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Bleeding Time and Vascular Factor in von Willebrand's Disease

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READING the literature on bleeding times is a frustrating experience, because it is so difficult to standardize conditions and make valid observations. Unfortunately, this is the general background for the discussion on the vascular factor in von Willebrand's disease. It is my purpose to review the experience of our group in Oslo (4) and also to compare this experience with that of others.

The Two Bleeding Times. At present, two methods are in general use for the measurement of the bleeding time (BT): the Duke (6) and the Ivy (7) methods. The main difference is the use of a backpressure of 40 mm Hg in the Ivy method, but the site, size and type of wound also differ. It is important that these wounds are made with sharp instruments, preferably with a new blade, to avoid crushing the tissues. The normal values vary from laboratory to laboratory. The upper limit of normal was considered to be 3 min by Duke (6) and 4 min by Ivy (7). There has been a tendency to increase these values, and I believe that 5 min for Duke and 10 min for Ivy would more truly reflect the present experience.

The Bleeding Time in von Willebrand's Disease. Patients with von Willebrand's disease have by definition a prolonged BT, but there is a marked variation, both between individuals and at different times in the same individual. We have found that the Ivy BT usually is more than 30 min. An occasional patient may have a normal BT and may nevertheless have the disease. Cornu *et al.* (5) have proved this by showing that

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The Hemophilias (edit. K.M. Brinkhous). Univ. N.C. Press. Chapel Hill 1964, 412 pp.

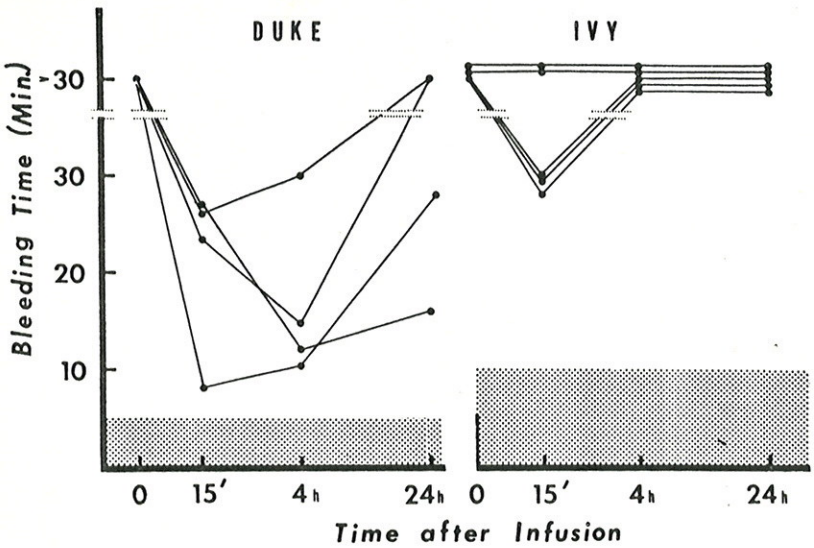

FIG. 1. The effect of plasma infusions on the Duke and Ivy bleeding times in five patients with von Willebrand's disease. Blood was collected in plastic bags with acid-citrate-dextrose as an anticoagulant. Plasma was separated (ca 1,400 *g* for 30 min at 4°C) and immediately infused into the patients; the total volume infused was 705-1135 ml.

