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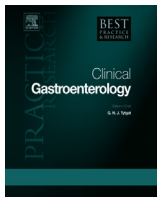

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Mechanisms of intestinal adaptation

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A B S T R A C T

Following loss of functional small bowel surface area due to surgical resection for therapy of Crohn's disease, ischemia, trauma or other disorders, the remnant gut undergoes a morphometric and functional compensatory adaptive response which has been best characterized in preclinical models. Increased crypt cell proliferation results in increased villus height, crypt depth and villus hyperplasia, accompanied by increased nutrient, fluid and electrolyte absorption. Clinical observations suggest that functional adaptation occurs in humans. In the immediate postoperative period, patients with substantial small bowel resection have massive fluid and electrolyte loss with reduced nutrient absorption. For many patients, the adaptive response permits partial or complete weaning from parenteral nutrition (PN), within two years following resection. However, others have life-long PN dependence. An understanding of the molecular mechanisms that regulate the gut adaptive response is critical for developing novel therapies for short bowel syndrome. Herein we present a summary of key studies that seek to elucidate the mechanisms that regulate post-resection adaptation, focusing on stem and crypt cell proliferation, epithelial differentiation, apoptosis, enterocyte function and the role of growth factors and the enteric nervous system.

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Introduction

Following loss of functional small bowel surface area due to surgical resection for therapy of Crohn's disease, ischemia, trauma or other disorders, the remnant gut undergoes a morphometric and functional compensatory adaptive response. In experimental rodent surgical models of short bowel syndrome in which 50–75% of the small bowel is resected, morphometric adaptation is characterized by increased crypt cell proliferation resulting in increased villus height, crypt depth and villus hyperplasia (Fig. 1; [1,2]). Morphometric adaptation is also accompanied by a functional adaptive response, with increased nutrient, fluid and electrolyte absorption.

Studies of the gut adaptive response have focused on understanding the molecular mechanisms that regulate post-resection changes in stem and crypt cell proliferation, enterocyte migration, apoptosis and enterocyte function (Fig. 2). .Although the morphometric changes following resection in humans have not been well-described due to the inaccessibility of tissue for biopsy, clinical observations indicate that functional adaptation occurs in humans [1,3,4]. In the immediate postoperative period, patients with substantial small bowel resection have massive fluid and electrolyte loss with reduced nutrient absorption. However, in the majority of patients with at least 100 cm of small bowel or 50 cm of small bowel with residual colon, the adaptive response permits partial or complete weaning from parenteral nutrition (PN) within two years following resection. However, patients with residual small bowel length <100 cm or <50 cm with residual colon generally exhibit life-long PN dependence [4,5].

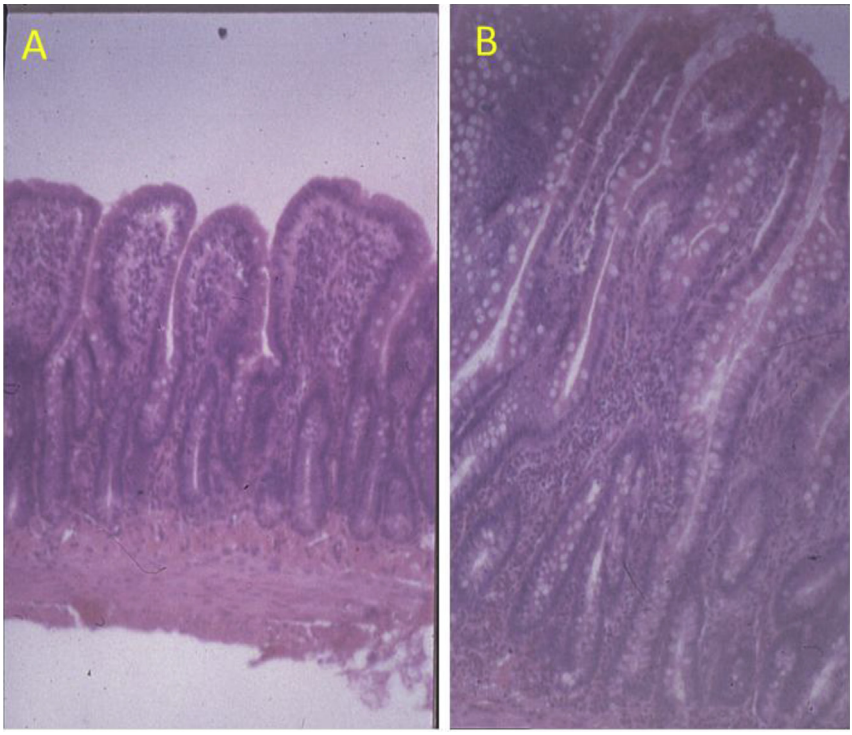

Fig. 1. The intestinal morphometric response post-resection. Rats were subjected to 70% intestinal resection and the residual adaptive ileum was removed at two weeks postop. Hematoxylin and eosin staining was performed. A. Preoperative ileum. B. Adaptive ileum at two weeks postop. The structural adaptive response is characterized by an increase in intestinal villus height and crypt depth, with an expansion in the goblet cell population.