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Research Article

THE EFFECT OF THE INTRAVENOUS ADMINISTRATION OF DEXTRAN ON CARDIAC OUTPUT AND OTHER CIRCULATORY DYNAMICS [1]

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INTRODUCTION

It has been well established that partially hydrolyzed dextran is effective in expanding and maintaining the plasma volume (1–3). Previously, there have been numerous investigations concerning the effects of plasma volume expansion on the circulatory dynamics (4–7). Many of these studies have used saline or plasma protein preparations. The former only temporarily expands the plasma volume and then rapidly distributes itself in the extracellular fluid; whereas the plasma protein has a more permanent intravascular residence. Other investigators have utilized solutions of gelatin (8), gram arabic, and acacia.

Dextran provides another opportunity to study the effects of hemodilution and plasma volume increase on certain physiological aspects of the circulation. Investigations of this nature have been reported by Bull and associates (2) on two patients studied with the cardiac catheter during a surgical operation.

Using the dye dilution technique (9, 10) for determining cardiac output also provides a unique opportunity to study the effect on the pulmonary circulation associated with blood volume expansion.

Data to be presented show that dextran consistently increased the plasma volume proportionally to the amount administered and that the effect was prolonged. Cardiac output was increased in every case. The increased plasma volume was associated with prolonged elevations of pressure in the pulmonary circulation.

[1] Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or the policy of the Veterans Administration.

METHODS

The patients were studied in the fasting state. All were male, and their ages ranged from 22 to 44. Diagnoses and a summary of important data are listed in Table I. All of the patients with lung disease were afebrile, well hydrated, and their lesions were well localized. The partially hydrolyzed 6 per cent dextran [2] solution had a viscosity of 3.31 centistokes at 25° C and was made up in 0.85 per cent saline.

Pulmonary artery catheterizations were performed with a 6-F and 8-F intracardiac catheter. The systemic arterial blood samples and pressure records were obtained from an indwelling, femoral arterial needle. An electromanometer (Sanborn), recording through a single channel, direct-writing electrocardiograph (Sanborn) was used for all pressure tracings. Arbitrary reference point was 5 cm. below the level of the sternal *angle of Louis*. Mean pressures were obtained by electrical integration of the pulse contours. Pulmonary "capillary" pressures were obtained as described by Hellems, Haynes and Dexter (11).

Cardiac outputs were derived by the method of Hamilton (9, 10), using Evans Blue dye (T-1824). Concentration of the dye in the plasma was determined according to the method of Dow and Pickering (12). Dye output determinations have been shown to correlate well with the Fick procedure (13). A figure ("Q") was also derived from the dye curve as an index of pulmonary blood volume, as described by Ebert and co-workers (14). "Q" includes the blood volume in the lungs, left heart, aorta, and certain large arteries. Pulmonary arteriolar resistance and cardiac work were calculated according to the formulae mentioned by Dexter and associates (15).

Blood volume was determined according to the method of Gibson and Evans (16). Specimens were obtained 10 minutes following the injection of Evans Blue dye. Estimated changes in blood volume after dextran were made by assuming that the changes were proportional to the percent of changes in hematocrit. However, Leard and Freis (17) have shown that this method failed to show accurate quantitative changes in patients excessively hydrated over a period of five days, when blood volume determinations were done by the dye method before and after hydration. However, the hemodilution which occurs following dextran injection has been shown to be

[2] Supplied by Commercial Solvents Corporation.

