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Effects of Intravenous Administration of Dextran on Renal Function.*† (19460)

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Expansion of the plasma volume produced by the intravenous infusion of human albumin and plasma is usually associated with an increased rate of renal plasma flow and occasionally with increased rates of glomerular filtration(1-3). Since it has been demonstrated that partially hydrolyzed dextran is an effective plasma volume expander(4-6), a study has been made of the effects of the intravenous administration of this substance on various renal functions.

Methods. Thirteen World War II male veterans, ages 27 to 34, who were normotensive, afrebrile, and well hydrated and who had no evidence of renal disease, were studied at rest and in the fasting state. Since the presence of large amounts of dextran interferes with the determination of inulin in plasma and urine, glomerular filtration rate was measured by the endogenous creatinine clearance, using Hare's creatinine method(7). Para-aminohippurate clearance (C_{PAH}) and measurements of tubular excretory mass (Tm_{PAH}) were performed as described by Goldring and Chasis(8), including bladder catheterization. Hematocrit determinations were done according to Wintrobe. In subjects 1-7 the procedure was as follows: After 2 control clearance periods, 500 cc of 6% dextran in normal saline‡ were given intravenously at the rate of 25 cc/min. Eight to 45 minutes after the termination of the infusion, 2 or more clearance periods were obtained. Subjects 8 and 9 received 1000 cc of 6% dextran; patient 10 was given 1500 cc; repeat clearances were begun immediately after the infusion was completed. In subjects 11-13, control clearances and Tm_{PAH} determinations were done on the first day. The following day 1000 cc of 6% dextran were administered intravenously, and the above procedures were then repeated 45 minutes to 2 hours following infusion. In 2 additional subjects a catheter was placed in the renal vein and simultaneous arterial and renal venous samples obtained for determination of PAH extraction before and immediately after the injection of 1000 cc of 6% dextran. All figures for clearances and Tm_{PAH} in the tables have been converted to a body surface area of 1.73 sq.m.

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‡ "Expandex," supplied by Commercial Solvents Corp., Terre Haute, Ind.

TABLE I. Studies with 500-1500 cc 6% Dextran.

Pt.	Amt dextran (cc)	Creatinine clearance Before	Creatinine clearance After	PAH clearance Before	PAH clearance After	Filtration fraction Before	Filtration fraction After
1	500	132	146	508	588	.26	.25
2		106	132	565	722	.19	.18
3		122	128	559	704	.22	.18
4		94	102	455	472	.21	.22
5		126	155	640	829	.20	.19
6		156	162	675	701	.23	.23
7		157	166	777	732	.20	.23
8	1000	121	111	489	435	.25	.25
9		113	118	360	456	.31	.26
10	1500	193	204	973	859	.20	.24

TABLE II. Studies with 1000 cc 6% Dextran (24-48 Hr Between Before and After).

Pt.	Creatinine clearance Before	Creatinine clearance After	PAH clearance Before	PAH clearance After	Filtration fraction Before	Filtration fraction After	Tm PAH (mg/min) Before	Tm PAH (mg/min) After
11	113	105	525	523	.22	.20	85	84
12	131	124	623	593	.21	.21	71	78
13	114	106	600	410	.19	.26	70	79

Results. Results of the administration of 500-1500 cc of dextran are presented in Table I. Creatinine clearance increased in all but one of the subjects, but the increase, based on previous experience, was considered significant only in subjects 2 and 5. PAH clearance increased in 3 subjects (Subjects 2, 3, and 5), changed very little in 4, and decreased in subjects 7, 8, and 10. Calculations of renal whole blood flow from C_{PAH} and hematocrit determination revealed increases of 103 cc/min. and 252 cc/min. in subjects 3 and 5, respectively, and a decrease of 43 cc/min. in subject 4. In subject 10, who received 1500 cc of dextran, the hematocrit fell from 41 to 32, and the renal blood flow decreased from 1650 to 1141 cc/min. From Table II it may be seen that with the exception of a decrease in C_{PAH} in subject 13, C_{Cr}, C_{PAH}, and Tm_{PAH} were not affected by the administration of 1000 cc of dextran.

