

AJCM Update

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Alternative Medicine

Acupuncture and Knee Osteoarthritis

This was a randomized, controlled trial designed to evaluate the efficacy of acupuncture therapy in the treatment of osteoarthritis (OA) of the knee. The trial compared traditional acupuncture, sham acupuncture and conservative treatment.

A total of 1,531 patients were assessed for eligibility into the trial, of which 1,039 were eligible and enrolled in the trial. Subsequently 32 patients withdrew consent, leaving 1,007 patients who participated in the study. Patients were all at least 40 years old, had more than six months of chronic pain in the knee joint, met the American College of Rheumatology criteria for OA and had radiological confirmation of osteoarthritis of one or both knees. The severity of OA was measured by the Western Ontario and McMaster University Osteoarthritis Index (WOMAC).

Conservative therapy involved 10 visits to practitioners with consultation and a prescription for either diclofenac or rofecoxib as needed for 23 weeks. Patients were permitted five additional visits in weeks seven to 13 if they were graded as having a partially successful result. The acupuncture groups had 10 acupuncture sessions over a 6-week period, and were entitled to five additional treatment sessions if they met criterion for partial success. Sham acupuncture was standardized as minimum depth needling without stimulation at 10 points at defined distances from traditional acupuncture points. Each of the three groups had up to six physiotherapy sessions. Acupuncture patients were blinded as to whether they were receiving traditional or sham acupuncture. Conservative therapy patients were not blinded.

The authors found success rates were 53.1% for traditional acupuncture, 51.0% for sham acupuncture and 29.1% for conservative therapy.

The authors conclude that compared with physiotherapy and as-needed anti-inflammatory drugs, addition of either traditional acupuncture or sham acupuncture led to greater improvement in WOMAC score at 26 weeks. No statistically significant difference was observed between traditional acupuncture and sham acupuncture, suggesting that the observed differences could be due to placebo effects, differences in intensity of provider contact, or a physiologic effect of needling regardless of whether it is done according to traditional acupuncture principals. - MSB

Scharf et al, Annals of Internal Medicine, July 4, 2006
Ann Intern Med. 2006;145:12-20

Cardiology

Dogma Disputed: Can Aggressively Lowering Blood Pressure in Hypertensive Patients with Coronary Artery Disease Be Dangerous?

Several reports have shown that low diastolic pressure is associated with an increased risk for coronary heart disease and related mortality in older patients and patients taking antihypertensive medications. Because coronary artery perfusion occurs mainly during diastole, patients with coronary artery disease (CAD) could be at increased risk for coronary events if diastolic pressure falls below critical levels.

To determine whether low blood pressure could be associated with excess mortality and morbidity in patients with CAD, the authors conducted a secondary analysis of data from the International Verapamil-Trandolapril Study (INVEST), which was conducted from September 1997 to February 2003. The INVEST study involved 22,576 patients from 862 sites in 14 countries. These patients were randomly assigned to receive verapamil sustained release, or atenolol based treatment. Blood pressure control and outcomes were equivalent in both groups.

The authors found that the relationship between blood pressure, all cause death and MI was a J-shaped curve. Diastolic pressures below 70-80mmHg had an increased risk of MI and all cause death, with the nadir 119/84. Patients who had undergone revascularization procedures had a lower risk of mortality at the lower diastolic pressures. The stroke rate remained constant at a wider range of lower diastolic pressures.

The authors conclude that the risk for the primary outcome, all-cause death, and MI, but not stroke, progressively increased with low diastolic blood pressure. Excessive reduction in diastolic pressure should be avoided in patients with CAD who are being treated for hypertension.

Messerli et al, Annals of Internal Medicine, June 20, 2006
Ann Intern Med 2006;144:884-893

Editors note: Further studies seem warranted to re-assess the therapeutic window, and risk-benefit of aggressive lowering blood pressure. - MSB

Migraine and Risk of Cardiovascular Disease in Women

Migraine with aura has been associated with an adverse cardiovascular risk profile and prothrombotic factors that, along with migraine-specific physiology, may increase the risk of cardiovascular events. Although migraine aura has been associated with increased risk of ischemic stroke, an association with cardiovascular disease (CVD) and, specifically coronary events remains unclear.

