

# ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

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## Dietary Supplements for Weight Loss

*By Adriane Fugh-Berman, MD,  
and Tieraona Low Dog, MD*

**W**EIGHT LOSS SUPPLEMENTS ABOUND. MANY SUPPLEMENTS contain ephedra, also called ma huang (*Ephedra sinica*); other popular ingredients include synephrine, from bitter orange (*Citrus aurantium*), green tea (*Camellia sinensis*), St. John's wort (*Hypericum perforatum*), and chitosan. This article will review data on efficacy and safety of these ingredients.

### Ephedra (*Ephedra sinica* and Others)

Ephedra contains ephedrine, an orally active  $\alpha$ -1 agonist and a non-selective  $\beta$ -agonist. Studies are about evenly split on whether ephedra is effective for weight loss (see Alternative Therapies in Women's Health, June 2002). The most recent trial, a randomized double-blind trial in 67 subjects (48 completed the study) compared Metabolife-356, containing 72 mg ephedrine and 240 mg caffeine, to placebo as an adjunct to diet and exercise for eight weeks.<sup>1</sup> The treated group lost 4.0 kg compared to 0.8 kg in the placebo group. Twenty-three percent of the treated group withdrew because of adverse effects, which included hypertension, chest pain, and palpitations. There were no withdrawals in the placebo group.

Health care practitioners should discourage the use of any ephedrine-containing products for weight loss, bodybuilding, or energy. Of 140 adverse events associated with ephedra-containing products reported to the Food and Drug Administration between June 1997 and March 1999, 62%, including 10 deaths, were considered definitely, probably, or possibly related to ingestion of these products.<sup>2</sup> Adverse events included hypertension, palpitations, tachycardia, stroke, and seizures. Quite low doses occasionally cause severe adverse events; one death, in a 38-year-old male without known concurrent risks, was associated with consumption of approximately 20 mg ephedrine/d.<sup>2</sup>

The fact that ephedrine raises blood pressure is no surprise to physicians, as ephedrine is used to treat hypotension during surgery, but ephedra manufacturers have argued that the herb ephedra has

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different effects than ephedrine. This isn't true. A recent pharmacokinetic study of a dietary supplement containing 20 mg ephedrine alkaloids and 200 mg caffeine found that mean systolic blood pressure increased by 14 mm Hg at 90 minutes after ingestion ( $P < 0.001$ ).<sup>3</sup> There was no change in diastolic blood pressure. Heart rate increased by 15 beats/min above baseline at six hours ( $P < 0.001$ ). Pharmacokinetics data for ephedrine, pseudoephedrine, and caffeine from ephedra correlated closely with previous studies of isolated ephedrine, pseudoephedrine, and caffeine. A mood and symptom questionnaire found that, compared to baseline, feelings of being energetic, relaxed, and contented were significantly higher at one hour, and shakiness was significantly higher at five hours.

Ephedra is used in small doses in traditional Chinese medicine as well as in Western herbal medicine, primarily for respiratory problems; this use does not appear to be dangerous. Both of us have personally used ephedra-containing preparations containing crude ephedra herb to treat respiratory problems; therapeutically, the herb is used in low doses, for short periods of time, for specific indications. Virtually all adverse effects reported with ephedra alkaloids have been associated with products for weight loss, exercise enhancement, energy enhance-

ment, or recreational use, none of which are traditional indications and all of which utilize doses meant to speed metabolism.

### Bitter Orange (*Citrus aurantium*)

Weight loss products containing synephrine and octopamine are apt to be the next wave in natural weight loss products. A double-blind, randomized, placebo-control, three-armed study of 23 subjects with body mass index greater than  $25 \text{ kg/m}^2$  compared treatment, placebo, and nothing as an adjunct to a 1,800 kcal American Heart Association step I diet and a weight circuit training exercise program three days a week under the direction of an exercise physiologist.<sup>4</sup> The product contained 975 mg *C. aurantium* extract (6% synephrine alkaloids), 528 mg caffeine, and 900 mg St. John's wort (3% hypericum [sic]) daily for six weeks. Outcome measures included weight, fat loss, and mood. Twenty subjects completed the study. The study reports that treated subjects lost a significant amount of weight (1.4 kg) compared to the placebo group (which lost 0.9 kg) and control group (which lost 0.04 kg). However, the table in the publication appears to indicate that the differences are significant compared to baseline but not in comparison to the other groups.

