

## ALTERNATIVE MEDICINE

AN EVIDENCE-BASED APPROACH

## Elderberry Extract for Influenza

## History of Use

The various constituents of the elder tree—leaves, bark, twigs, and berries—have a long and broad history of use in folklore, magic, and medicine. Legend holds that Judas Iscariot hanged himself from an elder tree, and, accordingly, it has often been considered an emblem of sorrow and death.

Elizabethan herbalist John Gerard observed, “The seeds contained within the berries dried are good for such as have the dropsie, and such as are too fat ... if they be taken in a morning to the quantity of a dram with wine.” He also attributed to the leaves purgative properties against phlegmatic and choleric humors and the ability “to assuage the pain of the gout.” He noted that in the first century, Greek physician Dioscorides had recommended the leaves for burns, “hot swellings,” and “for such as be bitten with a mad dog.”

Many cultures have ascribed various supernatural qualities to the elder: In the early 20th century in “The Book of Herb Lore,” Lady Rosalind Northcote wrote that “the Russians believe that elder trees drive away evil spirits, and the Bohemians go to it with a spell to take away fever. The Sicilians think that sticks of its wood will kill serpents and drive away robbers, and the Serbs introduce a stick of elder into their wedding ceremonies to bring good luck. In England it was thought that the elder was never struck by lightning, and a twig of it tied into three or four knots and carried in the pocket was a charm against rheumatism” (Mineola: Dover, 1971). Native Americans used the plant extracts for rheumatism and fever.

In “A Modern Herbal,” Mrs. M. Grieve wrote, “Elder flowers and elder berries have long been used in the English countryside for making many homemade drinks and preserves ... the berries make an excellent homemade wine and winter cordial, which improves with age, and taken hot with sugar just before going to bed is an old-fashioned and well-established cure for a cold.” She also wrote, “Like elderflower tea, [elderberry wine] is one of the best preventives known against the advance of influenza and the ill effects of a chill” (New York: Random House, 1973).

## Mechanisms of Action

Elderberry extract contains multiple active compounds such as bioflavonoids and anthocyanins that have antioxidant effects. Antiviral properties have been seen in vitro against herpesvirus type 1, respiratory syncytial virus, parainfluenza, and influenza types A and B. A standardized extract also has been shown to inhibit viral adhesion to cell receptors and replication of influenza viruses in vitro.

This extract also has been shown to increase cytokine production in human monocytes. Of particular note is its dose-dependent stimulatory effect on tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), according to a group of researchers from the Israeli Cytokine Standardization Laboratory in Jerusalem. These authors note that “TNF- $\alpha$  is a multipotential mediator of cellu-

lar immune responses with a wide variety of biologic activities. Under different conditions, TNF- $\alpha$  can exhibit favorable or unfavorable effects on the host immune response ... [Elderberry extract was] shown in this study to activate the immune system by strongly increasing inflammatory cytokine production” (Eur. Cytokine Netw. 2001;12:290-6).

## Clinical Studies

In a double-blind, placebo-controlled trial, 60 symptomatic influenza patients from four primary care sites in Norway were randomized to receive the proprietary formulation Sambucol (Razei Bar, Jerusalem), which contains 38% elderberry extract plus small amounts of raspberry extract, glucose, citric acid, and honey, or a placebo syrup. They started the medication within 48 hours of symptom onset, taking 15 mL of the syrup four times a day for 5 days.

Influenza A virus was isolated from 54 of the patients; influenza B was isolated from the other 6. All patients had a fever of at least 38°C.

Rescue medication consisting of oral acetaminophen and a nasal decongestant was permitted when needed.

The primary outcomes in the study were 10-point visual analog scale (VAS) scores for aches and pains, cough, mucus discharge, nasal congestion, and quality of sleep, as rated by the patient.

At baseline there were no differences in VAS scores between the active treatment group and the placebo group, but by day 4, scores in the elderberry group were 9 or greater for aches and pains, quality of sleep, mucus discharge, and nasal congestion, with 10 indicating the best outcome. By day 5, the mean VAS score for aches and pains was 10 in the elderberry group. These levels of improvement were not seen in the placebo group until days 7-8 (J. Int. Med. Res. 2004;32:132-40).

Significant improvements on global evaluation scores were seen in the active treatment group by a mean of 3.1 days, while in the placebo group this was achieved after a mean of 7.1 days. Among patients in the active treatment group, seven used acetaminophen and five used the decongestant nasal spray, while the corresponding figures in the placebo group were 26 and 21, respectively. No patients in either group reported adverse events, and all recovered by day 8.

The study was sponsored by the manufacturer of Sambucol.

