TABLE II. Effect of Oral Medication with Tri-Iodo-Thyronine Given Once a Day for 7 Days to 25 Normal Subjects. A) before starting treatment; B) 6th day on treatment; C) 7th day after treatment discontinued; A') uptake before treatment; B') uptake on 7th day of treatment.

Dose, mg	Protein bound iodine, γ %			Cholesterol, mg %			I^{131} uptake, %	
	A	B	C	A	B	C	A'	B'
.008	4.6	3.9					18.8	2.7
	6.5	4.7					31.2	5.7
	4.8	3.5					31.6	5.9
	4.2	3.0					40.2	15.9
	3.6	2.9					18.8	6.2
.0175	4.7	4.3	5.7	276	276	295	22.0	13.3
	5.4	4.4	4.4	165	146	177	26.9	15.7
	5.0	4.0		259	227		21.0	2.3
	5.1	4.4	3.9	192	162	200	14.5	7.0
	5.0	4.1	3.8	565	543	520	21.3	4.6
	4.0	4.0	6.5	317	295	350	16.0	4.3
.035	4.2	4.2	6.4	234	212	235	17.0	2.7
	4.6	3.4	4.9	213	162	259	23.0	5.0
	5.4	2.7		260	343		20.0	10.0
.070	5.7	5.2		256	262		28.0	3.1
	3.8	5.0	3.8	244	192		20.0	5.0
	5.0	3.0	4.2	200	204	238	18.0	4.0
.105	4.0	4.9		312	294		13.0	6.7
	4.0	3.9	3.5	272	192	273	32.0	8.9
	4.4	2.9	4.3	192	227	224	13.0	2.0
.140	5.8	4.7		235	194		18.9	6.5
	6.4	4.9	5.1	214	322	228	19.4	6.5
	5.3	5.7	4.6	255	208	277	30.0	5.4
	4.6	5.1		200	208		14.0	8.6
	3.2			255			19.0	4.3

in dosage as low as 0.008 mg orally also reduces the uptake. This is associated with a decrease in serum protein bound iodine.

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Effect of Piromen on Survival of Irradiated Mice.* (20263)

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Piromen‡ stimulates a leukocytic response very similar to that produced by treatment with ACTH(1-3). The mechanism of Piromen stimulation is unknown, but it is believed that the drug affects directly or indirectly the adrenal cortex(4). There is evidence, how-

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‡ Trade name for a sterile non-protein, non-anaphylactogenic bacterial pyrogen. Furnished through the courtesy of Dr. William F. Windle, Baxter Laboratories, Morton Groves, Ill.

ever, that its action is not identical with that of ACTH(5-7). It has also been shown to induce changes in the connective tissue mast cells(8). Jacobson, *et al.*(9) have postulated that it may be possible to stimulate the production of the factor responsible for rapid recovery from radiation injury. This factor seems to be intimately associated with the spleen. Since Piromen stimulates hemopoiesis and produces hyperplastic myeloid spleens, it seemed probable that this substance might effect an increase in production of the radiation-recovery factor. This possibility, plus the demonstrated importance of the role of adrenal response in alleviation of radiation sickness(10), prompted the inquiry into the possible protective action of Piromen.

