44 mg I/min/1.73 M^2 on 3 normal subjects; it is reached at a plasma level between 15 and 20 mg I per 100 cc and is unaffected by presence of inulin. This value is somewhat lower than Smith's latest figure of 57. The fall in Tm seen in Fig. 2 at the highest plasma I levels was obtained in experiments where a single large dose of D (35 to 60 cc) was given within 10 minutes and urine collections begun 5 minutes later. This transitory fall in Tm is presumably due to a renal vasoconstriction or to transitory tubular disturbance and is not seen when plasma D is maintained at a high constant level for some time before beginning urine collections, *i. e.*, in the latter case Tm at 50 mg % plasma I is not lower than at 20 mg %.

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Serum Albumin Regeneration Following Intravenous Amino-Acids (Hydrolyzed Casein) in Hypoproteinemia Produced by Severe Hemorrhage.*

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Acute hypoproteinemia was produced in fasting dogs by a single severe hemorrhage; the details have been described elsewhere.[1] One hour later injections were started, intravenously, which lasted 3 hours.[2] No symptoms were produced by this treatment. The solution injected consisted of 10% each of a mixture of amino-acids and dextrose. The dose varied with the weight of the dog, *i. e.*, 3.5 g per kilo of each (amino-acids and dextrose). The amino-acid mixture was obtained from casein by enzymic digestion.† As shown by preliminary observations it contained all of the essential amino-acids in that it required no additions in order to maintain nitrogen balance in dogs. It was not as completely digested as the acid hydrolysate of casein which was used in our previous experiments.[2] Thus, only 70% of its nitrogen could be accounted for an amino-acid nitrogen; the rest probably occurred as dipeptides.

In control experiments[1] it was observed that no change in the

* Aided by a grant from the Louis B. Beaumont Fund.

1 Elman, R., *Am. J. Physiol.*, Jan., 1940.

† Product 92-Z kindly furnished by the Mead Johnson & Company, Evansville, Ind.

2 Elman, R., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 867.

serum albumin or globulin occurred from the first to the sixth hour after a standard hemorrhage and replacement with Ringer's solution. In the present experiments, however, a definite increase from 2.60 to 2.95 g % in the albumin fraction was observed. That this was not due to a concentration of the plasma was indicated by two findings: first, that the hematocrit decreased indicating a dilution rather than a concentration; moreover, the magnitude of this dilution was the same as previously reported in the controls.[1] Secondly, the globulin fraction remained relatively unchanged indicating that mechanical alterations in the plasma volume were probably not responsible for the increase in the albumin.

From these considerations it is inferred that the injected amino-acid mixture was utilized by the body in the rapid regeneration of serum albumin. The magnitude of the change was not great; it is suggested that this is probably due to at least two factors. First, it is probable that under the stress of an acute hemorrhage amino-acids are drawn upon from all tissues and this deficit must be met. There is evidence, moreover, which will be described in a subsequent communication, that large amounts of nitrogen are actually lost in the urine during the course of a severe hemorrhage. Second, the amino-acid composition of casein is considerably different from serum albumin in that a number of essential amino-acids are present in quite insufficient concentration, thus acting as limiting factors as far as the utilization gram for gram is concerned and requiring a much larger dose of casein in order to make up for the deficiency.

The methods used in the present experiments are described in another communication.[1] The findings in 6 animals are summarized in Table I. The change in serum albumin herein reported (.35 g %) compares well with the change in serum protein (.38 g %) previously reported with similar experiments in which a fortified acid hydrolysate of casein was used.[2]

TABLE I.

Changes in hematocrit in percent of whole blood (H), serum globulin in g % (Glob.) and serum albumin in g % (Alb.), one and six hours after hemorrhage and replacement.

	One-hr determinations			6-hr determinations		
Dog	H.	Glob.	Alb.	H.	Glob.	Alb.
F16	24.8	1.17	2.23	24.2	1.09	2.32
G5	29.2	1.84	2.12	26.8	1.48	2.71
G6	36.0	1.10	2.86	32.2	.87	3.21
27	53.9	2.56	3.00	50.3	2.65	3.24
28	44.3	2.19	3.03	41.7	1.90	3.62
30	44.5	2.19	2.36	44.5	2.47	2.59
Avg	38.5	1.84	2.60	36.7	1.74	2.95

Summary. The intravenous injection of a mixture of amino-acids (enzymic hydrolysate of casein) was followed in a few hours by a significant increase in the serum albumin concentration of fasting dogs rendered hypoproteinemic by a severe hemorrhage. Since the serum globulin concentration and the relative red cell volume both decreased, it is inferred that the increase in serum albumin concentration was due to a regeneration.

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Further Studies of Antigenic Properties of Bacteriophage.

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Although bacteriophage is antigenic, it has not been found possible to induce active anaphylaxis in guinea pigs with bacteriophage,[1] even when employing for the test-injection active purified bacteriophage-protein containing 2.6×10^{13} lytic units, (1.79 mg of specific protein,[2] equivalent to 5 liters of crude phage). In seeking another method of demonstrating the interaction of bacteriophage with its antibody *in vivo,* we attempted to utilize the Shwartzman test.

Four rabbits were sensitized by repeated injections of crude *B. coli* bacteriophage, and their sera, 10 days after the last (ninth) injection, were found to be capable (in a dilution up to 1:320) of neutralizing an equal volume of undiluted crude phage having a titer of 10^9 lytic units per cubic centimeter. Two of these rabbits were then prepared by the intracutaneous injection of 0.25 cc of meningococcal filtrate, kindly sent us by Dr. Shwartzman, and 24 hours later one of them received intravenously 5 cc of crude phage and the other 9.5 cc of freshly prepared active purified phage containing a total of 5.7×10^{13} active lytic units (or 3.42 mg of specific protein equivalent to 11.4 liters of crude phage).

The animal that had received crude phage responded within 3 hours with a typical reaction at the site of the preparatory injection, while the one that had received the purified phage had no reaction. This difference indicated that the reaction in the animal receiving

1 Bronfenbrenner, J., and Kalmanson, G. M., *J. Bact.*, in press.

2 Kalmanson, G. M., and Bronfenbrenner, J., *J. Gen. Physiol.*, 1939, **23**, 203.