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credibly well tolerated" is very gratifying, Dr. Jankowski said, because many people were skeptical that it could be done.

"One of the major criticisms of the study when we tried to get it funded in the first place was that people thought we were mad and dangerous, and that we would kill patients with low-dose aspirin. But about 90% of our patients are still on low-dose aspirin and esomeprazole 2 years into the study with hardly any adverse events, showing the drug combination is very well tolerated."

So far, 12% of patients randomized to 20 mg esomeprazole have required an increase to 40 mg for symptom control, Dr. Jankowski said.

**Being able to show that aspirin 'is incredibly well tolerated' is very gratifying because many people were skeptical.**

**DR. JANKOWSKI**

Besides conversion to high-grade dysplasia or cancer, the other primary end point of the study is all-cause mortality.

Additionally, it will look at the pharmacokinetics of aspirin resistance, genetic markers as potential risk factors for esophageal cancer, and quality of life.

The first planned efficacy analysis is scheduled for 2010, a second interim analysis is due in 2012, and the final analysis is due in 2016.

The trial is funded by Cancer Research UK, Oxford University, and AstraZeneca.

Dr. Jankowski disclosed that he is a consultant to and receives research funding from AstraZeneca. ■

# Perception of Pain Altered in IBS Patients

BY KATE JOHNSON

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Patients with irritable bowel syndrome have altered brain responses to the anticipation of pain and to pain itself, which may make them more sensitive to painful stimuli.

"During expectation of pain, IBS [irritable bowel syndrome] patients generate higher levels of tonic noradrenergic activity, producing a bias toward interpretation of network activity as pain (speed over accuracy), and are inefficient at reducing such activity when discrimination of nonpainful stimulation should be maximized, or pain should be inhibited," wrote Dr. Steven M. Berman and his colleagues from the Center for the Neurobiology of Stress at the University of California, Los Angeles (J. Neurosci. 2008;28:349-59).

They used functional magnetic resonance imaging (fMRI) to measure the blood oxygen level-dependent response to anticipated and delivered rectal distention in 14 female IBS patients and 12 healthy controls (mean age 36 years). The imaging showed that, when the control subjects were anticipating a painful stimulus, brain activity decreased in the insula, supragenual anterior cingulate cortex, amygdala, and dorsal brainstem, but there was less of this anticipatory deactivation in the IBS patients.

Visceral distention of the rectum was then performed using a computer-driven pump and rectal balloon, which was inflated, in random order, to pressures of 25 mm Hg, 45 mm Hg, or 5 mm Hg (sham distension). The distention was performed after an 8-hour fast and two enemas.

Four to six sessions of 16 inflations were performed. Each inflation was preceded by an anticipatory cue, then 15 seconds of inflation at the designated pressure.

During rectal distention, increases in activity in the insula, dorsal anterior cingulate cortex, and dorsal brainstem were more extensive in IBS patients than in controls. "The DBS [dorsal brainstem] region contains multiple small structures implicated in the modulation of pain," the authors wrote.

Patients rated their mood, before and after the visceral distention, using the Stress Symptom Rating scale and they rated the intensity of their discomfort on a 3-point scale. In addition, they were all evaluated for depression and anxiety symptoms.

Overall, depression and anxiety scores fell within the normal range for all controls and 12 of the 14 IBS patients, but both scores were higher in IBS patients than controls, even when the two clinically elevated patients were excluded. Self-reported stress, anxiety, and anger were also higher in IBS patients. "The current results demonstrate that during certain expectation of experimental abdominal/pelvic discomfort, female IBS-C [IBS with constipation] patients are more anxious and less able than healthy controls to down-regulate activity within the CNS network activated by potentially aversive interoceptive stimuli," the authors noted. ■