Severe Adverse Reaction to Dextran Therapy

By Dr. Ali Akbar Murad *

ANTIBODIES to Dextran can develop without prior Dextran infusion. In such cases when Dextran is infused, a severe immunological disturbance can occur immediately which may lead to anaphalactic shock.

Mr. A. F. aged 24, was admitted to Crumpsall Hospital (Manchester) with classical clinical diagnosis of sub-acute bacterial endocarditis. There was early finger clubbing, mild splenic enlargement, raised E.S.R., raised temperature but no oslers nodes, Janeways Lesions, Roth spots and no Lipman 's spots. There were signs of aortic regurgitation to account for aortic lesion but there was no previous history of rheumatic fever or for that account any disease whatsoever. This was subsequently confirmed by blood culture which was positive non-haemolytic streptococci (strep. mutans) in nine bottles cultures out of nine. Three days after admission, while he was on chemotherapy, it was noted that his blood pressure had dropped from the original recording of 130/50 to 100/30. An attempt was made to raise the blood pressure with Dextran 70 in normal saline infusion. Following a 5 ml. infusion a sudden, severe reaction was noted in this patient characterised by severe abdominal discomfort, cyanosis, sweating, dyspnoea, dryness of the mouth, urgency, anxiety and fear. The pulse was rapid and of very low volume, and blood pressure unrecordable. This was thought to be an anaphylactic type of reaction and was immediately reversed to normal following subcutaneous injection of adrenalin and intravenous Piriton. Cultures of the infusion from the same bottle of Dextran produced no growth and no contamination. The remarkably interesting association between the findings of strep. mutans on blood culture (these produce Dextran substance and are only found on teeth enamel) and the anaphylactic reaction to Dextran therapy made us search as to whether the same micro-organism produced Dextran substance which earlier on circulated in the blood stream and produced antibodies on further transfusion of Dextran — hence the anaphylactic reaction. We therefore proceeded to estimate the level of Dextran antibodies and found to our great interest that the level was significantly raised. No case has been recorded of such severe anaphlactic type of reaction.

Discussion:

The substance known as plasma volume expander, of which Dextran is one, when infused intravenously restores a diminished volume and maintains it in the manner similar to homologous plasma or serum. Dextrans are glucose polymers produced by bacterial fermentation of sucrose. They have a molecular weight range from a few thousand to many million and the biological properties depend on the molecular weight. Clinically these have two important properties:

a) Colloidal osmotic effect
b) Promotion of blood flow in the mocrovasculature.

Fractions with molecular weight above 70,000 are most commonly use for colloidal osmotic effect. Below that is indicated for promotion of blood flow. Molecules of 50,000 MW and below are excreted through the kidneys. Molecules of 250,000 MW and above exert only low colloidal osmotic pressure. Also the larger molecules have been shown to be responsible for such side effects as red cell aggregation. Dextran has a number of advantages over plasma therapy and briefly these are as follows:

i. Very low incidence of side-effects.

ii. No risk of transmission of viral hepatitis, syphilis, Herpes simplex, or other blood transmitted infections.

iii. No storage problems; stable in extreme climatic conditions with no refrigeration necessary.

iv. Stable for at least five yers.

v. Very much less expensive than blood or plasma.

vi. Freely available for immediate use in the emergency treatment of hypovolaemic shock.

vii. Compatible with all blood groups.

viii. Dextran injection is used when up to one litre of fluid is to be infused. This saves blood and plasma for cases where the required volume is greater than a litre.

As a general rule Dextran 110 and 150 are more suitable for prolonged blood volume expansion whereas Dextran 40 and 70 have particular use as an emergency measure. The relationship between the colloid concentration and colloidal osmotic pressure with a Dextran with an average molecular weight of 70,000 is graphically depicted.

