Production of Achlorhydria in Rats by Direct Irradiation of the Stomach* (33965)

M. John Murray, Nell Stein, John Mathews, and Rita Deyo

Departments of Medicine and Radiotherapy, University of Minnesota, Minneapolis, Minnesota 55455

For some time we have been seeking an animal with achlorhydria without disturbance in the continuity of the gut to study the effect of gastric secretions on absorption. In view of previous studies of gastric irradiation in man (1), we decided to observe the effects of direct local irradiation of the stomach in rats.

Materials and Methods. To follow the effects of irradiation, a technique was devised for obtaining a small sample of gastric juice from live rats. Rats were housed singly and fasted overnight. An intragastric Barbic no. 8 premature baby feeding tube was fitted on a 30-ml syringe. The rat was then wrapped in a towel and the tube was introduced through the side of the mouth for a distance of 18.5 cm in a 250-g rat. The stomach was washed twice with 6–8 ml of warm saline and the contents were discarded. The rat was then deprived of water for 2–4 hr and the tube was reintroduced to aspirate a few drops of gastric juice which were tested for pH with hydrion papers.

For irradiation the rats were fasted for 24 hr. They were then anesthetized and the stomach was exposed and immobilized through a midline incision 3 cm long. The stomach was carefully placed on a lead shield devised for the purpose (Fig. 1). It was kept moist with warm saline during the procedure. Pairs of rats were then exposed to increasing doses of irradiation to find the optimum dose required for the production of long-term achlorhydria. The dosage levels were 800, 1000, 1250, 1500, 1750, 2000, 2250, and 2500 rads. The object of this technique was to produce achlorhydria but protect all other tissues, *e.g.*, pancreas and bone marrow, from irradiation injury. At the end of the exposure, the abdomens were closed and the rats were returned to their regular diet and water. The method of irradiation was as follows. A General Electric Maximar 220 operated at 220 kVp and 15 mA was employed with a 1-mm aluminum filter. A dose rate of 208 R/min was obtained at 40 cm source–skin distance. The half-value layer was 0.38 mm copper. A special lead shield was used to elevate the stomach of the rat into the primary beam while shielding the rest of the animal from irradiation (see Fig. 1). With the assistance of a light centering device, the beam was focused upon the presented stomach but blocked from the rest of the animal by 6 mm of lead. Adjacent areas of the animal were protected from scattering effects by 3 mm of lead. The actual primary beam port measured 3.5 $\times$ 3.5 cm and was focused in its entirety upon the lead surface, thus precluding scattering effects. In the event that pancreas was found adhering to the stomach wall, small crescent shaped lead shields were provided to obtain nearly total protection for the exposed tissue. Transmission through these 3-mm lead shileds was estimated to be less than 1%. The lead shields were coated with paraffin to forestall possible toxic effects upon exposed tissue. The rate of delivery of radiation was adjusted so that 1750 rads were given the stomach in 8.68 min. No ill effects were noted.

All rats were kept 15 weeks during which time the hemoglobin, weights, and pH values of gastric juice were recorded. They were finally fasted for 48 hr and a 4-hr Shay procedure (2) for determination of pH and total gastric acidity was carried out.

Results. Figure 2 shows the pH recordings made during the 15 weeks in each rat correlated with the amount of stomach irradiation. It appears that at least 1750 rads are required to produce enduring achlorhydria in

Supported by the John Hartford Foundation and by the National Institute of Arthritis and Metabolic Diseases Research Grant No. AM 10976-01.

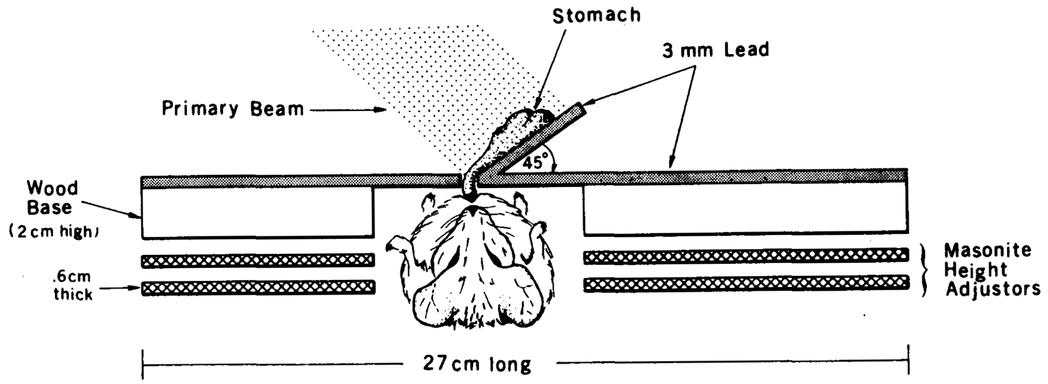

FIG. 1. Diagram of apparatus.

rats by this method. During the time of irradiation, there was an initial fall in hemoglobin and weight, depending on the size of the dose. Only those receiving over 2000 rads failed to show the normal expected weight gain at the end of 15 weeks but hemoglobin levels at this time were normal. The hemoglobin fall seems likely to be due to gastric mucosal hyperemia and hemorrhage resulting from irradiation. Table I records the results of the 4-hr Shay study after 15 weeks and relates the acid production and concentration to the gastric acid pH produced by varying amounts of irradiation. At 1750 rads or more, the gastric mucosa showed complete atrophy of its glandular portion on microscopic section.

