

Table 1 Platelet factor VIII-related antigen (F VIII-RA) in VWD

Patient	FVIII-RA/mg platelet protein (U)	FVIII-RA/10 <sup>11</sup> platelets (U)	FVIII activity plasma (U ml <sup>-1</sup> )	FVIII-RA plasma (U ml <sup>-1</sup> )	Bleeding time <sup>25</sup> (min)
1	0.18	35	0.14	< 0.05	7
2	0.14	56	0.23	< 0.05	9
3	0.04	16	0.13	< 0.05	7
4	< 0.01	< 0.01	0.12	< 0.05	> 15
5	0.15	35	0.11	< 0.05	—
6	0.27	60	0.05	< 0.05	> 15
7	0.18	52	0.15	< 0.05	> 15
8	0.26	67	0.12	< 0.05	10
9	0.23	90	0.18	< 0.05	—
10	0.24	47	0.44	0.80	> 15
11	< 0.01	< 0.01	0.15	0.10	—
12	0.08	14	0.10	0.10	—
13	0.14	38	0.11	0.05	—
14	0.36	120	0.35	0.40	9
15	0.16	34	0.21	0.25	6

with antibodies produced in rabbits against platelet fragments, which may be carried along in the purification of factor VIII. The following observations suggest that in our experiments the antigen detected by rabbit anti-factor VIII in platelets is indeed F VIII-RA.

(1) The platelet antigen could not be distinguished from plasma factor VIII when tested in immunodiffusion and cross immunoelectrophoresis, using antifactor VIII and the antisera against the low ionic strength components of factor VIII. (2) The positive immunofluorescence of haemostatic plugs was completely blocked by absorption of antifactor VIII with purified factor VIII, the characteristics of which have been described in detail<sup>15,26</sup>. (3) In preliminary experiments antibodies were prepared against normal and VWD platelet F VIII-RA. These antisera precipitated with purified factor VIII when tested in immunodiffusion experiments.

Previously it has been suggested that the capacity to synthesise F VIII-RA is reduced in VWD. This was concluded from the fact that F VIII-RA is reduced or absent in plasma of patients with VWD. Our findings, however, suggest that the platelets, or more likely the megakaryocytes retain the capacity to synthesise F VIII-RA. Another possible explanation for the presence of F VIII-RA in VWD platelets is that the platelets selectively sequester F VIII-RA from an extracellular source such as plasma or endothelial cells. The fact that F VIII-RA from normal as well as from VWD platelets supports ristocetin-induced aggregation may indicate that platelet F VIII-RA is also identical to VWF. VWF has been deemed necessary for normal haemostasis because patients with VWD who lack this factor have a prolonged bleeding time. The presence of F VIII-RA in haemostatic plugs<sup>20</sup>, and blood platelets suggests that it serves some useful function in haemostasis. A direct haemostatic role of platelet F VIII-RA seems unlikely because it is not released from intact platelets and is present in platelets of patients with VWD who have prolonged bleeding times. Although plasma F VIII-RA seems to be more important in haemostatic plug formation the presence and synthesis of F VIII-RA in endothelial cells and its localisation in blood platelets suggest additional haemostatic functions for this molecule.

We thank Dr Jean Dodds for criticising this manuscript. This investigation was supported in part by the Foundation for Medical Research (Fungo) which is subsidised by the Netherlands Organization for the Advancement of Pure Research (ZWO).

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Received June 30; accepted August 19, 1975.