TABLE I

Patient	Body surface area, *sq. m.*	Cardiac output, *L/min.*	Cardiac index, *L/sq. m./min.*	Pulse rate/*min.*	Stroke volume, *cc.*	Circulation time, *secs.*			"Q," *cc.*	Pulmonary artery pressure, *mm. Hg*			Mean pulmonary "capillary" pressure, *mm. Hg*	PA–"PC" gradient, *mm. Hg*	Pulmonary resistance, *dynes sec. cm.$^{-5}$*	Peripheral resistance, *dynes sec. cm.$^{-5}$*	"Work," *kg. m./min./sq. m.*		Femoral artery pressure, *mm. Hg*			Hematocrit, *cc.*	Per cent change in hematocrit	Blood volume, *cc.*	Estimated change in blood volume	Venous pressure, *mm. H_2O*	Diagnosis
						Lesser	Mean	Total		Systolic	Diastolic	Mean					R. vent.	L. vent.	Systolic	Diastolic	Mean						
1*	1.77	4.8	2.7	80	60	6	11	12	740	18	5	11	3	8	134	1542	.43	3.6	100	74	92	47	—	3960	—	60	Tbc. RUL
†		6.1	3.4	90	67	4	8	9	795	35	16	23	14	9	120	1338	1.18	4.9	130	78	100	40	15	—	590	72	cavity
2*	1.8	4.7	2.6	95	49	4	9	12	662	20	5	13	—	-	—	1199	.46	2.6	100	55	70	43	—	2700	—	—	Lung abscess
‡		5.5	3.1	90	61	6	11	12	960	27	13	20	—	-	—	1046	.88	3.2	100	56	72	—	—	—	—	—	LLL
3*	1.7	4.0	2.4	90	48	6	12	12	806	30	13	16	—	-	—	1832	.54	3.0	140	75	90	48	—	3180	—	—	Labile hyper-
†		5.5	3.3	90	61	4	12	16	1050	33	16	23	—	-	—	1504	1.05	4.8	159	90	103	42	12	—	367	—	tension
4*	1.95	6.1	3.2	90	68	5	12	16	1216	12	6	8	—	-	—	1178	.36	4.2	125	74	90	50	—	5430	—	—	Tbc. LUL
†		9.4	4.8	100	94	5	11	11	1760	16	6	10	—	-	—	785	.69	6.4	130	75	92	45	10	—	543	—	cavity
5*	1.96	5.7	2.9	75	74	6	12	11	1109	20	7	11	6	6	78	1298	.46	3.9	108	78	92	43	—	3862	—	57	Inactive tbs.
†		7.0	3.6	70	99	4	11	14	1280	23	8	14	8	6	63	1103	.69	5.0	115	80	96	39	9	—	360	—	partial
‡		7.3	3.7	70	103	2	11	15	1350	24	10	16	8	8	89	1000	.83	5.0	110	70	90	39	9	—	360	—	collapse
§		6.8	3.5	75	90	6	10	9	1134	26	7	16	8	8	89	1132	.77	4.8	114	80	96	—	—	—	—	67	left lung

* Before administration of dextran.
† 10 minutes after dextran administration completed.
‡ 25 minutes after dextran administration completed.
§ 90 minutes after dextran administration completed.

of the same order of magnitude by both hematocrit and serum protein determinations (18).

Venous pressure readings were made with a Burch-Winsor manometer (19).

The basic experiments were done as follows: the patients were given mild sedation (1 to 3 grains of sodium phenobarbital intramuscularly), the catheter tip passed in the pulmonary artery, and the indwelling, femoral arterial needle inserted. An initial dye injection was made, and several pressure tracings were taken. Patients were tested for sensitivity by the intradermal and conjunctival injection of dextran. Five hundred cc. of 6 per cent dextran were given intravenously at the rate of 25 cc. per minute. Pressure recordings were done midway in the administration of the dextran, immediately after its completion, and at frequent intervals thereafter. Second dye injections were done at about 10 minutes after administration in most cases and at 25 minutes in two cases. A third dye injection was made after 90 minutes in the last case. There were no untoward reactions to dextran.

TABLE II

Average determinations before and after dextran administration

	Before	After
Cardiac output (L/min.)	5.06	6.76
Cardiac index (L/min.)	2.70	3.65
Pulse rate (beats/min.)	86	88
Stroke volume (cc./stroke)	60	75
Pulmonary artery pressures (mm. Hg):		
Systolic	20	26
Diastolic	7	12
Mean	12	18
Blood volume (cc.)	3826	4291
"Q" (cc.)	800	1099
Femoral artery pressures:		
Systolic	114	122
Diastolic	71	76
Mean	87	93
Venous pressure (mm. water)	58	69
Work (kg. m./min./sq. m.):		
R. ventricle	.465	.923
L. ventricle	3.39	4.79
Circulation time in secs.:		
Lesser	5	4.2
Mean	11	10.4
Total	12.5	12.4

RESULTS

As shown in Tables I and II and in Figure 1, there were increases in cardiac output in every case following the administration of dextran. There was an average rise of 38 per cent if determinations were done within 10 minutes after injection. The change in stroke volume was commensurate with this increase, but the average pulse rate showed no appreciable change.

