907 ALTERATION OF TRANSFUSED VON WILLEBRAND FACTOR (VWF) IN A PATIENT WITH SEVERE VON WILLEBRAND DISEASE (VWD)

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Previous studies by others have demonstrated preferential loss of the high molecular weight vWf multimers after infusion of purified 125I-radiolabeled vWf but this abnormality might be the result of purification and radiolabeling the vWf. We studied plasma factor VIII molecular complex serially in a patient with severe vWd after transfusion with cryoprecipitate (cryo) and determined the multimeric composition of vWf by SDS-agarose electrophoresis. Studies before and after infusion of 1 donor unit cryo per 5 kg body weight were as follows:

	VIII:C	vW Ag	vWf	Subunits
Pre	2.6	<1.5	<1.5	None
1 hour	47	36	37	Normal
18 hours	69	14	13	Abnormal
39 hours	35	4	4	Abnormal

Multimeric analysis of vWf showed progressive loss of the larger multimers. A vW antigen fragment was identified following subsequent infusions. Thus, with infusion of vWf from cryo, we have confirmed the preferential loss of large multimers. The vW antigen frag may be the result of in vivo or in vitro proteolysis.

† 908 NORMALIZATION OF ABNORMAL VON WILLEBRAND FACTOR (VWF) MULTIMERS FOLLOWING CLOSURE OF VENTRICULAR SEPTAL DEFECT (VSD)

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Plasma samples from 8 children with ventricular septal defect (VSD) were previously found to lack the high molecular weight vWf multimers by electrophoresis in SDS-agarose followed by staining with 125I-radiolabeled anti-vWf and autoradiography. Low vWf by antigenic and ristocetin cofactor assays were found in 4 whereas all had normal VIII:C; none had evidence of intravascular coagulation. To determine if these children were different from others with VSD, cardiac catheterization findings were evaluated. All had a sealed foramen ovale and high or high normal end diastolic pulmonary artery pressure. To date, 3 of the children have been re-studied after surgical correction of their VSD. Two had normalization of vWf multimers; the third, whose vWf was abnormal postoperatively, had a residual pressure gradient across a previous pulmonary artery banding site. Multimeric abnormalities were not found in the parents of 3 patients. Thus, some patients with VSD and an abnormal hemodynamic state may have an "acquired" loss of the high vWf multimers that is normalized with correction of the hemodynamic defect.

● 909 COMPARATIVE ACTIVITY OF ADENOSINE DEAMINASE (ADA) AND OROTIDINE DECARBOXYLASE (ODC) IN RED BLOOD CELLS (RBC) FROM PATIENTS WITH DIAMOND-BLACKFAN SYNDROME (DBS).

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We previously reported that ADA activity is increased in RBC from patients with DBS, but not in RBC from patients with other RBC-hypoplastic disorders (NEJM 307:1486, 1983). It also has been reported that the pyrimidine synthetic enzyme ODC is increased in RBC from patients with DBS (Br J Haematol 42:381, 1979). In the present study we compared the activity of these two enzymes in RBC from patients with DBS:

ODC (Eu/Gm Hgb)		ADA (Eu/Gm Hgb)	
Normal (19)	290 ± 170	Normal (50)	0.62 ± 0.13
DBS (7)	680 ± 140	DBS (16)	2.21 ± 0.78
Retic-rich (7)	1510 ± 650	Retic-rich (19)	0.75 ± 0.16
Cord Blood (19)	1810 ± 920	Cord Blood (14)	0.58 ± 0.08

In support of the previous observations we observed elevated ODC activity in RBC from patients with DBS compared to normal. Since ODC is an age-dependent enzyme, however, activity of this enzyme in DBS RBC was less than that observed in retic-rich blood or cord blood erythrocytes. In contrast, ADA activity is markedly elevated in DBS RBC compared to normal, retic-rich and cord blood RBC. These data support the concept that purine and pyrimidine metabolism may be deranged in DBS RBC. In terms of sensitivity, however, ADA activity appears to be the most discriminate biochemical abnormality to aid in the diagnosis of this RBC disorder.

† 910 EVIDENCE FOR REDUCTION OF CONTACT FACTORS IN SICKLE CELL DISEASE.