The treatment group lost 2.9% of fat; there was no significant change in the placebo or control groups. No significant changes were seen in any group in the profile of mood states questionnaire, blood lipids, blood pressure, heart rate, EKG, serum chemistries, or urinalysis. Basal metabolic rate increased significantly in the treated group and decreased significantly in the placebo group; there was no change in the control group. No side effects were reported.

Bitter orange extract is made from the fruit with the rind. Also called Seville or sour orange, *C. aurantium* contains synephrine and octopamine, which are phenolamines found in sympathetic nerve fibers. Synephrine is similar to epinephrine, and octopamine is similar to norepinephrine (they differ only in the number of hydroxyl groups on the aromatic ring).<sup>5</sup> Synephrine activates both alpha-adrenoreceptors and beta-3 adrenoreceptors; both synephrine and octopamine also inhibit cyclic adenosine monophosphate production. Beta-3 adrenoreceptors agonists are full lipolytic agents in rats, hamsters, and dogs, but are much less active in humans and guinea pigs.<sup>6</sup> Octopamine appears to be more potent than synephrine. There are almost no safety data on synephrine or octopamine. Any sympathomimetic agents in sufficient dosages increase thermogenesis and blood pressure and cannot be presumed to be safe, especially in those with cardiovascular disease.

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The juice from the bitter orange (without the rind) contains 6',7'-dihydroxybergamottin, and is used to selectively knock out intestinal cytochrome P450 CYP3A4 in bioavailability studies. CYP3A4 metabolizes about a quarter of all drugs, so inhibition of this isoenzyme would be expected to increase blood levels of some drugs. It would be interesting to test the extract to see if the effect is as strong as the fruit juice. Juice contains fewer phenolamines than extract; octopamine was not detected at all in Seville orange juice.<sup>7</sup>

No pharmacokinetic studies of the extract were identified, but a safety study has been done of the juice. A crossover, open-label study in 12 normotensive subjects ages 20-27 tested the cardiovascular effects of two doses of *C. aurantium* juice (eight ounces, eight hours apart); the test was repeated with water a week later. Blood pressure was taken every hour for five hours after the second dose of juice; systolic and diastolic blood pressure, mean arterial pressure, and heart rate were not significantly altered. Oddly, hemodynamic indices were not measured after initial bitter orange juice consumption. It was estimated that subjects consumed approximately 13-14 mg of synephrine, approximately comparable to a dose of phenylephrine in decongestant-containing cold preparations.

If bitter orange extract contains 6',7'-dihydroxybergamottin, which knocks out CYP3A4, it would be expected to increase blood levels of many drugs. St. John's wort has an opposing effect: It induces CYP3A4 as well as p-glycoprotein, thus lowering drug levels (*see Alternative Therapies in Women's Health, August 2002*). A product containing both could have unpredictable interactions with drugs.

Assuming that the 3% hypericum actually means 0.3% hypericin, the dose of St. John's wort in this particular product would be a therapeutic antidepressant dose. There is no clinical evidence that St. John's wort helps weight loss, but depression can certainly predispose to overeating.

### Caffeinated Herbs

The bitter orange product described above contains a lot of caffeine—the equivalent of four cups of coffee or 10 cups of tea. Caffeine has thermogenic effects, which can be synergistic with other sympathomimetic agents. At least this product acknowledged the presence of caffeine, which can be hidden by listing herbs that contain caffeine. Besides tea, kola nuts (*Cola nitida*, *C. acuminata*), mate (*Ilex paraguariensis*), and guarana (*Paullinia cupana*) contain significant amounts of caffeine.

A double-blind placebo-controlled study tested several herbs in non-obese subjects, using indirect calorime-

ters, including guarana (*P. cupana* 2.72 g seed powder, with 4% caffeine), ephedra (*E. sinica* 2.0 g powder, 2% alkaloids), and mate (*I. paraguariensis* 1.5 g dry extract).<sup>8</sup> Only mate decreased respiratory quotient (indicating an increase in fat oxidized); none of the herbs increased energy expenditure.

