PROLIFERATIVE ACTIVITY OF CELLS OF THE RAT GASTRIC MUCOSA AFTER ORAL ADMINISTRATION OF RADON WATERS AT VARIOUS TIMES AFTER RESECTION

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At various times after resection of 50% of the fundal part of the stomach in adult rats, water containing different concentrations of radon was introduced into the stomach. A clear decrease in the diurnal number of DNA-synthesizing cells was observed in the gastric rats one month after the operation compared with the controls. This parameter was indistinguishable from normal 4 and 6 months after the operation. Injection of radon waters into the gastrectomized animals stimulated or inhibited DNA synthesis in the gland cells depending on the postoperative period and the radon concentration in the water.

Adaptive changes in the mucous membrane of the stomach after resection have frequently been investigated [3, 5-11]. However, the quantitative characteristics of repair in the resected stomach have received little study [13-16].

In gastrointestinal diseases the therapeutic administration of radon waters (possessing α-ray activity) is known to be beneficial [1, 2, 4, 12]. The therapeutic action of radon waters in the treatment of postoperative gastritis has been observed experimentally [1].

In the present investigation the effect of α rays of radon waters given by mouth was studied on the proliferative activity or, more precisely, DNA synthesis of the epithelium of the rat stomach after resection.

EXPERIMENTAL METHOD

Altogether 120 noninbred male rats weighing from 120 to 250 g were used. In the experimental animals 50% of the fundal part of the stomach was resected [13]. The experiments were divided into four series,

TABLE 1. Diurnal Number of Glandular Cells in Fundus of Stomach Synthesizing DNA (in %; ±m)

Group of animals	Time after operation when treatment began			
	8 days	2 months 10 days		5 months 10 days
	time of sacrifice (months)			
	1	3	4	6
Intact	13,70±0,61	14,78±2,33	14,80±2,23	14,69±0,96
Gastrectomized	7,45±0,32	13,69±2,21	14,81±1,10	17,36±2,05
Receiving tap water	8,09±0,53	12,15±0,87	12,89±1,25	21,89±1,87
Receiving radon water (activity 1.1 μCi per course)	9,27±0,67	9,20±0,39	14,78±0,75	19,48±1,18
Receiving radon water (activity 11 μCi per course)	12,32±0,73	9,87±1,22	13,56±0,81	11,65±0,94

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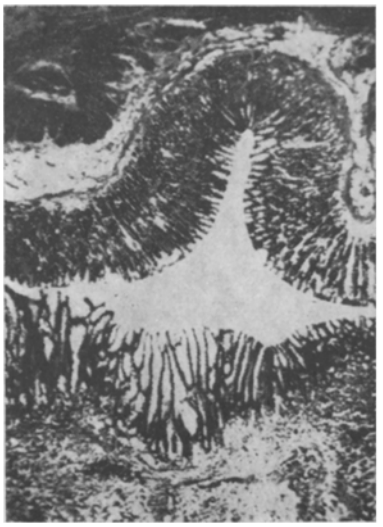

Fig. 1

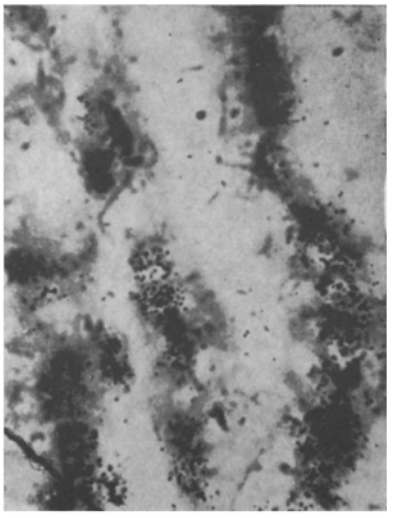

Fig. 2

Fig. 1. Section through fundal part of the stomach remaining after resection (3 months after operation). Glands of normal structure seen above, glands consisting entirely of mucous cells below, 250×.

Fig. 2. Autoradiograph of fundal part of resected stomach (3 months after operation). Increased DNA synthesis in cells of "mucous" glands, 1000×.

