can get away with—because they can," said Hagop Kantarjian, M.D., a leukemia researcher at the University of Texas M. D. Anderson Cancer Center in Houston, who also writes about this topic. “Drug companies are increasing drug prices to the extent it is harming our patients. Advocating for lower drug prices is a necessity to save the lives of patients who can’t afford them.”

Elsewhere, Kantarjian, Fojo, and colleagues have endorsed value pricing. In this alternative model, a drug's price reflects the proportional benefit to patients, such as prolonging OS and improving quality of life—concepts that guide price negotiations in Europe and elsewhere. Drugs with greater benefit may cost more, and those that adversely affect quality of life should compensate by offering more benefits in survival.

“It requires all of us to agree on benchmarks,” Fojo said. “For example, a smaller gain could be valued more in pancreatic or rare cancers that currently have no effective therapy.”

According to Yu, ASCO is developing a framework to compare value of treatments on the basis of clinical benefit, toxic effects, and cost.

How much is society pressing to move in this direction?

“My patients aren't complaining. They don't actually know what these drugs cost because insurance pays for them,” Flaherty said. “The groundswell of protest over pricing is among insurance companies, and I can see why,” said Lowe, also agreeing with the other researchers that having Medicare negotiate drug prices would be one straightforward way to better align them with clinical value. How likely is that?

“I’m an optimist,” Yu said. “All oncologists are.”

Notes

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Renewed Focus on Preventing Gastric Cancer

By Susan Jenks

With the heavy burden of gastric cancer in the developing world, researchers have begun to target its principal cause, Helicobacter pylori, in hope of preventing it.

This ancient microbe has resided in the human gut for at least 100,000 years. Eradicating it still raises concerns about swapping one deadly cancer for another. Even so, data from several recent randomized trials have shown enough benefit, researchers say, to warrant a more aggressive prevention approach. The World Health Organization declared H. pylori a class I human carcinogen in 1994.

“Ignoring gastric cancer in the hope that it will soon disappear is not a tenable health policy,” three scientists wrote in an editorial (JAMA 2014;312:1197–8). Their recommendation: Countries with high rates of gastric cancers should begin large population-based evaluation programs to screen for and treat H. pylori while awaiting results of four long-term clinical trials. One prevention trial in China involves more than 200,000 people.

An International Agency for Research on Cancer working group made similar recommendations in a 2013 report amid “an acute need to commit more public health resources to gastric cancer control.”

Often diagnosed at advanced stages, gastric (or stomach) cancers kill more people globally than any other cancer, except lung and liver, according to the World Health Organization. More than 700,000 men and women are expected to die of this disease in 2014, most in East Asia and South America, where poor socioeconomic conditions favor H. pylori’s easy transmission, usually during childhood.

H. pylori is responsible for an estimated 75%–80% of gastric cancers. These spiral-shaped bacteria burrow into the stomach’s protective mucosal lining, where they cause inflammation and extensive cellular damage over time. Although about half the world’s population harbors H. pylori, individual risk for developing stomach cancer is less than 2%. Nevertheless, chronic H. pylori infection carries the blame for many clinical conditions, including peptic ulcers, pernicious anemia, and dyspepsia.

U.S. gastric cancer rates have fallen precipitously since the 1950s, partly because of dietary changes and a dramatic decline in smoking, according to Philip Taylor, M.D., senior investigator in the National Cancer Institute’s genetic epidemiology branch. The “so-called hygiene theory” also comes into play, he said, as the U.S. and other industrialized nations have improved food storage and sanitation measures, thwarting H. pylori’s ability to spread.

Even globally, gastric cancer rates have been decreasing, Taylor said. But as the world’s population increases and ages, epidemiologists expect to see a rise in these cancers.

Still Divisive

How best to screen and treat H. pylori remains a divisive issue within the gastrointestinal community, however. Two prominent scientists still sit on opposite sides of the controversy—one calling for eradication of the bacterium whenever possible, the other suggesting that doing so indiscriminately could cause more harm than good. Others take a middle ground.

“From a cancer prevention point of view, the theory is wonderful,” an infectious disease whose cure lies in a vaccine, Taylor said. But no promising vaccine yet exists for H. pylori, and eradicating it may be “a good idea only if you don’t look at the downside.”

One possible downside: losing protection against esophageal cancers. Several observational studies have shown that H. pylori infection decreases stomach acid secretion. So eliminating the infection would lead to more acid secretion as the stomach recovers, possibly worsening gastroesophageal reflux disease, a major risk factor for esophageal cancer.
“If that’s real, it’s a fairly striking effect,” Taylor said. “The question then becomes, would we be trading one cancer for another?”