An earlier study randomized 27 Israeli adults and children to Sambucol or placebo for 3 days during an outbreak of influenza B Panama in 1993. The adult dose was 4 tablespoons per day, while the pediatric dose was 2 tablespoons per day. Significant symptom improvements were seen in 93.3% of patients within 2 days; 91.7% of patients in the placebo group had significant improvement by day 6. Significantly higher hemagglutination inhibition titers to influenza B also were seen in the active treatment group (J. Altern. Complement. Med. 1995;1:361-9).

—Nancy Walsh

► Constituents of the elder tree, *Sambucus nigra*, have been used in folk medicine for a variety of indications ranging from driving away evil spirits to curing the common cold.

► Two clinical trials have found significant benefits for a standardized extract of elderberries as a treatment for influenza.

## FDG-PET Scans Find Secondary Infections

BY PAM HARRISON  
Contributing Writer

TORONTO — Positron emission tomography using <sup>18</sup>F-fluorodeoxyglucose enhancement can identify underlying infectious foci in most patients with bacteremia or fungal infections in the blood, even when other diagnostic findings are normal, Wim J.G. Oyen, M.D., reported at the annual meeting of the Society of Nuclear Medicine.

Dr. Oyen, professor of nuclear medicine at Radboud University Nijmegen (Netherlands) Medical Centre, and colleagues assessed the value of FDG-PET in helping detect infectious lesions that may have spread to other sites in patients with bacteremia or fungemia—what they term “secondary metastatic infection.” Prior to undergoing FDG-PET, each patient had undergone a mean of four conventional diagnostic procedures, including blood work, ultrasound studies, and CT scans.

The retrospective review included 40 FDG-PET scans performed at the center between October 1998 and September 2004. A total of 41 FDG-PET scans were performed in 39 patients, but 1 scan was excluded because the patient’s claustrophobia led to an incomplete scan. The scans were ordered by referring physicians because patients had persistent fever despite an adequate course of antibiotics, and therefore were sus-

pected of harboring a secondary metastatic infection. Blood cultures confirmed that about 60% of the episodes resulted from gram-positive bacteria, whereas about 18% resulted from gram-negative bacteria and about 20% resulted from *Candida* species. The source of infection was polymicrobial in the remaining episodes.

Of the group, “30% had abnormalities on previous diagnostic techniques, but physicians were not satisfied with the conventional diagnoses, and these abnormalities were confirmed by FDG-PET,” Dr. Oyen said in an interview.

Overall, 45% of the 40 scans provided clinically relevant, new information. FDG-PET confirmed already diagnosed abnormalities in another 30% of the scans, yielding a positive predictive value of 91%. No patient developed infectious complications when the FDG-PET was negative, yielding a negative predictive value of 100% in this small series of patients.

The high diagnostic accuracy of FDG-PET in this series may not apply to lower-risk patients whose bacteremia or fungemia is less likely to have spread. Nevertheless, FDG-PET appears to be a “valuable imaging technique” for high-risk patients, he noted.

The researchers are planning a prospective study to test whether FDG-PET is useful in lower-risk patients with bacterial or fungal infections in the blood. ■

## Transfusions Up Trauma Patients’ Risk of VAP

MIAMI — Blood product transfusion was an independent risk factor for ventilator-associated pneumonia in a study of 766 adult trauma patients, said Grant Bochicchio, M.D., at the joint annual meeting of the Surgical Infection Society and Surgical Infection Society—Europe.

In a prospective, observational cohort study, 26 patients developed ventilator-associated pneumonia, and 22 of the 26 (85%) received blood transfusions prior to their VAP diagnoses, noted Dr. Bochicchio, of the R. Adams Cowley Shock Trauma Center in Baltimore.

The patients, who did not have pneumonia on admission to the ICU, were on ventilators for at least 48 hours. Transfusions of any blood product—red blood cells, plasma, and platelets—were independent risk factors for VAP after controlling for gender, injury

severity, number of days on the ventilator, and number of days in the ICU prior to developing VAP.

The odds ratio for VAP due to blood transfusion was significantly higher for trauma patients compared with other ICU patients. In trauma patients, the odds ratio for developing VAP was 3.34 for fresh frozen plasma transfusion, 4.19 for platelet transfusion, and 4.41 for red blood cell transfusion, compared with a 1.8 odds ratio for VAP among nontrauma patients in the ICU, Dr. Bochicchio noted.

Patients with VAP spent significantly more days on ventilators compared with non-VAP patients (35 vs. 11) and significantly more days in the ICU (31 vs. 12). There were no significant differences between VAP and non-VAP patients in terms of age or race, and most patients in each group were male.

—Heidi Splete