plasmin) rest mainly on the evidence that INR results obtained with different reagents for individual patients with LA while on warfarin are less concordant than those of controls, i.e., patients without LA and on warfarin. It should be emphasized that the INR obtained with different reagents on individual patients may differ even though the reagents have been properly calibrated to assign them an ISI value. This may be due to a variety of effects, such as (i) the influence of non vitamin K dependent clotting factors on the PT with different reagents; (ii) whether or not the stable phase of the therapy has been attained and (iii) whether or not the INR is outside the range from 1.5 to 4.5 for which this scale is valid (4). The small number of patients and controls so far investigated and the lack of information on the stability of therapy do not permit us to draw definite conclusions. Futhermore, Lawrie et al. (2) in their recent report on the same topic conclude that the INR values in patients with LA are concordant provided that the reagents are calibrated to assign them an instrument-specific ISI. Their opinion is that the discrepancies so far reported are mainly due to the incorrect application of the ISI rather than to the influence of LAs on the PT (2). These conflicting findings leave room for further investigation. Important limitations of previous studies are the relatively small numbers of patients and controls investigated and the fact that thromboplastin reagents have not been calibrated as part of the study on the same instrument (1), or they have been calibrated by procedures not endorsed by WHO (2, 3). These limitations may be circumvented by a joint effort involving investigation of a larger number of patients from different centers. Plasmas from these patients should be centralized and the INR determined with different reagents, all calibrated against the same International Standard on the same instrument by the recommended WHO procedure with fresh plasmas from healthy individuals and anticoagulated patients (4). This approach would make it possible to separate the artefactual effects due to incorrect assignment of the ISI from the genuine effect of LAs on the PT test. We feel that any decision on the issue of oral anticoagulant monitoring in patients with LA should be deferred until more information becomes available.

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References

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In Vivo Photoactivation of Caged Thrombin

Dear Sir,

Arroyo and colleagues (1) claim to have produced intravascular thrombosis in abnormal vessels of the rabbit eye using photoactivation of intravenously injected caged-thrombin but have failed to present convincing histological verification for this. The black and white photomicrograph accompanying their article and its color counterpart on the front cover of the Journal are said to show “corneal vessels filled with blood cells that stain positive for fibrin” using the phosphotungstic acid hematoxylin (PTAH) technique. It is well known that the PTAH stain is a sensitive but nonspecific marker for fibrin since it binds equally well to red blood cells and a number of other structures (2). The photomicrographs exhibit no evidence of “intraluminal fibrin clots” as stated in the paper; the vessels are filled with erythrocytes and a few leukocytes with no sign of intravascular fibrin deposition. Blue-staining of the red cells does not indicate that fibrin has precipitated on those cells. The intensity of blue coloration of red blood cells and fibrin with the PTAH method varies with minor modifications of the staining technique (Fig. 1).

Fig. 1 Photomicrograph of thin-walled, blood-filled vessels in subcutaneous tissue shows deep blue staining of red cells with phosphotungstic acid hematoxylin (original magnification = 400x).
Dear Sir,

We have read with interest the recent publication of Aygören-Pürsün et al. (1) in which they ascribe 5 seroconversions for human parvovirus B19, among 16 previously untreated and susceptible persons receiving recombinant factor VIII, to possible B19 contamination of the albumin excipient.

A more likely explanation, in the absence of a close temporal association with infusion of a particular product batch, is that this just represents community-acquired infection of this endemic virus, particularly in a group of young age. We have suggested this previously (2-4) and such an explanation would also be supported by a study we performed in 1995 showing similar age dependence of B19 seroprevalence in the Scottish population and Scots persons with haemophilia (Fig. 1), and by other studies that include an appropriate control group, such as that of Williams et al. (5).

Yours sincerely,

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Fig. 1 Seroprevalence of IgG antibody to human parvovirus B19 in the Scottish normal and haemophilic population, 1995. Samples (1036 normals, 143 haemophiliacs) were assayed using the Biotrin ELISA for IgG to B19. Clearance to obtain samples for this purpose was obtained from the appropriate local ethical committee for control children, blood donors and persons with haemophilia respectively. The higher prevalence in very young children is ascribed to passive maternal antibody transfer.