As illustrated in Figure 2, when dextran was given, there was a gradual rise in pulmonary artery pressure during the infusion. The peak rise was noted immediately after the completion of the dextran administration. There was usually a gradual decline in the pressure; however, the peak was maintained for only 12 to 20 minutes in two

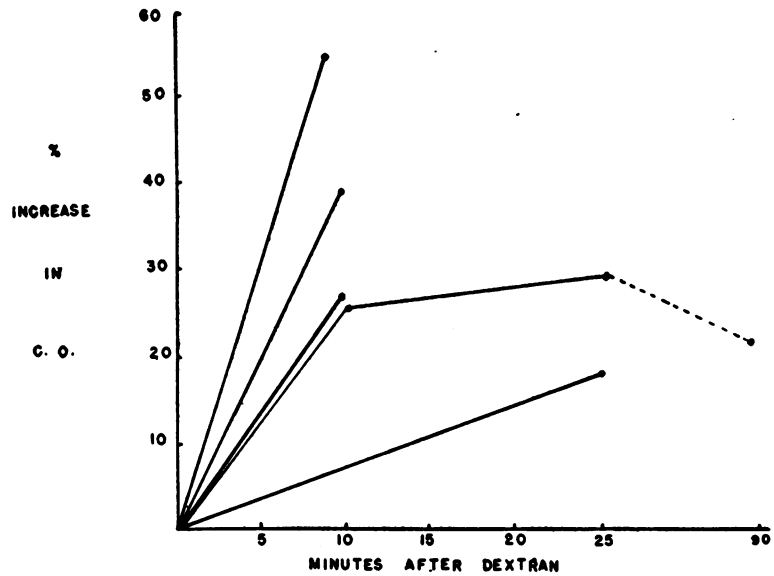

FIG. 1. PER CENT CHANGE IN CARDIAC OUTPUT AFTER 500 CC. DEXTRAN

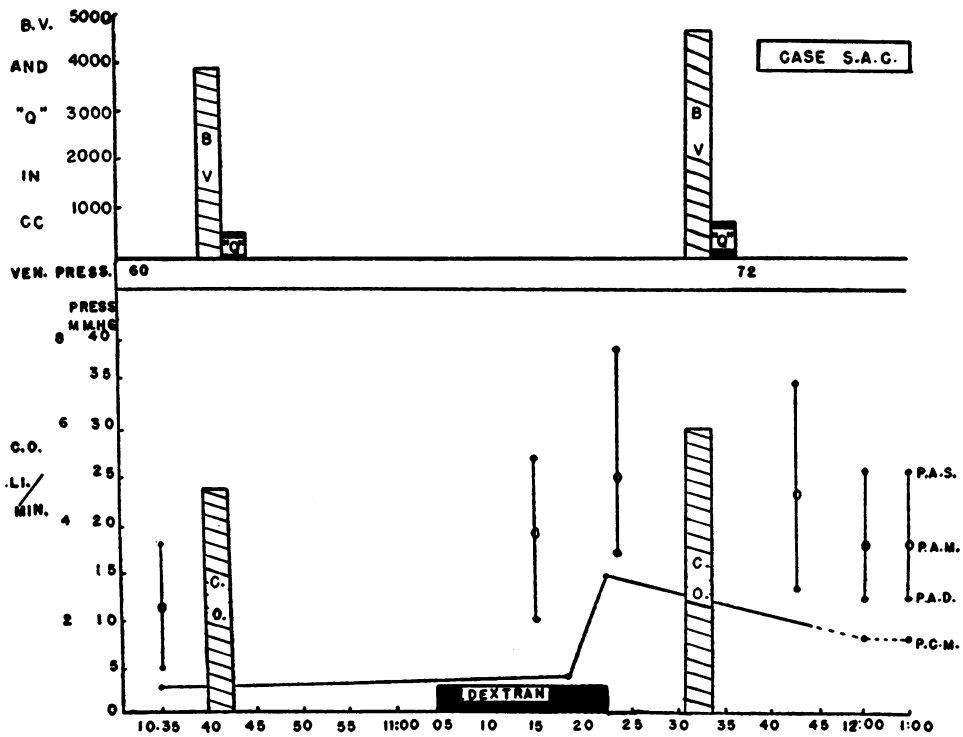

FIG. 2. HEMODYNAMIC CHANGES FOLLOWING INFUSION OF 500 CC. OF DEXTRAN, AS OBSERVED IN CASE 1

C.O. = cardiac output
B.V. = total blood volume
"Q" = index of pulmonary blood volume
P.A.S. = systolic pulmonary artery pressure
P.A.M. = mean pulmonary artery pressure
P.A.D. = diastolic pulmonary artery pressure
P.C.M. = pulmonary "capillary" mean pressure

cases, then fell to lower but still elevated levels. Four patients showed increases in mean pulmonary artery pressure of 5 to 10 mm. Hg after 45 to 90 minutes, and the pressure in one patient fell to normal limits after 32 minutes. The rise was due to a greater increase in the systolic than in the diastolic pressure in three cases, and the rises were about the same in both pressures in two cases. The average rise in the mean pulmonary artery pressure was 6 mm. Hg 10 minutes after dextran, at which time the dye was injected, but the average mean peak rise, which occurred earlier, was 9 mm. Hg, with a range from 4.5 to 15 mm. Hg.

