The medicinal use of black cohosh (Actaea racemosa or Cimicifuga racemosa) has a long herbal tradition in North America and Europe. A member of the buttercup family, black cohosh is native to the eastern part of North America and found as far west as Arkansas. Black cohosh was used by Native Americans for a range of disorders, including menstrual cramps, labor pains, general malaise, malaria, kidney ailments, and rheumatism. Additional uses by early settlers in the US colonies included amenorrhea, bronchitis, fevers, back pains, nervous disorders, yellow fever, and diverse problems of the uterus. The Eclectic physicians of the 1800s used Cimicifuga for similar problems such as rheumatism, influenza, labor pains, headaches, nervous disorders, and even smallpox. The root of black cohosh has been approved by the German Commission E to treat premenstrual syndrome, dysmenorrheal, and a variety of menopausal symptoms, including hot flashes, heart palpitations, nervousness, irritability, vertigo, insomnia, and depression. For the last 50-plus years, numerous clinical trials have been conducted on black cohosh for women's disorders in particular, largely in the area of menopause issues. Much of the research on Cimicifuga racemosa indicating use for menopausal symptoms was conducted in Germany in the 1980s and 1990s. New research in the last several years and new studies in the last two years highlight the role of black cohosh in menopause and make it the single most studied botanical for perimenopause and menopause symptoms.

Up until 2003, there had been five placebo-controlled trials studying black cohosh. These studies used different black cohosh preparations and different doses, which has made it difficult to come to some clear conclusion about what form and dose of black cohosh is best to utilize. Some of these studies indicate that black cohosh can reduce some important symptoms associated with perimenopause and menopause. The Stoll study reports a statistically significant reduction in the Kupperman Index and the Hamilton Anxiety scores in women taking black cohosh. The Wuttke study demonstrated a statistically significant reduction in the Menopause Rating Scale in women taking black cohosh and taking black cohosh with conjugated equine estrogens. The Jacobsen study found a decrease in sweat, but not in the frequency and severity of hot flashes in women taking black cohosh. The results of this study were tempered by its use of a lower dose of black cohosh and the fact that a large number of women in the study were taking tamoxifen, known to induce hot flashes. Lehmann-Willenbrock and colleagues found no significant differences in the Kupperman Index scores in women taking black cohosh, compared to women taking hormone therapy.

Four new studies on black cohosh and menopause symptoms, three in 2005 and one in 2006, demonstrated positive results in two studies, mixed results in one, and no effect in one. A randomized, multicenter, double-blind clinical trial compared the efficacy of black cohosh extract with placebo in 304 postmenopausal women. Participants were given 40 mg of a standardized extract or placebo for 12 weeks. Clinical efficacy was measured using the Menopause Rating Scale (MRS). The standardized extract of black cohosh was more effective than placebo (P<0.001), but was more pronounced during the early menopause years. Hot flashes were the most significant symptom affected by black cohosh, but atopic changes and moods also decreased statistically significantly in the black cohosh group compared with the placebo group.

In a Swiss study, researchers compared the efficacy and safety of the black cohosh root with placebo in women with menopause symptoms. This multicenter, 12-week, clinical trial was conducted in 122 menopausal women with three or more hot flashes a day. Measures included weekly scores of hot flashes, the Kupperman Index, and the Menopause Rating Scale. In the primary analysis using the hot flash scores and the Kupperman Index, black cohosh showed no superiority over placebo. There was also no benefit of black cohosh in the Menopause Rating Scale. However, in a subgroup of patients with a high Kupperman Index (more symptoms), there was a significantly superior benefit of the black cohosh (P< 0.018). A decrease of 47% was observed in the black cohosh group vs. 21% in the placebo group.

