coccal disease have up to an 800 times greater risk of developing meningococcal disease, such as septicaemia, than those of the general population.[10] The systemic treatment of a person with a meningococcal conjunctivitis and the screening and treatment of their contacts with prophylactic antimicrobials is thus important. This case reaffirms the necessary practise of microbiologically investigating patients with conjunctivitis.

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Sir

Retinal Signs in Sickle Cell Anaemia

Patients with sickle cell anaemia may have retinal abnormalities ranging in severity from simple arteriolar occlusion to proliferative sickle cell retinopathy (PSR) with visual loss.[1,2] To date, studies examining haematological factors in relation to the severity of sickle cell retinopathy have yielded negative or conflicting results.[3,4] Goldberg[5] has suggested that intravascular red blood cell sickling and increased blood viscosity may be the cause of this retinal vascular occlusion. However, it might then be expected that such sickling would occur at that point in the circulation where oxygen is the lowest, i.e. on the venular end of the capillary or in the venule itself.

It is now known that erythrocytes of sickle cell patients contain varying amounts of polymerised sickle haemoglobin (Hbs) at arteriolar saturation values.[6] The tendency of HbS to polymerise is determined by the intracellular haemoglobin concentration and composition.[6] The resulting heterogeneity in red cell haemoglobin concentration can be assessed by using the calibrated phthalate ester technique.[7] The middle 60% density range (R60 values) serves as an indicator of the heterogeneity of the density of the red cells. We used the phthalate ester technique and red cell indices to examine whether HbS is the primary determinant of the retinal lesions found in sickle cell patients.

We studied a consecutive series of 30 patients, nine women and 21 men, with stable sickle cell anaemia admitted for routine follow-up to the National Institutes of Health. Their mean age was 30.0 + 8.1 years. The diagnosis of sickle cell anaemia was made on the basis of red cell haemoglobin electrophoresis, DNA analysis of bone marrow aspirates and peripheral blood examination. No patient was included who had a sickle cell crisis during either the month before or after the study, who had received a blood transfusion in the four months before the study or who was taking long term medication other than folic acid.

A detailed retinal examination was performed using Goldmann 3 mirror contact lens, and recorded on a fundus drawing. Fundus photographs were obtained in 29 of the 30 patients and fluorescein angiography (FA) in 19 patients. Severity of the sickle cell retinopathy was graded using Goldberg's classification.[1]

Haematological tests, performed independently (by GPR) on the day of the ocular examination included total haemoglobin levels, reticulocyte count, absolute reticulocyte count calculated from the red cell count and the percentage of reticulocytes, the fraction of fetal haemoglobin (HbF), mean red cell corpuscular haemoglobin concentration (MCHC) and red cell density profile using the phthalate ester technique.[7] The median density (D50), middle 60% density range (R60), and fraction of dense cells (specific gravity 1.120, CHC>37 gm/dl) were calculated.[7]

In the statistical analysis non normally distributed data were analysed using the Wilcoxon rank sum test, and Student's *t* test on log transformed data. Spearman method of correlation was also used.

Retinal arteriolar occlusion, in the form of an engorged vascular segment on biomicroscopic examination, no sheathing and no perfusion on fluorescein angiography was present at the posterior pole in three patients and in peripheral arterioles in another two (Fig. 1). Such occlusions were transient and normal perfusion on FA was subsequently observed in these patients. Patients with such retinal arteriolar occlusions (N=5) had a significantly higher percentage of reticulocytes (14.1 (6.2) % *vs* 8.6 (4.2) % or absolute reticulocytes (3.5 (1.1) × 10^9/l SI units *vs* 2.5 (1.1) (10^9/l SI units) than patients without those signs (N=23) (p=0.02 and p=0.03, respectively) (Table).

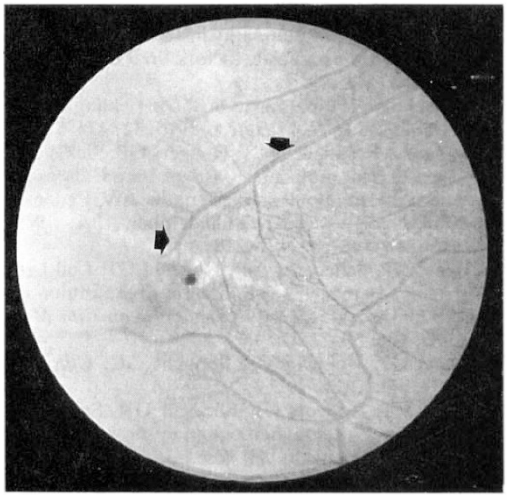

Fig. 1(a) *Fundus photograph showing an engorged retinal arteriole (arrows).*

Patients with PSR (N=7) had significantly lower blood levels of HbF than those without PSR (N=22) (1.0 (0.5) % *vs* 1.8 (1.1) %, p=0.03) (Table). There were no significant differences on any haematological factor between patients with (N=18) or without (N=10) Stage I substages 3 or 4 retinal changes (Table).