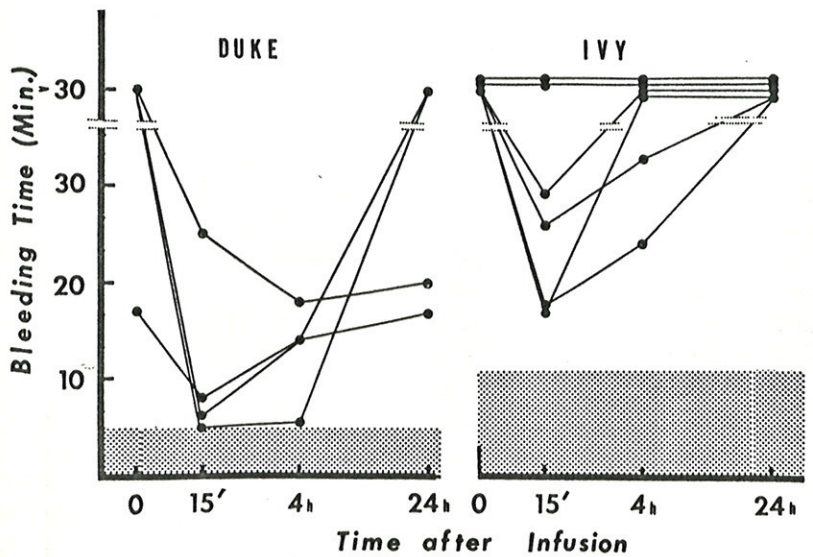

FIG. 2. The effect of Cohn's Fraction I infusions on the Duke and Ivy bleeding times in five patients with von Willebrand's disease. Fraction I was prepared from 4-6 donors and infused within 4 hours of collection of the blood.

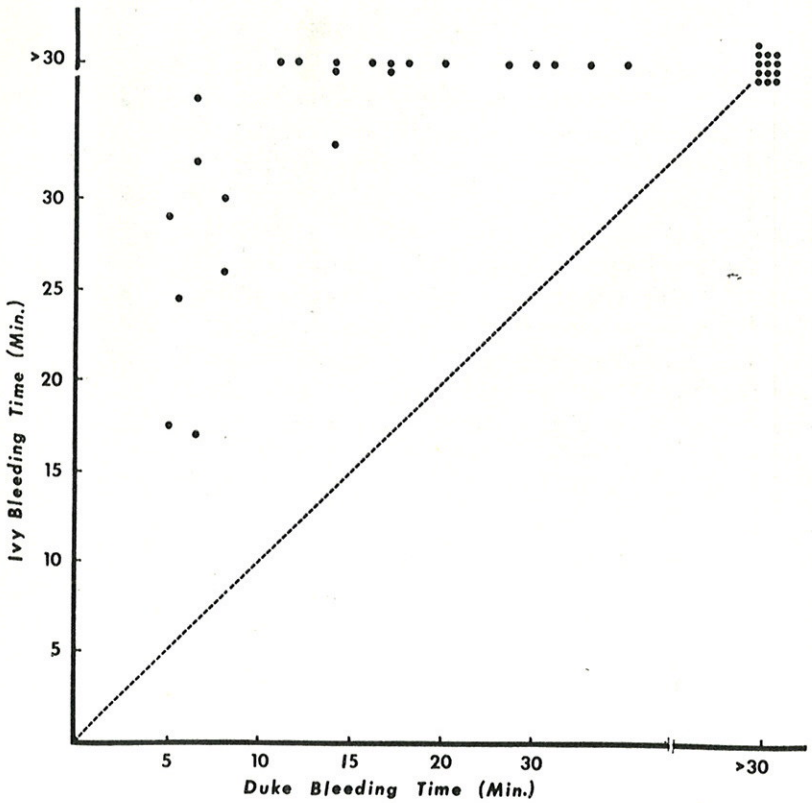

FIG. 3. Comparison of Duke and Ivy bleeding times after transfusion of patients with von Willebrand's disease. The figure is based on the data in Fig. 1 and 2.

hemophilic plasma increased the level of Factor VIII in such a patient. It is important that these variations in the BT are not paralleled by similar variations in the level of Factor VIII.

The Effect of Transfusion on the Bleeding Time. Our own experience with transfusions of about 1 liter of fresh, citrated plasma collected in plastic bags is summarized in Fig. 1. Fig. 2 shows the results with infusions of Cohn's Fraction I. Clearly, there is a significant effect on the Duke BT, but the effect on the Ivy BT is disappointing. Our experience seems to reflect the general situation: those who use the Duke BT are convinced that there is a marked effect of transfusions, but those who use the Ivy BT have expressed doubts. In fact, I believe that the Swedish group would never have discovered the effect if they had used the Ivy method. In spite of these discrepancies, there can now be little doubt that there *is* an effect of infused plasma, and the "bleeding time factor" must therefore be accepted. The studies of Borchgrevink (3), Weiss (8)