As recorded in Table I, there was a marked and prolonged rise in pulmonary "capillary" pressure in Case 1. In Case 5, the pulmonary "capillary" pressure rose from 6 to 13 mm. Hg immediately after dextran but then fell quickly to a very slightly elevated level. Figure 3 illustrates the pressure changes noted in Case 1.

The average estimated increase in blood volume was close to the amount administered (500 cc.), but the "Q" value average increase was about 300 cc., as shown in Table II; however, if Case 4 is omitted because of its unusually large increase, the average increase in "Q" is only 192 cc.

Relatively small changes were noted in the systemic arterial and venous pressure following dextran injection. Table II indicates that there was a 98 per cent average increase in right ventricular work and a 41 per cent average work increase of the left ventricle following dextran injection; however, absolute changes in work indicate that the left ventricle increases its work output considerably more than the right ventricle.

In general, the lesser circulation and total circulation times usually showed no constant or marked changes, and the mean pulmonary circulation time decreased slightly in most cases.

Studies on two of our patients and on numerous other patients receiving either 500 or 1000 cc. of 6 per cent dextran have shown no changes in the vital capacity.

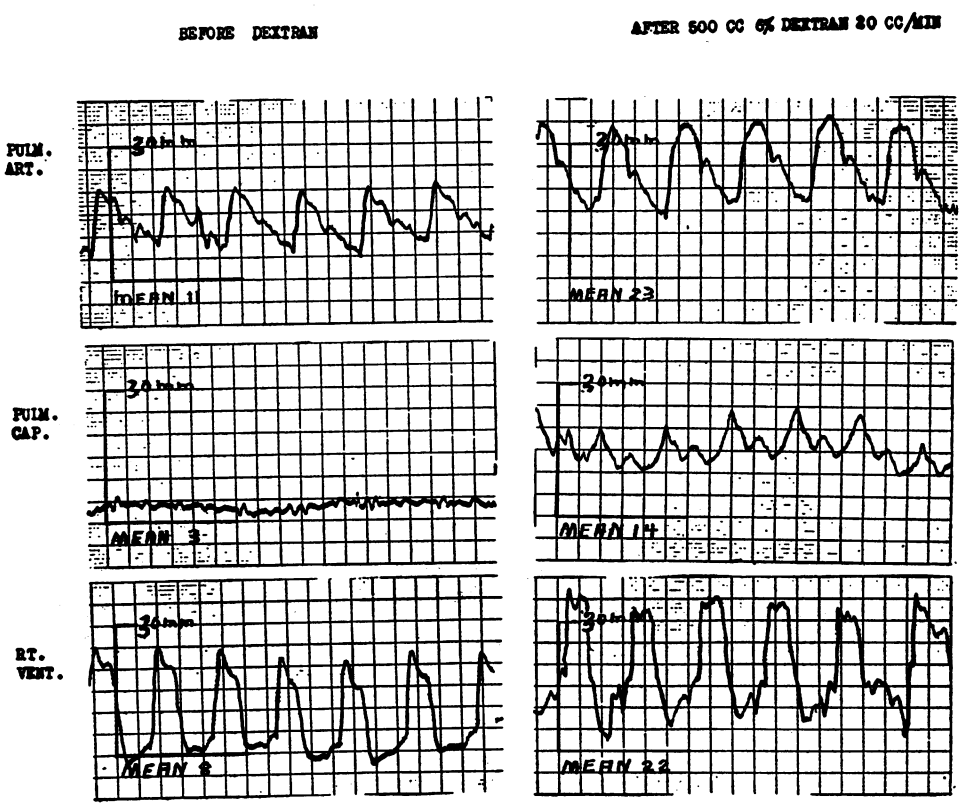

FIG. 3. PULMONARY ARTERY, PULMONARY "CAPILLARY," AND RIGHT VENTRICULAR PRESSURE RECORDINGS NOTED BEFORE AND 10 MINUTES AFTER THE ADMINISTRATION OF 500 CC. OF DEXTRAN TO CASE 1

DISCUSSION

There have been conflicting reports concerning the ability of increased blood volume to enhance consistently the cardiac output in normal subjects. Whereas McMichael and Sharpey-Schafer (4) have stated that elevations in diastolic filling pressure will produce an increase in cardiac output in man, Warren and associates (5) have denied that this occurs regularly in normal humans when the right atrial pressure is increased by intravenous saline or human serum albumin. In both of these studies the cardiac output was measured by the Fick principle. Also, Doyle and co-workers (20), using saline and both the dye and Fick procedures, have found no consistent increase in output.