Since a decreased renal extraction of PAH has been found after the rapid infusion of human serum albumin(1), this was measured in 2 additional subjects and found to be 89% and 92% before and 88% and 91% after dextran.

Discussion. The dextran solution used in these studies was essentially isosmotic with plasma, and previous work(4-6,9) has shown that the increases in plasma volume produced by it are roughly equivalent to the amount administered. In this respect our results might be expected to differ from those reported by Bradley(2) and Cargill(1) where plasma volume expansion was produced by the oncotic action of concentrated albumin solution. A more comparable study is that of Wilson and Harrison(3) who administered 900-1955 cc of plasma to normal human subjects and found that the blood volume was increased in each instance by approximately the amount infused. These authors report changes in exogenous creatinine clearance ranging from —4 to +228 cc/min., with an average of +83 cc/min. C_{PAH} increased in every instance, ranging from +92 to +1008 cc/min. and averaging +514 cc/min. We are unable to explain our failure to find similar changes when the plasma volume is expanded by dextran. It is possible that the renal vasodilatation produced by plasma and albumin is due to the direct action on the kidney of an unidentified substance in these solutions and not to the concomitant increase in plasma volume.

Summary. Following the intravenous administration of 500-1500 cc of 6% dextran solution in 13 normal subjects there were no

marked changes in clearance of PAH and creatinine or in Tm_{PAH}.

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Rapidity of Calcification *in vitro*.* (19461)

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Most experiments reported in the literature on the calcification of hypertrophic rachitic cartilage *in vitro* depend on 16 to 20 hour incubation periods. Generally, these have been performed with minimal concentrations of calcium and inorganic phosphate. We have observed that calcification can proceed with unexpected rapidity in organic phosphate ester, and that the characteristic line of calcification may be observed after as little as 5 minutes incubation.

Methods. Slices of epiphyseal cartilage were prepared from bones removed from young rats, which had been made rachitic by feeding them a modified Steenbock and Black diet No. 2965(1). They were shaken in a water bath at 37°C for varying periods of time in calcification medium, as described by Miller, Waldman, and McLean(2), then stained with 2% $AgNO_3$, and cleared with oil of isosafrol. Phosphate was supplied as inorganic phosphate, from a stock solution of 0.1 M phosphate buffer, pH 7.4, or as disodium monophenyl phosphate. Inorganic phosphate liberated from the organic ester was determined by the method of Gomori(3) after removal of the slices and precipitation of the contents of the flask with an equal volume of 10% CCl_3COOH. The calcification score used is that described by Sobel, Goldfarb, and Kramer(4).

Results. In a medium which contained only inorganic phosphate a wide line of calcification was noted in 5 of 6 slices after 8 hours incubation in the highest concentration of phosphate, 5.0 mM (Exp. 1, Table I). The density of the calcium phosphate deposit increased after 22 hours incubation. Little or no calcification was noted up to this time with 2.0 or 3.0 mM inorganic phosphate. In the presence of organic phosphate ester, however, all the slices showed calcification after only one hour incubation. At this time, the concentration of inorganic phosphate attained in the medium due to hydrolysis of disodium monophenyl phosphate was only 1.7 mM. As in the experiment with inorganic phosphate, the density of the bone salt deposit became greater with more prolonged incubation.

In order to determine how rapidly salt deposit can occur in organic phosphate ester, a second experiment was performed with a higher concentration of Ca^{++}, 2.0 mM. Flasks were removed from the incubator after various intervals of time, from 5 to 60 minutes. Beginning calcification was noted in 1 of 4 slices after only 5 minutes, when the inorganic phosphate content of the medium had reached

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