

vomiting (11.0%), chronic constipation (9.9%), diarrhea (3.3%), unexplained weight loss (3.3%) and other symptoms (7.7%).

In 49.5% of the cases the clinical indication for which the test was performed was to demonstrate or exclude a generalized motor disorder, followed by unexplained symptoms without vomiting (17.6%), unexplained vomiting (12.1%), problems after surgery of the proximal digestive tract (8.8%), a systemic illness (5.5%) and others (6.6%).

A normal outcome was found in 37 (40.7%) studies. Four studies (4.4%) failed due to technical problems. Non-specific motor abnormalities constituted the majority (72%) of studies with an abnormal outcome. A pseudo-obstruction syndrome was diagnosed in 20%, rumination in 4% and abnormalities related to a vagotomy in 4%.

The manometric studies resulted in a new therapy in 13%, a new diagnosis in 15%, another investigation in 1% and referral to another specialist in 8%. A positive clinical impact was found in 28.7% of the patients.

Conclusion: Antroduodenal manometry can be a helpful diagnostic tool in a specialized center. More insight is needed in the significance of the non-specific motor abnormalities that are often found.

### ● G3509

**GASTROPARESIS AND AUTONOMIC DYSFUNCTION IN CIRRHOSIS.** GN Verne, C Soldevila-Pico, KM Spicer\*, A Reuben\*\*, Division of Gastroenterology and Hepatology and Department of Radiology\*, University of Florida, Gainesville FL, \*\*Medical University of South Carolina, Charleston SC.

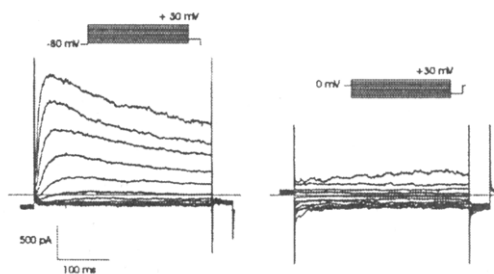
**Background:** Patients with cirrhosis frequently have gastrointestinal complaints including nausea, vomiting, abdominal pain, abdominal distention, and anorexia. Although the etiology of these symptoms is unclear, they may be due to altered gastrointestinal motility resulting in gastroparesis. These motility abnormalities are felt to be due to autonomic dysfunction that has previously been described in patients with cirrhosis (Hendrickse et al. Lancet 1992;339:1462). **Aims:** 1. To determine the prevalence of gastroparesis in patients with cirrhosis 2. To correlate the presence of autonomic dysfunction with gastroparesis and the etiology and Child's classification of cirrhosis. **Methods:** We prospectively studied 28 patients (14 males, 14 females, ages  $46 \pm 10.3$ ) with cirrhosis (12 viral, 8 alcoholic, 1 NASH, 5 autoimmune, 2 cryptogenic). All patients had abdominal pain and/or nausea and bloating. None of the patients studied had prior gastrointestinal surgery, massive ascites, or were on medications that might effect gastrointestinal motility, heart rate, or blood pressure. Two patients had insulin-dependent mellitus without neuropathy. All patients underwent 5 standardized cardiovascular tests to assess autonomic dysfunction: heart rate response to standing up, Valsalva maneuver, and deep breathing; blood pressure response to standing up and sustained handgrip. Results were expressed as either "autonomic dysfunction" or normal. Each patient underwent a solid phase gastric emptying study with  $^{99m}\text{Tc}$  sulfur colloid-labeled scrambled egg. Both anterior and posterior images were obtained at the onset of the study and every 10 minutes for a total of 100 minutes. Gastroparesis was defined as retention of the sulfur colloid of  $> 50\%$  at 100 minutes. **Results:** Autonomic dysfunction occurred in 18/28 patients (64%) [5 Child's class A, 8 class B, and 5 class C], with cirrhosis due to alcohol (8), viral hepatitis (5), autoimmune liver disease(4), and cryptogenic (1). Gastroparesis occurred in 13/28 patients(46%), all of whom had autonomic dysfunction. Five of 15 patients with normal gastric emptying had autonomic dysfunction. Of the 10 patients with normal autonomic function, the etiology of cirrhosis was viral(7), autoimmune(1), cryptogenic(1), and NASH(1). **Conclusions:** Gastrointestinal symptoms of anorexia, nausea, and abdominal pain are common in patients with cirrhosis. Gastroparesis is common in these patients, especially those with underlying autonomic dysfunction. Gastrointestinal motility disorders in cirrhosis may be due to underlying autonomic dysfunction and may account for their gastrointestinal symptoms.

### ● G3510

**A SLOWLY INACTIVATING VOLTAGE-DEPENDENT  $\text{K}^+$  CHANNEL CURRENT IN SMOOTH MUSCLE CELLS OF THE OPOSSUM SPHINCTER OF ODDI.** Fivos Vogalis, Harvard Med. School & West Roxbury VA, 1400 VFW Pky, Boston, MA 02132.