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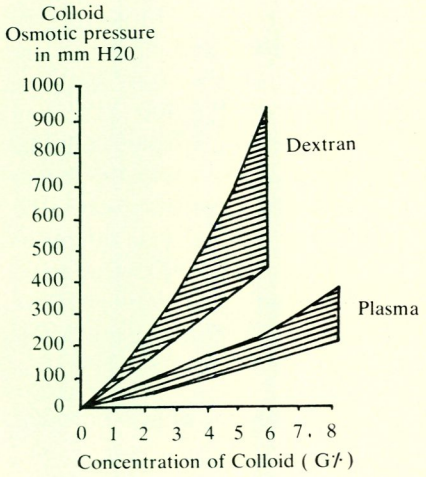

The straight lines represent the osmotic pressure while the shaded areas signify the osmotic contribution from molecular interaction. The colloid osmotic pressure of Dextran 70 is about 800 mmH 2 0 and of Dextran 40 about 230 mmH $_2$ 0. This means that both solutions have a considerably higher c.o.p. than normal plasma which exerts a colloid osmotic pressure of 350 mmH $_2$ 0. Finally, the effect of Dextran on blood rheology and flow is well documented by the fact that the degree of erythrocyte aggregation is influenced by composition of the plasma colloids and quantitively correlated to the physiochemical properties of these colloids.

Thorsen and Hint (1950) suggested that the effect of Dextran on erythrocyte aggregation may be due to absorption of Dextran layer on the red cells. Later it was shown by Rothman (1957) and by Lee (1963) that the Dextran has an anti-thrombotic effect and these properties are most likely related to its action on the platelets. The difference between Dextran and Heparin effects on the initial thrombus formation has been demonstrated by Berman (1964) on experimental animals. Their thrombus threshold ratio for animals treated with clinical Dextran 70 twenty-four hours before testing were 3:4, animals treated with 500 u.s.p. of Heparin showed a thrombus threshold ratio of 1:7. Dextran was consequently more potent than Heparin in these experiments. There was however, an interesting difference between the Dextran and Heparin effects; in animals treated with Dextran the whole blood clotting time was thirty-eight seconds while it exceeded twenty-four hours in animals treated with Heparin with all controlled animals it was twenty-two to twenty-six seconds. The effect of Heparin seems consequently to be connected with its effect on blood clotting, while no significant effect on clotting was found with Dextran. Berman concludes that Dextran is effective in inhibiting platelet agglutination without being an anticoagulant. The anti-thrombotic effect of Dextran is probably due to some physio-chemical interference with platelet aggregation as yet not clear.

REACTIONS:

Isolated cases of anaphylactoid reactions (flushing, blood pressure drop, oppression, pain in the lumbar region, urticaria) immediately after commencing a Dextran infusion, have been reported. The frequency of such reactions is low . It is considerably lower than in connection with blood transfusions. The aetiology of such a reaction is unknown. A cross-reaction with antibodies against bacterial, for example pneumococcal, polysaccharides may be responsible. Such reactions have, however, without any scientific evidence been considered an expression of the antigenicity of Dextran.

Kabat and Bezer (1958) have shown that precipitating antibodies against Dextran may be produced by intra-cutaneous injections of minute amounts if relatively high molecular weight Dextran is used.

It must therefore be concluded that Dextran gives rise to anaphylactoid reactions in isolated cases only. These reactions are not caused by the antigenicity of Dextran. They must therfore be considered as drug reactions of unknown origin in certain sensitive patients.

R. Brisman J. Med. Ass. 1968 204 , 824, has recorded that in four patients anaphylactic type reaction developed within two minutes or less of Dextran 70 infusion in small amounts (5, 10, 15, 25 ml. respectively). Reactions were characterised by subjective discomfort, severe gastro-intestinal disturbance and hypotension. All these patients recovered. Allergic reactions to Dextran 40 are in the order of an angio-neurotic type, asthma, rhinitis and urticaria. Aggregation of red cells and hypotension are only noted in Dextran 110 and 150. □

REFERENCES :

1. Ricketts, C.R.,
British Medical Journal (1966) 1423/26.

2. Squire, J.R., Bull, Maycock and Ricketts
"Dextran, its properties and use in Medicine".
Blackwell, Oxford (1955)

3. Thorsen, G., Hint, H.C.,
Acta. Chir. Scand. (1950) Suppl. 154.

4. Rothman, Adelson, Schevebel, Langdell,
Vox Sanguinis 2 (1957) p. 104-109.

5. Lee, W.H.,
Conference on evaluation of low molecular weight Dextran in shock.
Washington (1963) p. 40-45.

6. Berman, J.H.,
Bibliotheca Anat. 4 (1964) p. 736-743.

7. Kabat, E.A., Bezer, A.E.,
Arch. Bioch. Biophys. 78 (1958) p. 306-318.

8. Brisman, R.,
J. Med. Ass. (1968) 204, 824.