CONCLUSION
The remarkably complex pathophysiology of sickle cell disease is influenced by multiple genetic factors and by the pleiotropic effects of the sickle haemoglobin gene. It is evident that crises are complicated events that almost certainly are multifactorial in etiology. Indeed, it is entirely possible that the genesis of vasoocclusion various among patients or, for a given patient, from time to time or even from vascular region to region. Such variability easily could derived from consequence of concomitant illnesses or from the simple stochastic effect of the aggregate participation of Multiple variables. The waxing and waning if such influence could engender critical changes, for example, in the receptor complement of endothelial surfaces or the degree of homeostatic activation. This realization perhaps jeopardizes the long held, comforting distinction between “steady-state” and acute vassocclusive/anemic crisis. Condition which may prove to be less discrete and more illusory than is suggested at the customary threshold of clinical observation.

It has been suspected for some time that sickle cell disease severity results from the net influence of a great verity of genetic, vascular, environmental, and red cell cytoplasmic and membrane factors. This perplexing array can be envisioned as acting at two distinct level to produce diverse clinical phenotypes.

The appearance role of these cellular, biochemical, and physiologic variables is to modulate the basic level of severity imparted by the genetic factors. The impact of some of these variables undoubtedly is minor.

Both extravascular and intravascular hemolysis appears to contribute to the pathogenesis of hemolytic anemia in sickle cell disease, although the precise contribution of each has not been defined.

Chronic organ damage is due to the compounding or accumulation of many small injuries over time; the disorders described below can and do occur in children,
but are distinctly more common as patient age. The order in which disorders are listed is not intended to imply either frequency or severity.

Hyposthurea occurs early and increases likelihood of dehydration during painful crises because water cannot be conserved. Renal papillary necrosis and hematuria represent extensions or magnification of the same process, which is thought to be caused by the hypertonic renal medulla and occlusion of the vasa reacta with infracruion. Hyposthuria and hematuria are seen in sickle cell trait and reflect almost the only relatively common clinical manifestation of that condition.

There are both less and more dramatic disorders of the liver in patients with sickle cell with various anemic crises. Small hepatic infraction do occur and can lead to a type of postnecrotic cirrhosis. Most adult have abnormal levels of serum transaminase and alkaline phosphate all the time, and those abnormalities become more marked (along with increases in serum Bilirubin) when crises occur.

Viral hepatitis in sickle cell anemia is associated with amazingly high Bilirubin levels due to the combination of rapid red cell destruction and impaired hepatic function. Patients with viral hepatitis usually recover spontaneously, but those with acute hepatic sequestration often do not. Pathogenesis of the latter syndrome is probably similar to that acute splenic sequestration in children: The liver enlarges, liver function deteriorate, the hemoglobin level falls, there may be fever, and patients become seriously ill.

The evidence in support of nutritional deficiencies in individuals with HbSS has been increasing. The role of micronutrient deficiencies has been more easily addressed and research in that area continues to reveal a range of individual deficiencies in HbSS patients, some of which can be corrected by supplements.

We report here that SCD patients showed a significant elevation in TNF-α, IL-6, CRP and homocystein in various crises state, when compared to normal controls. Precipitation of crisis resulted in augmentation of type I cytokine response with elevation in TNF- when compared with steady state, with further accentuation of the type II response as indicated by the sustained progressive rise in IL-6.