the intradermal test injections (1 cc) only 2 showed a doubtful positive local reaction (Grade 1).

Comment. The absence of toxic effects following the transfusion of bovine serum albumin into human beings and into mice tends to substantiate our previous statement[1] that it is the globulins of bovine serum which are responsible for the toxicity of the whole serum. The results of the transfusion of bovine serum in human beings are promising from the viewpoint of its use as a substitute for blood. The absence of albuminuria following these transfusions possibly indicates that bovine serum albumin is utilized by the human being.

Summary. The intravenous administration of bovine serum albumin to 13 human beings has given encouraging results, inasmuch as no reactions were noted. The blood pressure was maintained at, or rose above, the initial level. Vasodepression was not observed. The significance of these results in relation to the use of bovine serum albumin as a blood substitute in human beings is discussed.

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A Study of the Effect of Desoxycorticosterone Acetate on Capillary Permeability.*

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The adrenal cortical hormones may increase the circulating plasma volume in adrenal insufficiency (1) by the control of renal function and (2) by the transfer of water and electrolytes to the blood stream from the tissues.[1] Whether these mechanisms operate by an alteration of capillary permeability is not known. The purpose of this communication is to report data bearing on this point.

The diffusion of dyes from the blood stream was utilized as a means of observing the capacity of desoxycorticosterone to influence the flow of fluids across the capillary membrane. Normal white rabbits were given one intravenous dose of one of 3 different dyes: trypan blue, brom phenol blue or patent blue V.† For each rabbit

* Aided in part by a grant from the Proctor Fund, Harvard Medical School.

1 Kendall, E. C., *Proc. Staff Meetings, Mayo Clinic*, 1940, **15**, 297.

injected with a definite dose of a given dye, a corresponding white rabbit, which had received desoxycorticosterone acetate‡ parenterally several hours in advance, was observed simultaneously. The rate of appearance of dye in the ears, mucous membranes, conjunctivae and skin of the abdominal wall was noted and compared with the controls.

Obvious delay in the appearance of trypan blue in these areas in animals under the influence of desoxycorticosterone acetate was noted. The difference was marked not only in the time of appearance but in the intensity of staining. Although there is no way of quantitating these differences, agreement was uniform as to the reality of the differences to 6 different observers, who rendered judgment without knowing which of the pair had received the hormone.

In the case of brom phenol blue the difference in time and intensity were in the same direction, though less marked.

No such striking difference was noted with patent blue V (and in a few instances with eosin and fluorescin). But a striking difference was noted in the time of disappearance of patent blue V, in that the rabbit which received hormone retained its greenish blue color for a perceptibly longer period in 3 out of 4 experiments (Table I).

The difference in staining of tissues under the influence of desoxycorticosterone acetate was not due to chemical alteration of the dye by the hormone because there was no difference in the concentration of dye (as measured by the photoelectric colorimeter) in samples of blood taken at intervals from the hormone-treated and untreated rabbits or *in vitro*, using horse serum or phosphate-buffered physiological saline solution (pH 7.4) with appropriate concentrations of desoxycorticosterone acetate and dye.

The specificity of desoxycorticosterone acetate in these reactions was shown by substituting testosterone propionate or progesterone, which are ketosteroids closely related to desoxycorticosterone in chemical structure, in three rabbits. These showed the same appearance time and intensity of staining with trypan blue as control rabbits. It is therefore clear that desoxycorticosterone acetate possesses an effect on the diffusion of dyes which is apparently specifically related

† These dyes, in the order named, possess increasing degrees of diffusibility: trypan blue a vital dye, being the slowest to appear in the tissues, while patent blue V, like eosin, is so rapidly diffusible that the normal animal usually becomes intensely blue before the injection of the dye solution is completed. The disappearance of these dyes from the tissues is of a corresponding order: patent blue V is completely excreted as a rule within an hour, while trypan blue remains fixed in the tissues for many days.

‡ Kindly furnished by Schering Corporation under the trade name "Cortate" and by the Ciba Co. under the trade name "Percorten."

TABLE I.

The Effect of Desoxycorticosterone Acetate on the Diffusion of Intravenously Injected Dyes in Rabbits.

