Changes in Serum Proteins Produced by Infusions of Dextran. (21939)

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(Introduced by David Seligson.)
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In the course of studies of possible metabolic effects of dextran infusions, a patient with chronic liver disease was given repeated infusions of dextran. A marked decrease in the concentration of serum proteins was observed, with a greater reduction in globulin than in albumin. Detailed studies were undertaken to confirm and evaluate these particular findings. For this purpose, 4 additional patients with liver disease and 8 patients convalescent from diseases other than liver disease were studied.

Methods. One patient was given only a single infusion of dextran, 750 cc of 12% dextran in water, the other 12 received daily infusions of 1000 cc of 6% dextran in saline. Five of these 12 men were given infusions for 4 successive days, 4 for 5 days, one for 6 days, and 2 for 15 days. Other than prolonged bleeding time(1), slightly prolonged one-stage prothrombin time, and minor headaches, no difficulties were encountered. Some patients gained as much as 3 kg of weight, but none developed overt edema.

Serum proteins were measured daily in most cases by the method of Reinhold(2), in which the globulins are precipitated by a sulfate-sulfite solution, and the protein in solution measured by the biuret reaction. On selected serums drawn both before and after dextran infusions the serum proteins were also checked by sulfate-sulfite precipitation and the analysis of supernatant nitrogen content by the Kjeldahl method. Filter paper electrophoresis was also used to check the partition of serum proteins, using the dye elution technique for colorimetric quantitation of the bromphenol blue bound by each protein zone. Dextran levels were measured by the turbidity method(3). In 3 of the liver disease patients serum cholinesterase(4), zinc turbidity (5), and thymol turbidity(6) were also measured.

Results. With repeated infusions of dextran, levels of dextran as high as 2.5 g % were found in the serum. Dextran was but slowly removed; appreciable levels were still present in the serum 10 to 15 days after infusion. Hematocrits and total serum protein concentrations changed inversely with the dextran level. In general the sum of the concentrations of protein and dextran remained constant, and roughly equalled the total pro-

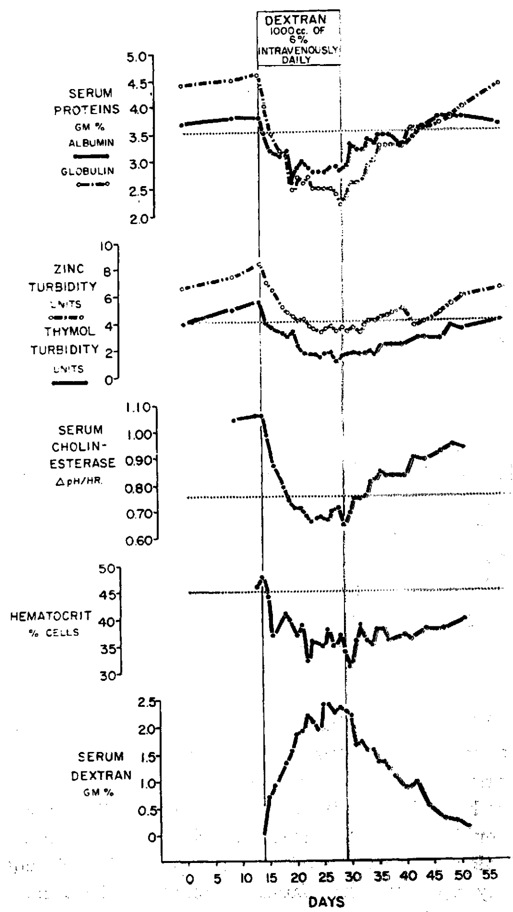

FIG. 1. Changes in serum proteins, hematocrit, serum dextran, serum cholinesterase, and zinc and thymol turbidity tests with repeated infusions of dextran in a patient with biliary cirrhosis convalescent from surgical relief of jaundice.

TABLE I. Correlations among Serum Proteins, Serum Dextran, and Hematocrit.

	Dextran, g %	Change in hematocrit, % cells
Change in total protein, g %	−.80	+.61*
" " albumin, "	−.77	+.44*
" " globulin, "	−.76	+.63*
" " A/G ratio	+.57	−.55
" " hematocrit, % cells	−.44	—

All correlations are highly significant. With 80 degrees of freedom (all correlations are based on 83 or more pairs) a correlation coefficient of .28 has a probability of .01.

* Correlation coefficients between percentage changes in serum proteins and hematocrit differ from those above by .03 or less.

tein concentration before dextran infusion.

In all patients, both liver disease patients and others, the serum globulin concentration decreased more than that of the serum albumin, so that the albumin:globulin ratios rose. These differential changes in albumin and globulin fractions were observed by both chemical methods used for analysis, and also in the paper electrophoresis patterns. By the latter technique the various globulins were found to be reduced equally.

In the patients in whom it was measured, the serum cholinesterase fell with dextran infusion. Abnormally high zinc and thymol turbidity values fell to the low normal range. (Fig. 1).

