

# QUIETING THE GRUMBLING

BY TONI BAKER

## Study Targets Irritable Bowel Syndrome Pain



DR. SATISH S.C. RAO

**THE NEWEST** drug for irritable bowel syndrome has the benefit of relieving the excruciating stomach pain affecting about a third of patients, and researchers want to know how.

### *Misfired Signals*

**"THESE** patients seem to have a magnification and misfiring of signals from their gut to their brain," said Dr. Satish S.C. Rao, Chief of the Medical College of Georgia Section of Gastroenterology and Hepatology and founding Director of the GRU Digestive Health Center. "Our hypothesis is that linaclotide dampens and essentially normalizes that communication."

Physicians don't fully understand why belly pain affects some patients with IBS, a condition characterized by chronic diarrhea, constipation, or bouts of both. The condition affects about 15 percent of the population, primarily women age 30-50.

Interestingly, individuals can have normal bowel habits and be pain-free for years before trouble starts, then problems can subside as mysteriously as they began.

Rao has documented how long it takes the brain and gut to communicate, as well as the size of the signals normally received. Sophisticated brain imagery reveals the communication is much faster and bigger in IBS patients.

## Gut/Brain Interaction

**"WE KNOW** that these basic mechanics seemed to be disturbed in IBS, based on our previous work," Rao said. "Let's see whether the drug truly works by changing how the gut and brain interact with each other."

Linaclotide, or Linzess, is only

agonist, mimics the work of two hormones normally secreted after eating, Rao said.

Animal studies, which show a decreased firing of nerves after taking the drug, support Rao's hypothesis about how it also eases stomach pain. To determine whether it works in humans, Rao is using his safe, well-established model for studying gut-to-brain and brain-to-gut communication. He uses a magnet to stimulate the portion of the brain that controls gut activity, then measures resulting nerve activity in the gut. He then stimulates the anus and rectum and measures the brain's response.

He is assessing this two-way communication in 45 IBS patients, half of whom will get linaclotide and the remainder a placebo, for 10 weeks.

### Heightened Sensitivity

**PREVIOUS** work has shown that IBS patients also have a heightened sensitivity in the gut. By slowly inflating balloons in the rectum, Rao has found significantly lower pain thresholds in IBS patients than in healthy individuals. "They feel the balloon at thresholds healthy individ-

in the gut," said Rao. "There are secretions; the stomach is churning and smashing up food; the bowel is contracting; nerves are firing. But we don't feel any of that" unless afflicted with IBS.

Those with the disease "start feeling normal things as painful and abnormal," Rao said. "We all feel a little bloated, a little gassy sometimes, but these people experience the same things with excruciating pain." (See "You Are What You Eat," page 30.)

One theory of what triggers IBS is some sort of acute gastrointestinal event, such as food poisoning or a viral or bacterial infection. "They get sick; they get better; then three to six months later, they start getting this grumbling sensation that is IBS," Rao said. He suspects a virus changes the sensitivity of the nerves just behind endothelial cells in the gut that manage the gut's communication with the brain.

Rao was involved in the clinical trials of linaclotide, which was approved by the FDA in 2012. The new investigator-initiated studies are funded by drug developers Forest Laboratories Inc. and Ironwood Pharmaceuticals. ■

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the second drug approved by the Food and Drug Administration for IBS. It latches onto a receptor on the surface of gastrointestinal cells that line the gut, triggering release of secretions that relieve constipation. The drug, a guanylate cyclase

agonist, mimics the work of two hormones normally secreted after eating, Rao said. Ultramicroscopy and special stains reveal inflammation in the gut lining undetectable with the eye and standard tests, Rao said.

"As soon as we eat, there is tremendous activity going on

For more information about IBS studies, call Research Coordinator Amanda Schmeltz at 706-721-1968.