CORRESPONDENCE

To the Editor:

Dr. Chediak and his colleagues[1] have reported that carriers of hemophilia A who inherit the defective gene from their father have a lower level of factor VIII coagulant activity (VIII:C) than carriers who inherit the gene from their mother. Their findings are very similar to ours[2] and prompt us to report the results we have obtained in carriers seen at Oxford in recent years.

Since 1972 we have examined 123 obligatory carriers of hemophilia A; 64 were the daughters of known hemophiliacs and 46 had inherited the defect from their mother. The remaining 13 had two or more hemophilic sons or one son and one or more grandsons with the condition but with no other history of hemophilia in the family. It was therefore not possible to say whether or not these women had received the defective gene from their mothers.

The results of our assays of plasma factor VIII:C and factor-VIII-related antigen (VIIIR:ag) are shown in Table 1, as are the ages of the women studied.

Table 1.

	VIII:C (% Average Normal)	VIIIR:ag (% Average Normal)	Age (yr)
Paternal			
$n = 64$			
Mean	44.9	101.7	20.1
SEM	2.27	6.04	1.53
Range	11–85	44–302	1–43
Maternal			
$n = 46$			
Mean	56.6	119.2	37.8
SEM	2.58	6.06	1.53
Range	19–109	57–240	18–59
No previous family history			
$n = 13$			
Mean	61.07	110.84	39.4
SEM	7.09	11.36	2.43
Range	27–125	56–197	28–48

The "paternal carriers" have a significantly lower level of factor VIII:C than the "maternal carriers" ($p < 0.001$). Those results are similar to our previous findings and agree with those of Chediak et al. Unlike the latter authors, however, we have found that paternal carriers have a lower level of factor-VIII-related antigen than maternal carriers. The difference seen was not as great as with factor VIII:C but was statistically significant ($p < 0.05$).

It is interesting to note that the carriers with no previous family history had a mean factor VIII:C level comparable to that of women who had received the defective gene from their mothers. The numbers in this group are small and more carriers in this category are required to be studied.

Like Professor Graham,[3] we were concerned that the observed differences between the carrier groups might have been brought about by nonrandom selection of carriers or by some vagary in the assay of factor VIII:C or in the standards used for the assay during the 8-yr period. We have checked back over our results to see how many carriers in each category were studied in each year and have also studied the assay figures, the value placed on the standards, and the factor VIII:C results obtained on many normal plasma samples in relation to the standards used during those years. Having done this, we cannot find any fault with the assays or with the standards. The possibility that the difference in factor VIII:C observed was due to the difference in ages in the two groups was studied by regression analysis. The effect of age within each group was very small and not significant. On the basis of our results we concluded as before[2] that carriers of hemophilia A who have inherited the abnormal gene from their hemophilic father have a lower level of factor VIII:C than those who have inherited it from their mother.

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REFERENCES

1. Chediak J, Telfer MC, Jaojaroenkul T, Green D: Low factor VIII coagulant activity in daughters of subjects with hemophilia A compared to other obligate carriers. Blood 55:552–558, 1980

2. Biggs R, Rizza CR: The sporadic case of haemophilia A. Lancet 2:431–433, 1976

3. Graham JB: Letter to the Editor. Blood 56:742, 1980

To the Editor:

The review by Koeffler and Golde,[1] "Human Myeloid Cell Lines," prompts us to report the results of studies in progress on the differentiation of the K-562 leukemia cells. The original K-562 blasts were characterized as very early precursors of the granulocytic series with a block for differentiation.[2,3] Since K-562 blasts did not differentiate in agar-gel cultures, although the average platting efficiency was as high as 70%, an attempt was made to stimulate their potential for spontaneous differentiation in prolonged suspension cultures to have most cells at the steady state rather than during expotential growth. Perplexingly enough, the cultivation of K-562 cells for 10 days in media gradually depleted of the essential nutrients needed for cell division induced their differentiation into early precursors of the monocytic, granulocytic, erythrocytic, and probably of the megakaryocytic series.

The peroxidase reaction for hemoglobin demonstrates benzidine-positive material limited to the region of the Golgi apparatus in about 14% of large blasts with undifferentiated nuclei containing numerous nucleoli. Intermediate forms, such as normoblasts, were rarely seen and up to 20% were glycophorin-positive cells. The nature of hemoglobins synthesized by K-562 cells were analyzed by isoelectric focusing and indicated major bands in the region of hemoglobin F and Bart's.

The majority of the cells (80%–90%) give a strong reaction for α-naphtyl acetate esterase typical (fluoride sensitive) of monocytic series and as many as 30%–40% of the cells have abundant red