### Garcinia (Hydroxycitrate)

Hydroxycitrate, found in *Garcinia cambogia*, inhibits fatty acid synthesis. There have been eight trials of garcinia thus far. The best trial was a 12-week randomized double-blind placebo-controlled trial in an outpatient weight control research unit in New York of 135 overweight men and women ages 18-65; mean body mass index was 32 kg/m<sup>2</sup>.<sup>9</sup> Both groups went on a high-fiber, low-energy diet and were given placebo or hydroxycitric acid 500 mg three times a day 30 minutes before meals for 12 weeks. The total daily dose was 3,000 mg herb, containing 1,500 mg hydroxycitric acid. Both groups lost weight, but there was no significant difference between the two groups. Reported adverse effects were minor and not significantly different between the two groups. Although this trial is the best study available, it has some limitations, including lack of monitoring of diet compliance and a high dropout rate; only 62% of the subjects completed the trial. However, this trial indicates that there is no benefit to adding hydroxycitrate to a weight loss plan.

Although seven previous trials have been conducted (five of which claimed a positive result for garcinia), only two were published in peer-reviewed journals. Also, five trials tested garcinia in mixed formulations, and none of the trials were more than eight weeks long.

### Chitosan

Chitosan is a cationic polysaccharide derived by alkaline deacetylation from chitin in the exoskeletons of arthropods; the usual commercial source is from the shells of shrimp and crab. Chitosan forms a positively charged gel in the stomach, and can bind negatively charged fats to its tertiary amine group; it also can decrease normal cholesterol emulsification through hydrophobic binding. It becomes insoluble in the alkaline environment of the intestine, forming aggregates with fats and bile acids, and interrupting enterohepatic recirculation.<sup>10</sup>

A randomized double-blind placebo-controlled trial in 34 overweight volunteers (30 completed) tested chitosan (four capsules, each containing 250 mg deacetylated chitin biopolymer) twice daily for four weeks.<sup>11</sup> Volunteers maintained their normal diet. There was no difference between groups in weight, blood pressure,

cholesterol, triglycerides, vitamin A, vitamin D, vitamin E, or beta-carotene levels; the chitosan-treated group had significantly higher vitamin K levels. An analysis of five previous trials in which chitosan was given with a hypocaloric diet (1,000-1,200 kcal/d) found a significant decrease in body weight in chitosan-treated groups vs. placebo.<sup>11</sup>

An abstract presented at a recent toxicology meeting attributes a case of possible arsenic toxicity to chitosan ingestion.<sup>12</sup> A 39-year-old woman who had been taking Chitosan® (six capsules daily for a year) was evaluated after presenting to an emergency department with a six-month history of fatigue, headache, and weakness. A sensory peripheral neuropathy was noted, and a 24-h urine collection (on a seafood-free diet) was found to contain arsenic levels of 186 µg/L (normal range 0-50 µg/L). Chitosan was discontinued; 19 days later, urinary arsenic level was 100 µg/L, and four months later, the 24-h urinary arsenic level was less than 10 µg/L, at which point the patient's neurological manifestations had resolved. Shellfish contains arsenic, and no other sources of arsenic in the patient's water, diet, or environment were identified. FDA analysis of the product found 135.5 ng/g/capsule of arsenic (equivalent to 0.015 µg/kg/d).

### **Tea (*Camellia sinensis*)**

Tea may have thermogenic effects that are not entirely due to caffeine. A crossover study in 10 healthy men utilizing a respiratory chamber at the University of Geneva tested green tea extract on energy expenditure and fat oxidation in humans.<sup>13</sup> On separate occasions subjects were given green tea extract (50 mg caffeine and 90 mg epigallocatechin gallate), caffeine (50 mg), or placebo, which they ingested at breakfast, lunch, and dinner. Twenty-four-hour energy expenditure, respiratory quotient, and urinary excretion of nitrogen and catecholamines were measured.

Ingestion of green tea extract resulted in a significant increase in 24-h energy expenditure (4%, P < 0.01) and a significant decrease in 24-h respiratory quotient (from 0.88 to 0.85, P < 0.001) with no change in urinary nitrogen. Norepinephrine excretion was 40% higher during treatment with green tea than with placebo (P < 0.05). Caffeine had no effect on energy expenditure, respiratory quotient, urinary nitrogen, or urinary catecholamines. No significant changes in heart rate were noted during the first eight hours the subjects were assessed. Caffeine is thermogenic, but only in doses of more than 100 mg for one to two hours. A dose of 600-1,000 mg/d is necessary to affect 24-h energy expenditure in a respiratory chamber.