“There’s a lot of controversy about whether H. pylori is good or bad,” said David Metz, M.D., associate chief for clinical affairs in gastroenterology and professor of medicine at the University of Pennsylvania in Philadelphia. “What is clear is it’s the cause of most gastric cancers.”

Julie Parsonnet, M.D., professor of medicine at Stanford University Medical Center in Palo Alto, Calif., cowrote the JAMA editorial. She said these studies, including a 2012 trial in a general population of adults in China, showed that testing and treating H. pylori had a clear benefit in reducing gastric cancer risk (J. Natl. Cancer Inst. 2012;104:488–92).

A meta-analysis of six studies found a similar benefit. That analysis, Parsonnet said, prompted her to write the JAMA editorial with her colleagues Rolando Herrero, M.D., Ph.D., of the International Agency for Research on Cancer, and Edwin Robert Greenberg, M.D., of Seattle’s Fred Hutchinson Cancer Research Center.

“We wrote the article because there’s a cheap treatment to prevent it,” she said, and also to encourage high-risk countries to investigate strategies to reduce gastric cancer’s burden. Those treatments include two or three generic antibiotics, plus a proton pump inhibitor, used in combination to eradicate H. pylori.

All Benefit or Some Risk?

For at least one researcher, David Graham, M.D., professor of medicine, molecular virology, and microbiology at Houston’s Baylor College of Medicine, the important question no longer is whether to eradicate H. pylori. Rather, is doing so cost effective in any particular population, since population risks vary?

In Japan, for example, gastric cancer rates are high. The government has approved an unprecedented test-and-treat strategy to eradicate the bacterium through the country’s universal insurance system, Graham said. Because so many individuals already have irreversible damage to their stomachs from years of infection, he said, the government also offers follow-up surveillance to identify new cancers at their earliest stages.

“There’s a lot of controversy about whether H. pylori is good or bad. What is clear is it’s the cause of most gastric cancers.”

But offering similar preventive measures in the U.S. may not be cost effective, according to Graham. Although immigrants from nations where gastric cancer occurs frequently constitute high-risk populations, he said, H. pylori and gastric cancer have a low overall prevalence. So universal screening might not be economically viable without first working out the best approach.

Still, he describes H. pylori treatment as a one-off—meaning once completed, reinfection is highly unlikely, except in impoverished countries where environmental risk factors remain high. And everyone benefits from intervention, Graham said, in light of the infection’s progressive pathology: Some compare H. pylori infection to gastric termites that nibble away at the stomach silently, undiscovered, for many years.

“Eradication of H. pylori among those infected, if done before it causes irreversible damage to the stomach, will prevent cancer,” Graham said in an e-mail. “And, when done later, it will reduce the risk of cancer.”

Martin Blaser, M.D., the Muriel and George Singer professor of translational medicine at New York University’s Langone Medical Center, offers a more nuanced view. Blaser supports, in part, H. pylori eradication efforts in certain high-risk populations. But he warned against a blanket approach, not only because of the bacterium’s presumed protection against esophageal cancer but also because of possible early-life benefits and even unrecognized ones, including protection against stroke.

His concerns are twofold: one ecological, the other epidemiological. H. pylori is disappearing rapidly over most of the world as a result of modern life, especially in developing countries, he said. However, we still don’t fully understand the consequences of losing this ancient bacterium that has coexisted inside us for hundreds of thousands of years. The obvious good consequence would be less gastric cancer, Blaser said. But the bad consequences include a wide body of evidence that H. pylori protects the esophagus, he said, as well as protects against early-onset childhood asthma and possibly tuberculosis.

“Right now, doctors have extrapolated way beyond the data,” he said. “What I think is that H. pylori is bad for you when you are old but good for you when you’re young.”

This assertion raises the possibility that, as they learn more, doctors may give H. pylori to children to preserve the bacterium’s benefits, while eradicating it to undercut its harms once people pass age 40 or 50 years.

Meanwhile, Blaser said, he considers eradicating H. pylori infection in adults in high-risk areas reasonable, to see whether it’s working and to document any tradeoffs in risk. But we need to proceed cautiously, he said, to minimize unanticipated results.

In Memoriam:

Dr. Joe McLaughlin, M.P.H., Ph.D., International Epidemiology Institute, passed away on December 9, 2014. In addition to his work at NIH, Dr. McLaughlin served as an associate Editor of the JNCI for 5 years. We wish to express our sincerest condolences to Dr. McLaughlin’s family. Dr. McLaughlin was a wonderful member of our Editorial Board and will always be appreciated for his efforts with the Journal. He will be greatly missed.

In addition to his work at NIH, Dr. McLaughlin served as an associate