INTRODUCTION

The main function of gut smooth muscle is to mix intraluminal contents with secretions and to propel these anally in a coordinated manner. This process insures that digestion and absorption of nutrients is complete, and that unabsorbable residue is expelled. The process responsible for postprandial propulsion is a propagated reflex, the peristaltic reflex. This reflex can be initiated by distension (i.e., radial muscle stretch) of the gut wall or as a result of either mechanical or chemical stimulation of the mucosa, and consists of two phases or components: contraction of the circular muscle layer orad (ascending contraction), and relaxation of the circular muscle layer caudad (descending relaxation) to the site of stimulation. During each phase, the longitudinal muscle layer responds in a reciprocal fashion (i.e., ascending or orad relaxation and descending or caudad contraction).

The peristaltic reflex is mediated by the enteric nervous system, an autonomous component of the peripheral nervous system, which is located wholly within the wall of the gut. This basic reflex is modified by neural inputs to the enteric nervous system from the autonomic and central nervous systems, locally released paracrine agents, and by circulating hormones. This chapter will focus on the role of enteric peptidergic and nonpeptidergic neurons in the regulation of this reflex.
CHARACTERISTICS AND NEUROPEPTIDE CONTENT OF THE ENTERIC NERVOUS SYSTEM

The enteric nervous system consists of two ganglionated plexuses, the myenteric and submucosal plexuses. The myenteric plexus is located between the outer longitudinal and inner circular muscle layers. Neurons of this plexus synapse with other neurons in both plexuses and project fibers into both muscle layers (1-6). The submucosal plexus is located in the submucosa, adjacent to the circular muscle layer. Neurons of this plexus synapse with other neurons in both plexuses and project fibers to the mucosa and additionally, in some species (human, dog, and rat), to the innermost layer of circular muscle (1-6). Neurons of the enteric nervous system also project to, and receive projections, from neurons outside of the gut in the prevertebral ganglia. These extramural ganglia act as centers for integration of information as it passes between the central nervous system and the enteric nervous system (7,8).

Neurons of the enteric nervous system have been characterized by their morphology as described originally by Dogiel (Type I, II, and III) (3,9-11), electrophysiological properties (S and AH neurons) (12-18), and neurotransmitter content (1,2,4-6,17-20). S neurons possess Type I morphology and exhibit fast excitatory postsynaptic potentials (EPSP), which are followed by rapid repolarization. In contrast, AH neurons possess Type II morphology and undergo prolonged after-hyperpolarization (AH).

The most successful method of categorizing enteric neurons has been the use of immunocytochemistry to identify the transmitter content (1,2,4-6,17-20). Application of this approach to the neurons of the myenteric plexus, the main source of innervation of smooth muscle, has identified two main populations of neurons that do not overlap. One population of neurons contain vasoactive intestinal peptide (VIP) or pituitary adenylate cyclase-activating peptide (PACAP), and nitric oxide synthase (NOS), the enzyme responsible for generation of nitric oxide (NO) from L-arginine. These neurons project fibers anally to other neurons within the myenteric plexus, and into underlying circular muscle, and are most likely interneurons and the relaxant (i.e., inhibitory) motor neurons to circular muscle (1,2,5,21-25). The second main population of neurons contain the tachykinins, substance P (SP) and neurokinin A (NKA), which are cosynthesized in the same precursor, β-preprotachykinin (26). These neurons probably also contain acetylcholine. This population of neurons projects to other myenteric neurons and into both the circular and longitudinal muscle layers, and are most likely interneurons and contractile (i.e., excitatory) motor neurons to circular and longitudinal muscle (1,2,5,17,21,22,27,28).

Subsets of VIP neurons contain other peptides, such as bombesin (also know as gastrin-releasing peptide or GRP), neuropeptide Y (NPY), and galanin (1,2,4-6,19). The opioid peptides, dynorphin, and [Met]enkephalin, are present in both VIP/NOS and tachykinin/ acetylcholine neurons (1,2,17-19,22). Some neurons contain somatostatin, γ-amino butyric acid (GABA), or serotonin (1,2,17,22,29). These neurons do not directly innervate smooth muscle cells; their influence on smooth muscle is exerted indirectly via other myenteric neurons (8,9).

METHODS OF MEASURING THE PERISTALTIC REFLEX

The early studies of peristalsis by Bayliss and Starling (30) identified the neural nature of this reflex and described the essential characteristics of contraction of circular muscle orad and relaxation of circular muscle caudad to a site of stimulation. Subsequent studies,