One possible explanation for additional thermogenic activity is that flavonoids called catechins in tea inhibit COMT, the enzyme that degrades norepinephrine (which helps to control thermogenesis and fat oxidation). Mice made obese through a high-fat diet were treated with oolong tea for 10 weeks. Food consumption was not affected but oolong tea prevented the obesity and fatty liver induced by a high-fat diet.<sup>14</sup> Lipolysis of fat cells was enhanced, an effect found to be due to caffeine; however, oolong tea extract inhibited pancreatic lipase activity, which would not be expected by caffeine.

### **Chili Peppers (*Capsicum spp.*)**

Capsaicin (the major capsaicinoid in the fruit that gives chili its hot taste) has been shown to stimulate lipid mobilization in rats.<sup>15</sup> In humans, capsicum ingestion may stimulate carbohydrate oxidation. In a crossover study in eight long distance male runners who exercised for an hour after a breakfast spiked with 10 g of hot red pepper (a pepper-free breakfast was used as a control), red pepper significantly elevated respiratory quotient and blood lactate levels at rest and during exercise; plasma triacylglycerol concentrations during exercise were significantly higher after the red pepper meal.<sup>16</sup> There was no significant difference in oxygen consumption.

### **Chinese Herbal Products**

Adulteration has been an ongoing problem with dietary supplements. Researchers in the United Kingdom reported high concentrations of fenfluramine (a prescription drug banned in 1997 because of its association with pulmonary hypertension) in two Chinese herbal remedies sold as Qian Er and Ma zin dol.<sup>17</sup>

Laboratory analysis by the Health Sciences Authority (HSA) of Singapore found that Slim 10, a Chinese herbal slimming product, was adulterated with fenfluramine and contained a second undeclared ingredient, nicotinamide. HSA advised consumers to stop taking the product immediately. The Japanese Health Ministry reported that more than 15 different Chinese diet products, many labeled as being made from herbs or tea, were associated with adverse effects in at least 317 people. The reported adverse effects included liver disorders, thyroid problems, and four deaths.<sup>18</sup>

In Belgium, approximately 100 cases of renal disease were reported in patients who took weight-reducing pills purportedly containing the Chinese herb *Stephania tetrandra* between 1990 and 1992. In fact, the preparations contained *Aristolochia fangchi*. Since then, 11 cases of interstitial fibrosis have been linked to botanical preparations containing aristolochic acid. In 2000, it was

reported that among 39 patients with end-stage renal disease from the original Belgian cohort who underwent surgery, 18 cases (46%) of urothelial carcinoma were identified; all tissue samples contained aristolochic acid-related DNA adducts.

The FDA has warned health professionals to watch for interstitial fibrosis associated with end-stage renal disease, or urothelial tract tumors, connected with aristolochic acid-containing dietary supplements.<sup>19</sup>

## Conclusion

Although marketers would have consumers believe that "miracle" weight loss products are available on the health food store shelves, the reality is that none have been shown to be both safe and effective. Although drinking green tea and eating chili peppers are not likely to cause any harm, the use of ephedra and guarana products has been associated with severe side effects, including death. Given the growing number of obese individuals in the United States, there is certainly a need for rigorous research to determine if there are safe and effective over-the-counter products for managing and losing weight. However, none can be readily recommended at this time. ♦

