mL, the test has better accuracy than either NHANES criteria or Framingham criteria. However, whether use of this new test will improve patient outcomes is unknown.

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Hair apposition technique is better than suturing scalp lacerations

Hock MO, Ooi SB, Saw SM, Lim SH. A randomized controlled trial comparing the hair apposition technique with tissue glue to standard suturing in scalp lacerations (HAT study). Ann Emerg Med 2002; 40:19–26.

■ BACKGROUND Suturing scalp lacerations can be a painful, time-consuming procedure. It often requires shaving a portion of the scalp and subsequent suture removal. The search for a less invasive means of wound closure led the authors to develop the hair apposition technique. After cleaning the wound, and without anesthesia, about 4 to 5 strands of hair from each side of the laceration are twisted together once and a drop of tissue adhesive is placed on the twist to hold it in place. A series of twists are placed over the laceration to appose the wound. Patients are instructed not to wash their hair for 2 days. This study compared the hair apposition technique with standard suturing methods.

■ POPULATION STUDIED This study was performed at emergency departments at 2 tertiary care centers in Singapore. The authors enrolled 189 patients who had linear, nonstellate scalp lacerations less than 10 cm in length. They did not include patients with severely contaminated wounds, arterial bleeding not controlled with 5 minutes of pressure, hair length less than 3 cm, and medically unstable patients.

■ STUDY DESIGN AND VALIDITY This study was a randomized, controlled clinical trial. In a concealed fashion, 93 patients were randomized to suturing and 96 patients to the hair apposition technique. Both groups had their wounds irrigated and cleansed in a similar fashion. The control group was shaved according to local practice and received an injection of local anesthetic; young children sometimes received oral sedation. Hair washing was discouraged for 1 week in the suture group. No subject in the study group received anesthesia or sedation. A senior physician who was not involved in the initial treatment evaluated subjects after 1 week; sutures were removed at that time as well. If complications were noted, the patient was followed weekly for as long as 4 weeks.

This study used reasonable methods. Because blinding was not possible in this study, subjective assessments, such as scarring, might have been biased. Follow-up was nearly complete, with only 1 person not completing the study. Two patients were randomized to the suture group but were treated with the hair apposition technique because of protocol noncompliance. These 2 patients were analyzed as part of the suture group according to the intention-to-treat principle.

■ OUTCOMES MEASURED Primary outcome measures were wound healing and the presence of complications including infection, scarring, bleeding, wound breakdown, and allergy. Secondary outcome measures were duration of procedure, pain perception, and patient preference.

■ RESULTS Overall, complications were reduced by the hair apposition technique (7.4% vs 21.5%; $P = .005$, NNT = 7). Most of the difference in complication rates can be attributed to the decreased scarring (at 1 week) found in the hair apposition technique group. Wound breakdown, bleeding, and infection rates were similar in both groups. The hair apposition technique was quicker than suturing (median time of 5 vs 15 minutes; $P < .001$). Less pain was reported in the hair apposition technique group (median score 2 vs 4 [out of 10 possible]); $P < .001$). In the hair apposition technique group, 84% claimed they would be willing to have the procedure in the future compared with only 10% in the suture group.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Using hair apposition with tissue adhesive appears to be an effective technique for closing simple scalp lacerations. It is faster and better tolerated than suturing, and appears to result in less scarring. The superficial apposition provided by this technique will not be adequate in those cases were deep sutures are required. Using the hair apposition technique appears to be a practical method of treating scalp lacerations.

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Do the risks of estrogen plus progestin outweigh the benefits in healthy postmenopausal women?

Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA 2002; 288:321–33.

■ BACKGROUND One of the proposed benefits of postmenopausal hormone replacement therapy (HRT) is the prevention of coronary heart disease. This proposal is based on evidence from nonrandomized observational studies and intermediate outcomes such as improved lipid profiles. The possibility of harm from HRT has also been reported, particularly regarding breast cancer and thromboembolic disease. The Heart and Estrogen/progestin Replacement Study recently challenged the benefits of HRT, showing no overall protective effect on coronary heart disease (and an increased risk of harm in the first year of treatment) for women with prior coronary heart disease.

■ POPULATION STUDIED The Women's Health Initiative is a set of clinical trials with more than 160,000 women enrolled in studies of low-fat diet, calcium and vitamin D supplementation, and postmenopausal hormone use. This particular report focused on the trial of estrogen plus progestin in women with an intact uterus. A total of 16,608 postmenopausal women were randomized to receive either 1 daily tablet of conjugated equine estrogen 0.625 mg and medroxyprogesterone acetate 2.5 mg (Prempro) or placebo. Women were excluded if they had a history of breast cancer, other cancer within 10 years, hysterectomy, anemia, thrombocytopenia, alcoholism, or dementia. Ages ranged from 50 to 79 years (mean 63 years). Approximately 36% of the women were being treated for hypertension, 4.4% had diabetes, and 7.7% reported a history of cardiovascular disease.

