sure. The blood pressure usually fell about 10 to 20 mm Hg following doses of 10 mg/kg and about 30-40 mm Hg following doses of 20 mg/kg. Such hypotensive effects were, in most instances, of short duration and were occasionally followed by slight hypertensive effects when a tachycardia was reverted.

Effect of Procaine Amide on the "Cat Unit" of Ouabain. Procaine amide failed to increase the lethal dose of ouabain in cats. In 5 experiments, the drug was infused concomitantly with the cardiac glycoside at rates of from 2 mg/cc/min. (total dose of 23 mg/kg) to 20 mg/cc/min. (total dose of 157 mg/kg). In 2 other experiments, procaine amide was injected repeatedly in a 10% solution in doses of 10 and 20 mg/kg (total doses of 70 and 80 mg/kg) beginning with the first appearance of ventricular tachycardia and continuing until the end of the experiment. The ouabain was constantly infused as in the other cat experiments. The "cat unit" values, as determined with ouabain and procaine amide, were compared with the values obtained with a previously conducted series of 11 cats in which ouabain alone was used. The value for the ouabain-procaine amide "cat unit" as well as the standard deviation was the same as that obtained with the ouabain series (0.11 mg/kg SD$\pm$0.015).

Summary. Rapid intravenous administration of procaine amide was found effective in reverting ventricular tachycardia, produced in dogs by large doses of cardiac glycosides, to normal sinus rhythm. In most instances, the reversion was temporary and additional injections of procaine amide were necessary in order to maintain the normal rhythm. Such additional injections, repeated several times in these experiments, did not produce electrocardiographic signs of cumulative toxicity.

Although procaine amide effectively reverted ventricular tachycardia in the dog experiments, the same agent failed to increase the lethal dose as determined by limited "cat unit" studies. A similar relation was noted by Emerson in studies on procaine(6) and by Stanbury and Farah(7) in studies on magnesium.

The development of slow idioventricular rhythms and cardiac arrest in several experiments following procaine amide administration demonstrates a danger of drug termination of digitalis-induced ventricular tachycardia. As Gold(8) has emphasized, complete A-V heart block concomitantly produced by the digitalis may be masked in the electrocardiogram by the ventricular tachycardia and the abolition of the latter arrythmia by quinidine or other drugs may result in ventricular arrest.

We are obliged to Dr. P. C. Gazes for his review of the electrocardiographic interpretations.

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Effect of Vitamin B_{12}, Folic Acid, and Nicotinamide on Urinary Coproporphyrin Excretion in Photosensitized Rabbits.* (18913)

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Nicotinic acid has been claimed to cause a decrease in the urinary coproporphyrin in certain pathologic states. Thus Spies and co-workers reported marked diminution in patients with pellagra(1) and in painters(2).

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The method(3) employed, however, was subsequently shown to be nonspecific and correlated much more with urorosein than with porphyrin(3-7).

Boulin *et al.*(8) administered nicotinamide (0.5 g orally and 0.4 g intramuscularly per day) for 8 days to a patient with coproporphyrinuria and a history of alcoholism. A decrease from 646 mg in 24 hours to a normal level was reported. The same investigators studied a case of porphyria before and after administration of nicotinamide (0.5 g orally per day) and noted a decrease in the amount of uroporphyrin excreted from 2.88 mg to 1.056 in 24 hours. No definite clinical improvement was observed. The decreases in both of these instances are of doubtful significance because of the well known spontaneous fluctuations in porphyrin excretion in both conditions. A somewhat more convincing effect was described by Scolari(9) in several individuals receiving antiluetic arsenical therapy. Here it appeared that significant decreases in urinary coproporphyrin, primarily elevated following the arsenic, resulted from the administration of nicotinamide.

A relation of folic acid to porphyrin metabolism has been suggested by several investigators. Steinkamp *et al.*(10) reported an increase in urinary coproporphyrin in cases of pernicious anemia after folic acid therapy. This report, however, was not based on a quantitative procedure. Totter and coworkers(11), studying the influence of folic acid on glycine and porphyrin metabolism in rats, concluded that the folic acid significantly increased the fecal and probably the urinary porphyrin excretion of animals fed a purified diet. Although of fundamental interest, it should be noted that the principal porphyrin of rat feces is protoporphyrin, derived from the Harderian glands(12).

Kvasnickova(13), administered 15 mg of folic acid daily to a patient suffering from a cutaneous form of porphyria and who was excreting 200 mg each of uroporphyrin and coproporphyrin per liter of urine. She reported it to be highly effective; it was stated that the skin manifestations disappeared, the pigmentation cleared up and the general feeling of well-being improved; the uroporphyrin disappeared from the urine entirely. Castex, Lopez Garcia and others(14) observed two cases of porphyria, one of abdominal and another of cutaneous type, in which there was said to be a complete return of urinary coproporphyrin excretion to the normal level after the administration of 20 mg of folic acid daily. With this a complete disappearance of clinical symptoms was also noted. However, serial data were not given, and the possibility of spontaneous remissions was not excluded.

In a previous paper(15) it was shown that the photodynamic effect of Rose Bengal and ultraviolet light produces a marked increase in urinary coproporphyrin in rabbits within 24-48 hours. The purpose of the present investigation was to study the effect of folic acid, nicotinamide and vitamin B_{12} on the urinary coproporphyrin excretion under these circumstances.

Methods. Adult rabbits of either sex were

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14. Castex, M. R., Garcia, A. L., and Zelasco, *Prensa Med. Argent.*, 1948, v35, 907.

