Does *H. pylori* Impair Glucose Tolerance?

BY NEIL OSTERWEIL

FROM THE ANNUAL MEETING OF THE INFECTIOUS DISEASES SOCIETY OF AMERICA

BOSTON – Already convicted for its role in causing peptic ulcers, *Helicobacter pylori* is also being indicted as a possible co-conspirator in the development of diabetes, investigators from two separate studies said at the meeting.

In a study of nearly 1,800 older Latinos in California, *H. pylori* infection was associated with a more than twofold greater risk for diabetes, reported Dr. Christine Y. Jeon of the Columbia University School of Nursing, New York.

VITALS

Major Finding: *Helicobacter pylori* infection was associated with a hazard ratio of 2.69 for diabetes among Latinos older than 60 years.

Data Source: Epidemiologic studies examining the relationship between *H. pylori* infections, glycated hemoglobin levels, and diabetes.

Disclosures: Dr. Jeon's study was supported by grants from the National Institutes of Health. Dr. Chen did not disclose a funding source. Both investigators reported that they had no relevant financial disclosures.

In addition, a separate study of National Health and Nutrition Examination Survey (NHANES) data found that, after excluding for diabetes and controlling for other risk factors, *H. pylori* seropositivity was positively associated with hemoglobin A_{1c} levels – suggesting that the bacterium may play a role in impaired glucose tolerance, said Dr. Yu Chen of New York University Langone Medical Center, New York.

Dr. Jeon noted that, although the mechanism for the association between *H. pylori* infection and diabetes is unknown, it does not appear to be mediated by either the inflammatory pathway or insulin resistance.

"This highlights the need for future studies on how the timing and severity of *H. pylori* infection affect glucose control in younger individuals, and how *H. pylori* alters gut microbiota and subsequent host gene expression and energy uptake," she said.

Dr. Jeon and her colleagues conducted a study to examine whether risk of diabetes changes with various common chronic infections, including herpes simplex virus 1, varicella virus, cytomegalovirus, *Toxoplasma gondii,* and *H. pylori*.

The study and its focus on *H. pylori* in particular were motivated in part by observation of a racial gradient in both diabetes prevalence and *H. pylori* infection in the United States, with Mexican Americans having a higher prevalence of both than either whites or non-Hispanic blacks.

Additionally, studies have found evidence of association between periodontal bacteria and increased diabetes risk, as well as links between decreased insulin sensitivity and higher antibody titers to herpes simplex virus 2 and *Chlamydia pneumoniae*.

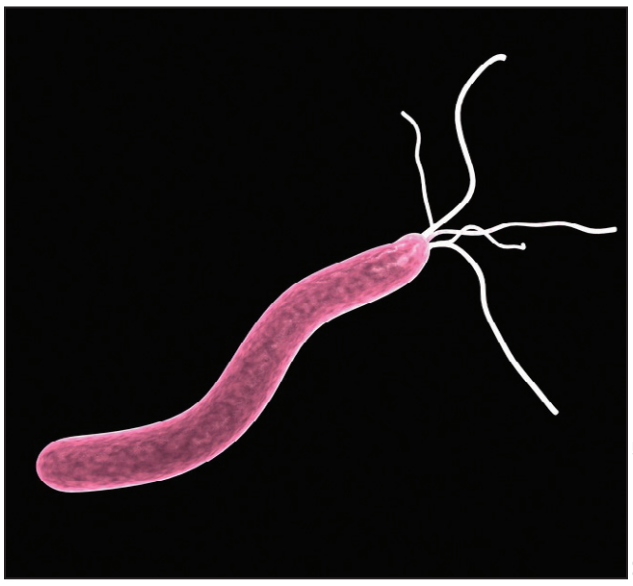
The *H. pylori* association was stronger than that for either vascular disease or being a former smoker.

DR. JEON

Other studies, however, have not shown an association between common infections and insulin resistance or diabetes.

Dr. Jeon and colleagues analyzed data on 1,789 men and women older than 60 years who were enrolled in the Sacramento Area Latino Study on Aging (SALSA). Of that group, 782 people did not have diabetes and had available baseline pathogen data.

During the 10-year study, 144 of those 782 people developed diabetes (18% incidence rate), with diabetes defined as self-report of a physician's diagnosis of diabetes or of taking hypoglycemic medication, including insulin, at semiannual interviews; fasting glucose of at least 126 mg/dL at four follow-up visits; or death certificate inclusion of diabetes as a cause of death.



