Genetic variations associated with susceptibility to bacteria linked to stomach disorders

May 7 2013

Two genome-wide association studies and a subsequent meta-analysis have found that certain genetic variations are associated with susceptibility to *Helicobacter pylori*, a bacteria that is a major cause of gastritis and stomach ulcers and is linked to stomach cancer, findings that may help explain some of the observed variation in individual risk for *H pylori* infection, according to a study in the May 8 issue of *JAMA*.

"[*H pylori*] is the major cause of gastritis (80 percent) and gastroduodenal ulcer disease (15 percent-20 percent) and the only bacterial pathogen believed to cause cancer," according to background information in the article. "*H pylori* prevalence is as high as 90 percent in some developing countries but 10 percent of a given population is never colonized, regardless of exposure. Genetic factors are hypothesized to confer *H pylori* susceptibility."

Julia Mayerle, M.D., of University Medicine Greifswald, Greifswald, Germany, and colleagues conducted a study to identify genetic loci associated with *H pylori* seroprevalence. Two independent genome-wide association studies (GWASs) and a subsequent meta-analysis were conducted for anti-*H pylori* immunoglobulin G (IgG) serology in the Study of Health in Pomerania (SHIP) (recruitment, 1997-2001 [n =3,830]) as well as the Rotterdam Study (RS-I) (recruitment, 1990-1993) and RS-II (recruitment, 2000-2001 [n=7,108]) populations. Whole-blood RNA gene expression profiles were analyzed in RS-III

(recruitment, 2006-2008 [n = 762]) and SHIP-TREND (recruitment, 2008-2012 [n=991]), and fecal *H pylori* antigen in SHIP-TREND (n=961).

Of 10,938 participants, 6,160 (56.3 percent) were seropositive for *H pylori*. GWAS meta-analysis identified an association between the gene TLR1 and *H pylori* seroprevalence, "a finding that requires replication in non-white populations," the authors write.

"At this time, the clinical implications of the current findings are unknown. Based on these data, genetic testing to evaluate *H pylori* susceptibility outside of research projects would be premature."

"If confirmed, genetic variations in TLR1 may help explain some of the observed variation in individual risk for *H pylori* infection," the researchers conclude.

In an accompanying editorial, Emad M. El-Omar, M.D., of Aberdeen University, Aberdeen, United Kingdom, writes that the authors of this study are appropriate to state, "based on their data, genetic testing to evaluate *H pylori* susceptibility is premature."

"This would be superfluous, because nongenetic testing for the infection can be accomplished at a fraction of the cost. There is a bigger picture: understanding genetic susceptibility to *H pylori* is essential for understanding how to overcome this infection. The current approach to eradication of the infection is limited and based entirely on prescribing a cocktail of antibiotics with an acid inhibitor to symptomatic individuals. However, *H pylori* antibiotic resistance is increasing steadily, and eventually curing even benign conditions such as peptic ulcer disease arising from *H pylori* will be difficult. When considering gastric cancer, another *H pylori*-induced global killer, the necessity for understanding the pathogenesis of the infection and the role of host genetics in

susceptibility is even greater. The corollary is that better understanding of infections, including genetic epidemiology, is crucial to design measures to eradicate the downstream consequences of *H pylori* in large populations."

More information: JAMA. 2013;309(18):1912-1920
JAMA. 2013;309(18):1939-1940