Discussion. Lasting achlorhydria in rats can be produced by direct irradiation of the exposed stomach with large doses, *i.e.*, more than 1750 rads. It is possible to follow the response to irradiation in living rats by intu-

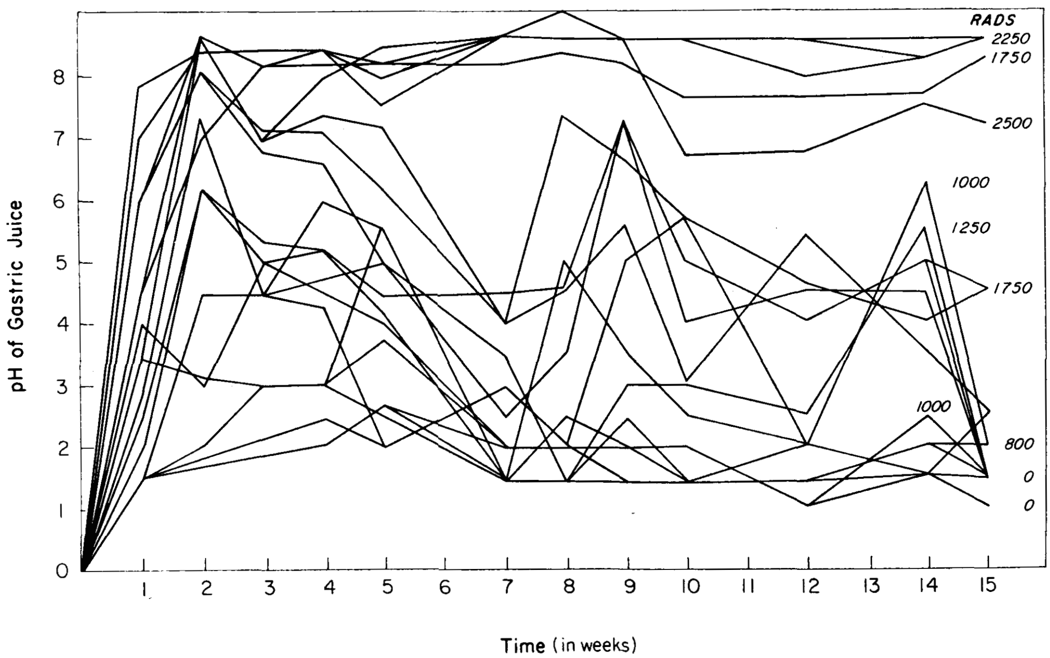

FIG. 2. Effect of varying amounts of irradiation on pH of gastric juice in rats.

TABLE I. Gastric Acid in Rats 15 Weeks after Stomach Irradiation.

		4-hr Shay	
(rads)	Gastric juice (pH)	Total acid (meq)	Acid (meq/liter)
800	1.0	0.350	40
1000	2.0	0.180	95
	1.5	0.130	45
1250	1.5	0.120	50
	1.5	0.054	45
1500	4.5	0.09	22.5
	2.5	0.008	40
1750	8.4	0.0275	11
	2.5	0.0325	32.5
2000	1.0	0.282	56.5
	8.6	0.00325	12.5
2250	8.6	0.0026	7.5
	8.6	0.0025	12.5
2500	7.2	0.0025	12.5
	1.5	0.19975	42.5
None	2.0	0.100	50
	1.5	0.192	60
	2.5	0.06	50

bation in the fasting state and determination of the pH of the gastric juice. The pH values relate well to the gastric acid production as determined by the Shay method. Rats treated in this way make a good experimental model for the study of achlorhydria and its effects on other physiological mechanisms such as absorption.

Summary. Lasting achlorhydria was produced in rats by irradiation of the exposed stomach. Gastric pH determination in the living animal correlates well with the degree of impairment of gastric acid secretion induced by irradiation. Rats treated in this way provide a good experimental model comparable to an animal with total gastrectomy but without the disadvantage of an interrupted gut.

The authors gratefully acknowledge the technical assistance of Richard Kenyon who devised the shielding apparatus for the rats.

1. Clayman, C. B., Palmer, W. L., and Kirsner, J. B., Gastroenterology **55**, 403 (1968).

2. Shay, H., Sun, D. C. H., and Gruenstein, M., Gastroenterology **26**, 906 (1954).

Received Feb. 19, 1969. P.S.E.B.M., 1969, Vol. 131.