Ischemia and Post-Ischemic Regeneration of the Small Intestinal Mucosa

A Light Microscopic and Autoradiographic Study* **

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Summary. After reversible ligation of the arcade vessels of the proximal jejunum, the intestinal mucosa was investigated by light microscopic and autoradiographic methods after 15, 30, 60, 120 and 300 min of ischemia. Early ischemic damage to the mucosa (after about 15 min) is characterized by shedding of not yet irreversibly damaged enterocytes from the tips of the villi into the intestinal lumen and bleb formation starting at the base of the epithelia. This process advances from the tips to the bases of the villi with increasing duration of ischemia, and the villi are completely denuded of epithelium after ischemia lasting 2 h. Remains of the small intestinal crypts are still present at this time. After ischemia lasting for 5 h, almost the entire intestinal wall is necrotic.

The post-ischemic repair of the small intestinal mucosa was investigated using light microscopic and autoradiographic methods 12 and 24 h and 3 and 8 days after a 2 h ischemic episode.

Reepithelialization takes place from the crypt residues still preserved at this time. After 12 h a flat epithelium is present, but by 24 h the epithelial cells are cuboidal or columnar and incipient development of small intestinal villi is apparent. After 8 days, the regenerated small intestinal mucosa shows a normal morphological appearance. This rapid repair of the small intestinal mucosa is brought about by an above-normal proliferation of the epithelia derived from the residual crypts.

Key words: Small intestinal ischemia – Histology – Autoradiography – Rat.

Introduction

Ischemia has an important role in pathogenetic intestinal processes. The pathological spectrum of ischemic damage extends from minor lesions of the

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mucosa, such as are present for example in ischemic enteritis, to total intestinal infarction.

Intestinal ischemia is usually due to vascular stenosis or occlusion (arterial and/or venous) (review paper: Jackson, 1963). Only recently has it become recognized that ischemic enteropathies may also occur without morphologically detectable vascular changes (so-called “non-occlusive mesenteric ischemia”), e.g., in shock or following treatment with certain drugs (Gazes et al., 1961; Marston, 1962; Baker et al., 1964; Boley et al., 1965; Muggi, 1967; Britt and Cheek, 1969; Davies and Brightmore, 1970; Manohar and Tyagi, 1973; Pawlik and Jacobson, 1974; Haglund et al., 1976). However, severe cardiac insufficiency with simultaneous arteriosclerosis of the mesenteric vessels underlies the majority of these cases (Berger and Byrne, 1961; Grosh et al., 1965; Fogarthy and Fletcher, 1966; Williams et al., 1967; Renton, 1972; Whitehead, 1976).

Since neither the development nor the regeneration of ischemic lesions of the intestinal wall can be followed in man, it seemed appropriate to investigate these problems in animal models. Previous experiments have led to variable and in some cases contradictory results, especially with regard to the extent and the course of ischemic mesenteric infarcts (Khanna, 1959; Marston, 1964; Robinson et al., 1966; David and Uerlings, 1967; Nylander and Wikström, 1968; Brown et al., 1970; Aho et al., 1973). There are only isolated investigations concerned with posts ischemic regeneration of the small intestinal mucosa (Cameron and Khanna, 1959; Glotzer et al., 1962; Pitha, 1971; Robinson, 1974; Rijke et al., 1976; Menge and Robinson, 1979).

The object of the present study was to examine the development and (under appropriate conditions) regeneration of an ischemic injury to the small intestine in a standardized experimental model. The experiment was arranged in such a way that the ischemia was not affected by uncalculable venous and collateral influences. This enabled a clear delineation of the consecutive phases. Besides the visualization of the morphological alterations in the small intestine, the proliferation behavior of the mucosa during ischemia and posts ischemic regeneration could be followed by autoradiography.

Materials and Methods

1. Experimental Animals

51 male wistar rats, three to four months old (weight 250 to 300 g) were used. The animals received food (Altromin R10 mixed feed) and water ad libitum.

2. Induction of Ischemia and Tissue Sampling

The animals were anesthetized by the intraperitoneal injection of 3.6% chloral hydrate solution (1 ml/100 mg body weight). The abdomen was opened by a median incision. The proximal jejunal loops were displaced forwards. The mesenteric arteries and veins of a 15 cm long jejunal segment were ligated using an elastic rubber band guided by a plastic drain (Fig. 1). The intestine was then replaced into the abdomen. The duration of ischemia was 15, 30, 60, 120 or 300 min.