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***H. pylori* was associated with diabetes and increased HbA_{1c} in two separate investigations. A mechanism to explain the curious finding is unknown.**

In bivariate analysis adjusted for gender and education, none of the pathogens reached statistical significance for an association with diabetes.

In multivariate analysis, however, the only significant association seen with diabetes was *H. pylori* (hazard ratio, 2.69). The association was stronger than that for either vascular disease (HR, 1.78) or being a former smoker (HR of 1.34 in bivariate analysis).

Possible explanations for the association include *H. pylori*–induced alterations in gut microbiota, changes in nutrient metabolism in the gut, increased energy harvesting, or altered host gene expression, Dr. Jeon said.

In the second study, Dr. Chen and her colleague Dr. Martin Blaser looked at data from NHANES III (1988-1994) and IV (1999-2004).

In NHANES III, they found a positive association between *H. pylori* infection and HbA_{1c} in the overall cohort and in people with body mass indexes (BMIs) both below 25 and 25 and higher (*P* for interaction for each comparison less than .01).

They also saw a synergistic interaction between *H. pylori* and higher levels of BMI in both NHANES III and IV (*P* for interaction less than .01), suggesting that *H. pylori* exacerbated the rise in HbA_{1c} often seen with weight increase.

In addition, in NHANES III but not NHANES IV, the synergistic effect was seen among patients seropositive for the cagA strain of *H. pylori*, which has been associated with virulence.

The investigators did not, however, find an association between self-reported diabetes and *H. pylori* infection. ■

In Diabetes, Fatty Food May Trigger 'Leaky Gut' Effect

BY MICHELE G. SULLIVAN

FROM THE ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

LISBON – Snacking throughout the day might not be the best way to help control type 2 diabetes, especially if the snacks contain much fat.

A high-fat meal in people with diabetes and impaired glucose tolerance appears to trigger the passage of bacterial endotoxins through the intestinal wall, adding to the load of inflammatory cytokines that have already been implicated in the disease, Alison Harte, Ph.D., said at the meeting.

Because people with diabetes are often counseled to consume food in smaller, but more frequent, meals, this "leaky gut" effect could be compounded by this eating pattern, building up more and more of the lipopolysaccharide endotoxin – the main component of a gram-negative bacterium's cell membrane – in the blood.

"Our data highlight that these people can be exposed to as much as 126% more circulating lipopolysaccharide after a high-fat meal," said Dr. Harte of the University of Warwick (England). "A continual grazing routine will cumulatively promote their pathogenic condition more rapidly than other individuals' due to the elevated exposure to endotoxin."

Dr. Harte and her colleagues tested this hypothesis in 54 participants: 9 nonobese controls, 15 obese subjects, 12 with impaired glucose tolerance, and 18 with type 2 diabetes. The mean body mass index was 25 kg/m^2 in the healthy controls, 33 kg/m^2 in the obese subjects, 32 kg/m^2 in those with impaired glucose tolerance, and 30 kg/m^2 in those with type 2 diabetes.

VITALS

Major Finding: A high-fat meal increased bacterial endotoxins by 126% in subjects with type 2 diabetes, compared with healthy controls.

Data Source: A prospective food study performed in 54 volunteers.

Disclosures: Dr. Harte reported no financial conflicts.

Each of the subjects ate a high-fat meal composed of 75 g of fat, 5 g of carbohydrate, and 6 g of protein after an overnight fast. Blood was drawn at baseline and at 1, 2, 3, and 4 hours after eating.

At baseline, lipopolysaccharide was already significantly higher in obese subjects and those with diabetes and impaired glucose tolerance (mean of 5.7 endotoxin units [EU]/mL), compared with the control subjects (mean of 3.5 EU/mL).

The high-fat meal caused a significant jump in lipopolysaccharides in those with diabetes and impaired glucose tolerance. By 4 hours, those with diabetes had a mean lipopolysaccharide load of 17 EU/mL. The load increased to 8 EU/mL in those with impaired glucose tolerance. At 4 hours after the meal, the obese controls had a nonsignificant increase but still had a mean of 22% more circulating lipopolysaccharide than the healthy controls. This group had a slight, nonsignificant increase in the endotoxin.

Triglycerides followed a parallel course, she said, increasing over the 4-hour period significantly more in those with type 2 diabetes, impaired glucose tolerance, and obesity, compared with the controls.

"A high-fat diet raises endotoxin and triglycerides over 4 hours, and this increase could be further compounded by subsequent eating during the day, potentially resulting in continually raised levels," Dr. Harte said. "The fasting studies that we do might actually be masking the true impact of these circulating endotoxins and lipids." ■