## References

1. Boozer CN, et al. An herbal supplement containing Ma Huang-Guarana for weight loss: A randomized, double-blind trial. *Int J Obes Relat Metab Disord* 2001; 25:316-324.
2. Haller CA, Benowitz NL. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N Engl J Med* 2000;343:1833-1838.
3. Haller CA, et al. Pharmacology of ephedra alkaloids and caffeine after single-dose dietary supplement use. *Clin Pharmacol Ther* 2002;71:421-432.
4. Colker CM, et al. Effects of *Citrus aurantium* extract, caffeine, and St. John's wort on body fat loss, lipid levels, and mood states in overweight healthy adults. *Curr Ther Res* 1999;60:145-153.
5. Airriess CN, et al. Selective inhibition of adenylyl cyclase by octopamine via a human cloned alpha 2A-adrenoceptor. *Br J Pharmacol* 1997;122:191-198.
6. Carpene C, et al. Selective activation of beta3-adrenoreceptors by octopamine: Comparative studies in mammalian fat cells. *Naunyn Schmiedebergs Arch Pharmacol* 1999;359:310-321.
7. Penzak SR, et al. Seville (sour) orange juice: Synephrine content and cardiovascular effects in normotensive adults. *J Clin Pharmacol* 2001;41: 1059-1063.
8. Martinet A, et al. Thermogenic effects of commercially available plant preparations aimed at treating human obesity. *Phytomedicine* 1999;6:231-238.
9. Heymsfield SB, et al. *Garcinia cambogia* (hydroxycitric acid) as a potential antiobesity agent: A randomized controlled trial. *JAMA* 1998;280:1596-1600.
10. Ylitalo R, et al. Cholesterol-lowering properties and safety of chitosan. *Arzneimittelforschung* 2002;52:1-7.
11. Pittler MH, et al. Randomized, double-blind trial of chitosan for body weight reduction. *Eur J Clin Nutr* 1999;53:379-381.
12. Caraccio TR, et al. Chronic arsenic (As) toxicity from chitosan supplement [abstract # 109]. *J Tox Clin Toxicol* 2002;40:644. Presented at the 2002 North American Congress of Clinical Toxicology Meeting, Palm Springs CA, September 24-29, 2002.
13. Dulloo AG, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr* 1999;70:1040-1045.
14. Han LK, et al. Anti-obesity action of oolong tea. *Int J Obes Relat Metab Disord* 1999;23:98-105.
15. Kawada T, et al. Effects of capsaicin on lipid metabolism in rats fed a high fat diet. *J Nutr* 1986;116: 1272-1278.
16. Lim K, et al. Dietary red pepper ingestion increases carbohydrate oxidation at rest and during exercise in runners. *Med Sci Sports Exerc* 1997;29:355-361.
17. Metcalfe K, et al. Chinese medicines for slimming still cause health problems. *BMJ* 2002;324:679.
18. Japanese Health Ministry. Available at: [www.mhlw.go.jp/english/index.html](http://www.mhlw.go.jp/english/index.html).
19. U.S. Food and Drug Administration. Available at: [www.cfsan.fda.gov/~dms/ds-bot.html](http://www.cfsan.fda.gov/~dms/ds-bot.html).

## Acupoint Stimulation for Postoperative Nausea and Vomiting

By Carmen Tamayo, MD

ALTHOUGH POSTOPERATIVE NAUSEA AND VOMITING (PONV) is less common now than when ether and cyclopropane were commonly used anesthetics, the overall incidence is about 30%, with up to 70% of high-risk patients experiencing PONV.<sup>1</sup> Risk factors include being female, being a nonsmoker, having a history of motion sickness or PONV, and use of postoperative

opioids.<sup>1</sup> Type of surgery also affects risk: PONV is quite common after craniotomy, ear, nose and throat procedures, major breast procedures, strabismus surgery, laparoscopy, and laparotomy.<sup>1</sup> Nitrous oxide, volatile inhalational agents, and intra-operative opioids also increase risk. PONV can lead to aspiration, dehydration, electrolyte disturbances, and disruption of the surgical site. PONV increases treatment costs and may be associated with increased anxiety, dissatisfaction with the surgical experience, and anticipatory nausea in the future.<sup>2</sup> Although PONV rarely causes medically serious complications, patients feel that avoiding PONV is more important than avoiding postoperative pain.<sup>1</sup>

Acupuncture point stimulation has been assessed to prevent nausea and vomiting of various etiologies, including PONV. A MEDLINE search (1966-2002) of prospective randomized controlled trials of acupuncture or acupressure for nausea or emesis, supplemented by my own files, identified 23 trials of acupoint stimulation for postoperative nausea and vomiting in adults (*see Table*). Pediatric trials will not be covered here. Sixteen of 23 trials found a benefit for acupuncture stimulation for nausea and/or vomiting. Five trials were negative, and two trials reported mixed results.

Acupuncture points (or acupoints) can be stimulated by needles, pressure, heat, or transcutaneous electrical stimulation (TENS) devices. At least 11 trials tested acupressure bands, which are elastic bracelets with a button that presses on the P6 point, which is two thumb-widths proximal to the distal wrist crease, between the flexor carpi radialis and palmaris longus tendons. Acupressure band trials are easily controlled by misplacing the band on the wrist so that it doesn't stimulate the P6 point; alternatively, a placebo band, lacking a button, may be used. All but two trials applied stimulation at the P6 acupoint; the Boehler trial tested acupressure "seeds" taped to a Korean hand acupressure point (K9, on the middle phalanx of the fourth finger), and the Kotani trial tested acupuncture at the bladder meridian point (about 2.5 cm from the spinal vertebrae).