■ STUDY DESIGN AND VALIDITY This was a well-designed double-blind, randomized controlled trial with concealed allocation. Baseline characteristics were similar between groups. Follow-up was conducted 6 weeks after randomization, every 6 months with questionnaires, and annually with in-clinic visits. Intention-to-treat analysis was appropriate and would tend to find smaller differences between groups given the high dropout rates (42% in the HRT group and 38% in the placebo group). The trial was originally designed to last more than 8 years, but the independent safety monitoring board recommended stopping the trial when the difference in breast cancer rates exceeded a predetermined threshold and the global index was supportive of harm. When the trial was stopped in the spring of 2002, the average follow-up period was 5.2 years.

■ OUTCOMES MEASURED The primary outcome measure was the rate of coronary heart disease, defined as acute myocardial infarction requiring overnight hospitalization, silent myocardial infarction determined from serial electrocardiograms, or coronary heart disease death. The secondary outcome measure was hip fracture rate. The primary adverse outcome measure was invasive breast cancer rate. Reported outcomes also included other cancers, total fractures, stroke, pulmonary embolism, deep vein thrombosis, and total mortality. A global index of outcomes was also calculated as a summary measure of risks and benefits. No measures of vasomotor symptoms or quality of life were reported.

■ RESULTS Women in the HRT group had a higher annual incidence of coronary heart disease (0.37% vs 0.30%, NNH = 1429), invasive breast cancer (0.38% vs 0.30%, NNH = 1250), stroke (0.29% vs 0.21%, NNH = 1250), and venous thromboembolic disease (0.34% vs 0.16%, NNH = 556). Bone fractures were less prevalent in the HRT group (total annual fracture rate, 1.47% vs 1.91%, NNT = 228), as was colorectal cancer (0.10% vs 0.16%, NNT = 1667). All of these differences except thromboembolic disease lost statistical significance when adjusting for multiple comparisons, but subgroup analyses showed these differences in adverse events regardless of baseline risks of coronary heart disease and breast cancer. Individuals who adhered to the study medication showed greater differences in adverse events, and individuals who had already used HRT before the study had higher rates of breast cancer. Overall mortality was not different in the 2 groups. The excess risk of events in the global index was 19 per 10,000 person-years. In other words, an average of 1 additional adverse event would be expected over 5 years of treatment for every 100 women meeting these criteria.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Combined HRT with estrogen plus progestin should not be used for prevention of coronary heart disease, and other agents should be considered for the prevention and treatment of osteoporosis. HRT may still be a reasonable option for perimenopausal, otherwise healthy women with significant vasomotor symptoms, provided they are informed of a slightly increased risk of adverse events. Use of HRT in these women should be limited if possible to 5 years or less. Ongoing questions include the potential benefit of estrogen alone in women without a uterus (that trial is ongoing) as well as the risks and benefits of other forms of estrogen and progestin.

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POEMS

DEET is the most effective mosquito repellent

Fradin MS, Day JF. Comparative efficacy of insect repellents against mosquito bites. N Engl J Med 2002; 347:13–8.

■ BACKGROUND The search for optimal protection against mosquitoes is particularly timely, with West Nile virus infection becoming more of a threat in the United States. Internationally, malaria is the primary infectious disease transmitted by mosquito. Mosquito-transmitted diseases are responsible for 1 in 17 deaths worldwide. New repellents have come out on the market, but their relative effectiveness has not been delineated.

■ POPULATION STUDIED The researchers recruited 15 volunteers from the staff of the Medical Entomology Laboratory at the University of Florida (10 were women). Age, ethnicity, and medical histories were not reported.

■ STUDY DESIGN AND VALIDITY The goal of the researchers was to compare the effectiveness of 16 products containing 7 botanical repellents. The products included those containing 4 different concentrations of DEET (N,N-diethyl-3-methylbenzamide), 2% soybean oil, 5 different formulations of citronella, and IR3535; in addition, 3 repellent-impregnated wristbands were tested. All products are nationally available in the United States. The study used an "arm-in-cage" design; volunteers inserted their repellent-treated bare arms into a cage with 10 hungry, disease-free female mosquitoes. This low mosquito density environment was considered to be similar to typical exposures. The order of tests was randomized and the volunteers were blinded to the repellent used. Hours of light and dark, humidity, and temperature were constant. Each repellent was tested 3 times on each subject. No more than 1 repellent was tested per day. The repellents were applied according to the instructions on the product's label. Subjects inserted an arm into the cage for 1 minute every 5 minutes. If they were not bitten after 20 minutes, the insertion interval was changed to every 15 minutes. The test was stopped with the first bite. The study was funded by the State of Florida.

The study was designed to show the relative efficacy of the repellents, not their absolute effectiveness. However, the applicability to real-world circumstances is questionable. We do not know, for instance, the influence of characteristics of the subjects (eg, skin color or texture) or use of perfumed skin products, which are known to attract mosquitoes. In addition, men are bitten more than women, but in this study women outnumbered men 2:1. Because the same subjects were used to test all the products, they served as their own controls, lessening the impact of those differences on the results. Although blinding was attempted, the differences in product smell and methods of application made blinding difficult.

■ OUTCOMES MEASURED Time to the first mosquito bite using different repellents in a controlled situation.