This was a prospective, cohort study of 27,841 women aged 45 years or older, who were participating in the Women's Health Study, were free of CVD and angina at study entry, and who had information on self-reported migraine and aura status, and lipid measurements. The primary outcome measure was the combined end point of major CVD. This included ischemic stroke, myocardial infarction, coronary revascularization, angina and death due to ischemic CVD.

Of the 27,841 participants, 5,125 reported any history of migraine, and 3,610 women reported active migraine. Of the 2,610 who reported active migraine, 1,434 (39.7%) reported aura. During a mean 10 year follow-up, 580 major CVD events occurred. Compared to patients with no migraine history, women with any history of migraine had a relative risk of 1.42 for a major cardiovascular event, 1.22 for ischemic stroke, 1.41 for myocardial infarction, 1.35 for coronary revascularization, 1.63 for death due to CVD. Women with migraine with aura had a relative risk of 2.15 for a major cardiovascular event, 1.91 for ischemic stroke, 2.08 for myocardial infarction, 1.74 for coronary revascularization, and 2.33 for death due to cardiovascular disease. Rates are adjusted for age, numerous cardiovascular risk factors, use of oral contraception and hormone replacement therapy.

The authors conclude that in this large, prospective cohort of women, active migraine with aura was associated with increased of major CVD, myocardial infarction, ischemic stroke, and death due to ischemic CVD, as well as coronary revascularization and angina. Active migraine without aura was not associated with increased risk of any CVD event. - MSB

Kurth et al, Journal of the American Medical Society, July 19, 2006 JAMA 2006;296:283-91

Emergency Medicine

Intravenous Morphine Plus Ketorolac Is Superior to Either Drug Alone For Treatment Of Acute Renal Colic

This was a randomized, double blinded, prospective study designed to study the efficacy of ketorolac, morphine and both drugs in combination in reducing the pain of acute renal colic.

Patients aged 18 to 55, and with a clinical diagnosis of acute renal colic were eligible. Consecutive patients presenting to

the ED in a six month period were screened for inclusion. Patients were excluded if they were pregnant or had suspected pregnancy, had taken analgesics six hours prior to presentation, history of renal dysfunction, bleeding diathesis, peptic ulcer disease, drug dependence, were on warfarin, or peritoneal signs on physical examination. A total of 130 patients were enrolled into the study.

Patients were randomized and received either morphine 5mg, ketorolac 15mg, or a combination of the two. Patients were intravenously administered study analgesic medications at time 0 and, if pain persisted, at 20 minutes. If pain still persisted at 40 minutes, patients were given a rescue dose or morphine 5mg IV.

Rescue morphine was required in 18/ 43 (42%) morphine patients, 14/43 (33%) ketorolac patients, and 7/44 (16%) combination patients.

The authors conclude that a combination of morphine and ketorolac offered pain relief superior to either drug alone and was associated with a decreased requirement for rescue analgesia.

Safdar te al, Annals of Emergency Medicine, August 2006 Ann Emerg Med 2006;48:173-81

Editors Note: While the data presented is valid, the standard dose of ketorolac for patients in this age group is 30mg IV. Although the authors did administer 30mg total, it was in divided doses. There is also no mention of how aggressively patients were hydrated, and if there was any standardization of hydration in the study. - MSB

Gastroenterology

Body-Mass Index and Symptoms of Gastroesophageal Reflux in Women

Gastroesophageal Reflux Disease (GERD) is a common disorder, affecting up to 60% of people at some point during the course of a year, and 20-30% of people on a weekly basis. It accounts for nine million office visits to physicians per year, and costs approximately \$10 billion dollars annually. Body Mass Index is defined as the weight in kilograms divided by the square of the height in meters. The association between increased body mass index (BMI) and GERD is well known, however the studies to date all involved obese and overweight persons. This study evaluated BMI and GERD in persons of normal weight.

The cohort of the Nurses Health Study was established in 1976 when 121,700 female registered nurses, 30 to 55 years of age, completed a mailed questionnaire about risk factors for cancer and cardiovascular disease. Participants have subsequently received supplemental follow-up questionnaires every two years.

In 2000, 10,545 randomly selected women from the Nurses Health Study completed questionnaires (response rate 86%) designed to determine the frequency and duration of GERD.

GERD was defined as heartburn, acid regurgitation or both. Women were then characterized based on their BMI as measured in 1998. Women were stratified according to BMI, age, smoking status, total activity, caloric intake, alcohol intake, coffee intake, tea intake, chocolate intake, use of hormone therapy, anti hypertension medication, asthma medication and history of diabetes.