Materials and methods. A total body dose (skin) of 550 r was delivered in each experiment by a deep therapy General Electric Maximar X-ray machine. Factors used were: 220 kvp, 15 ma, 1.0 mm Al, 0.5 mm Cu and 0.5 mm Cu equivalent (inherent in machine) filters, 50 cm target-center of animal distance, 1.25 mm Cu half-value layer, and 49.2 r per minute dose rate. An Oddman localizer was used to determine the exact location of the 15 cm square field. To avoid possible stress and complications due to hormonal influences, the animals were neither anaesthetized nor closely confined during irradiation. With small animals such as mice, body irradiation may be considered to be uniform throughout. The irradiation chamber was constructed of ⅛ inch lucite with ample ventilation ports. The total dose was determined by summing repeated r-readings with a 100 r Victoreen Condenser meter and correcting for temperature and barometric pressure. Animals were maintained in an air-conditioned room at 25°C, and allowed free access to Purina Laboratory Chow and water (controls), or Piromen-treated water. Preliminary experiments with C3H and several Swiss Albino strains indicated that results were comparable. The HN strain of Rockefeller Institute Swiss albino mice was used in all experiments reported here. *Exp. I.* Thirty-two 10-week-old mice (18 males, 14 females) received an average daily dose of 0.37 γ of Piromen, calculated on the basis of the amount added to drinking water, 4 successive days prior to irradiation (total dose, 1.48 γ). The control group, which received no Piromen, consisted of 32 animals (18 males, 14 females) of the same age. *Exp. II.* Another experiment was conducted in which Piromen was administered intraperitoneally. Seven-week-old mice were used. Group 1 (37 mice, 25 males) received 0.1 γ Piromen/day for 5 days before irradiation. Group 2 (37 mice, 25 males) received the same dose of Piromen for 5 days after irradiation, and group 3 (39 mice, 26 males) received one ml physiological saline 5 days before and 5 days after irradiation. Group 4 (10 mice, 5 males) received 0.1 γ Piromen/day for 10 days, but was not irradiated. *Exp. III.* The effect of post-irradiation treatment with larger Piromen doses was determined by using 2 groups of 8-week-old mice. Twenty-six mice, half male and half female, were employed in each group. Due to the fact that there is a decrease in water consumption immediately after irradiation, Piromen was administered as follows: Group 1 received 0.5 γ intraperitoneally immediately after exposure and thereafter the daily dose, calculated on the basis of Piromen contained in water consumed, was 0.34 γ/day/mouse for 6 days (total dose 2.55 γ). Mice of group 2 were given an injection of saline containing no Piromen.

Results and discussion. Results of these experiments are presented in Table I.

When Piromen was administered intraperitoneally before irradiation, as in Exp. II, it had a significant protective effect. Piromen, even at twice the experimental dose did not impair health or survival. Post-irradiation treatment, on the other hand, significantly decreased survival time. When the post-irradiation dose was increased, as in Exp. III, all Piromen-treated animals died within 11 days, whereas 4 of the control group survived at least 30 days. This is a significant difference and indicates how a small change in dosage may affect survival. No sex differences were observed in any experiments.

It appears that as regards survival the primary action of Piromen is very similar to that of ACTH. As in the case of ACTH treatment under similar conditions(11), a protective ac-

TABLE I. Survival of X-Irradiated Piromen-Treated Mice.

Exp. No.	Treatment	Survival			
		Fraction*	%	Mean	Significance†
I	Small oral Piromen doses before irradiation (.37 γ/day for 4 days)	13/32	59.4	14.15	P >.05
	Control (no Piromen)	13/32	59.4	12.31	—
II	Piromen inj. i.p. before irradiation (0.1 γ/day for 5 days)	22/37	40.6	19.00	P <.05
	Piromen inj. i.p. after irradiation (0.1 γ/day for 5 days)	32/37	13.5	12.95	P <.05
	Control, saline only, inj. i.p. 5 days before and 5 days after irradiation	30/39	23.1	14.54	
	Piromen control, (no irradiation) (0.1 γ/day for 10 days)	10/10	100	30.00+	
III	Larger Piromen dose after irradiation (1 ml saline containing 0.5 γ/ml i.p. 1st day after irradiation, then 0.34 γ orally for 6 days)	26/26	0	8.04	P <.05
	Control. One ml saline i.p. first day after irradiation. No Piromen	21/26	19.0	16.65	

* No. died/total.
† No. surviving as compared with control in each experiment, based on "t" test.

tion is obtained, but post-irradiation treatment lowers the number of survivors. Perhaps Piromen and ACTH exert an additive deleterious effect upon tissues already damaged by irradiation. The leukocytosis-promoting factor, isolated by Menkin(12), which produces a pharmacological effect somewhat like that of Piromen, has been shown, however, to have no effect upon survival of X-irradiated mice(13).

Summary. Intraperitoneal injection of 0.1 γ Piromen/day/mouse for a 5-day period effected a significant increase in the mean survival time of X-irradiated (550 r) mice of the HN Rockefeller Institute strain. Piromen administered with the drinking water at the rate of 0.37 γ/day/mouse for 4 days failed to significantly alter survival time. This may have been due to the small dose actually absorbed. Administration of a larger dose (total dosage, 2.55 γ) after irradiation resulted in fewer survivals than in the untreated controls. The action of Piromen following irradiation appears to be similar to ACTH with respect to survival. The dosage of Piromen is apparently of critical importance.

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