Exp. No.	Dye (in distilled water)	Amt of dose in mg	Dye		Time of appearance of dye after injection		Time of disappearance of dye after injection	
			Amt, cc	Conc., %	Control	Hormone	Control	Hormone
1	Trypan Blue	1	2.5	1	immediate	40 min	10-14 days	10-14 days
2	" "	1	2	1	"	45 "	10-14 "	10-14 "
3	" "	1	3	1	"	a. 45 " b. 50 "	10-14 "	10-14 "
4	" "	5	2	1	8 min	a. 45 " b. 2½ "	— died 10 hr after inject.	10-14 "
5	" "	5	1	0.5	30 "	3 hr	10 days	10 "
6	Bromphenol Blue	2	3	1	30 "	60 min	5 "	5 "
7	" "	2	3	1	3 "	a. 12 " b. 12 "	5 "	5 "
8	Patent Blue V.	1	2	1	immediate	a. immediate b. "	3 hr	a. 2½ hr
9	" " "	5	1	1	"	"	½ "	1 "
10	" " "	10	1	0.5	"	5 min	20 min	1 "
11	" " "	10	1	0.3	"	3 "	40 "	1½ "
12	Eosin	1	2	5	"	a. 16 " b. 15 "	2-3 days	2-3 days
13	Fluorescin	2	1.8	10	"	immediate	1 hr	1 hr
14	"	5	1.6	10	"	"	1 "	1 "

to the $COCH_2OH$ radical attached to the phenanthrene ring.

In vitro experiments on the diffusion of these dyes showed no uniform effect from the presence of the hormone, but certain clear-cut differences appeared when the intact frog or the surviving frog's skin were used as diffusion membranes.

It is clear from the fact that trypan blue is not excreted by the kidneys that these dye phenomena cannot be related to renal function.

That this effect on the diffusion of dyes is not related to an alteration in capillary permeability is suggested by the following observations:

I. In 2 normal subjects the rate of disappearance of intravenously injected NaCNS from the blood stream was not altered by the intramuscular injection of 25 mg of desoxycorticosterone acetate 3 hours previously.

II. In 2 normal subjects the time of disappearance of an intracutaneous wheal produced by injecting physiological saline solution was not altered by the intramuscular injection of 25 mg of desoxycorticosterone acetate.

III. In 3 normal subjects the rate of appearance and the size of the wheal and flare at the site of injection of 1/10 cc of 1/1000 solution of histamine hydrochloride was the same before and 3 hours after the intramuscular injection of 25 mg of desoxycorticosterone acetate.

IV. In a case of nephrosis the average 24-hour loss of albumin in the urine was substantially the same for 10 days preceding and for 6 days during which a daily intramuscular dose of 25 mg of desoxycorticosterone acetate was administered.

V. In dogs the rate of absorption of water, isotonic sodium chloride or glucose from loops of ileum or colon was not altered appreciably by the intravenous injection of 5 mg of desoxycorticosterone.

These observations do not support the concept that desoxycorticosterone acetate has an effect on capillary permeability to water and electrolytes.

Desoxycorticosterone acetate produced no change in the concentration of plasma proteins in the following 3 subjects: (a) a normal person, (b) a patient with nephrosis, and (c) a patient with probable cirrhosis of the liver.

The negative effect of this hormone on the function of the normal capillary indicates that its positive effect, as in adrenal insufficiency and on the diffusion of dyes, is exerted elsewhere. Menkin[2] reported

[2] Menkin, V., *Am. J. Physiol.*, 1940, **129**, 691.

that the permeability of capillaries damaged by the local injection of irritants was altered, as indicated by the local diffusion of intravenously injected trypan blue, by the local injection of desoxycorticosterone acetate. We were unable to confirm these findings when this hormone was injected intravenously.

If the primary pathology in traumatic shock is an altered permeability of the capillaries, the foregoing observations are consistent with evidence recently presented by us that desoxycorticosterone acetate exerted no beneficial effect in shock following hemorrhage.[3]

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Fixation of Iodine by Thyroids of Rats Given Diets Deficient in Iodine.*

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Iodine fixation in the thyroids of rats given a goitrogenic diet was examined with the help of radio-iodine. One group of animals received Remington's diet No. 342,[1] modified after Steenbock and Black's diet No. 2965[2-5] by adding liver extract to improve growth, and by reducing the amount of calcium, so that the results could be ascribed to the low iodine content of the diet and not to the goitrogenic effect of calcium.[1] The amount of iodine estimated by the method of Matthews, *et al.*,[6] after destruction according to Kolnitz and Remington,[7] was found to be 19 μg per kilo. The animals ate

[3] Fine, J., Fischmann, J., and Frank, Howard A., *Surgery*, in press.

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[1] Remington, R. E., *J. Nutr.*, 1937, **13**, 223; Remington, R. E., and Levine, H., *J. Nutr.*, 1936, **11**, 343.

[2] Steenbock, H., and Black, A., *J. Biol. Chem.*, 1925, **64**, 263.

[3] Krauss, W. E., and Monroe, C. F., *J. Biol. Chem.*, 1930, **89**, 581.

[4] Thompson, J., *J. Nutr.*, 1932, **5**, 359.

[5] Levine, H., Remington, R. E., and von Kolnitz, H., *J. Nutr.*, 1933, **6**, 325.

[6] Matthews, N. L., Curtis, G. M., and Brode, W. R., *Ind. Eng. Chem.*, 1938, **10**, 612.

[7] Kolnitz, H. v., and Remington, R. E., *Ind. Eng. Chem.*, 1933, **5**, 38.