Of the respondents, 2,497 (24%) women reported reflux symptoms less than once a month, 1,302 (12%) women reported GERD symptoms once a month, 986 (9%) women reported symptoms once a week, and 1,027 (10%) of women reported symptoms several times a week. The authors observed a positive relationship between increasing BMI and frequency of GERD. Compared to women with a BMI of 20.0 to 22.4, the odds ratio for frequency of GERD was 0.67 women with a BMI less than 20, 1.38 for women with a BMI of 22.5 to 24.9, 2.20 for women with a BMI of 25.0 to 27.4, 2.43 for a BMI of 27.5 to 29.9, 2.92 for a BMI 30.0 to 34.9, and 2.93 for women with a BMI greater than 35.

The authors conclude that BMI is associated with symptoms of gastroesophageal reflux disease in both normal and overweight women. Even moderate weight gain among persons of normal weight may cause or exacerbate symptoms of reflux. - MSB

Jacobson et al, New England Journal of Medicine, June 1, 2006 NEJM 2006;354:2340-8

Hematology

Effect of Hypobaric Hypoxia, Simulating Conditions During Long-Haul Air Travel on Coagulation, Fibrinolysis, Platelet Function and Endothelial Activation

This study was a single blind, crossover study designed to evaluate the effect of hypobaric hypoxia and the risk of venous thromboembolism.

The authors enrolled 73 healthy volunteers. They further stratified the volunteers into three subgroups. Group 1 was composed of individuals ages 18 to 40 years, group 2 was composed of women ages 18 to 40 years who were taking oral contraceptives, and group three were individuals ages 50 or greater. Individuals were excluded if they had a first degree relative with a history of thromboembolism, or if they had taken an anticoagulant or an antiplatelet medication with the preceding two weeks. Air travel was not permitted within one week of each exposure.

Individuals were exposed to both conditions, at least one week apart. The participants were placed in a normobaric or hypobaric chamber for eight hours, equivalent to conditions at ground level or an altitude of 2,438 meters. Patients were seated, but permitted to stand up and move for five minutes each hour. Multiple markers for coagulation

activation, fibrinolysis, platelet activation and endothelial cell activation were obtained prior to and within 20 minutes after exposure. Blood samples were obtained by venipuncture.

The authors found no significant difference in the change in markers when comparing normobaric and hypobaric exposure before and after exposure. Markers included (but not limited to), D-dimer, thrombin-antithrombin complex, tissue plasminogen activator, PT, PTT.

The authors conclude that their findings do not support the hypothesis that hypobaric hypoxia, of the degree that might be encountered during long-haul air travel, is associated with prothrombotic alterations in the hemostatic system in healthy individuals at low risk of venous thromboembolism. - MSB

Toff et al, Journal of the American Medical Association, May 17, 2006 JAMA 2006;295:2251-61

Infectious Disease

Single-Dose Azithromycin in the Treatment of Cholera in Adults

Single dose azithromycin is effective in the treatment of cholera in children. It's effectiveness has not been studied in children. This was a randomized, double blinded study comparing the efficacy of single dose azithromycin to ciprofloxacin.

Patients were eligible if they were men between the ages of 16 and 60. Patients had watery diarrhea for more than 24 hours, severe dehydration, a high purging rate (stool volume > 20ml per kilogram body weight during a four hour period) and had vibrio cholera O1 or O139 isolated from a culture of stool or a rectal swab.

Consecutive patients meeting eligibility requirements who presented for care to the Dhaka Diarrhea Treatment Center between 6 am and 6 pm daily were identified. The patients were re-hydrated over a period of two to four hours and screened for V. cholera with dark field microscopy of a stool specimen. Of the 325 patients screened, 198 patients met eligibility criteria.

Patients were given either two 500mg tablets of azithromycin and a placebo formulation of ciprofloxacin, or two 500mg tablets of ciprofloxacin and a placebo formulation of azithromycin. Patients were admitted to the study ward of the treatment center for five days. Every six hours vital signs, the presence of watery stool, and fluid balance were assessed. Fluid balance was maintained with oral hydration, and where oral intake was inadequate, intravenous hydration. Stool specimens were obtained before administration of the drug, on day three and on a follow-up visit. The primary study outcomes were the clinical success of the therapy, and the bacteriological success of therapy. Clinical success was defined as the cessation of watery stools within 48 hours, and bacteriological success was defined as negative

cultures 48 hours after administration of the study drug. Secondary outcome measures were defined as clinical or bacteriological relapse.