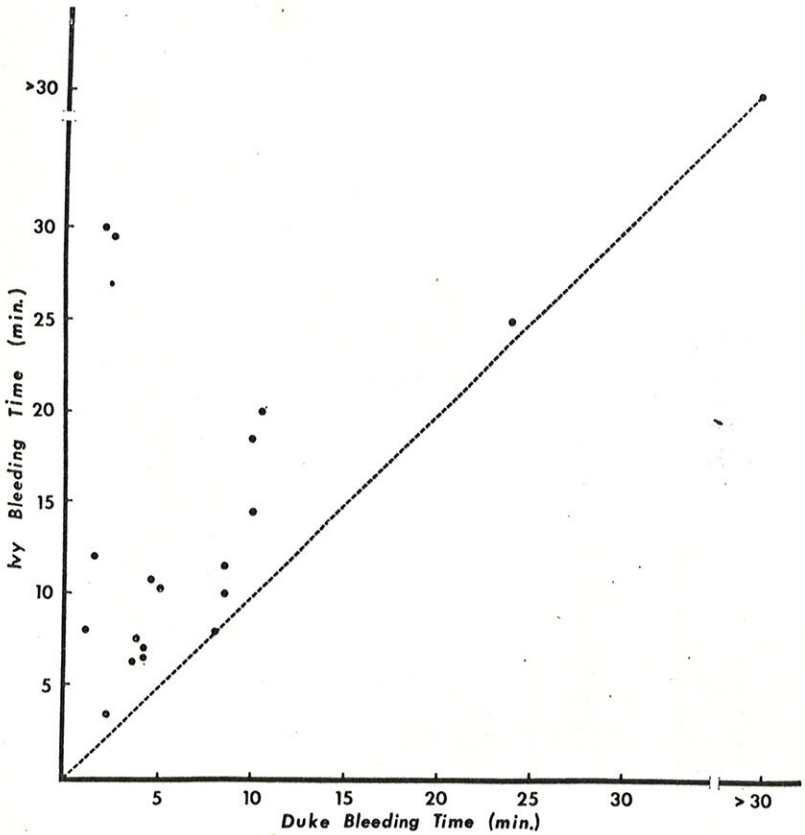

FIG. 4. Comparison of Duke and Ivy bleeding times in patients with thrombocytopenia.

and Cornu *et al.* (5) suggest that the factor is necessary for the adherence of platelets to injured vessels.

The Discrepancy Between the Two Bleeding Times. This discrepancy is so marked in von Willebrand's disease (Fig. 3) that we have compared the two methods also in patients with thrombocytopenia. These data are still not complete (Fig. 4), but it is possible that the difference between the two methods is smaller in these patients than in patients with von Willebrand's disease.

The explanation for the discrepancy between the two bleeding times is not known. We have found, as did also Duke (6), that the size of the wound plays a minor role: large cuts bleed a little longer than do small cuts, but the difference is small. The difference is probably not due to the use of pressure in the Ivy method. In some of the transfusion experiments we measured the Ivy BT without pressure, and found that the bleeding

was then only slightly shorter. At present, therefore, the difference between the two methods cannot be explained.

Which Test is the Better Clinical Tool? There can be little doubt that the sensitive Ivy method is better for diagnostic purposes, especially when there is reason to suspect von Willebrand's disease. However, this may no longer be true when the purpose is to use the BT as a practical guide to evaluate the risk of bleeding. There are reports of little or no bleeding following surgery in patients with von Willebrand's disease, in spite of a greatly prolonged Ivy BT (2, 4). Thus, practical experience has shown that it is not necessary to maintain a normal Ivy BT during and after surgery. However, there may also be a discrepancy between the actual hemostatic effect of transfusions and the effect on the Duke BT (1). Thus, we do not know the significance of the "bleeding time factor" for hemostasis. At present, Factor VIII levels appear to be a better practical guide than the BT in patients with von Willebrand's disease. To settle this problem, we need serial studies of Factor VIII levels and of the two bleeding times in patients who undergo surgery and tooth extractions. Such studies should also be done in patients with a prolonged BT due to other hemostatic defects.

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