

tory depressant factor in gastric juice is identical with that factor described as "urogastrone" and obtained from the urine. Gray² reported the consistent recovery of this gastric secretory depressant factor from urine by precipitation with benzoic acid, extraction with acid-aqueous-acetone and reprecipitation with alcohol-aniline-acetone.

One gram quantities of 80% alcohol precipitates of human gastric juice, 300 to 500 mg of which, as stated, always produced prolonged achlorhydrias in the stimulated gastric pouch, were extracted twice with 20 cc of 70% acid acetone (1 cc concentrated HCl per 100 cc solution) and these combined. The latter were then treated with one volume of absolute alcohol, 3 cc of aniline and 3 volumes of absolute acetone (Gray's meth-

od); this afforded a flocculent precipitate which was separated by centrifugation and dried. This precipitate weighing about 300 mg was found to be soluble in slightly acidified normal saline solution, and when injected into pouched dogs failed to produce achlorhydria on 8 separate occasions.

The residue of the original alcohol precipitate of gastric juice which was insoluble in 70% acid acetone was suspended in 20 cc of slightly acidified normal saline and injected into pouched dogs. In each of 6 separate experiments achlorhydria of the stimulated pouch, lasting over 2½ hr, obtained.

Conclusions. A method for extraction of the gastric secretory depressant factor from urine (urogastrone) does not extract the gastric secretory depressant from an alcohol precipitate of human gastric juice, hence evidence is offered that these two factors are not identical.

² Gray, J. S., *et al.*, *Endocrinology*, 1942, **30**, 129.

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Observations on the Intravenous Injection of Gelatin for Nutritional Purposes.*

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In view of the recent interest in parenteral injection of nitrogenous nutriment, the question of nutritive value of gelatin injected intravenously is being investigated. Observations of this type apparently have not been hitherto recorded. Such a study is complicated by the heterogeneous nature of gelatin. The sample employed in this study was designated as 3 Cu, and consisted of a light brown moderately coarse powder. Aqueous solutions were prepared by adding 120 to 125 g to 1000 cc of hot water. This was autoclaved at 15 pounds pressure and 250°F for 45 min prior to injections in animals. Total nitrogen determinations were made on each sample and this data employed to calculate

nitrogen intake. Non-protein nitrogen varied widely in the several liter samples prepared, the maximum in one sample being 570 mg % but in most others it was under 100 mg %. This gelatin was found to contain no cysteine or tryptophane and .8% tyrosine (analyses by Mr. Carter Johnston, Department of Biochemistry).

Dogs depleted of protein stores by maintenance on a Weech diet¹ for about one month received 150 cc of the gelatin solution (which was approximately 12% by weight) a day intravenously as the sole source of protein. During the injection period Weech diet was afforded *ad libitum* but the appetite varied widely. Urine (and feces) was collected every 24 hr and the daily loss of

* This work was conducted under a grant from the Edible Gelatin Manufacturers' Research Society.

¹ Weech, A., *et al.*, *J. Exp. Med.*, 1935, **61**, 299. (505 g of diet contains 1.23 g N.)

TABLE I.
Nitrogen Balance in Dogs Receiving Intravenous Injections of Gelatin.

Dog	No inj.			Inj. period*				
	No. days	N loss, g	Avg daily N loss, g	No. days	Total N inj., g	Total N loss, g	Avg daily N bal., g	N balance total period, g
352 (4.3 kg)				7	18.5	10.17	+1.2	+ 8.33
354 (6.4 kg)								
Exp. I	8	4.58	.57	8	27.9	14.32	+1.69	+13.58
Exp. II	5	2.92	.58	7	18.5	17.25	+ .18	+ 1.25
357 (5.6 kg)	7	4.77	.68	10	28.00	30.58	— .26	— 2.58
358 (5.6 kg)								
Exp. I	5	3.38	.68	15	41.70	41.30	+ .03	+ .40
Exp. II	5	1.28	.26	7	18.30	11.02	+1.04	+ 7.28

* Each dog received 150 cc of 12% gelatin solution daily.

nitrogen determined. This was compared with nitrogen intake as represented by the gelatin injections. Results are summarized in Table I. In 5 of the 6 experiments a positive nitrogen balance or a nitrogen equilibrium was obtained; in one instance there was a negative balance. In the latter (Dog 357) however, the daily net loss of nitrogen was less than in the period during which no injections of gelatin were received.