Azithromycin was clinically successful in 71 of 91 patients (73%), and ciprofloxacin was successful in 26 of 98 patients (27%). Bacteriological success was achieved in 76 patients (78%) treated with azithromycin and in 10 patients (10%) treated with ciprofloxacin. Patients who were treated with azithromycin had a significantly shorter duration of diarrhea, fewer stools, a lower volume of stool, and a lower frequency of vomiting than did patients who received ciprofloxacin. They also required less intravenous and oral fluids, and excreted *V. cholera* for a shorter period.

The authors conclude that single-dose azithromycin was effective in the treatment of severe cholera in adults. The lack of efficacy of ciprofloxacin may result from its diminished activity against *V. cholera* O1 strains currently circulating in Bangladesh. - MSB

Saha et al, New England Journal of Medicine, June 8, 2006 NEJM 2006;354:2452-62

Single-Dose, Patient Initiated Famciclovir: A Randomized, Double-Blind, Placebo Controlled Trial For Episodic Treatment Of Herpes Labialis

Herpes Simplex virus type 1 infects at least 40% of Americans by the time they reach adolescence, increasing with age so that up to 90% of persons older than 50 years are seropositive for HSV-1. Since the period of viral replication resulting in HSV outbreaks is short, the authors evaluated whether a shorter treatment time would be effective in controlling an episode of herpes labialis.

This was a multinational, randomized, double blind, placebo controlled study of patient initiated therapy with famciclovir in immunocompetent patients with recurrent herpes labialis. The study was conducted at 28 centers in the United States, 10 centers in Canada and three centers in Australia between October 2003 and January 2005. Patients were men and women at least 18 years of age, in good health and had at least three or more episodes of cold sores with the preceding 12 months. Patients were also required to have a history of prodromal symptoms, as defined by the patient, preceding at least 50% of the outbreaks, and at least 50% of the episodes had to progress to vesicular lesions. Women of childbearing age agreed to use reliable birth control.

A total of 1,417 patients were screened, and 1,376 met eligibility requirements. The patients were randomized into one of three study arms, famciclovir 1500mg once, famciclovir 750mg bid for one day, or placebo.

A total of 701 patients developed symptoms of recurrence, and 477 developed vesicles. Time to healing of primary vesicular lesions was 4.4 days for single dose famciclovir, 4.0 days for divided dose famciclovir, and 6.2 days for placebo.

Time to healing of all vesicular lesions was 4.5 days for single dose famciclovir, 4.1 days for divided dose famciclovir, and 6.6 days for placebo. Adverse events were similar in all three groups.

The authors conclude that single dose famciclovir reduced time to healing of herpes labialis by approximately two days when compared to placebo. - MSB

Spruance et al, Journal of the American Academy of Dermatology, July 2006 J Am Acad Dermatol 2006;55:47-53

Neurology

High Dose Atorvastatin after Stroke or Transient Ischemic Attack

Statins reduce the incidence of strokes among patients at increased risk for cardiovascular disease. Whether they reduce the risk of stroke or transient ischemic attack (TIA) had not been established. This was a randomized, double blinded study which looked at the effectiveness of atorvastatin in reducing the risk of stroke in patients with a history of stroke or TIA.

The authors assessed 6,670 patients for inclusion into the study, of which 4,731 met the inclusion criteria. Patients already on lipid lowering drugs had to stop these medications 30 days prior to the screening phase of the study. Patients were randomized to receive either 80mg atorvastatin daily or placebo. The primary outcome was a fatal or non-fatal stroke.

The mean LDL level was 73mg/dl in the atorvastatin group, and 129mg/dl in the placebo group. During a median follow-up of 4.9 years, 265 patients (11.2%) on atorvastatin and 311 (13.1%) placebo patients had a fatal or non-fatal stroke. The atorvastatin group had 218 ischemic strokes and 55 hemorrhagic strokes, while the placebo group had 274 ischemic strokes and 33 hemorrhagic strokes. The risk of cardiovascular events were reduced in the atorvastatin group. There were 216 deaths in the atorvastatin group, and 211 deaths in the placebo group. While cardiovascular and ischemic stroke deaths were lower in the atorvastatin group, deaths from all other causes were lower in the placebo group.