- Nilsson, I. M., Blombäck, M., Jorpes, E., Blombäck, B., and Jönansson, S. A., *Acta Med. scand.*, **159**, 179–188 (1957).
- Bouma, B. N., Wiegierink, Y., and Sixma, J. J., Van Mourik, J. A., and Mochtar, I. A., *Nature new Biol.*, **236**, 104–106 (1972).
- Weiss, H. J., Rogers, J., and Brand, H., *Blood*, **41**, 809–815 (1973).
- Meyer, D., Jenkins, C., Dreyfus, M., and Larrieu, M. J., *Nature*, **243**, 293–294 (1973).
- Weiss, H. J., Rogers, J., and Brand, H., *J. clin. Invest.*, **52**, 2697–2707 (1973).
- Zimmerman, T. S., and Edgington, T. S., *J. exp. Med.*, **138**, 1015–1020 (1973).
- Hougie, C., Sargeant, R. B., Brown, J. E., Baugh, R. F., *Proc. Soc. exp. biol. Med.*, **147**, 58–61 (1974).
- Zimmerman, T. S., Ratnoff, O. D., and Powell, A. E., *J. clin. Invest.*, **50**, 244–254 (1971).
- Weiss, H. J., Hoyer, L. W., Rickles, F. R., Varma, A., and Rogers, J., *J. clin. Invest.*, **52**, 2708–2716 (1973).
- Karparkin, S., *J. clin. Invest.*, **46**, 409–417 (1967).
- Lowry, O. H., Rosebrough, N. J., Farr, A. L., and Randall, R. J., *J. biol. Chem.*, **193**, 265–275 (1951).
- Bouma, B. N., Van der Klaauw, M. M., Veltkamp, J. J., Starckenburg, A. E., Van Tilburg, N. H., and Hermans, J., *Thromb. Res.*, **7**, 339–350 (1975).
- Born, G. V. B., *J. Physiol., Lond.*, **209**, 487–512 (1970).
- Nachman, R. L., and Jaffe, E. A., *J. exp. Med.*, **141**, 1101–1113 (1975).
- Van Mourik, J. A., Bouma, B. N., LaBruyère, W. T., de Graaf, S., and Mochtar, I. A., *Thromb. Res.*, **4**, 155–164 (1974).
- Howard, M. A., Montgomery, D. C., and Hardisty, R. M., *Thromb. Res.*, **4**, 617–624 (1974).
- Bloom, A. L., Giddings, J. C., and Wilks, C. J., *Nature new Biol.*, **241**, 217–219 (1973).
- Hoyer, L. W., de los Santos, R. P., and Hoyer, J. R., *J. clin. Invest.*, **52**, 2737–2744 (1973).
- Kater, L., Borst-Eilers, E., and Van Gorp, L. H. M., *Pathol. Europ.*, **7**, 299–306 (1972).
- Sixma, J. J., et al., *J. Lab. clin. Med.* (in the press).
- Bouma, B. N., and Starckenburg, A. E., *Haemostasis*, **3**, 94–97 (1974).
- Jaffe, E. A., Hoyer, L. W., and Nachman, R. L., *J. clin. Invest.*, **52**, 2757–2764 (1973).
- Hovig, T., Rowsell, H. C., Dodds, W. J., Jørgensen, L., and Mustard, J. F., *Blood*, **30**, 636–668 (1967).
- Holmberg, L., and Nilsson, I. M., *Br. Med. J.*, **3**, 317–320 (1972).
- Ivy, A. C., Nelson, D., and Bucher, G., *J. Lab. clin. Med.*, **26**, 1812–1822 (1941).
- Van Mourik, J. A., and Mochtar, I. A., *Biochim. biophys. Acta*, **221**, 677–679 (1970).
- Bouma, B. N., *Scand. J. Haemat. Suppl.*, **13**, 391–392 (1971).
- Coller, B. S., Hirschman, R. J., and Gralnick, H. R., *Thromb. Res.*, **6**, 469–480 (1975).
- Shearn, S. A. M., Giddings, J. C., Peake, I. R., and Bloom, A. L., *Thromb. Res.*, **5**, 583–599 (1974).

## Corrigendum

In the article "The origin of nuclei and of eukaryotic cells" by T. Cavalier-Smith (*Nature*, **256**, 463; 1975) the two unlabelled arrows at the top right of Fig. 5 should read (from the top) Prasinophyta and Charophyta, respectively.

## Erratum

In the article by B. Donzel and M. Goodman (*Nature*, **256**, 750; 1975) the title should have read "Synthesis and conformations of hypothalamic hormone releasing factors: two TRF analogues containing backbone N-methyl groups" and not as printed.