In the highly anticipated Herbal Alternatives for Menopause (HALT) Study, results were disappointing for black cohosh. This randomized, double-blind, controlled trial set out to test the efficacy of three herbal regimens for menopause symptoms, compared to placebo and compared to hormone therapy. Women were given either 1) black cohosh standardized extract 160 mg daily; or 2) a combination herbal product (black cohosh, alfalfa, chastetree, dong quai, false unicorn, licorice, oats, pomegranate, Siberian ginseng, boron) four capsules daily; or 3) 625 conjugated equine estrogen + 2.5 mg medroxyprogesterone acetate; or 4) placebo. Participants were 351 women, ages 45-55, who experienced two or more vasomotor symptoms daily. After one year, there was no difference in frequency or intensity of vasomotor symptoms between those in the herb groups and those taking...
the placebo. At three months, the mean number of night sweats was 12% lower in the black cohosh group and 83% lower with hormone therapy vs. placebo. At three months, the overall Wiklund score was 22% lower, and the mean vasomotor symptoms score was 22% lower with black cohosh vs. placebo. At three months, the overall Wiklund score was 22% lower, and the mean vasomotor symptoms score was 22% lower with black cohosh vs. placebo. At three months, the mean number of night sweats was 83% lower with black cohosh vs. placebo. Hormone therapy was 61% and 73% lower than placebo. Black cohosh vs. placebo differences were not seen after six months or 12 months. (The Wiklund Menopause Symptoms Index is an instrument validated to evaluate the most common complaints in peri- and early post-menopausal women: hot flashes, sweats, vaginal dryness, sleep, fatigue, depression, headache, irritability, arthralgia, nervousness, palpitations, and vertigo.)

What happened? There have been seven published randomized trials of black cohosh and various menopause symptoms. Five of the seven have reported a decrease in hot flashes/night sweats or the Kupperman index. However, the difficulties with these studies have included lack of placebo controls, small sample sizes, and shorter durations of 12 weeks. With the current study, we could scrutinize the statistics and the statistical power, we could note differences from in-office practice to mail questionnaires, we could cite that the multi-herb formula has some less-than-ideal selections, we could cite the flaw of expecting dietary compliance with soy foods, and we could note the problematic issue of studying peri-menopausal women with inconsistent symptoms vs. post-menopausal women. In addition, perhaps a better multi-herb formulation, especially when seeking results with hot flashes, would be to use the three herbs with some positive results for vasomotor symptoms: black cohosh, red clover, and kava. In the end, it was a disappointing result for black cohosh.

In the most recent double-blind, randomized, placebo-controlled study, 301 peri- and post-menopausal women who had climacteric symptoms, including psychological symptoms, for at least three months were studied. Symptoms were evaluated by means of the Menopause Rating Scale and the Hamilton Depression Rating Scale. Patients were treated with an extract of St. John’s Wort and black cohosh extract or a placebo for 16 weeks. The mean Menopause Rating Scale score decreased 50% in the treatment group and 19.6% in the placebo group. The Hamilton Depression Rating Scale score decreased 41.8% in the treatment group and 12.7% in the placebo group. In both measures, the St. John’s Wort + black cohosh group was significantly superior to placebo (P < .001).

What about reports of liver damage? In the past three years, there have been several reports that black cohosh resulted in liver damage. The first report was from Australia, where six patients taking a variety of herbal products acquired hepatitis. Two of the individuals were taking black cohosh, and one of the two was also taking a hepatotoxic genus of skullcap. In the case of the woman taking black cohosh alone, she had been taking black cohosh for one week, although no dose was reported. Her liver biopsy confirmed severe hepatitis and early fibrosis. Hepatitis testing was negative. In another publication, also reporting on a case in Australia, a 52-year-old woman had acute liver failure. She was taking a liquid extract of black cohosh, although, upon analysis, there was also goldenseal and ginkgo in the mixture, along with ground ivy and oats seed. The publication stated that an extensive investigation excluded other causes of liver failure, although they do not reveal the details of any investigation. The third report was a case report in the US of a woman developing autoimmune hepatitis that was possibly due to black cohosh. Tests for infectious causes of hepatitis were negative. The woman was also taking six different medications for two years, then black cohosh for three weeks. The last case was a case report of a 50-year-old woman suffering from acute jaundice, with a possible diagnosis of autoimmune hepatitis again. She had been taking black cohosh for five months and no other medications. She underwent a liver transplant.

