Obata[5] observed lesions in 3 of 12 rabbits injected intravenously with saline extracts of fresh placenta. He mentioned hemorrhagic liver lesions in his injected mice. Oden[6] upon repeating the methods of Young with 3 guinea pigs and 7 rabbits, declared that the liver lesions were diffuse, with "no lesions in any manner resembling those of eclampsia." No mention was made of liver lesions in his mice that received injections of extract. Bartholomew and Kracke[7] reported liver and kidney lesions in rabbits and guinea pigs.

From these reported observations and from the circumstances leading to the development of the liver lesions here reported, it is apparent that there is a relationship between the development of focal liver necrosis and the injection of toxic extracts of endometrium and of placenta. However, the appearance of a few similar foci of necrosis in animals which received injections of extracts of a variety of tissues, or occasionally too soon after injection to be a result of the treatment, suggests that the experimental lesions may not result directly from the action of the extract, but may follow activation of some latent process. Since most of the changes in the liver developed after the animals that received injections of extract had suffered a temporary collapse or shock-like state, this non-specific influence may have been a factor in the pathogenesis of the lesions. The possibility that the lesions are identical with the spontaneous focal liver necrosis in mice reported by Olitsky and Casals[8] has been considered, but the lesions described here were grossly visible and involved larger zones than did the spontaneous lesions. No inclusion bodies have been found in any of the sections of liver from animals used in this study.

Summary. Focal liver necrosis occurred in 30% of 500 mice which survived the intravenous injection of single sublethal quantities of toxic extracts of endometrium or placenta. Occasional similar lesions were seen in mice which were injected with other tissue extracts. Although related to the effect of the injected toxic material from endometrium or placenta, the lesions may be indirect or nonspecific effects of the injections.

Special appreciation is due Miss Carol Spaulding for assistance in conducting this investigation.

[5] Obata, I., *J. Immunology*, 1919, **4**, 111.

[6] Oden, C. L. A., *J. Mich. Med. Soc.*, 1925, **24**, 110.

[7] Bartholomew, R. A., and Kracke, R. R., *Am. J. Obs. and Gyn.*, 1932, **24**, 797.

[8] Olitsky, P. K., and Casals, J., PROC. SOC. EXP. BIOL. AND MED., 1945, **60**, 48.

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Influence of Dietary Iodine on Susceptibility of Rats to Alpha Naphthylthiourea Poisoning.*

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Richter[1] proposed the use of α-naphthylthiourea (ANTU) as a rodenticide for the control of Norway rats because of its high toxicity to carnivorous species and its relatively low toxicity to omnivorous and herbivorous species.

While it has not yet been reported that any

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† The experimental data in this paper are taken from a thesis submitted *in absentia* in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biochemistry in the Graduate School of the University of Illinois.

[1] Richter, C. P., *J. A. M. A.*, 1945, **129**, 927.

dietary factor will influence an animal's resistance to ANTU, Griesbach *et al.*[2] have shown that iodide, a normal dietary component, when injected in doses of 1.30 mg per rat every 4 days protected the animals against poisoning by thiourea, the parent compound from which ANTU is derived. DuBois and Erway[3] have demonstrated that ANTU and related compounds inhibit tyrosinase, and that this inhibition can be prevented by iodine.

Therefore, a study of the effect of iodine fed in the diet on the resistance of rats to ANTU poisoning was undertaken.

Methods and Materials. Three- to 4-month-old albino rats of the Sprague-Dawley strain averaging 200 g in weight were used throughout these experiments. Iodine was given to the animals either dissolved in the drinking water or mixed into the diet. Both food and water, containing iodine, were provided *ad libitum* but the actual iodine intake was recorded for each rat individually. The animals had eaten Purina Laboratory Chow for at least 3 weeks before receiving the experimental diets.

