## CASE REPORT

# Anaphylaxis Associated with the Use of Dextran

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The use of dextran as a plasma-expander has occasionally been associated with adverse reactions. Most have been "allergic" in nature, with urticaria, angioedema, vasomotor rhinitis, and wheezing developing after the infusion of about 500 to 1,000 ml. dextran. A few reports,[1-6] however, have described more serious reactions, anaphylactic in type associated with much smaller doses; as little as 2 ml. has been known to produce anaphylactic shock.[7] This report describes an example of such a reaction.

### CASE REPORT

A 54 year old white man was admitted to hospital having sustained compound fractures of tibia and fibula. Examination revealed, in addition to the injury, an obese, plethoric man in pain; the pulse rate was 100 per minute, hepatomegaly and ascites were detected moved poorly, was increased antero-posteriorly, but the lungs were clear on auscultation; hepatomegaly and ascites were detected by abdominal palpation. The past history revealed that he had suffered from pneumonia on three occasions, and from chronic emphysema for several years. He was known to have had cirrhosis of the liver since 1956, when he had been treated for hepatic coma; cirrhosis was attributed to exposure to carbon tetrachloride and alcoholic intake. Apart from a rash associated with the use of adhesive tape, there were no positive allergic features, and questioning later revealed that he had never received dextran.

Under spinal anesthesia (producing analgesia to the sixth thoracic dermatome) debridement and open reduction of fractures was done. During this procedure there was moderate blood loss, the systolic blood pressure falling to 90 mm. of mercury at one point. An infusion of 6 per cent dextran (Abbott) was started, about two hours after the beginning of the procedure, replacing a 5 per cent solution of dextrose in water. Two minutes later, the patient complained that the veins of his left hand, the site of the intravenous needle, felt tight; after another minute he reported that the veins all over his body felt tight; immediately thereafter he said he felt "no good." By this time he had received 15 to 20 ml. dextran. He was now cyanotic, salivating and sweating. Oxygen was administered by mask, but within one minute he became unconscious, and no pulse was palpable at the wrist; despite positive-pressure oxygenation he remained cyanotic, and there was no movement of his chest. Five minutes after the start of the dextran infusion, which had by now been stopped, the blood pressure was unrecordable, and heart sounds could not be heard. After injection of methoxamine (5 mg. intravenously, 15 mg. intramuscularly), the trachea was intubated, ventilation with 100 per cent oxygen was continued, and external cardiac manual systole was begun.

With this treatment the radial and femoral pulses became palpable, and upon attachment of electrodes, a normal electrocardiographic complex was seen. An infusion of Neo-Synephrine supported the blood pressure. Within fifteen minutes his color returned to normal, and spontaneous cardiac activity was resumed. Forty-five minutes after the crisis, the status of the cardiovascular and respiratory systems appeared normal, with the exception of mild bronchospasm, and he was conscious and reflexic.

His postoperative course was remarkably benign. ECG and enzyme studies revealed no evidence of myocardial damage; chest roentgen-ray films were likewise negative, and his neurologic status appeared unaltered. Of interest was the appearance of hives on the

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twelfth, thirteenth and fourteenth postoperative days, which were attributed to drugs he was receiving at that time (Darvon (dextropropoxphane hydrochloride), Aldactone (spironolactone)), although a possible association with the original reaction was suggested. The dextran used during the operation was examined and found free of pyrogens and bacteria; skin testing was done on three occasions with different samples of dextran, but these tests also yielded negative results.

## Discussion

The reaction reported here was evidently an anaphylactic one. Both fat embolism and pulmonary embolism were considered at one time to be possible causes, but no evidence appeared for these. The most likely factor seemed to be the infusion of dextran. As noted above, the association of anaphylactic reactions with dextran is recognized. The most striking feature of the present case was the *timing* of the reaction, highlighted by the subjective phenomena described by the patient. Although the skin tests were negative, it should be pointed out that while there is a correlation between systemic reactions to dextran and positive skin tests, this is by no means consistent[8] (an observation applicable to many drugs). This reaction was, therefore, attributed to dextran.

Much thought has been directed towards elucidation of the nature of reactions to dextran. Before the clinical use of dextran (which is a macromolecular polysaccharide of bacterial origin) immunologic and serologic properties of the crude, unhydrolyzed form were established. Of particular interest was the occurrence of precipitin reactions between dextran and antisera for bacteria such as salmonella,[9] streptococci[10] and pneumococci,[11] as was the demonstration that dextran could contaminate commercial sugar.[12]

The concept of antigenicity in relation to dextran was, therefore, a logical one. After a warning that clinical dextran might possess antibody combining properties in persons with high titers of antipneumococcal antibodies,[13] it was indeed shown to be antigenic.[14] A rational basis for allergic reactions associated with dextran thus became available. For example, cross-reactivity between dextran and bacterial antibodies present in the body at the time of infusion provided one explanation, especially in those who had not previously received dextran. It is interesting that a number of cases reported, like the present one, were associated with a previous history of pneumonia. However, Maurer's work[15] on the specificity of dextran antibodies argued against this.

Another aspect of allergy lay in the variation of molecular size and structure of different commercial dextrans. Thus, marked variation was reported in the incidence of reactions to different preparations.[16] Later it became clear that the particular strain of organism (*Leuconostoc mesenteroides*) used in preparation of dextran, the average molecular weight of the preparation, and the arrangement of the polysaccharide molecule,[17] were all of importance in relation to antibody formation and manifestations of allergy. It was found, for example, that dextran derived from the B 512 strain of *Leuconostoc mesenteroides* had a particularly low degree of antigenicity, together with a low molecular weight and a high ratio of 1:6 to non-1:6 linkages in the molecule. The effect of variation in molecular weight on dextran antigenicity was also demonstrated.[18]

While such work has enlarged our knowledge of dextran serology, the cause of these reactions, as emphasized by Grönwall,[19] has not been clarified. He therefore suggested another possibility, namely, the mechanism of histamine-release. Although direct evidence in man is lacking, this has sound experimental backing. Dextran causes an "anaphylactoid" reaction when injected into rats,[20] and also such a reaction is associated with a rise in plasma-histamine.[21] It is therefore interesting that, in man, liver disease may be associated with a raised plasma-histamine level,[22, 23] and it seems significant that the report of Henley *et al.*,[6] and the present one, are both concerned with anaphylactic reactions to dextran in persons with a history of alcohol intake and hepatomegaly. The liver may play a part in histamine metabolism,[24] and if, as has been suggested,[25] cirrhosis causes a reduction in stores of liver histaminase, thus causing more free histamine to reach the general circulation, then it may well be that histamine-release is

the major factor in the production of anaphylactic reactions to dextran in man.

Such reactions are rare. However, dextran is widely used as a plasma-expander; and the recent development of low viscous dextran has extended its use to the management of conditions with low tissue blood flow and to that of the extra-corporeal circulation. Low viscous dextran has an average molecular weight about one-half that of the older preparation, so that the incidence of reactions should be very small. Nevertheless, with the increasing applications of dextran in medicine, it would seem desirable to draw attention to the occurrence of adverse reactions to this substance.


## Summary

A case is reported in which an anaphylactic reaction occurred in association with the infusion of 15 to 20 ml. dextran. The literature concerned with such reactions is reviewed, and the factors relating to anaphylaxis resulting from dextran infusion are discussed.


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