FREQUENCY OF MAIN GRAFT VESSEL THROMBOSES IN RENAL TRANSPLANTS TREATED WITH OKT3 AT CONVENTIONAL DOSES

—	Thromboses		
	Yes	No	Total
OKT3			
Yes	7	21	28
No	12	156	168
Total	19	177	196

because of main graft/vessel disease. 2 of these cases with, respectively, venous suture dehiscence and pedicular torsion were excluded from the analysis. In the 19 remaining patients there was histologically proven thrombosis of the main artery (12 patients) or vein (7).

25% of patients treated with OKT3 (table) had acute vascular thrombosis, compared with 7% who did not receive OKT3 ($p = 0.009$ Fisher's exact test). There was no statistically significant difference between the two groups with respect to age, sex, donor age, and number of vessels of the donor graft.

These data suggest a strong relation between OKT3 use and main graft/vessel thromboses, perhaps through lymphokine production. Furthermore, these results underline that these complications can also appear with conventional doses, since our patients have never received OKT3 doses larger than 5 mg. The seemingly higher incidence of vascular thrombosis in OKT3-treated patients should call for more caution in the prescription of this potent immunosuppressor. The encouraging findings of some workers about adequate immunosuppression obtained with lower OKT3 doses[1] should be further explored to reduce these severe complications.

Service of Nephrology,
Hospital Covadonga,
C. C. Villamil s/n. 33006 Oviedo,
Spain

E. GÓMEZ
S. AGUADO
E. GAGO
P. ESCALADA
J. ALVAREZ-GRANDE

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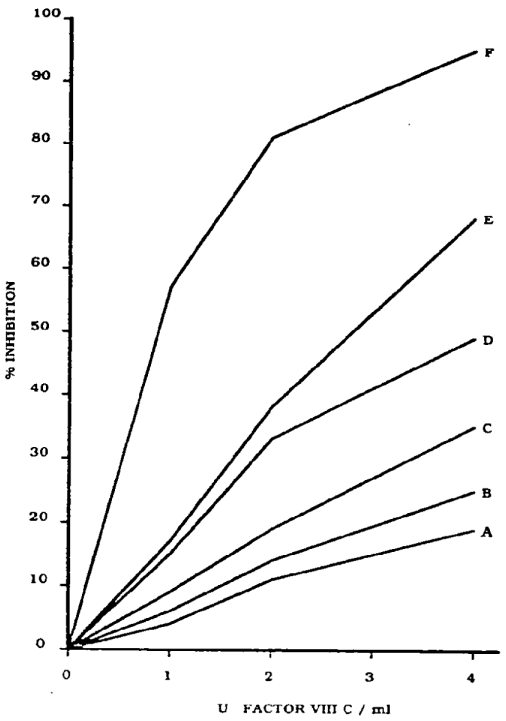
Purity of factor VIII concentrates

SIR,—UK regional haemophilia centre directors recommend that intermediate-purity factor VIII (FVIII) concentrates should be replaced by high-purity concentrates in HIV-seropositive patients with haemophilia.[1] This advice was based on evidence that impurities in intermediate-purity concentrates cause lymphocyte and monocyte dysfunction; abnormalities not observed in patients treated exclusively with monoclonally purified high-purity products. Furthermore, two studies of CD4 counts in HIV-seropositive patients treated with intermediate-purity or monoclonally-purified FVIII concentrates have suggested that intermediate-purity products may adversely affect the course of HIV infection.[2,3] CD4 counts remained stable in those using monoclonally purified products but declined progressively in patients using intermediate-purity concentrates.

These recommendations have been widely adopted, although patients in England and Wales are generally being switched to monoclonally-purified concentrates (produced commercially or under licence by the Blood Products Laboratory) whereas the Scottish National Blood Transfusion Service has chosen to manufacture ion-exchange-purified FVIII (under licence from CRTS Lille) and this is replacing intermediate-purity concentrate in Scotland and Northern Ireland. (Similar preparations are already widely used elsewhere in Europe but lack a full UK product licence.) Although the two processes yield products of similar specific activity, the impurity profiles are very different and they cannot be assumed to have similar effects on immune function.

We have compared the effect of various concentrates on lymphocyte transformation with lectins in vitro. Monoclonally purified concentrates (A and B) did not significantly inhibit lymphocyte function but equivalent concentrations of three brands of intermediate-purity concentrate (C, E, and F) and one brand of



Mean inhibition of lymphocyte transformation with phytohaemagglutinin caused by six FVIII concentrates.

All experiments done with three batches of concentrate in triplicate with cells from five healthy individuals.
A = Monoclate (Armour), B = 8SM (BPL), C = 8Y (BPL), D = Facteur VIII HP (CRTS Lille), E = Profilate SD (Alpha), F = Haemate P (Behring).

ion-exchange purified concentrate (D) significantly inhibited lymphocyte function. The data (figure) suggest that ion-exchange-purified and intermediate-purity concentrates will cause similar immunosuppression, an impression supported by a comparison of CD4 counts in HIV-seropositive haemophilic patients treated with intermediate-purity (Kryobulin, Immuno) or ion-exchange-purified (Beriate P, Behring) concentrates.[4] The use of ion-exchange-purified concentrate conferred no advantage and CD4 counts declined at a similar rate in both groups over a 24-month follow-up.

It cannot be assumed that the use of ion-exchange-purified FVIII concentrates will limit immunosuppression to the same degree as monoclonally purified products. There is no convincing evidence that ion-exchange-purified products cause less immunosuppression than intermediate-purity products and further clinical trials are required.

University Department of Haematology,
Royal Liverpool Hospital,
Liverpool L7 3BX, UK

C. R. M. HAY
P. MCEVOY

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