each with five groups of animals as follows: group 1) intact, 2) resection of the stomach only, 3) resection of the stomach and administration of 3 ml tap water by gastric tube, 4) resection of the stomach and administration of radon water in a concentration of 17.5 μCi/liter, and 5, administration of radon water with a concentration of 175 μCi/liter. The series of experiments differed in the time after the operation when administration of the radon waters began. In series I the waters started to be given 8 days after the operation (the animals were sacrificed one month after the operation); in series II treatment began after 2 months, 10 days, and the animals were sacrificed three months after the operation; in series III treatment began 2 months, 10 days after the operation also, but the rats were sacrificed 1 month after the end of the course; and in series IV treatment began 5 months, 10 days after and the animals were sacrificed 6 months after the operation. Before sacrifice and after starvation for 24 h the animals of each experimental group and the intact rats received injections of thymidine-H^3 in doses of 0.3 μCi/g body weight 5 times in 24 h (every 5 h). The animals were killed by decapitation at 9:30 A.M. The material was fixed by filling the stomach with Carnoy's fluid, and sections 5 μ in thickness were coated with type M (NIIKHIM-FOTO) emulsion and exposed for 1 month. The autoradiographs were developed and then stained by the Dominici–Kedrovskii method. Labeled cells were counted in 50 longitudinally divided glands, in the fundus of the stomach which still preserved their characteristic structure. The number of cells synthesizing DNA in 24 h was expressed as a percentage. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The general changes in the gastric mucosa of rats after resection of the fundal part have been described previously [13]. After administration of radon waters no significant abnormalities were found in the structure of the mucous membrane of the gastrectomized animals. All that was observed was a sharp decrease in the number of adhesions between the serous membrane of the stomach and other organs: the intestine, liver, and omentum.

In the early period (one month after the operation) no distinct changes were observed in the structure of the surface epithelium and the epithelium of the pits. At later periods (3-6 months after the operation) the pits became deeper, and the accessory cells penetrated into the basal parts of the glands and replaced the chief cells. Lymphoid follicles were seen near the muscularis mucosae, and bands of connective tissue were observed in some places between the glands. At this stage hypertrophy of the mucous membrane of the resected stomach and increased DNA synthesis were clearly detected. At all periods glands consisting entirely of mucous cells could be seen in some places in the mucous membrane, and the level of DNA syn-

thesis in these glands was 2-3 times or, in some cases, as much as 8-10 times higher than in the rest of the stomach (Figs. 1 and 2). Atypical glandular structures also were seen in the position of the fundal glands (gland-free zones). Cysts lined with cylindrical epithelium were visible in the basal parts of the glands.

In all groups of animals determination of the diurnal number of DNA-synthesizing cells showed that most were located in and at the base of the pits of the gastric glands: from 30 to 40% of the total number of surface epithelial cells, from 49 to 59% of the mucous cells at the base of the pit, from 6 to 18% of the accessory cells of the neck, from 0.2 to 0.8% of the chief cells in the basal portion, and from 0.1 to 0.6% of the parietal cells.

The results of series I (treatment beginning 8 days and sacrifice 1 month after the operation) demonstrated a significant general tendency for the diurnal number of labeled cells in the gastric glands to decrease in the gastrectomized animals compared with the intact contral. A decrease was observed in all groups except the group of animals treated with a higher concentration of radon water (Table 1).

In the gastrectomized animals the proliferative activity of the glandular cells of the stomach was thus reduced 1 month after the operation. However, under the influence of radon water with an activity of 11 μCi per course, it increased up to the characteristic level for intact animals. In all the gastrectomized rats at this period, regardless of whether they were treated or not, the gain in weight at the time of sacrifice was significantly smaller than in the intact animals.

In all subsequent series the diurnal number of cells synthesizing DNA in the gastrectomized rats receiving no additional treatment was indistinguishable from their number in intact animals. The number of labeled cells, i.e., the proliferative activity of the glandular cells of the stomach, 3 months after the operation was thus back to the normal level.

Administration of tap water to the gastrectomized animals had no significant effect on the proliferative activity of the gland cells. Only at one period (sacrifice 6 months after the operation) was a significant increase in the diurnal number of labeled cells observed.

Administration of radon water to the gastrectomized rats 2 months 10 days after the operation led to a decrease in the proliferative activity of the glandular cells when both concentrations of radon were used. However, if treatment was given at the same time and the rats were sacrificed 1 month after the end of the course, no effect of the α rays of the radon waters could be detected. The changes which occurred were evidently transient in character.

In the experiment in which water with a lower radon concentration was given 5 months, 10 days after the operation a significant increase in the percentage of DNA-synthesizing cells compared with the intact group was observed. However, the higher level of DNA synthesis than in the gastrectomized animals receiving no additional treatment was not statistically significant. In animals treated with water containing a high concentration of radon at the same time after gastrectomy a significant decrease in the diurnal number of DNA-synthesizing cells was observed in the gastric glands by comparison with the animals of all experimental and intact groups.

These results show that administration of radon waters to the gastrectomized animals had a definite influence on the level of DNA synthesis in the gland cells. This effect varied with the time at which the radon waters are administered. For instance, 2 months, 10 days after the operation radon waters of both concentrations lowered the level of synthesis in the gland cells, while radon water with an activity of 11 μCi led to an increase in the diurnal number of labeled cells in the gastric glands 8 days after the operation but to a decrease in their number 5 months 10 days after the operation.

Administration of radon waters can thus have a definite effect on the proliferative activity of the gastric glands of the resected stomach.

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