■ RESULTS DEET was the clear winner in these tests, especially in the highest concentration. The highest DEET concentration (23.8%) protected for an average of 301.5 ± 37.6 minutes. This concentration, which was alcohol based, protected significantly longer than the 20% controlled-release formulation (245.5 ± 31.8 minutes). Only DEET-containing repellents protected longer than 1.5 hours. The soybean oil repellent protected similar to the lowest concentration of DEET (94.6 vs 88 minutes, respectively). The wristbands were essentially not effective. Citronella-based lotions worked for only 10.3 ± 7.9 minutes at best.

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RECOMMENDATIONS FOR CLINICAL PRACTICE

Unquestionably, DEET should be the only mosquito repellent recommended by physicians. No other repellent came close to DEET in effectiveness in this study. Despite the carefully controlled laboratory conditions of this study, the results were so dramatic that it is hard to conceive that any other repellent would be as effective in the field. Concentrations up to 23.8% should be used; given the known safety of DEET, it can be used by children and adults, although the American Pediatric Association recommends a concentration of no more than 10% for children. The repellent should be applied to exposed skin. The study showed protection for 5 hours, but given the controlled conditions of the study, it would be wise to assume that in the field protection time will likely be shorter. Citronella candles have not been shown to protect much better than plain candles or incense and are effective only when the user is near the candle.[1]

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POEMS

Topical steroids more effective than antifungals for chronic paronychia

Tosti A, Piraccini BM, Ghetti E, Colombo MD. Topical steroids versus systemic antifungals in the treatment of chronic paronychia: an open, randomized double-blind and double dummy study. J Am Acad Dermatol 2002; 47:73–6.

■ BACKGROUND Although *Candida* is often isolated from nails afflicted with chronic paronychia, the benefit of treating chronic paronychia with antifungal agents has never been proved. More recently, chronic paronychia is thought to be an eczematous condition better treated with corticosteroids.

■ POPULATION STUDIED A total of 45 patients, 22 to 69 years of age, presenting to a dermatology clinic in Italy with chronic paronychia were enrolled. The diagnosis of chronic paronychia was established by the following criteria: absence of the cuticle with swelling and erythema of the proximal nail fold. Exclusion criteria included hypersensitivity to imidazoles or terbinafine, use of drugs interfering with itraconazole or terbinafine metabolism, pregnancy, liver or renal dysfunction, history of contact dermatitis from steroids, onychomycosis, psoriasis, lichen planus, and self-induced or manicure-related nail abnormalities. Disease duration before the study ranged from 1 month to 40 years (mean 2.3 years).

■ STUDY DESIGN AND VALIDITY Patients were randomized in a double blind fashion to receive either itraconazole 200 mg daily; terbinafine 250 mg daily; or topical methylprednisolone aceponate cream 0.1%, 5 mg daily. Treatment duration was 3 weeks and patients were followed for an additional 6 weeks. Mycological samples were obtained and a clinical examination performed at baseline, the end of treatment, and the end of follow-up. Nail abnormalities were rated as cured (regrowth of cuticle with normal proximal nail fold), improved (proximal nail fold not inflamed, absence of cuticle, nail plate growing normally), stable (proximal nail fold still inflamed), or worsened (acute flare with purulent inflammation of the proximal nail fold).

Analysis was by intention to treat. The authors did not clarify if assignment to treatment group was concealed. Throughout the study, nails were evaluated by the same investigator, who was blind to treatment group assignment. The clinical evaluation of the patients was limited by a lack of standard criteria for chronic paronychia and therefore some subjective bias was expected. The authors attempted to overcome this potential limitation by using distinct, though not objective, criteria for observations. There was adequate power to evaluate the treatment groups by the number of affected nails, but not by the number of patients treated.

■ OUTCOMES MEASURED The primary outcomes measured were the presence of *Candida* in the proximal nail fold and the clinical status of nails and patients at the end of the follow-up period. No measure of patient satisfaction was determined.

■ RESULTS The 3 groups were similar at baseline in terms of sex, age, and number of fingernails affected by chronic paronychia. A total of 42 patients (93%) completed 6 weeks of follow-up. The presence of *Candida* was not linked to disease activity; mycological examination before treatment revealed the presence of *Candida* in the proximal nail fold of only 18 of 45 patients. Only 2 of these patients had simultaneous eradication of *Candida* and clinical cure by the end of the study, both of whom were in the topical steroid group. Clinical improvement or cure of total nails at the end of follow-up was superior with topical steroids compared with either terbinafine or itraconazole (85% vs 53% vs 45%; $P < .01$; NNT = 3 and 2.5, respectively). Improvement or cure was observed in 60% of patients treated with topical steroids compared with 33% treated with itraconazole and 20% treated with terbinafine.

RECOMMENDATIONS FOR CLINICAL PRACTICE

In this small but well-designed study, topical steroids were more effective than systemic antifungal agents in the treatment of chronic paronychia. Given their lower risks and costs compared with systemic antifungals, topical steroids should be the first treatment offered to patients with chronic paronychia. Although *Candida* is often isolated from these nails, its presence or absence appears to be unrelated to effective treatment of this disorder.

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