Helicobacter pylori May Protect Against Asthma

BY NANCY WALSH
New York Bureau

Early childhood colonization with the major human commensal microbe *Helicobacter pylori* may be protective against asthma, study findings show.

According to the "hygiene hypothesis," the rise in asthma and allergic disorders that occurred during the 20th century relates to a reduction in exposure to environmental antigens and alterations in gut microbiota during development of the immune system.

Changes in human colonization with *H. pylori* represent a "biologically plausible" candidate in the hygiene hypothesis, asserted Dr. Yu Chen of New York University and Dr. Martin J. Blaser of New York University and the Veterans Affairs Medical Center, New York..

The investigators explained that there has been a near universal association of this organism and humans for at least 58,000 years, since the time of the initial human migration out of Africa. Seropositivity is generally acquired during the first few years of life and remains lifelong unless eradicated by antibiotics.

The prevalence of seropositivity began to decline early in the last century, a trend that was paralleled by an increase in asthma. Today the seroprevalence in native-born children younger than 10 years in the United States stands at less than 10%, wrote the researchers (J. Infect. Dis. 2008;198: 553-60).

To investigate whether this decline in *H. pylori* colonization could be linked to the increase in asthma in children, the investigators analyzed data from the National Health and Nutrition Examination Survey (NHANES) 1999-2000, which is a representative sample of the U.S. population.

They estimated odds ratios for asthma, wheezing, and other allergic conditions such as allergic rhinitis and eczema, with adjustment for age, body mass index, smoking, education level, race, country of origin, and also for antibiotic and corticosteroid use in the previous month, medical insurance status, and household income.

The sample included 7,412 participants, 3,327 of whom were younger than 20 years. Overall seroprevalence for *H. pylori* was 26%, but prevalence was lower in younger groups, with only 5% of children younger than 10 years being seropositive.

For the entire cohort there was a trend toward an inverse association between seropositivity for *H. pylori* and ever having had asthma and for having had one or more asthma attacks during the past year. There was a significant inverse association between *H. pylori* seropositivity and having had eczema or dermatitis in the past year, with an odds ratio of 0.73.

Among the 3,327 subjects who were age 19 years or younger at the time of data collection, there was a strong inverse association between *H. pylori* positivity and onset of asthma before 5 years of age, with an odds ratio of 0.58.

Furthermore, among those aged 3-13 years, strong inverse associations were seen for seropositivity and current asthma, ever having had asthma, and having had allergic rhinitis during the previous year.

A possible explanation for the recent decline in *H. pylori* colonization is the widespread use of antibiotics in children for conditions such as otitis media, according to Dr. Chen and Dr. Blaser. In fact, they noted, their study population was "strongly impacted" by antibiotics, with 11% of those younger than 10 years having had an antibiotic during the month before data collection. Eradication rates of *H. pylori* with antibiotic monotherapy range from 10% to 50%.

"Our findings suggest *H. pylori* status is one of the measurable risk factors for asthma and atopic conditions in children," they wrote. Among the characteristics favoring *H. pylori* as protective is its dominance in the gastric microbiota and its "intimate relationship with the gastric mucosa, where it injects bacterial constituents into epithelial cells."

In seropositive subjects, lymphoid cells such as helper and regulatory T cells are found in the gastric lamina propria. These lymphoid cell populations are absent in seronegative persons.

Dr. Chen and Dr. Blaser commented that the loss of the lymphoid compartment in the stomach, with its activator and regulatory T cells, could potentially lower an age-dependent threshold for allergic sensitization. ■

Nut Consumption in Pregnancy May Increase Asthma Risk in Child

BY JONATHAN GARDNER
London Bureau

Women who eat nut products such as peanut butter daily throughout pregnancy may significantly increase their children's risk of developing asthma symptoms, according to a Dutch cohort study.

At 8 years of age, children whose mothers reported daily consumption of nut products were at significantly increased risk for steroid use (odds ratio 1.62), dyspnea (OR 1.58), and wheeze (OR 1.42), compared with children of women who reported only rarely (no more than three times per month) eating nut products. The data were adjusted for factors such as parental atopy, maternal smoking in pregnancy, and breastfeeding. The associations were independent of the children's diets.

The investigators stressed that these findings should be replicated in other studies "before influencing dietary advice given to pregnant women" (Am. J. Respir. Crit. Care Med.;177:1-8).

