Results. The results are tabulated in terms of average daily nitrogen intake and average daily nitrogen excretion in the urine.

Dog No. 4, Table I, lost 2.16 g urinary nitrogen, or 65.4% of the intake after infusion of protein hydrolysate intravenously. 1.84 g urinary nitrogen or 55.6% of intake was lost when protein hydrolysate was given orally. 1.37 g urinary nitrogen, or 41.5% of intake was lost when calcium caseinate was given orally.

Dog No. 5, Table II, lost 1.83 g urinary nitrogen, or 51.2% of the intake after infusion of protein hydrolysate intravenously. 1.34 g of urinary nitrogen, or 37.3% of intake was lost when protein hydrolysate was given orally. 0.96 g urinary nitrogen, or 26.8% of the intake was lost when calcium caseinate was given orally.

Dog No. 6, Table III, lost 2.61 g urinary nitrogen, or 70% of intake when protein hydrolysate was given intravenously. 2.02 g urinary nitrogen, or 53.6% of intake was lost when protein hydrolysate was given orally. 1.64 g of urinary nitrogen, or 44% of the intake was lost when calcium caseinate was given orally.

Summary. It has been observed that with the oral ingestion of native protein (Casec), there is the greatest nitrogen retention; with the protein hydrolysate enterally there is less nitrogen retention; and with protein hydrolysate intravenously there is least nitrogen retention.

16525

Nitrogen Retention after Injection of Protein Hydrolysate into the Portal and Systemic Veins.*

YOSHIO SAKO,† ARNOLD J. KREMEN, AND RICHARD L. VARCO.
From the Department of Surgery, University of Minnesota.

Numerous reports[1-3] suggest that positive nitrogen balance can be obtained by the parenteral administration of essential amino acid mixtures or protein hydrolysates. Regularly there is a sharp rise in the total urinary nitrogen following the infusion of these mixtures. Under these circumstances, theoretically, significant quantities of amino acids might be lost through renal excretory mechanisms before circulation through, and protein fabrication in, the liver could take place.

Method. Mongrel dogs were used in this study. Dogs No. 3, 4, and 5 were placed on a low protein diet consisting essentially of potatoes, apples, carrots, and sucrose. The diet was fortified with substantial quantities of vitamin B complex, cod liver oil, choline, and minerals. Caloric intake was limited to 40 calories per kg body weight daily. The animals were not studied until a weight loss of 30% had been reached. Dog No. 6 was placed on the low protein diet and the study begun prior to any significant weight loss. Caloric intake in this dog was similarly limited to 40 calories per kg of body weight.

Prior to the beginning of the study the animals were operated upon and a polythene tubing with an outside diameter of 1 millimeter and an inside diameter of 0.5 mm was threaded into a radicle of the splenic vein until it reached the entrance to the portal vein. The tube was brought to the outside through a separate stab wound. During infusion a blunt end 25 gauge needle was inserted into the tube. Four % sodium citrate solution was used to irrigate and fill the tube daily. A small glass plug was kept in the needle when not in use

* The researches presented here were supported by grants of the Graduate School of the University of Minnesota.

† Fellow of the United States Public Health Service.

1 Elman, R., *Ann. Surg.*, 1940, **112**, 594.

2 Brunschwig, Al., Clark, D. E., and Corbin, N., *Ann. Surg.*, 1942, **115**, 1091.

3 Kremen, A. J., *Surgery*, 1948, **23**, 92.

TABLE I.
Nitrogen Loss After Administration of Protein Hydrolysate into the Portal and Systemic Veins. Dog. No. 3.*

No. of days	N intake, g		N output, g		Avg daily diff.	Urine amino acid N, g	
	Total	Avg daily	Total	Avg daily		Total	Avg daily
7, control	3.35	0.48	4.15	0.59	—0.12	1.61	.23
5, Amigen† through portal vein	9.43	1.89	7.22	1.44	+0.44	1.72	.34
9, control	4.30	0.48	5.33	0.59	—0.11	0.88	.10
5, Amigen through peripheral vein	9.43	1.89	6.54	1.31	+0.58	1.02	.20

* Original wt, 13.55 kg; 33.6% wt loss at start of exp.; 44.0% wt loss at termination.
† Casein hydrolysate equivalent to 1 g protein per kg body wt.

TABLE II.
Nitrogen Loss After Administration of Protein Hydrolysate into the Portal and Systemic Veins. Dog No. 4.*

No. of days	N intake, g		N output, g		Avg daily diff.	Urine amino acid N, g	
	Total	Avg daily	Total	Avg daily		Total	Avg daily
7, control	3.35	0.48	2.53	0.37	+0.11	—	—
5, Amigen† through portal vein	16.57	3.31	9.91	2.00	+1.33	1.78	0.36
9, control	4.30	0.48	5.09	0.57	—0.09	1.05	0.12
5, intravenous Amigen	16.57	3.31	10.82	2.16	+1.15	2.14	0.43
9, control	4.30	0.48	7.81	0.87	—0.39	1.52	0.17

* Original wt, 13.55 kg; wt loss at start of exp., 33.6%; wt loss at end of exp., 37.0%.
† Casein hydrolysate equivalent to 2 g protein per kg body wt.

