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Letter to the Editor

A Method to Eradicate Fibrosarcoma in the Rectum of Rats by Selective Hyperthermia*

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A TUMOR in the foot of a mouse may be cured by immersion of the whole leg into hot water [1]. It appears that a modification of this immersion method enables the cure of fibrosarcoma in the rectum of rats.

Male Lewis/han rats (200–400 g) were used throughout the experiment. Three days prior to the heating experiment the rat received 60 mg Neomycinsulfate + 3000 I.E. Bacitracin (1/4 tablet Nebacitin®/day) mixed with 2 g commercial margarine, as a low residual diet, to decrease bacterial contamination of the gut.

Tumor

The fibrosarcoma was originally induced by methylcholanthrene and maintained by injection of approximately 1 mm^3 solid tumor mass into the wall of the rectum. The injection gives rise to a barely palpable tumor within 8–12 days. The tumor is 100% transplantable and lethal within 6–8 weeks. The tumors were in the 90–102 transplanted generation. Spontaneous cures were not observed during the experimental period in untreated animals.

Hyperthermia

The rats were anesthetized with 2 Br-2Cl-1,1,1-trifluorethane (Halothan®) + O_2. Prior to hyperthermia 1/4 tablet of Nebacetin® dissolved in 10 ml Ringer was infused via the rectum into the colon descendens. After infusion the colon was ligated and remained so during the experiment.

After a midline incision in the skin of the scrotum the rectum tube was freed, thus forming a free space between the rectum wall and the surrounding tissues. This gap around the rectum was irrigated with heated Ringer-solution (8 l/hr) for 60 min by means of 10 perforated steel or silicon tubes inserted into the gap ($\phi = 1$ mm, $l = 12$ mm).

Additional to the external gap-heating, the rectum lumen and the lower part of the colon descendens up to the ligation was perfused with heated Ringer-solution (4 l/hr) by means of a perforated Plexiglas tube ($\phi = 5$ mm, $l = 32$ mm).

The temperature of the fluid within the rectum-gap, the rectum-lumen and occasionally within the tumor was monitored with thermistor probes with an accuracy better than ±0.1°C. The whole-body temperature was controlled with a thermistor inserted into the esophagus.

The optimal temperature of the irrigation fluid to eradicate fibrosarcoma (Tu-diameter 2–5 mm) in the rectum wall of rats was 44.2–44.3°C. The tumor showed exactly the temperature of the irrigation fluid. The heated area became moderately swollen, with a maximum 3–6 days after heating. Palpation showed normal consistency in most cases 2–3 weeks later.

To avoid necrosis of the rectum wall bacterial contamination of the gut must be lowered by antibiotics 3 days prior to heating. As demonstrated in experiment C, the rectum not protected was destroyed if heated to 44.2°C. The rats died within 1 week. Histological control showed total necrosis of all layers of the wall. Peritonitis was a common finding.

In all successful experiments the rectum mucosa, though destroyed by heating, began to regenerate approximately 3 months later. Six months later histological control showed the

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Table 1. *Temperature of irrigation fluid and tumor response (time of irrigation* = 60 min)

Experiment	44.0 ± 0.1°C				44.2 ± 0.1°C				44.4 ± 0.1°C			
	n	Cured	Tu	Died	*n*	Cured	Tu	Died	*n*	Cured	Tu	Died
A	22	4	18	0	23	13	5	5	21	9	0	12
B		-					-		11	3	8	0
C		-			4	0	0	4			-	
D	13	1	3	9			-				-	

A = Antibiotics, O_2-gassing; B = antibiotics, no irrigation of rectum lumen, O_2-gassing; C = no antibiotics, O_2-gassing; D = antibiotics, no O_2-gassing. Cured = histological control showed no tumor 2–10 months after heating. Tu = Tumor reappeared 1–6 weeks after heating.

heated rectum with a normal mucosa. Gross inspection showed no difference between normal and heated rats.

If the irrigation fluid was allowed to stand in the open air in a reservoir for 24 hr, the rectum became necrotic if heated with this fluid (experiment D). Gassing the fluid with oxygen prevents tissue destruction (experiment A), and enables the temperature to be raised by about 0.2°C, i.e. to reach the therapeutically effective temperature of 44.3°C.

In experiment B only the external gap was irrigated. These experiments were performed to exclude the possibility that washing out the mucus by irrigation of the lumen would render the mucosa of the rectum more susceptible to heating. Histological control showed no difference between experiments A and B. The temperature of the rectum lumen and of the tumor remained about 0.2°C below the external gap temperature. This may explain the relatively small rate of cure. This experiment shows that, under the given conditions, it is not possible to heat the cooler arterial inflow sufficiently if the space available for heat transfer between irrigation fluid and blood vessels in the rectum is only 12 mm, the length of the perforated irrigation tubes. The rectum wall obviously needs to be heated from both sides.

REFERENCE

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