Medical Xpress

Genetic factor undermines H. pylori treatment

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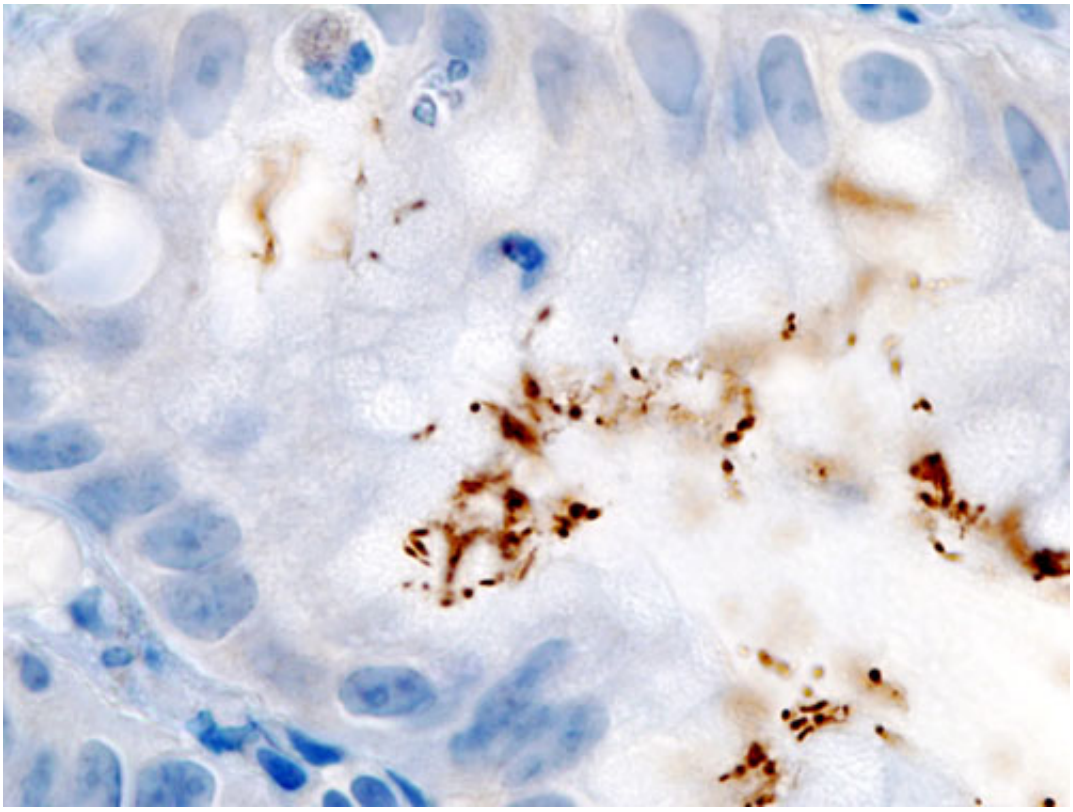

Histopathology of Helicobacter pylori infection in a gastric foveolar pit demonstrated in endoscopic gastric biopsy. Credit: Wikipedia.

Helicobacter pylori, a stomach-dwelling bacterium, is a strong risk factor for gastric cancer, peptic ulcers and other debilitating gastrointestinal disorders. Yet efforts to eradicate it using a combination of antibiotics and proton pump inhibitors (PPIs), which suppress gastric acid

production, often fail.

Now a team led by scientists at Vanderbilt University Medical Center and the Nashville Veterans Affairs Medical Center has linked eradication failure with polymorphisms or genetic variations that increase the activity of the CYP2C19 enzyme, which metabolizes or breaks down first-generation PPIs.

These so-called "fast metabolizers" may prevent adequate suppression by PPIs of gastric acid production, which is necessary for successful H. pylori eradication.

Reporting Aug. 3 in the journal *Gastroenterology*, the researchers analyzed 57 studies from 11 countries, and found that the failure rate of H. pylori eradication more than doubled in people who carried a version of the CYP2C19 gene that enhanced its metabolic activity.

There was no association between CYP2C19 variants and eradication failure, however, if the rapid metabolizers were treated with newer PPIs such as esomeprazole and rabeprazole, which are less metabolized by the enzyme or which bypass CYP2C19 metabolism entirely.

Further well-designed studies, especially in U.S. populations, are needed to determine whether giving higher or more frequent dosages of first-generation PPIs to people who have rapid-metabolizer variants of CYP2C19 might improve eradication rates, noted the paper's corresponding author, Shailja Shah, MD, MPH.

Studies of U.S. populations are needed because the majority of the studies have been conducted in Asian-Pacific countries, she said. Shah, a gastroenterologist and former assistant professor of Medicine at VUMC, is now at the University of California San Diego and the VA San Diego Healthcare System.

"Even small improvements in H. pylori eradication rates would likely translate to substantial collateral health, economic and societal benefits," the researchers concluded.

More information: Shailja C. Shah et al, Host genetic determinants associated with Helicobacter pylori eradication treatment failure: A systematic review and meta-analysis, *Gastroenterology* (2021). DOI: 10.1053/j.gastro.2021.07.043

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