LOW MOLECULAR WEIGHT FACTOR VIII: A COMPARISON OF THE ELECTROPHORETIC MAPS OF THE NORMAL AND HEMOPHILIAC MOLECULE. G.A. Rock and W.H. Cruickshank, Canadian Red Cross Blood Transfusion Service, Ottawa, Ontario, Canada.

Considerable debate exists as to the relative structure of normal and hemophilic Factor VIII. In order to obtain some insight into the differences which exist at the molecular level we examined the various subunits found after dissociation of Factor VIII from these two populations.

Factor VIII was obtained by column chromatography of either cryoprecipitate or concentrated plasma on Sepharose CL6B. The protein eluting at the void volume was rechromatographed in buffer containing 0.25 M CaCl_2 . Under these conditions, both normal and hemophilic Factor VIII underwent dissociation with an identical elution pattern. The low molecular weight fraction from normal Factor VIII displayed procoagulant activity; that from the hemophilic did not.

As determined by their elution volume and ultrafiltration, the molecular weights were identical. When digested with pepsin (protein: pepsin 50:1) for 16 hours at 37°C and "mapped" by pH 6.5/2.1 paper electrophoresis the two compounds were significantly different in the neutral and acidic peptide regions and identical in the basic region.

It therefore appears that the inactivity of hemophilic Factor VIII is a consequence of an amino acid substitution or deletion in the low molecular weight portion of the molecule rather than a complete absence of the procoagulant molecule.