Structural and Functional Studies on the Transformation of the Intestinal Mucosa in Rats with Experimental Diabetes

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Summary: Twenty days after the onset of alloxan-induced diabetes, a villous hyperplasia has developed in the intestines of rats having free access to food. The transformation is characterised by a considerable increase in the area of the villous surface, caused by an enhanced mitotic activity in the crypts. The absorption of glucose or methionine by jejunal loops, whether expressed in terms of serosal area or villous area, is unchanged at this stage. On the other hand, the specific activity of certain disaccharidases and dipeptidases in crude mucosal homogenates is greater in diabetic animals, but quantitative histochemistry revealed no changes in the activities of alkaline phosphatase, leucine amino-peptidase and non-specific esterase in the individual enterocytes. Thus the biochemical changes may simply reflect the hyperplasia of the mucosa. The blood sugar level does not appear to be directly responsible for the mucosal transformation; however, the positive correlation between the daily food intake and the villus height suggests a role of hyperphagia and consequent increased luminal nutrition in the development of the hyperplasia.

Key words: Transformation - Intestinal mucosa - Experimental diabetes

From studies of intestinal function at different stages of the development of alloxan- or streptozotocin-induced diabetes, SCHEDL and WILSON [1] described two distinct phases in the adaptive response: During the first 5-8 days after the alloxan administration, at a time when the weight of the intestine was still unchanged, an increased absorptive capacity for sugars, both in vivo and in vitro, was observed. At a later stage, the absorptive capacity of the entire intestine was increased, since the organ had gained in size, but the absorption per unit weight of intestine resumed values similar to those of control animals.

Kinetic studies have demonstrated that during the early phase of experimental diabetes, the maximal velocities of transport for sugars, amino-acids and bile acids are increased, whereas the Michaelis-constants for the transport processes remain unchanged [2]. At the same stage, enhanced specific activities of certain intestinal disaccharidases have been reported [3].
The behaviour of the animals is different in the two phases of the intoxication. During the first few days after the poisoning, the animals lose weight, the food intake is reduced, but glucosuria develops. After 5-8 days, the body weight stabilises, and the animals become hyperphagic [4].

Much uncertainty exists as to the aetiology of the intestinal changes occurring in experimental diabetes. The increased transport capacity and enzymatic activities observed during the early phase of the intoxication can be attributed to a semistarvation state, a condition that is known to provoke increased transport capacities [5]. The role played by other factors arising from the destruction of the β-cells, such as hyperglucagonaemia [6], in the regulation of intestinal structure and function remains unknown. Since both morphological and functional changes can be prevented by replacing the missing insulin [2,7], it seems clear that they must be provoked primarily by the diabetic state.

The hyperphagia that sets in about 8 days after the intoxication is probably responsible for the changes occurring during the second phase of the transformation [8]. The trophic effect of the increased ingesta is believed to lead to the development of a larger and longer small intestine. It is uncertain whether the high blood glucose level can inhibit the net intestinal absorption of glucose in vivo by providing a finite back-diffusion component from the blood into the lumen; under such conditions, an unusually high concentration of glucose might persist in the intestinal lumen and play a role in the development of the mucosal transformation [9].

In the present study, various features of the aetiology of the mucosal transformation have been examined during the second phase of experimental diabetes. These include:

1. Cell-kinetic aspects of the transformation;
2. Relationship between the absorptive surface area and the absorption of various actively transported substrates in vivo;
3. Alterations in biochemically and histochemically determined enzyme activities;
4. Relationship between the daily food intake and the blood sugar level on the one hand, and various morphological and functional parameters on the other;
5. Role played by a hypothetical back-diffusion of glucose from the blood into the intestinal lumen.