The authors conclude that in patients with a recent stroke or TIA and without known coronary artery disease, 80mg of atorvastatin per day reduced the overall incidence of strokes and of cardiovascular events, despite a small increase in the number of hemorrhagic strokes.

The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators, New England Journal of Medicine, August 10, 2006 NEJM 2006;355:549-59

Editors note: While the incidence of cardiovascular events and ischemic strokes were reduced in the atorvastatin group, overall mortality was slightly higher in the atorvastatin

group, although not statistically significant. Death from causes other than cardiovascular events and ischemic stroke was higher in the atorvastatin group. - MSB

Obstetrics and Gynecology

Major Congenital Malformations after First-Trimester Exposure to ACE Inhibitors

Angiotensin converting-enzyme (ACE) inhibitors are contraindicated in the second and third trimester of pregnancy due their increased risk of fetopathy. The use of ACE inhibitors in the first trimester has not been linked to any adverse birth outcomes.

This was a cohort study of 29,507 infants enrolled in Tennessee Medicaid and born between 1985 and 2000. The authors identified 209 infants exposed to ACE inhibitors in the first trimester alone, 202 infants with exposure to other antihypertensive medications in the first trimester alone, and 29,096 infants with no exposure to antihypertensive drugs at any time during gestation. Infants born to women with diabetes were excluded.

The authors found that 411 infants were exposed to antihypertensive medications, of which 209 had been exposed to ACE inhibitors only, and 202 other antihypertensive medications. The rate of congenital malformations was 834/29069 (2.63%) for infants with no exposure, 18/209 (7.12%) for infants exposed to ACE inhibitors during the first trimester, and 4/202 (1.73%) for infants exposed to other antihypertensive medications. Compared to no antihypertensive medications, use of ACE inhibitors in the first trimester of pregnancy had an overall relative risk of congenital malformation of 2.71, the relative risk of cardiovascular malformation was 3.72, and the relative risk of central nervous system malformation was 4.39. Use of other antihypertensive medications had an overall relative risk of congenital malformation was 0.66, the relative risk of cardiovascular malformation was 0.89, and the relative risk of nervous system malformation was 0. Odds ratios were adjusted for numerous underlying medical conditions.

The authors conclude that exposure to ACE inhibitors in the first trimester cannot be considered safe and should be avoided. - MSB

Cooper et al, New England Journal of Medicine, June 8, 2006 NEJM 2006;254:2443-51

Psychiatry

Fluoxetine After Weight Restoration in Anorexia Nervosa

Despite lack of evidence, a substantial number of patients with Anorexia Nervosa are on antidepressant medication. This was a randomized, double blinded, placebo controlled trial designed to study the efficacy of fluoxetine in promot-

ing recovery and prolonged time to relapse inpatients with anorexia nervosa following weight restoration.

Patients were eligible if they were a woman between the ages of 16 and 45, met DSM-IV criteria for anorexia nervosa, with the exception of amenorrhea. Prior to enrollment, the patients had successfully completed treatment at one of the study sites. Additionally they had maintained a BMI of 19 for two weeks, were not a suicide risk, did not have another serious underlying medical condition, and were medication free (with the exception of lorazepam, 0.5mg or zopiclone, 7.5mg for anxiety or sleep disturbance).

A total of 150 patients were evaluated for eligibility into the study. After evaluation, 93 patients were randomized to received either fluoxetine (49 patient) or placebo (44 patients). Medication was administered in a double blind fashion one week prior to discharge from the hospital. The dose increased from 20mg/day to 60mg/day (1 to 3 pills) over one week under close supervision for any adverse effects. If adverse effects were present, the dose was lowered at the discretion of the psychiatrist. If the patient's clinical status was deteriorating, the dose could be raised to 80mg/day (4 pills). After the first week receiving study medication, patients were discharged home and treated for 12 months or until they met criteria for premature study withdrawal or voluntarily withdrew.

Of the 93 patients who were enrolled, 40 patients completed the study. The number of patients and their reasons for termination were comparable in both the treatment and the placebo group. In comparing the two groups, the authors found no statistically significant difference in the two groups in BMI or time to relapse during the study period.

