THE EFFECT OF ADRENALECTOMY, ACTH, AND HYDROCORTISONE ON THE DEVELOPMENT OF EXPERIMENTAL STOMACH ULCERS*

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The important role of the pituitary—adrenal system in the regulation of the status of the mucous membranes of the gastroinestinal tract and in the various pathologic states which arise there have been demonstrated by a number of investigators [3, 5, 6, 9, 11]. In this connection, and in view of the accumulation of a large number of clinical observations by numerous workers [1, 2, 4, 8, 10], doctors are called upon to use corticosteroids with great care, since with them it is possible to aggravate the ulcer process or to induce ulcers in persons with normal gastrointestinal tract function. Other authors reject a similar point of view [7].

Our goal was to study experimentally the characteristics of the development of the ulcerative process in the stomach in experimental animals under conditions of various states of endocrine regulation.

EXPERIMENTAL

As experimental animals we used 359 white rats of weight 120-140 g , in which stomach ulcers were produced by the method of Shea, with our own modifications. Three series of experiments were done. Rats were not fed for 48 h. Then, under ether anesthesia, laparotomy was performed and a ligature tied around the pyloric portion of the stomach. When the animals (series I and II) awakened from the anesthesia they were given orally 2 ml of pickle cabbage containing 3% sodium chloride. Animals in series III on awakening were given per os a much weaker stimulus: two ml of 7% dry cabbage broth. The cabbage broth was titrated with 0.1N solution of hydrochloric acid; the broth titer corresponded to 20-24. Sodium chloride was added to the broth to a concentration of three percent.

At 24 h after the operation all the animals were killed, autopsied and their stomachs removed. Macroscopically (with a lens) the stomach mucosa was examined, the number of erosions and ulcers counted and the size of the ulcers determined. The ulcers were divided into small, medium and large on the basis of diameter: small, from 0.5 to 1.5 mm; medium, from 1.5 to 2.5 mm; and large, greater than 2.5 mm.

In series I, 91 rats underwent bilateral adrenalectomy under ether anesthesia. Immediately after the operation and thereafter the animals were maintained on the usual nutrient ration, but instead of water received a 1.5% solution of NaCl. In the first postoperative days 21 animals died. After two to three weeks the adrenalectomized animals were subjected to the ulcerogenic stimulation. At different times after ligation of the pylorus ten animals died.

In series II, 70 rats were given ACTH (brand Gideon Richter), to ensure a gradual level of action over 24 h. The preparation was injected once intramuscularly in a dose of one international unit per 100 g on the day the rats were transferred to a starvation regimen. After the ligature had been placed in the pylorus ten animals were killed

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TABLE 1. Injury to the Gastric Mucosa in Rats being Subjected to Adrenalectomy and Receiving ACTH

Type of influence	Number of animals	Pathologic-anatomical injuries found at autopsy				total	Number of animals in which injury was observed	
		erosion	ulcers				absolute number	%
			small	medium	large			
Adrenalectomy	60	118	135	58	24	335	25	41
Injection of ACTH	60	310	175	183	63	731	56	93.5
Control	60	169	174	123	42	508	39	65

TABLE 2. Injury to the Gastric Mucosa in Rats Receiving Hydrocortisone

Type of influence	Number of animals	Pathologic-anatomical injuries found at autopsy				total	Number of animals in which injury was observed	
		erosion	ulcers				absolute number	%
			small	medium	large			
Hydrocortisone injections	56	368	145	50	12	575	48	85.7
Control	56	257	109	6	11	383	34	60.7

at different intervals (before 24 h, i.e., up to the moment of autopsy); damage to the mucosa was not expected in these animals. Since series I and II were carried out simultaneously, a single control was provided for them (experimental animals which had undergone only the ulcerogenic treatment).

In series III, 76 rats were injected intramuscularly with hydrocortisone, (brand Gideon Richter) in a dose of one mg/100 g. The injections were given daily for five to ten days, preceding the sacrifice of the animals. On the sixth to eighth day before laparotomy and placement of a ligature on the pylorus, four rats died (on autopsy no ulcers were found); 12 rats died at different periods after placement of the ligature. These 16 animals were not included in the experiment.

RESULTS

Results of series I and II experiments are presented in Table 1.

It follows from these data that in animals with extirpated adrenals, morphological changes in the gastric mucosa are less marked than in control rats. In addition, injury to the gastric mucosa is encountered more often in control rats than in adrenalectomized ones. It is entirely clear that the effect of ulcerogenic factors in animals which are lacking adrenals is weaker than that in controls.

In distinction to this, the pathomorphologic changes in the gastric mucosa in animals given ACTH are more strongly marked and are encountered more frequently than in control rats.

The results of the third series of experiments are presented in Table 2.

It follows from the data presented in Table 2 that with multiple injections of hydrocortisone, the number of animals in which ulceration of the gastric mucosa is observed increases.

This study suggests that the glands of internal secretion as well as the nervous system play a not unimportant part in the development of gastric ulcers. Evidently, the adrenal cortical hormones, which appear to act on the functional state of the stomach, increase the sensitivity of its mucosa to ulcerogenic factors. Our experiments confirm the truth of the impression of many clinicians that it is necessary to carefully supervise the therapeutic use of certain corticosteriods, in view of their capacity to provoke dyspepsic phenomena in patients and to aggravate or provoke ulcer processes.

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