Kerry Bone, a practicing herbalist and research chemist, offers an analysis of the case reports which I will paraphrase. He states that case reports linking black cohosh to liver injury have some serious flaws. For all the cases, the presence of black cohosh in the products consumed was not definitely established. In most of the cases, the name and dosage of the product were not specified. In case 1, there were no details of the results on the contents of the mixture or even the amount of black cohosh in the mixture. In case 1, the subject was only taking black cohosh for one week, which would presumably imply a hypersensitivity reaction if the herb were the etiology. However, there were no other symptoms reported of an allergic reaction, and eosinophilia was specifically absent. In addition, the liver biopsy showed early signs of fibrosis which develops only after months of exposure to a toxic substance. For case 3, the authors claimed that none of the drugs the patient was taking had been linked to any previous cases of autoimmune hepatitis. However, one of her drugs, labetalol has been a cause of at least 11 cases, as reported by the FDA. In case 4, they blame the black cohosh based on the Australian reports without offering any real academic analysis of their case.

Additional problems with the four cases include the lack of positive identification of black cohosh, lack of product information, and lack of dosage information. It is likely that these cases of non-infectious hepatitis were, in fact, idiopathic hepatitis, consistent with the demographics of idiopathic hepatitis, female between the ages 40-50. I would add that uncontrolled reports and human clinical trials including more than 2,800 patients demonstrate the low incidence of adverse events associated with black cohosh. The World Health
Black Cohosh

Organization (WHO) Collaborating Center for International Drug Monitoring keeps a database for all reported adverse reactions to pharmaceutical products and herbal products, including adverse black cohosh. As of July 31, 2000, it revealed a total of 35 adverse reactions. The reactions were primarily general and temporary symptoms and were not concentrated on a particular organ system. This list did include one case of liver failure, one case of hepatitis, and one case of elevated liver enzymes. These cases were related to unspecified amounts of black cohosh and unspecified products. In animal studies, there have been some reports of increased liver weights associated with very large doses over an extended period of time.

The National Herbalists Association of Australia had this response to the three Australian cases: "The authors supply no details regarding verification of the herbal ingredients. Failing to authenticate the plant preparations or review their quality and dosages means that any conclusion is subject to doubt. No information about plant part used, solvent, concentration, type of manufacturing, or chemical analysis is supplied. Secondly is the fact that no information is supplied about the woman's past or present medical history, concurrent use of medical or recreational drugs, lifestyle, dietary intake, and other factors, which may have influenced her health status. No attempt was made by the authors to investigate the adverse reaction in detail. Biopsies were typical of acute hepatitis, such as is seen in severe viral hepatitis, and changes that are not typically found in severe immunological reactions and are not the changes of direct toxic injury. In other words, the reaction was not the result of herbal toxicity but of some immunological situation. Without further pathological and biochemical investigation into the specific reaction, no conclusion can be made as to the exact mechanism causing the acute hepatitis."

I have also learned that a herbal manufacturer in Australia, which produces 90% of Australia's black cohosh products, was cited and shut down for misidentification of raw materials, cross-contamination, microbiological contamination, and poor handling, sourcing, and hygiene practices during the time period when these cases occurred. Although their products have not been directly traced to the hepatitis cases, since they were producing most of the black cohosh products in Australia, it appears possible that some manufacturing contamination process may have been involved.

I have been advised by expert scientists in botanical toxicology that, in women without a history of liver disorders or in women using less than one gram of crude herb per day, we need not be concerned. Currently, in a study of black cohosh and menopause at Columbia University, researchers are checking liver function tests after two to three months. No problems have been detected. In addition, given the vast use of the product in Europe for more than twenty years, the likelihood of liver problems is extremely low, given the low reported incidences of adverse events.