Previous research on the effectiveness of maternal dietary allergen avoidance during pregnancy in prevention of childhood allergic disease has been "inconclusive," wrote Saskia M. Willers of the environmental epidemiology division at Utrecht University, the Netherlands, and associates. They added that their study is the first to use longitudinal statistical methods to assess the relationship over an extended period.

The researchers enrolled 4,146 women (1,327 atopic and 2,819 nonatopic). Complete data were available for 2,832 children whose mothers completed questionnaires at baseline on their dietary habits during pregnancy. The questionnaires assessed frequency of the women's consumption of vegetables, fresh fruit, fish, eggs, milk, milk products, nuts, and nut products; possible responses ranged from "never" to "several times per day."

"Because we mentioned peanut butter as an example of nut products in the questionnaire and because peanut butter is a commonly used spread on sandwiches in the Netherlands … we assumed that the largest proportion of nut products is peanut butter," the researchers wrote.

Children were followed up at 3 months and then once a year from ages 1 through 8; a dietary assessment was conducted at age 2. At age 8, 13.2% of the children had asthma symptoms, and another 3.9% had asthma diagnosed by a doctor.

Daily consumption of nut products was the only factor assessed that showed a significant association with increased incidence of asthma symptoms. In an interview, Ms. Willers noted that the lack of a significant association between asthma symptoms and daily consumption of nuts—as opposed to nut products—may have been due to the small sample size of women (1.4%) who ate nuts daily. In addition, she said, the nut products consumed were made largely from peanuts, but women who ate nuts daily also may have eaten less allergenic types of nuts.

In a crude analysis, women who ate fruit daily were significantly less likely to have children who wheezed than were those who ate fruit only regularly or rarely (odds ratio 0.82), but that association disappeared after adjustment for socioeconomic factors, parental atopy, and other factors.

The researchers said their findings are limited by their inability to obtain more information on specific foods and portion sizes. They said they included the main food groups associated with asthma, but other foods and nutrients cannot be ruled out as having been responsible for the asthmatic symptoms identified.

One of the study investigators reported having received an unrestricted research grant from Glaxo SmithKline over a 3-year period; the remaining authors reported no financial conflicts. ■

Pirfenidone Is Promising as Pulmonary Fibrosis Therapy

BY NANCY WALSH
New York Bureau

TORONTO — Treatment of patients with idiopathic pulmonary fibrosis with pirfenidone was "encouraging" in a phase III study conducted in Japan.

Few treatment options are available for patients with idiopathic pulmonary fibrosis (IPF), Dr. Takashi Ogura said at an international conference of the American Thoracic Society.

A previous phase II study suggested the agent, which has antifibrotic, anti-inflammatory, and antioxidant effects, could be beneficial.

In that study, 107 patients aged 20-75 years were randomized to receive pirfenidone in dosages up to 1,800 mg/day or placebo, and were followed for 9 months, during which time improvements were seen on vital capacity (VC), although not on a 6-minute walk test (Am. J. Respir. Crit. Care Med. 2005;171:1040-7).

The current study included 267 patients from 73 centers. Two radiologists verified the diagnosis in each patient after reviewing chest x-rays and high-resolution CT scans.

Patients were then randomized to receive pirfenidone 1,800 mg/day or 1,200 mg/day, or placebo. Vital capacity was measured every 4 weeks, and lowest oxygen saturation by pulse oximetry (SpO_2) on exertion was measured every 12 weeks.

Statistically significant improvements were seen in both pirfenidone groups on the primary end point, which was change in VC, as well as in an overall slowing of deterioration from the progressive, fatal disease, Dr. Ogura said.

"At week 52, the difference between the pirfenidone high-dose group and placebo was 70 mL, and the difference between the lower-dose group and placebo was 80 mL," said Dr. Ogura of Kanagawa Cardiovascular and Respiratory Center, Yokohama, Japan.

Statistically significant changes also were seen in progression-free survival, although not in the lowest SpO_2 on exertion or the incidence of acute exacerbations.

The most common adverse events associated with the treatment were photosensitivity, dizziness, anorexia, and elevated γ-glutamyl transpeptidase. The drug was generally well tolerated, with no significant differences being seen among the three groups for serious adverse events.

A total of 32% of patients dropped out during the course of the study, including 37% of the patients taking 1,800 mg of pirfenidone, 28% of those taking 1,200 mg, and 27% of patients in the placebo group.

The researchers will continue to follow the patients to see if pirfenidone can improve survival, and to see if the drug also may prove useful in other fibrotic lung diseases.

Dr. Ogura noted that he had no relevant financial disclosures. ■