The fact that a positive nitrogen balance or equilibrium was obtained, does not indicate necessarily a utilization of gelatin for body or plasma protein synthesis or for energy. At least some gelatin remains un-

changed and circulates in the plasma since samples of blood withdrawn 24 hr after an injection gel when placed in the ice box, and after several daily injections, some samples of urine also geled at 8°C. On the other hand it would appear that some of the gelatin is broken down by the organism since, as shown in Tables I and III, after daily injections were begun the nitrogen output exhibited a substantial increase and this was for the most part in the form of non-protein nitrogen.

When 2, 2.5 and 5% aqueous solutions of gelatin were analyzed as "blood plasma" for plasma proteins by the semi-micro Kjeldahl

TABLE II.
Plasma Protein Changes Resulting from Intravenous Injection of Gelatin.

Dog		Hematocrit, %	N. P. N., mg %	Plasma prot., g %	A/G
352	Before injection	44.5	18.2	4.52	2.09/2.43
	After 6 injections*	32	50	6.54	2.25/4.29
	4 days after last injection	38	28	5.54	2.03/3.51
	8 days after last injection	32	22	4.93	2.56/2.33
354	Before injection	37	17.5	4.73	2.65/2.08
	After 9 injections	30	26	6.10	1.52/4.58
	7 days after last injection	32	17	5.35	1.68/3.67
358	Before injection	48	23	4.22	2.41/1.81
	After 14 injections	23	—	5.79	2.65/3.14
	7 days after last injection	30	34	5.18	2.23/2.95
	14 days after last injection	28	26	4.30	2.22/2.08
356	Before injection	40	21	3.87	1.56/2.31
	After 5 injections	25	32	4.88	1.84/3.04
353	Before injection	49	17	3.90	2.15/1.75
	After 3 injections	38	322†	8.63	2.71/5.92

*Daily injection of 150 cc of 12% gelatin solution.

†Dog was uremic, died 24 hours after last injection.

TABLE III.
Showing Increased Urinary N Output During Period of Intravenous Injection with Gelatin.
Dog 358. On Weech Diet. (Partial data.)

	No injections				Daily inj. 150 cc gelatin solution 6th to 20th day				No injection after 20th day			
Days	1	2	3	4	7	8	9	10	21	22	23	24
Urine vol., cc	280	240	250	160	240	380	400	300	200	100	140	120
Total N excreted, g	.47	.61	.56	.44	2.90	3.71	3.98	2.03	1.81	.76	1.06	.75
Total N.P.N. excreted, g					2.88	3.61	3.80	1.93	1.66	.68	.96	.65

method for total nitrogen, and precipitation with 21% sodium sulphite carried out as for separation of albumin from globulin, it was found that most of the gelatin precipitated as "globulin." For example, a 2.1% aqueous solution of gelatin yielded .68% "albumin" and 1.41% "globulin." A 5.33% solution of gelatin yielded 1.72% "albumin" and 3.61% "globulin." In another series of experiments gelatin was added to dog plasma low in proteins and the greater part of the gelatin was precipitated with the globulin fraction.

In the protein depleted dogs, the injections of gelatin resulted in a rather rapid and appreciable rise in plasma protein, this being in a large measure due to the presence of circulating gelatin. From the above mentioned observations it would therefore appear that the increase in "plasma proteins" thus brought about would constitute essentially an increase in the "globulins." Some of the data illustrating this is shown in Table II. Following the cessation of injections the nitrogen output fell appreciably and there was a gradual fall in the plasma protein level, the decrease being again principally the globulin fraction with relatively less fluctuation in the albumin fraction (with exception of Dog 354).

The animals tolerated the injections quite well. Occasionally there was emesis; in one animal marked erythema about the head and over the extremities developed after each in-

jection. Severe reactions were not observed. Elevations in temperature were likewise not observed. Since the animals were depleted of proteins, being on a very low protein diet, they were not in good condition at the onset of the experiments. Throughout the injection period this diet was available in unlimited quantities but as stated they ate poorly and, although maintained for periods in positive nitrogen balance or in nitrogen equilibrium, they continued to lose weight and their condition deteriorated. The latter would be expected from maintenance on an incomplete diet.

Summary. 1. A positive nitrogen balance or nitrogen equilibrium may be maintained in protein-depleted dogs with a gelatin solution injected intravenously as practically the sole source of nitrogen.

2. Elevation of depressed blood plasma protein levels may obtain from intravenously administered gelatin as practically the sole source of nitrogen. The increase is apparently in the globulin fraction and represents to a large extent circulating gelatin. It was found that most of the gelatin used above in aqueous solution, or if added to plasma *in vitro*, precipitates with 21% sodium sulphite (thus behaving like a "globulin").

3. At least a portion of intravenously injected gelatin appears to be metabolized since there is a substantial increase in non-protein nitrogen excretion following injections.