Dear John,

HEAT TREATED FACTOR VIII

Thank you for your letter of 12 April following that of 24 March from Dr Ludlam; there is a Lancet leader of 2 April which also refers.

I agree that there is need to ensure that heat does not damage Factor VIII concentrates in a manner dangerous to recipients but find it difficult to follow the logic of the test system proposed by Dr Ludlam to that end.

The Lancet leader seems to confirm my understanding that certain patients, for poorly understood reasons, have a predilection to formation of antibody to homologous Factor VIIIc. This antibody is responsive to Factor VIII in transfused plasma, cryoprecipitate and various concentrates and I have assured (but cannot recall seeing proof) that different inhibitor patients may produce antibody of differing specificity and avidity.

If a production lot of concentrate is reacted with such antibody there may or may not be evidence of immunological binding irrespective of the source of the concentrate or its method of preparation. If such a reaction is seen it would be evidence that immunologically intact Factor VIII was present but failure to observe the reaction could mean one of two things:

1. The antibody does not detect a suitable site on the polypeptide present in the product containing Factor VIII activity.

2. The product has been so altered that none of the binding sites antigenic to inhibitor serum are intact.

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In short, if an antibody to existing concentrates reacts with the product, it suggests that the product has characters in common with existing product. If the evidence we are seeking is to be found in the clinical area it will occur in the shape of new antibody which is unique in reacting with heated product and not with product which has not been heated. Before then I would expect that PFC would have evidence of molecular structure variation using techniques such as HPLC.

If my thinking is correct one would suggest that the type of study proposed by Dr Ludlam is either unnecessary or premature; I'd believe the latter to be most probable.

With kind regards.

Yours sincerely

JOHN G WATT
Scientific Director