Discussion. Part of the reduction of serum protein concentration was certainly caused by expansion of the plasma volume by dextran. However, the increase in plasma volume calculated from changes in hematocrit accounted for only a part of the gain in body weight. Also it may be seen in Table I that the protein changes were less well correlated with the hematocrit changes than with the serum concentrations of dextran. The different percentage changes in albumin and globulin cannot be explained by plasma volume expansion. This difference was not caused by interference by dextran with the analytic method, because similar changes were found by the paper electrophoresis technique. Similar changes have been observed by Jaenike and Waterhouse(7).

Expansion of the interstitial fluid as well as the plasma volume must have occurred in these patients. Since the molecular size of the globulins is much greater than that of albumin the rate of transfer of globulins across the capillary wall should be slower than that of albumin. Therefore with transfer of fluid and protein from the plasma to interstitial fluid to compensate for the hypervolemia, the albumin concentration should fall faster than that of the globulin. A significant fall in total circulating albumin, but not in globulin, has been observed shortly after a rapid infusion of dextran(8). Later as dextran is metabolized and as fluid and dextran are excreted, albumin should return more rapidly to the plasma than globulin. This process of reequilibration may possibly explain the relatively greater reduction of globulin than of albumin which was observed.

The changes in albumin and globulin concentrations may also be explained by reductions in rates of synthesis. Since serum cholinesterase activity seems to parallel the rate of albumin synthesis(9), the observed reduction in cholinesterase may be taken as evidence of a decreased rate of albumin synthesis. Colloids similar to dextran are taken up by the reticulo-endothelial system, the site of globulin synthesis. Thus dextran might reasonably be expected to depress globulin synthesis. If dextran does reduce the rates of synthesis of albumin and globulin, there is no reason to expect, *a priori*, that the reductions need be the same.

The changes to normal of elevated zinc and thymol turbidity values are doubtless secondary to the relative changes in albumin and globulin.

Summary. Daily infusions of dextran were given to 13 patients for as long as 15 days. In addition to the decrease in total serum protein from plasma volume expansion, dextran was found to produce a relatively greater decrease in globulin than in albumin. Serum cholinesterase activity decreased, and zinc and thymol turbidity values fell.

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Effect of High Levels of Fat, Lactose, and Type of Bulk in Guinea Pig Diets.* (21940)

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Woolley and Sprince(1) reported that supplements of certain inert materials, such as powdered cellophane and Cellu flour, improved the growth of guinea pigs fed purified diets. Booth *et al.*(2) who found a similar beneficial action of bulk, reported gum acacia (formerly called gum arabic) to be slightly superior to Cellu flour. However, Reid and Briggs(3) could not always obtain consistent growth with diets containing gum acacia, and turned to the use of Spangles,† a coarsely-ground cellophane product.

In this paper we are presenting further studies on the effect of different types of bulk, especially Solka-floc,‡ a very pure, finely-ground and relatively inexpensive cellulose product, on the growth of guinea pigs as well as the effect of different levels of fat and lactose.

Methods. To test the effectiveness of these different materials, 3 types of diets were devised, including a "normal", a high-fat 24% corn oil, and one with lactose as the only carbohydrate. The latter 2 diets were chosen because more information was desired on the effect of these substances on the deposition of liver fat in guinea pigs fed milk diets(4). The basal or normal diet used in this experiment provided per 100 g of ration in g: sucrose, 43; casein, 30; bulk, 15; salts IV, 4(5); corn oil, 4; potassium acetate, 2.5; choline-Cl, 0.75; magnesium oxide, 0.50; and vitamin mix, 0.25. The vitamin mix provided per 100 g of ration in mg: inositol, 200; niacinamide, 20; p-aminobenzoic acid, 10; Ca-pantothenate, 8; riboflavin, 3; thiamine-HCl, 2; pyridoxine-HCl, 2; folic acid, 1; in μg: biotin, 100; B_{12}, 4. Fat soluble vitamins were provided weekly by dropper in the following amounts: A, 2000 I.U.; D, 20 I.U.; E, 12 mg; K, 0.2 mg. It should be noted that the diets contained 2.5 times the level of choline normally used in guinea pig diets to allow for any greater need with high-fat diets. The addition of corn oil to the high-fat diets and to those with graded levels of corn oil was made at the expense of sucrose. The care and feeding of guinea pigs have been described elsewhere(6). Since the diets differed so widely, the guinea pigs were initially divided into 3 groups with each group gradually being adapted to its particular diet. After adaptation, each of the 3 dietary groups was subdivided into 3 groups of 5 guinea pigs each, with the same average starting weight within each main group (normal, 194 g; high-fat, 221 g; and lactose, 217 g). The 3 normal groups were on experiment for 4 weeks after which they were redistributed into groups averaging 380 g. These groups were fed diets with 4, 8,

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† Rayon Processing Co., Pawtucket, R. I.

‡ Brown and Co., Berlin, N. H.