The authors conclude that this study failed to demonstrate any benefit from fluoxetine in the treatment of patients with anorexia nervosa following weight restoration. Future efforts should focus on developing new models to understand the persistence of this illness and on exploring new psychological and pharmacological treatment approaches. - MSB

Walsh et al, Journal of the American Medical Association, June 14, 2006 JAMA 2006;295:2605-2612

Rheumatology

Cyclophosphamide Versus Placebo in Scleroderma Lung Patients

Scleroderma is an autoimmune connective tissue disorder characterized by microvascular injury, excessive fibrosis of the skin and visceral changes that can involve the lungs, heart, kidneys and gastrointestinal tract. Forty percent of scleroderma patients have ventilary restriction, mainly as a result of interstitial lung disease.

Several agents have been evaluated as treatments for scleroderma related interstitial lung disease without success.

Cyclophosphamide has shown promise in retrospective studies. This was a multi-centered, double blinded, randomized prospective study designed to evaluate the effectiveness of cyclophosphamide in treating patients with active, symptomatic scleroderma related interstitial lung disease.

Patients were excluded if they had a single breath carbon monoxide diffusing capacity (DLCO) less than 30% of predicted value, a history of smoking within the past six months, other significant pulmonary abnormalities, or clinically significant pulmonary hypertension requiring drug therapy. Patients were also excluded if they had been treated with cyclophosphamide for more than four weeks, or had received more than two IV doses of cyclophosphamide, were taking more than 10mg prednisone a day, or had received other potentially disease modifying medications.

The authors screened 267 patients. 162 patients underwent randomization, of which four were later determined to be ineligible. Of the 158 eligible patients, 79 were randomized to receive cyclophosphamide and 79 received placebo. Cyclophosphamide was administered in 25mg capsules. Patients started with a dose of 1mg/kg, (to the nearest 25mg), and the dose increased by one capsule monthly until patients were receiving 2mg/kg per day. Placebo patients received matching gelpcaps.

Of the 158 patients, 145 completed at least six months of treatment and were included in the analysis. The mean absolute difference in adjusted 12-month FVC was 2.53% in favor of cyclophosphamide, and the difference was maintained at 24 months. The authors also found significant differences in favor of the cyclophosphamide group in disability score and skin thickness scores. The total lung capacity also showed a significant difference of 4.09% in total lung capacity, favoring the cyclophosphamide group. There was no significant difference in DLCO.

The authors conclude that one year of oral cyclophosphamide in patients with symptomatic scleroderma related interstitial lung disease had a significant, but modest beneficial effect on lung function, thickening of skin, and the health-related quality of life. The effects on lung function were maintained through the 24 months of the study.

Tashkin et al, New England Journal of Medicine, June 22, 2006 NEJM 2006;354:2655-66

Editors note: While the differences in the two groups was small, small differences in lung function make a big difference to patients with severe interstitial lung disease resulting from this debilitating disease. - MSB

Women's Health

Combined Estrogen Use And Testosterone Use And Risk of Breast Cancer in Post Menopausal Women

The role of androgens in breast cancer etiology has been unclear. Epidemiologic studies suggest that endogenous androgen levels are positively associated with breast cancer risk. This was a prospective cohort study in the Nurses Health Study from 1978 to 2002 to assess the risk of breast cancer associated with different types of postmenopausal hormone replacement (PMH) formulations containing testosterone.

During the 24 years of follow-up (1,359,323 person-years), 4,610 cases of breast cancer were identified among postmenopausal women. There were 18,754 women who never used PMH, 15,489 women who had used estrogen only PMH, 550 women who had used estrogen and testosterone PMH, and 37 women who had used testosterone only. The authors adjusted for age at menopause, family history of breast cancer, body mass index, age at menarche, age at first birth, alcohol use, and current use of other hormones.

Among all women, the relative risk of breast cancer as compared to no use of PMH was 1.15 for estrogen only PMH, 1.77 for estrogen and testosterone PMH, and 2.52 for testosterone only PMH. Among women with natural menopause, the relative risk was 1.23 for estrogen only PMH, 2.48 for estrogen and testosterone PMH, and 2.10 for testosterone only PMH.

The authors conclude that consistent with the elevation in risk for endogenous testosterone levels, women using estrogen and testosterone therapies have a significantly increased risk of breast cancer.

Tamini et al, Archives of Internal Medicine, July 24, 2006 Arch Intern Med 2006;166:1483-1489

Editors note: The authors correctly point out in their discussion that the number of women on testosterone was very small. - MSB

Section Editor: Matthew S. Berry, MD, FACP, FAAEP