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TABLE I. Effect of Folic Acid (F.A.), Vitamin B_{12}, and Nicotinamide (N.A.) on Coproporphyrinuria Following Rose Bengal and Ultraviolet Irradiation.

No. rabbits	Day	Coproporphyrin, μg per day 0*	1	2	3	Substance administered	
5	7	163	72	22			
1	7	48	9	9		F.A.	5 mg
1	6	45	34	34		F.A.	15 mg
3	7	10	8	8		F.A.	45 mg
1	5	15	5	13		B_{12}†	5 μg
2	7	12	11	10		B_{12}	10 μg
2	9	6	27	13		B_{12}	15 μg
1	3	6	19	4		B_{12}	30 μg
2	9	18	17	15		Cryst. B_{12}‡	15 μg
3	12	46	60	23		N.A.	50 mg
1	9	11	209	20		N.A.	200 mg
2	8	28	64	33		N.A.	300 mg
3	6	22	19	8		F.A.	5 mg
						B_{12}‡	5 μg

* A control analysis of urinary coproporphyrin excretion was carried out on the day preceding the administration of Rose Bengal and ultraviolet light. Mean values are given where more than 1 rabbit was employed.

† Rubramin (Squibb).

‡ Crystalline vit B_{12} (Merck).

given Rose Bengal intravenously in physiological saline solution, in an amount of 100 mg/kg body weight.

The ultraviolet light exposure of the rabbits was the same as previously described(15).

The concentration of total urinary coproporphyrin (UCP) was determined daily by the method of Schwartz and co-workers(16). It should be emphasized that this method relates in the main to preformed porphyrin, and the values are therefore smaller than those obtained with a new and more sensitive procedure which includes whatever porphyrin is excreted as chromogen(17,18).

In each experiment the folic acid and the vit. B_{12}‡ were injected 10 minutes before the Rose Bengal. In those rabbits receiving 200-300 mg nicotinamide, the dosage was divided in 3 equal parts and given the same day on which the Rose Bengal was given. The first dose of nicotinamide was given between 8 and 9 A.M., the Rose Bengal between 10 and 11 A.M. and the second and third doses of nicotinamide between 12 and 2 P.M., and 4 and 6 P.M. respectively. The other rabbits received the drug 10 minutes before the Rose Bengal.

Results. The results are summarized in Table I in terms of the control value (Day 0) and the values for the first 3 days following treatment. Mean values are listed where more than one rabbit was employed at a given dose level. Though analyses were done for 6 days, the data for days 4-6 are omitted from the table since values for all groups returned to the normal range in this period.

In 5 control animals injected with Rose Bengal and exposed to ultraviolet light the range of peak values during the subsequent 24 hours was from 110 to 300 μg/24 hr. (These rabbits have been discussed in detail elsewhere)(15). This may be compared with a normal range in untreated rabbits of 3.2 to 14.2 μg/24 hr (mean = 7.3 μg/24 hr) as determined in a series of 50 rabbits.

Folic acid and B_{12} were very effective in limiting or preventing the usual coproporphyrinuria. With a dose of 45 mg of folic acid no increase in urinary coproporphyrin oc-

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‡ Rubramin solution was provided through the courtesy of E. R. Squibb and Co. In certain experiments, as noted in Table I, crystalline B_{12} was used. This was provided through the courtesy of Merck and Co.

curred after Rose Bengal and ultraviolet light. The 5 and 15 mg doses, however, did not completely inhibit the effect. In general, vit. B_{12} in a dose from 5 to 35 μg almost completely prevented the increase of urinary coproporphyrin, while the combination of folic acid and B_{12} exhibited no special advantage.

Nicotinamide has a significant effect in reducing the coproporphyrinuria (type III) caused by the photodynamic action of ultraviolet light. Nevertheless, it is evident that the increases are only partially prevented.

Summary and Conclusions. The administration of large amounts of folic acid inhibited the increase of the urinary coproporphyrin in rabbits given Rose Bengal and exposed to ultraviolet light. The administration of small amounts of vit. B_{12} had the same effect. The combination of folic acid and vit. B_{12} had no advantage over either substance given separately. The administration of nicotinamide in large amount produced a significant but only partial inhibition.

In view of the fact that nicotinamide, folic acid, and vit. B_{12} are all intimately related to cellular metabolism, it seems highly likely that the marked increases of urinary coproporphyrin under these experimental conditions are likewise so related, but whether to the metabolism of the bone marrow, or some other system of cells is not clear. Further studies of these relationships are in progress.

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Effect of Total Body X-Irradiation on Glutathione Levels in Rats.* (18914)

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Recently the theory has been advanced that a relationship exists between x-irradiation effects and sulfhydryl groups. Barron(1) reported that irradiation decreases the metabolism of substances requiring sulfhydryl enzymes and other investigators that changes in glutathione levels affect the sensitivity of animals to irradiation,(2,3). Therefore, it appeared desirable to investigate glutathione levels following irradiation.

Method. Male and female Sprague-Dawley rats weighing from 170 to 275 g were used. Reduced glutathione in blood and liver was determined(4). Total glutathione was measured by treating the filtrates with H_2S at pH 8, acidifying, removing H_2S with CO_2, and determining total reduced glutathione. The difference between the glutathione before and after H_2S reduction was considered to represent oxidized glutathione. Known solutions gave good recoveries. Hematocrit values were obtained using 0.01 cc of blood(5). Somogyi's method was used to determine blood glucose(6). Reduced glutathione values on 0.2 cc of whole blood were determined one week before irradiation. Analyses one week apart showed no significant variation. No glutathione was found in rat plasma before or after irradiation. Red blood cell glutathione concentrations were calculated by

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