Phasic contractile activity of the musculature of the sphincter of Oddi (SO) meters bile release and propels bile into the duodenum. This activity is coordinated by "slow waves" that originate in the proximal SO and invade the smooth muscle syncytium.  $\text{K}^+$  conductances in the smooth muscle are likely to play an important role in determining the frequency and amplitude of these events. In the present study,  $\text{K}^+$  channel currents were characterized in smooth

muscle cells enzymatically dissociated from opossum SO. The SO was dissected from the duodenum and sectioned longitudinally while bathed in  $\text{Ca}^{2+}$ -free HEPES-bicarbonate physiological solution (PS). After the mucosa was removed by sharp dissection the muscle layer was cut into thin 1mm strips and incubated at  $35^\circ\text{C}$  in PS containing collagenase (0.6 mg/ml) for 1.5 hrs. The strips were then incubated in enzyme-free PS for a further 30 min after which they were gently triturated through a widebore glass pipette to release single smooth muscle cells. Aliquots of the cell suspension were placed on a glass chamber on top of an inverted microscope in preparation for patch-clamping. The chamber was perfused continuously (0.5 ml/min) with HEPES-containing Tyrode solution ( $\text{Ca}^{2+}$ , 1 mM) at room temperature. Recording pipettes were filled with high- $\text{K}^+$  (150 mM) solution ( $\text{Ca}^{2+}$ , 80 nM). In the whole-cell recording configuration, step depolarization of cells from a holding potential of -80 mV activated a slowly activating outward current ( $\text{I}_{\text{KV}}$ ) at potentials positive of -40 mV (see Figure). This current was fully inactivated at a holding potential of 0 mV (see Figure). The peak  $\text{K}^+$  conductance plotted as a function of voltage was fitted with a Boltzmann function and yielded  $+11.8 \pm 4.6$  mV for half-maximal activation and a slope of  $11.7 \pm 3.2$  mV in six cells.  $\text{I}_{\text{KV}}$  was insensitive to 1 mM TEA in the bath. The relatively positive activation voltage and weak voltage dependence of  $\text{I}_{\text{KV}}$  suggests that this current may be responsible for limiting the level of depolarization attained during electrical "slow waves" in the smooth muscle of the sphincter of Oddi.



Supported by NIDDK Grant DK50137.

### ● G3511

**INWARD CURRENTS THROUGH LARGE CONDUCTANCE CHANNELS IN SMOOTH MUSCLE CELLS OF THE OPOSSUM ESOPHAGUS.** Fivos Vogalis & Raj K. Goyal, Harvard Medical School & West Roxbury VAMC, 1400 VFW Pky, Boston, MA 02132.

The membrane potential of the circular muscle layer of the opossum esophagus lies positive of the predicted equilibrium potential of  $\text{K}^+$  ions. This suggests that the resting potential is established by a mixture of conductances that generate both inward and outward currents. We used the patch-clamp technique to further characterize in the circular muscle layer of the opossum esophagus the ionic currents responsible for the electrical behavior of this tissue. Smooth muscle cells were enzymatically dispersed from the circular muscle by treating strips (<1mm wide) with a mixture of collagenase (0.5 mg/ml) and trypsin (0.5 mg/ml) dissolved in  $\text{Ca}^{2+}$ -free HEPES-bicarbonate physiological solution for 30 min at  $35^\circ\text{C}$ . Ionic currents were recorded in the whole-cell recording configuration using conventional and nystatin-perforated patch clamp techniques at room temperature ( $22^\circ\text{C}$ ). Cells were perfused continuously (0.5 ml/min) with Tyrode's solution ( $\text{Ca}^{2+}$ , 1 mM). When cells were perfused internally with high- $\text{K}^+$  (150 mM) solution ( $\text{Ca}^{2+}$ , 100nM) through the recording pipette, spontaneous step-like fluctuations in current were recorded at a holding potential of -80 mV ( $n=22$  cells). Similar unitary currents were recorded from cells under perforated patch-clamp conditions ( $n=11$ ) and from 5 cells perfused internally with CsCl (150 mM) to block outward  $\text{K}^+$  currents. The conductance of these elementary events was estimated to be 300-400 pS and the unitary currents reversed near 0 mV. The frequency of channel openings increased with hyperpolarization and decreased with depolarization. The threshold potential for activation was  $\sim -50$  mV and overlapped with the activation of a transient outward  $\text{K}^+$  channel current. Boltzmann fits to the average current plotted as a function of test potentials negative of -50 mV yielded a voltage of half-maximal activation of  $-66 \pm 9$  mV ( $n=4$ ). Because these unitary currents activate at potentials near the resting level they may contribute to the depolarized state of esophageal circular muscle.

Supported by NIDDK grants DK50137 (F.V.) and DK31092 (R.K.G.)