These facts, and a review of the scientific literature, do not present a compelling case for concern or a reason for avoiding this herb. We are confident in the safety of black cohosh for menopause symptoms. Even minimal adverse events such as headaches, upset stomach, and nausea are rarely observed and resolve easily and quickly when the black cohosh is discontinued. If concern for liver function exists, then monitoring after three months (and possibly again at six months) with liver function tests (blood test) would be a consideration.

The average recommended dose of the standardized extract of black cohosh is 40-80 mg per day. The clinical studies performed prior to 1996 used doses of 40-140 mg of standardized extract. Although there is still some confusion about which dose of black cohosh may be most effective, the dosage used in most clinical trials to date is 40 mg twice daily. Another problem that has confused many is that the German Commission E has recommended that black cohosh be taken for only six months. However, it should be noted that this was not due to any noted toxicity within or after those six months. They have stated that their reason was to ensure that women would continue to have regular examinations with their physicians at six-month intervals. Short term studies on black cohosh indicate that it may be used safely for long-term use as well.14,15

Left unanswered is the question of how black cohosh works. Early studies found the herb has an estrogenic activity, whereas other studies in the last few years have demonstrated no phytoestrogens in black cohosh and no estrogen-like effect on LH or FSH. In addition, prolactin levels, estradiol, and endometrial thickness were not affected.17,18 At the moment, we would have to say that the mechanism of action is not clear, although some have postulated an effect on serotonin levels.

Currently, all published studies imply safety for breast cancer patients. In one, black cohosh demonstrated a lack of estrogenic activity and did not promote breast cancer cell growth.19 In another, black cohosh extract inhibits the proliferation of estrogen receptor positive and negative human breast cancer cell lines.20 There was a 50% growth inhibitory effect, and the mode of cell death was apoptosis. One fly in the ointment has been a presentation made at a meeting of the American Association of Cancer Research in July 2003. A researcher, Vicki Davis from the Mylan School of Pharmacy in Pittsburgh, fed black cohosh to female mice bred to be prone to breast cancer. She gave the mice the daily equivalent of the standard human dose of a 40 mg extract. The mice were not any more likely to develop breast cancer in the first place, but those who did develop breast cancer were more likely to develop lung metastases. She found that 27% of mice that ate black cohosh had the cancer spread to the lung, compared to 11% of the mice not given the black cohosh. This study has not been published as of this writing, and it is therefore difficult to analyze and make any conclusion. Some breast cancer individuals may choose to not use black cohosh due to the lack of long-term studies in women, but there is no published data to assert concern at this time.

There are no known contraindications to utilizing black cohosh. Occasional side effects have been reported and can include gastrointestinal discomfort, headache, nausea, vomiting, weight gain, and vertigo. No known drug interactions are known.

Standardized extracts of black cohosh continue to be one of the most reliable herbal approaches to treating a wide array of peri-menopausal and menopausal symptoms. The most common dosage utilized is 40 mg twice daily. One should expect results within four weeks. In my experience, about 85% of women will receive benefit, and maybe 50% will achieve complete amelioration of their hot flashes and night sweats. This is consistent with the largest (yet non-controlled) study ever done on black cohosh in 1982.21 When one menopause symptom is especially dominant, then I often use black cohosh.
Nutritional Influences on Illness continued from page 132

Based on the Textbook of Nutritional Medicine by Melvyn R. Werbach with Jeffrey Moss. Tarzana, California: Third Line Press, Inc., 1999. Allergy is only one of the 82 illnesses discussed in Dr. Werbach's Textbook of Nutritional Medicine. For information or a free brochure on all of his books, contact Third Line Press Inc., 4751 Viviana Drive, Tarzana, California 91356, USA; 818-996-0076; Fax: 818-774-1575; www.third-line.com; e-mail: tlp@third-line.com.

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