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Evidence supporting the existence of intravascular coagulation in homozygous sickle cell (HbSS) disease has been reported. In this study, surface-mediated reactions of clotting were compared in 21 black children with HbSS disease and 12 age-matched controls. Both the coagulant and antigen titers of Hageman factor were decreased (mean coagulant titer 0.49 ± S.D. 0.29 u/ml; mean antigen titer 0.77 ± 0.27 u/ml) in asymptomatic HbSS patients compared to the control group (mean coagulant titer 1.01 ± 0.39 u/ml; mean antigen titer 0.94 ± 0.25 u/ml). A disparate relationship between the Hageman factor coagulant and antigen titers were observed in HbSS patients. These findings were associated with a slight decrease in the plasma titers of prekallikrein and HMW kininogen (mean 0.78 ± 0.14 and 0.75 ± 0.15 u/ml respectively in HbSS patients compared to 1.05 ± 0.22 and 0.86 ± 0.09 u/ml respectively in the control group). A further reduction from the initially low titers of these contact factors was observed during vaso-occlusive crises (mean Hageman factor titer 0.32 ± 0.15 u/ml; mean prekallikrein titer 0.38 ± 0.18 u/ml; mean HMW kininogen titer 0.56 ± 0.17 u/ml). These data indicate that the initial participants of the intrinsic pathway of coagulation are consumed in patients with HbSS disease. Further, these processes appear to accelerate during vaso-occlusive crises.

● 911 SICKLE CELL BLOOD INCREASES PROSTACYCLIN (PGI_2) PRODUCTION BY CULTURED ENDOTHLIAL CELLS IN AN IN VITRO FLOW SYSTEM.

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We have shown that PGI_2 production by monolayers of bovine aortic endothelial cells (ECM) increases for several minutes when the ECM are suddenly exposed to heparinized (4 U/ml) normal blood under arterial-like flow conditions. The increase is dependent upon levels of shear rate (or shear stress) and the presence of platelets and red cells. Since vessel wall injury may occur in sickle cell disease, we exposed ECM to blood from children with SS disease vs normal controls in a parallel-plate chamber at 37°C, pH 7.4, and shear rates of 270 and 700 sec^{-1}. Despite a 36% lower hematocrit, sickle cell bloods had a whole blood viscosity at 350 sec^{-1} (Wells-Brookfield cone-plate viscometer) similar to controls, thereby ensuring similar shear stresses for the two kinds of blood at the shear rates studied. Chamber outflow samples were collected on ice into indomethacin and EDTA. PGI_2 in supernatant plasma was measured by RIA for 6-keto $PGF_{1\alpha}$. In six matched-pair (patient-control) experiments, initial PGI_2 production with SS blood exceeded that with normal blood ($p<0.01$) by 68 ± 33% (mean ± SE). Interestingly, the greatest PGI_2 response was seen with the one patient who had had no vasoocclusive crises in the past 5 years. Since PGI_2 is a potent vasodilator, its increased production may represent an important compensatory response of blood vessels to minimize the effects of local flow impairment due to sickle erythrocytes.

912 STUDIES RELATED TO THE CRISIS EPISODES IN SICKLE CELL PATIENTS

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In this study we have measured a variety of hematogical parameters in 17 sickle cell disease (SCD) patients (mean age: 35 years) for a period of 30 months. Several hematological parameters were measured under conditions of vaso-occulsive crisis as well as in the steady state noncrisis period. The mean serum calcium content (mg of calcium per dl) was found to be less ($P < 0.05$) during crisis (8.24 ± 0.73 , N = 7) than during the noncrisis states (8.81 ± 0.43 , N = 15). This decrease in serum calcium may be the result of calcium influx into Hb SS-erythrocytes. Irreversibly sickled Hb SS-erythrocytes are known to have a particularly high calcium content. Fibrinogen levels were also found to be much higher ($P < 0.01$) in the crisis state (426 ± 195 mg/dl , N = 3) compared to the noncrisis state (236 ± 47 mg/dl , N = 14). Measurements of serum LDH and of oxygen saturation (P-50 per cent) and blood gases were not significantly different in the two states (crisis vs steady state). There is an increased shift to the right of the optical density of sickle hemoglobin during crisis compared to the steady state. Measurement of the optical density of sickle hemoglobin may be useful in predicting the frequency of sickle cell crisis in some patients.