No serious adverse events have been associated with acupressure bands; occasional wrist swelling has been noted. Several studies in which the bands were placed prior to anesthesia noted that the bands did not interfere with the insertion of intravenous lines into the same arm. Adverse events following acupuncture are rare (*see Alternative Therapies in Women's Health, July 2002*).

Acupuncture and/or acupressure appear to be effective for PONV. Different methods of stimulating P6 (acupuncture, acupressure, electroacupuncture) appear to be equally effective, and all treatments appear to be benign.

Clinical trials of acupoint stimulation for PONV have used diverse populations and techniques. The wide variation in type of surgery, type of anesthesia, timing of administration of acupuncture or acupressure, duration of treatment, and duration of the study make it difficult to compare techniques and timing.

Future research evaluating acupoint stimulation should improve the quality of the existing evidence. Nevertheless, women undergoing surgery may consider acupressure bands, or other forms of acupoint stimulation, as a safe alternative or adjunct to pharmacological agents for preventing PONV. ♦

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## References

1. Gan TJ. Postoperative nausea and vomiting—Can it be eliminated? *JAMA* 2002;287:1233-1236.
2. Thompson HJ. The management of post-operative nausea and vomiting. *J Adv Nurs* 1999;29:1130-1136.
3. Boehler M, et al. Korean hand acupressure reduces postoperative nausea and vomiting after gynecological laparoscopic surgery. *Anesth Analg* 2002;94:872-875.
4. Kotani N, et al. Preoperative intradermal acupuncture reduces postoperative pain, nausea and vomiting, analgesic requirement, and sympathoadrenal responses. *Anesthesiology* 2001;95:349-356.
5. Ming JL, et al. Th efficacy of acupressure to prevent nausea and vomiting in post-operative patients. *J Advanced Nurs* 2002;39:343-351.
6. Agarwal A, et al. Acupressure wristbands do not prevent postoperative nausea and vomiting after urological endoscopic surgery. *Can J Anaesth* 2000;47: 319-324.
7. Harmon D, et al. Acupressure and prevention of nausea and vomiting during and after spinal anaesthesia for caesarean section. *Br J Anaesth* 2000;84:463-467.
8. Alkaissi A, et al. Effect and placebo effect of acupressure (P6) on nausea and vomiting after outpatient gynaecological surgery. *Acta Anaesthesiol Scand* 1999;43:270-274.
9. Harmon D, et al. Acupressure and the prevention of nausea and vomiting after laparoscopy. *Br J Anaesth* 1999;82:387-390.
10. al-Sadi M, et al. Acupuncture in the prevention of post-operative nausea and vomiting. *Anaesthesia* 1997;52: 658-661.
11. Yentis S, Vashisht S. The effect of timing of PC.6 acupuncture on post-operative vomiting following major gynaecological surgery. *Acupuncture Med* 1998; 16:10-13.