In the total group of sickle cell patients reticulocyte count and log R60 values were significantly associated (r = 0.48, p<0.05, N = 30).

Discussion

In the present study of sickle cell patients we found that transient arteriolar occlusion was significantly associated with high reticulocyte counts and PSR with low levels of HbF.

It is now generally accepted that the rate and extent of HbS polymerisation-depolymerisation is a function of intracellular HbS concentration.[6] Cellular dehydration accompanies this reversible polymerisation process and results in an heterogeneity of the density of the red cell population (R60 values) with the formation of progressively denser red cells. Denser red cells have diminished viscoelastic properties and are thought to be responsible for microvascular occlusion and chronic haemolysis. In sickle cell patients the degree of red cell haemolysis, which is mirrored by changes in reticulocyte count and indirect bilirubin levels, is significantly associated with R60 values.[8] Thus, the significant association that we found between transient arteriolar occlusion and high reticulocyte counts suggest that the extent of red cell hae

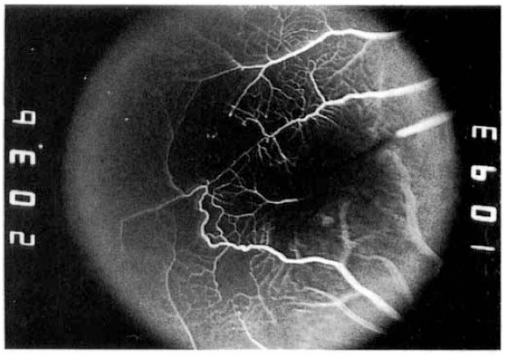

Fig. 1(b) *Fluorescein angiogram of the same area showing the non-perfusion of the engorged retinal arteriole.*

Table *Hematological indices and retinal findings in 30 patients with sickle cell anaemia*

	Patients with arteriolar occlusion		Patients with peripheral vessel closure*		Patients with proliferative sickle retinopathy+	
	Absent	Present	Absent	Present	Absent	Present
	(n=23)	(n=5)	(n=10)	(n=18)	(n=22)	(n=7)
Age (years)	29.5 (8.3)	31.2 (8.3)	32.4 (9.8)	29.4 (7.1)	29.0 (8.4)	33.7 (7.0)
Hb (g/dl)	9.0 (1.4)	8.6 (1.0)	9.2 (1.5)	8.8 (1.3)	9.0 (1.3)	8.9 (1.4)
MCHC (g/dl)	34.0 (1.9)	33.5 (1.7)	33.9 (1.5)	34.1 (2.1)	34.2 (1.6)	33.4 (2.6)
Reticulocyte (%)	8.6 (4.2)	14.1 (6.2)‡	9.8 (6.4)	9.4 (4.3)	8.6 (4.3)	14.1 (6.3)
absolute reticulocyte ($\times 10^9$/l)(SI units)	2.5 (1.1)	3.5 (1.1)	2.7 (1.4)	2.7 (1.0)	2.8 (1.3)	2.5 (0.6)
HbF†(%)	1.6 (0.5)	2.2 (2.6)	1.7 (1.3)	1.6 (0.6)	1.8 (1.1)	1.0 (0.5)§
Dense Cells† (%)	8.51 (5.82)	8.00 (3.92)	6.69 (6.88)	8.25 (4.43)	8.3 (6.7)	9.04 (4.09)
D50 (SG units)	1.102 (0.005)	1.104 (0.004)	1.101 (0.005)	1.103 (0.006)	1.103 (0.005)	1.101 (0.005)
R60† (SG units) $\times 10^{-3}$ Means (SD)	3.32 (0.99)	4.10 (1.22)	3.69 (1.19)	3.42 (1.06)	3.6 (1.04)	3.1 (1.17)

*Stage 1 substages 3 and 4, +Stage III, Goldberg's classification (1).
†Median (interquartile range/2); the interquartile range contains half the total frequency.
‡Patients with arteriolar occlusion had significantly higher% of reticulocytes than those without these signs (p=0.02).
§Patients with proliferative sickle cell retinopathy had significantly lower HbF values than those without these signs (p=0.03).

molysis and indirectly the factors associated with red cell heterogeneity may have a role in these vascular complications. We speculate that retinal blood flow may be compromised by repeated reversible arteriolar occlusive events occurring in response to red cells containing polymerised HbS.

In the present study we also confirmed the previous report by Hayes *et al.*[3] that patients without PSR have higher HbF levels than those with PSR. This result is consistent with data demonstrating both the sparing effect of HbF on the calculated HbS polymer fraction[9] and the inverse relationship between HbF levels and R60 values.[8] Thus, this finding also indirectly suggests that factors responsible for red cell heterogeneity may play a role in the pathogenesis of PSR.

The results of the present study indirectly support the hypothesis that HbS polymer within red cells may be a determinant of the severity of the retinal lesions found in sickle cell patients. However, studies in larger groups of patients are needed to replicate these findings.

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