that a new mutation occurred, could not be excluded. The possibility that the father is hemophilic, would imply that the examined father is not the child's father and has yet to be explored.

C. D. Forbes, A. D. McLaren and C. R. M. Prentice (Department of Medicine, Royal Infirmary and Department of Statistics, Glasgow University, Glasgow, Scotland): **Calculation of Predictive Odds for Possible Carriers of Haemophilia.** **(527)**

The predictive odds for possible carriers of haemophilia have been calculated using data derived from normal and known carrier populations. For each individual the concentration of factor VIII-related antigen (A) and factor VIII biological activity (B) was measured. The data has been studied by linear discriminant analysis linked to a Bayesian calculation of posterior odds using the predictive distributions of both the normal and obligatory carrier populations. The proportion of possible carriers assigned to the definite carrier group or control group is dependent on which betting odds are regarded as most suitable for counselling patients. For instance, if betting odds of 5 : 1 were given it was possible to assign 22 of 32 possible carriers (69 per cent) to control or carrier groups. Of this group of 22 possible carriers, 11 were thought to be normal and 11 were thought to be haemophilia carriers.

G. Casillas, C. Simonetti and A. Pavlovsky (Instituto de Investigaciones Hematológicas, P. de Melo 3081, Buenos Aires, Argentina): **Immunological Separation and Study of a F. VIII Inhibitor.** **(528)**

A potent F. VIII inhibitor developed by a patient with hemophilia A, polytransfused with homologous material, was studied. The ability of the inhibitor to inactivate human, bovine, and others mammals F. VIII activity showed its low species specificity. A crude gamma globulin preparation of the plasma with the inhibitor was mixed with higly purified bovine F. VIII. When the complex "bovine F. VIII-inhibitor" formed in the mixture was purified by gel filtration it did not show F. VIII activity or inhibitory action. By the use of specific antisera to bovine F. VIII and to human gamma globulins two antigens were found in the complex: a) bovine F. VIII and b) human IgG gamma globulin. Thus the nature of the inhibitor was seen in its purified form. For further evidence of the results, rabbit antiserum was prepared with the "bovine F. VIII-inhibitor" complex. This antiserum gave precipitation bands with: a) bovine F. VIII, b) human plasma (gamma globulins) and c) "Bovine F. VIII-inhibitor" complex. Even though this antiserum has a good precipitating capacity for bovine F. VIII, its neutralizing capacity against F. VIII biological activity is very low. Any way when the mixture antiserum-bovine F. VIII is ultracentrifuged, F. VIII activity disappears from the supernatant.

D. Frommel, A. Gaillandre, L. Meunier and J. P. Allain (Centre médicopédagogique pour jeunes hémophiles. Croix-Rouge Française & U 56 I.N.S.E.R.M.): **The Puzzle of Immunologic Reactivity to Factor VIII in Haemophilia A.** **(529)**

Factor VIII neutralizing antibodies occur in 6–21% of transfused haemophiliacs A. Two types of specific immune response can be observed. In high responding patients, anti-factor VIII antibodies develop after relatively short exposure to the antigen, and anamnestic responses are characterized by antibodies of high affinity and titer. In low responding haemophiliacs, occurrence of anti-factor VIII antibodies is delayed and secondary response is either inconstant or requires strong antigenic challenge. Both types of immune response can be observed in kindreds. Low responsiveness to human factor VIII can switch to high responsiveness as a result of stimulation with heterologous factor VIII.

In experimental situations, it has been found that immunologic reactivity to weak native isologous antigens is dose-dependent and shows extreme variations from one individual to another. The state of high, low or non responder is, in many instances, controlled by well defined genetic mechanisms. Considering possible analogies between