Table

**Acupoint stimulation to prevent postoperative nausea and vomiting in adults**

<b>Study</b>	<b>Subjects/Intervention</b>	<b>Results</b>
Boehler <sup>3</sup>	n = 80 women; acupressure “seeds” at Korean hand acupoint K9 (preoperatively, for 24 h) vs. inappropriate placement	Positive: Compared to control, fewer treated patients than placebo had N ( $P = 0.006$ ) or V ( $P = 0.007$ )
Kotani <sup>4</sup>	n = 189; acupuncture (preoperatively, for four days) vs. sham	Positive: Compared to controls, incidence of N/V was significantly less in the acupuncture group ( $P < 0.05$ )
Ming <sup>5</sup>	n = 150; finger acupressure before and after surgery vs. wristbands vs. no intervention	Positive: Compared to control, both types of acupressure reduced both N and V
Agarwal <sup>6</sup>	n = 200; P6 acupressure bands (preoperatively, until six hours post-op) vs. inappropriate placement	Negative: No difference between groups in N/V within 24 h
Harmon <sup>7</sup>	n = 94 women; P6 acupressure bands (preoperatively, until six hours post-op) vs. inappropriate placebo	Positive: Compared to control, treated subjects had less N/V during or after surgery ( $P \leq 0.003$ )
Alkaissi <sup>8</sup>	n = 60; P6 acupressure bands vs. inappropriate band placement (preoperatively) vs. no treatment	Mixed: P6 acupressure reduced V, compared to no treatment ( $P < 0.05$ ); two hours post-op, N was similar among groups
Harmon <sup>9</sup>	n = 104 women; P6 acupressure bands vs. inappropriate band placement (preoperatively) vs. no treatment	Positive: Compared to control, acupressure reduced the incidence (42% vs. 19%) but not severity of N/V
al-Sadi <sup>10</sup>	n = 81 women; P6 acupuncture (intra-operative only)	Positive: Acupuncture, compared to control, reduced N/V ( $P \leq 0.007$ )
Yentis <sup>11</sup>	n = 50; P6 acupuncture before anesthesia, after anesthesia, or postoperatively vs. sham	Negative: There were no differences among groups in N/V (secondary source used)
Fan <sup>12</sup>	n = 200; Acupressure bands (preoperatively, for six hours) vs. inappropriate band placement	Positive: Compared to controls, acupressure group had less N/V (23% vs. 41%, $P = 0.0058$ )
Stein <sup>13</sup>	n = 75 women; Acupressure bands (preoperatively) vs. metoclopramide vs. sham bands + IV saline (double dummy design)	Positive: Compared to control, acupressure and metoclopramide reduced N ( $P < 0.001$ ); only metoclopramide reduced V
Ho <sup>14</sup>	n = 60 women; P6 acupressure bands (preoperatively, for 48 h) vs. sham bands	Positive: Compared to sham, acupressure decreased N/V ( $P < 0.05$ )
Ferrara-Love <sup>15</sup>	n = 90; P6 acupressure bands (preoperatively through post-op) vs. sham bands vs. routine care	Negative: No differences among groups in N/V in OR or immediately post-op; compared to control, acupressure and sham reduced N/V ( $P \leq 0.003$ ) in second phase of recovery
Allen <sup>16</sup>	n = 46 women; P6 acupressure bands (preoperatively, apparently for 24 h) vs. inappropriate band placement	Negative: No difference in incidence of N/V
Philips <sup>17</sup>	n = 80 women; (apparently non-blinded) acupressure bands (preoperatively, apparently for 48 h) vs. no treatment	Mixed: Compared to controls, treated group had similar incidence of, but less severe, N ( $P = 0.002$ )
Yang <sup>18</sup>	n = 120 women; P6 glucose injection (intra-operatively) vs. IV droperidol vs. untreated controls	Positive: Compared to controls, droperidol and acupoint injection decreased incidence of V post-op ( $P < 0.05$ )
Gieron <sup>19</sup>	n = 60 women; P6 stimulation with metal “bullets” for 24 h vs. (apparently) misplaced bullets	Positive: Compared to controls, acupressure reduced post-op N (53% vs. 23%, $P = 0.03$ ) (German paper, read in abstract)
Barsoum <sup>20</sup>	n = 162; (apparently single-blind) P6 acupressure bands (post-op for seven days) vs. placebo bands with or without prochlorperazine	Positive: Compared to control or drug, acupressure reduced N on days 1 and 2 ( $P < 0.002$ ), but not later; no benefit for V
Rogers <sup>21</sup>	n = 19 men; P6 acupressure vs. no treatment	Positive: Compared to controls, the treated group had less (and less severe) N within six hours, but not later
Dundee <sup>22</sup>	n = 50 + n = 75 women; study 1: P6 acupuncture with or without meptazinol; study 2: acupuncture or sham with nalbuphine	Positive: P6 acupuncture significantly reduced N/V compared to meptazinol alone ( $P = 0.001$ ); compared to sham, acupuncture reduced N ( $P < 0.002$ )
Ghaly <sup>23</sup>	n = 93 women; P6 acupuncture vs. electroacupuncture vs. cyclizine vs. no intervention	Positive: All three active treatments superior to placebo for N/V ( $P \leq 0.001$ )
Weightman <sup>24</sup>	n = 44 women; P6 acupuncture (intra-operatively) vs. no acupuncture	Negative: No differences between groups in N/V
Fry <sup>25</sup>	n = 500; brief P6 acupressure before and after anesthesia vs. acupressure	Positive: Compared to control, fewer in the P6 group were sick ( $P < 0.001$ )