and the abdomen was protected with a heavy canvas binder.‡

Beginning one week post-operatively, urine was collected daily as a control period. Specimens were analyzed quantitatively by the macro Kjeldahl[4] method for total nitrogen. The amino acid nitrogen was determined by the method of Frame.[5] Each batch of diet and protein hydrolysate was analyzed for total nitrogen by the macro Kjeldahl method. One g of protein as protein hydrolysate (Amigen§) per kg of body weight was infused into Dog No. 3 and 2 g of protein as protein hydrolysate per kg body weight was infused into Dogs No. 4, 5, and 6. About 220 cc (on the average) of 10% solution of protein hydrolysate was diluted with distilled water to make a final volume of 500 cc and this was given over a 6 hour period, care being taken to maintain a uniform rate of infusion. After 5 to 6 days of infusion through the portal vein, the dogs were allowed to rest 9 days during which time urine was collected and analyzed for total urea, creatinine, and amino acid nitrogen. Protein hydrolysate in the same volume and amount was then given intravenously through a vein in the foreleg over a 6 hour period. For the most part direct needling was used but when the animals were too restless, a polythene tubing was inserted into the vein. In no instance was there any untoward reaction noted. Dogs No. 5 and 6 had rectal temperatures taken after the hydrolysate was given through the portal vein and no febrile reaction was noted.

Results. The results are tabulated in terms of average daily nitrogen intake and average daily nitrogen excretion for each period.

Dog No. 3, Table I, lost 1.44 g of total urinary nitrogen or 76.7% of the total nitrogen

‡ Dog No. 4 autopsied at conclusion of the study showed no thrombus or phlebitis from prolonged use of an indwelling polythene tube. In Dogs 5 and 6 the tube was removed without subsequent bleeding and the dogs have remained healthy.

4 Peters, J., and Van Slyke, D. D., *Quant. Clin. Chem.*, 1931, **2**, 602.

5 Frame, E., *et al.*, *J. Biol. Chem.*, 1943, **199**, 225.

§ Enzymatic casein hydrolysate kindly supplied by Mead Johnson and Co., Evansville, Ind.

TABLE III.
Nitrogen Loss After Administration of Protein Hydrolysate into the Portal and Systemic Veins
Dog No. 5.*

No. of days	Intake N, g		Urine N, g		Avg daily diff.	Urine amino acid N, g	
	Total	Avg daily	Total	Avg daily		Total	Avg daily
7, control	3.35	0.48	6.89	0.98	—0.51	0.18	0.03
6, Amigen† through portal vein	21.49	3.58	15.77	2.63	+ .95	1.10	0.18
8, control	3.82	0.48	12.18	1.52	—1.04	1.21	0.15
6, Amigen intravenously	21.49	3.58	1.00	1.83	+1.75	2.08	0.35
8, control	3.82	0.48	4.96	0.62	—0.14	0.90	0.11

* Original wt, 14.7 kg; 34% wt loss at start of exp.; 35.4 wt loss at end of exp.
† Protein hydrolysate equivalent to 2 g protein per kg body wt.

TABLE IV.
Nitrogen Loss After Administration of Protein Hydrolysate into the Portal and Systemic Veins.
Dog No. 6.*

No. of days	Intake N, g		Urine N, g		Avg daily diff.	Urine amino acid N, g	
	Total	Avg daily	Total	Avg daily		Total	Avg daily
6, control	2.87	0.48	17.53	2.92	—2.44	0.63	0.11
6, Amigen† through portal vein	22.45	3.74	15.78	2.63	+1.11	2.79	0.46
8, control	3.82	0.48	8.06	1.01	—0.53	1.04	0.13
5, Amigen intravenously	18.71	3.74	13.05	2.61	+1.13	2.41	0.48
9, control	4.30	0.48	9.14	1.01	—0.54	0.98	0.11

* Weight, 10.2 kg; no wt loss at start of exp.; 14.5% wt loss at end of exp.
† Casein hydrolysate equivalent to 2 g protein per kg body wt.

intake during infusion of protein hydrolysate into the portal circuit. The urine amino acid nitrogen lost was 0.34 g or 18.4% of the total nitrogen intake. There was 1.30 g urinary nitrogen excretion or 69.3% of intake when protein hydrolysate was given into a peripheral vein. The urine amino acid nitrogen was 0.20 g or 10.9% of total nitrogen intake.

Dog No. 4, Table II, lost 1.98 g of total urinary nitrogen or 60% of the total nitrogen intake during infusion of protein hydrolysate into the portal circuit. The urine amino acid nitrogen lost was 0.36 g or 10.7% of the total nitrogen intake. There were 2.16 g of urine nitrogen or 65.5% intake when protein hydrolysate was given into a peripheral vein. The urine amino acid nitrogen lost was 0.43 g or 12.9% of the total nitrogen intake.

Dog No. 5, Table III, lost 2.63 g urinary total nitrogen or 73.7% of intake during infusion of protein hydrolysate into the portal circuit. The urine amino acid nitrogen lost was 0.18 g or 5.1% of total nitrogen intake. There were 1.83 g of urine nitrogen or 51.4% of intake when protein hydrolysate was given into a peripheral vein. The urine amino acid nitrogen lost was 0.35 g or 9.7% of the total nitrogen intake.

Dog No. 6, Table IV, lost 2.63 g urinary nitrogen or 67.6% of intake during infusion of protein hydrolysate into the portal circuit. The urine amino acid nitrogen lost was 0.46 g or 12.4% of total nitrogen intake. There were 2.61 g urinary nitrogen or 69.7% of intake when protein hydrolysate was given into a peripheral vein. The urine amino acid nitrogen lost was 0.48 g or 12.9% of total nitrogen intake.

Conclusion. (1) No significant difference in the total nitrogen retention has been noted after infusion of protein hydrolysate into the portal or the systemic venous systems. (2) Polythene tube appears well tolerated and remains patulous for prolonged intravenous therapy in dogs.