

# Test Suspected Lyme Borreliosis in Children

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WARSAW — While erythema migrans is the presenting manifestation of Lyme borreliosis in the majority of cases, nonspecific symptoms predominate in many infected children.

Thus, serologic testing should be considered for these children who have a history of tick bite or who have visited a wooded area, Dr. n. med. Ewa Duszczek said in a poster at an international congress of the World Society for Pediatric Infectious Diseases.

A group of 171 children with suspected Lyme borreliosis who ranged in age from 6 months to 17.5 years underwent serologic testing with an enzyme-linked immunosorbent assay (ELISA). A total of 111 (65%) had a history of tick bite, and 60 (35%) had visited a wooded location.

They were divided into two groups: those with erythema migrans (104 children) and those with nonspecific symptoms such as other skin lesions, lymphadenopathy, fever, and pain and/or edema of joints (67 children).

In the group with erythema migrans, 74 children were seropositive, 72 with IgM antibodies to *Borrelia burgdorferi*, 17 with IgG antibodies, and 13 with both antibodies, noted Dr. Duszczek and her colleagues in the department of children's infectious diseases, Medical University of Warsaw.

In the group with nonspecific symptoms, antibodies were detected in 16 (24%) children. Of

these, IgM antibodies were detected in 13 children, IgG in 5, and both IgM and IgG in 2.

All children were treated to symptom resolution. In 35 seropositive children, serologic testing was repeated after 2-20 months; all showed a decline in IgM levels. In three cases followed for 13, 16, and 20 months, respectively, IgM antibodies were still present, but no clinical symptoms remained.

Serology can be used to monitor treatment to some extent, but the persistent presence of antibodies does not necessarily indicate treatment failure, she cautioned.

In another poster session, Prof. dr. hab. Teresa Wozniakowska-Gesicka noted that in a series of 87 children with confirmed Lyme borreliosis, only 57.4% had a history of contact with a tick.

In 42.5% of the infected children, symptoms were nonspecific, whereas in 28.7%, neuroborreliosis was diagnosed with symptoms that included facial palsy, meningitis, cranial nerve palsy, paresthesias, radiculoneuritis, and mental disturbances. Erythema migrans and acrodermatitis chronica atrophicans were observed in 19.5%, and arthritis in 9.3%, reported Dr. Wozniakowska-Gesicka of the department of pediatrics, Polish Mother's Hospital, Lodz, Poland.

Acrodermatitis chronica atrophicans is seen primarily in European borreliosis, and is usually associated with infection with *B. afzelii*.

Early diagnosis and treatment are needed in this serious diagnostic and therapeutic problem, Dr. Wozniakowska-Gesicka said. ■

## Lyme Without Erythema Migrans Is Not So Rare

SNOWMASS, COLO. — Lyme disease patients without erythema migrans were thought to be rare—until they showed up frequently in a large trial of the Lyme disease vaccine, Linda K. Bockenstedt, M.D., said at a symposium sponsored by the American College of Rheumatology.

In that trial, 269 cases of Lyme disease were detected by serum assay, of which 42, or about 16%, involved patients without erythema migrans. However, those patients did have flulike symptoms, such as malaise, fever, myalgia, migratory arthralgias, occipital headache, and neck stiffness. They did not have any upper respiratory symptoms, such as cough.

Additionally, Dr. Bockenstedt, of the rheumatology section at

Yale University, New Haven, Conn., noted that there may soon be a way to monitor Lyme disease treatment.

A new enzyme-linked immunoabsorbent assay for Lyme disease, the C6 ELISA (Immunitics Inc.), tests for a single small peptide expressed by the *Borrelia burgdorferi* spirochete during active infection, instead of the whole organism.

Research has shown that antibody titers to this antigen drop fourfold when an infected individual has been successfully treated. Dr. Bockenstedt added that forthcoming study results will confirm the ability of the assay to adequately detect a drop in the antigen level.

—Timothy F. Kirn

## 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 paine 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" (New York: 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 cellular 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 study outcomes 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. Intern. 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.