As shown in Figure 1, there was a consistent increase in the cardiac output following dextran in all of our cases using the dye method. Cardiac output was still elevated after 25 and 90 minutes, respectively, in two cases.

While, theoretically, there are several differences between raising the ventricular filling pressure with an osmotically inactive diluent such as saline and doing the same thing with an isotonic and isoncotic fluid such as dextran, it is difficult to see how the albumin and dextran solutions should differ hemodynamically in short term experiments such as these. Actually, in Warren's seven cases given albumin infusions, five had increases in cardiac output. The other two cases had relatively high "basal" outputs with subsequent falls into the normal range after albumin. Dye and Fick methods have been shown to be comparable (13), and it can be seen that our patients had lower basal outputs generally than those in Warren's series.

Hardy and Godfrey (6), using the ballistocardiograph, found that the intravenous infusion of physiological saline solution caused an increase in cardiac output in patients who were dehydrated but produced no change in normally hydrated subjects. Fletcher and associates (7), also using the ballistocardiograph, showed that the intravenous administration of 6 per cent ossein gelatin solution produced a marked increase in minute volume output in very debilitated patients, but the change in output was not very remarkable in normal patients. All of our patients were well hydrated, and none was debilitated.

Altschule and Gilligan (8), using the ethyl iodide technique for cardiac output, reported that there was a direct correlation between elevation of the peripheral venous pressure and increase in cardiac output. They stated that if over a liter of saline is given intravenously at a rate faster than 20 cc. per minute, normal individuals will respond with a temporary increase in cardiac output. Doyle and co-workers (20) state that their results are inconsistent following infusions of saline at rates of 100 cc. per minute. Our patients received only 25 cc. per minute. That venous pressure is elevated following dextran injection, has been shown by several investigations (2, 3, 18).

It has been reported (1, 2) that during administration of other preparations of dextran, more venous engorgement occurred than is noted with comparable amounts of blood or serum albumin. It was suggested that this resulted from osmotic withdrawal of fluid from the extracellular spaces. This excessive engorgement did not occur with our isotonic, isoncotic preparation of dextran, and the blood volume studies showed only increases comparable to the amount of dextran solution administered.

The data presented here might suggest that in these cases the increases in cardiac output are due to increases in the total plasma volume, resulting in increases in stroke volume.

In the calculation of the "Q" value, it is apparent that the average "Q" increase was around 300 cc. (or about 200 cc. if Case 4 is omitted), while the total blood volume increased only by the amount of fluid administered (500 cc.). It should be pointed out that this disproportionate increase in "Q" does not mean an increase of 300 cc. in the pulmonary blood volume, for the vascular bed of the lung is only a portion of "Q." Cournand (21) believes that the average human lung contains about 400 cc., whereas the average "Q" value is about 1000 cc. In our experience, the pulmonary blood volume index ("Q") usually does not vary more than 15 per cent in repeated determinations in the same patient with an undisturbed circulation. However, others feel that the "Q" determination is inaccurate and that changes of the magnitude mentioned in our discussion may not be significant.

Following the dextran administration, rises in

the peripheral venous pressure were relatively small (10 and 12 mm. H_2O), whereas most pulmonary artery pressure rises were around ten times that amount. Figure 2 shows that changes in mean pulmonary "capillary" pressure almost completely accounted for the rises in mean and diastolic pulmonary artery pressure in that case.

SUMMARY AND CONCLUSIONS

1. A study was made of the effect upon the circulation of increasing the plasma volume by the intravenous administration of 6 per cent dextran in five men.

2. In every case there was a prolonged rise in pulmonary artery pressure and an increase in the cardiac output. The changes in pulse rate and systemic blood pressure were slight and inconsistent.

3. Blood volumes after dextran showed only increases comparable to the amount of solution administered. The dextran used was isoncotic and isotonic.

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