The stock diet used in these experiments contained: casein 18%, cerelose 15%, dextrin 50%, cellu flour 2%, salt[4] 3%, lard 4%, corn oil 4%, and cod liver oil 4%. A vitamin supplement containing thiamine hydrochloride 250 γ, pyridoxine hydrochloride 250 γ, nicotinic acid 250 γ, riboflavin 500 γ, calcium pantothenate 2.5 mg, choline chloride 125 mg, α-tocopherol 10 mg, and Wilson's 1-20 liver concentrate 625 mg was added per 100 g of diet.

In experiments in which iodine was supplied in the drinking water it was given in dose equivalent to 2.52 mg I_2 per cc in the form of both Lugol's solution and potassium iodide.

After iodine feeding for various periods, the animals were injected intraperitoneally with ANTU dissolved in anhydrous propylene glycol.

Results. The effect upon the resistance of rats to ANTU of feeding iodine *ad libitum* at different concentrations in the drinking water and in the diet is shown in Table I.

TABLE I.
Relationship of Iodine Ingested in the Diet to Resistance of Rats to ANTU.

Avg I_2 intake mg/kg	ANTU mg/kg	Mortality	LD_{50} mg/kg
	4	0/5	
Purina Chow control	6	3/5	ca 6.5
	7	4/7	
	8	2/2	
	3	0/4	
	5	4/11	
0.2	7	2/7	" 7.0
	8	3/4	
	9	4/4	
	12	4/4	
	20	1/3	
	23	1/6	
20.8 (7.6-29.0)	26	1/4	" 29
	29	5/9	
	32	6/8	
	40	3/3	
	20	0/3	
	23	0/2	
	26	0/3	
	28	0/5	
44.8 (31-81.6)	32	1/7	" 46
	35	1/5	
	40	2/6	
	50	3/4	
	60	5/5	

After a 1-2-day feeding period a difference was noted in the protection provided by diluted Lugol's solution, potassium iodide in the water, or potassium iodide given in the diet. This difference was directly related to the quantity of iodine the animals had ingested. Those animals eating the greatest amount of iodine during the period were the most resistant to the rodenticide. It was noted that the intake of Lugol's solution at the concentrations used was 9 cc per day compared with an average intake of 16 cc per day by controls. Animals which drank water containing potassium iodide consumed an average of 14 cc per day. Animals receiving potassium iodide in the diet ate an average of 12 g of the food per day as compared with

[2] Griesbach, W. E., Kennedy, T. H., and Purves, H. D., *Nature*, 1944, **154**, 610.

[3] DuBois, K. P., and Erway, W. F., personal communication.

[4] Hubbel, R. B., Mendel, L. B., and Wakeman, A. J., *Nutrition*, 1937, **14**, 273.

13 g during the same period for the controls.

It will be noted that the dose of ANTU required to kill 50% of the animals (LD_{50}) was about 7.0 mg per kg for rats receiving the synthetic stock diet for 30 days. This value is not significantly different from an LD_{50} of 6.5 mg per kg for animals eating Purina Laboratory Chow for at least 3 weeks.

The rats receiving increased amounts of iodine in food and water were divided into 2 groups according to the quantity of iodine consumed. The average iodine intakes for the 2 groups expressed as mg iodine were 20.8 and 44.8 mg per kg. The LD_{50} for the group of animals which had ingested an average of 20.8 mg per kg of iodine during a 1-2-day feeding period was 29 mg per kg of ANTU, while the LD_{50} for animals having an average intake of 44.8 mg per kg of iodine over the feeding period was 46 mg per kg of ANTU. The animals were, therefore, able to tolerate some 4 to 7 times the amount of ANTU required to kill the controls. It is apparent that within these limits of iodine intake, the amount of iodine ingested over a 1-2-day feeding period increases the resistance of rats to the rodenticide.

Summary. This study has shown that iodine given either as Lugol's solution or as potassium iodide protected rats against ANTU poisoning. The ability of the animals to tolerate ANTU was proportional to the quantity of iodine which had been ingested over a 1-2-day period.