**Key:** N = nausea; V = vomiting

12. Fan CF, et al. Acupressure treatment for prevention of postoperative nausea and vomiting. *Anesth Analg* 1997;84: 821-825.
13. Stein DJ, et al. Acupressure versus intravenous metoclopramide to prevent nausea and vomiting during spinal anaesthesia for cesarean section. *Anesth Analg* 1997;84:342-345.
14. Ho CM, et al. Effect of P-6 acupressure on prevention of nausea and vomiting after epidural morphine for post-cesarean section pain relief. *Acta Anaesthesiol Scand* 1996;40:372-375.
15. Ferrara-Love R, et al. Nonpharmacologic treatment of postoperative nausea. *J Perianesth Nurs* 1996;11:378-383.
16. Allen DL, et al. P6 acupressure and nausea and vomiting after gynaecological surgery. *Anaesth Intensive Care* 1994; 22:691-693.
17. Phillips K, Gill L. The use of simple acupressure bands reduces post-operative nausea. *Complement Ther Med* 1994;2:158-160.
18. Yang LC, et al. Comparison of P6 acupoint injection with 50% glucose in water and intravenous droperidol for prevention of vomiting after gynecological laparoscopy. *Acta Anaesthesiol Scand* 1993;37:192-194.
19. Gieron C, et al. Acupressure in the prevention of postoperative nausea and vomiting [in German]. *Anaesthetist* 1993; 42:221-226.
20. Barsoum G, et al. Postoperative nausea is relieved by acupressure. *J R Soc Med* 1990;83:86-89.
21. Rogers P. Using acupressure bands for postoperative nausea. *Nurs Times* 1990;86:52-53.
22. Dundee JW, et al. Traditional Chinese acupuncture: A potentially useful antiemetic. *Br Med J* 1986;3:583-584.
23. Ghaly RG, et al. Antiemetic studies with traditional Chinese acupuncture. A comparison of manual needling with electrical stimulation and commonly used antiemetics. *Anaesthesia* 1987;42:1108-1110.
24. Weightman WM, et al. Traditional Chinese acupuncture as an antiemetic. *Br Med J* 1987;295:1379-1380.
25. Fry ENS. Acupressure and postoperative vomiting. *Anaesthesia* 1986;41:661-662.

## CME Questions

20. Dietary supplements containing ephedrine and caffeine:
  - a. have no effect on blood pressure and heart rate.
  - b. increase systolic blood pressure and heart rate.
21. Adverse effects of ephedra have *not* been reported with products used for:
  - a. weight loss.
  - b. ergogenics.
  - c. recreational use.
  - d. respiratory problems.
22. Chitosan has been associated with a case of:
  - a. hyperthyroidism.
  - b. mercury poisoning.
  - c. arsenic poisoning.
  - d. hepatotoxicity.
23. The majority of randomized controlled trials of acupuncture/acupressure for postoperative nausea and vomiting (PONV) have been:
  - a. positive.
  - b. negative.
24. For PONV, acupoint stimulation by which of the following techniques is superior?
  - a. Acupuncture
  - b. TENS stimulation
  - c. Acupressure bands
  - d. All are equivalent

## Clinical Abstracts

*With Comments by Adriane Fugh-Berman, MD*

### Homeopathy and Asthma

**Source:** Lewith GT, et al. Use of ultra-molecular potencies of allergen to treat asthmatic people allergic to house dust mite: Double-blind randomised controlled clinical trial. *BMJ* 2002;324:520.

**Design/Setting/Subjects:** A double-blind randomized controlled trial in 38 general practices in Hampshire and Dorset of 242 asthmatics allergic to house dust mites.

**Intervention:** Subjects received either oral homeopathic immunotherapy or

placebo and were assessed over four months (including three clinic visits and every other week diary assessments).

**Funding:** Smith's Charity, NHS Executive South and West Research and Development Directorate, Boiron.

**Results:** There was no difference between groups in most outcomes. Both groups improved significantly from baseline in forced expiratory volume in one second and asthma bother, as well as several diary measures, but homeopathy was not superior to placebo.

**Comments:** Several previous studies had suggested that homeopathy might be helpful in hay fever.<sup>1</sup> This larger

study focused on asthma, using both objective and subjective measures. There was a different pattern of response in the treated group, consisting of alternating deterioration and improvement, but the researchers point out that this is inconsistent with homeopathic theory (which holds that symptoms may initially be aggravated before improving). ♦

### Reference

1. Taylor MA, et al. Randomised controlled trial of homoeopathy versus placebo in perennial allergic rhinitis with overview of four trial series. *BMJ* 2000;321:471-476.