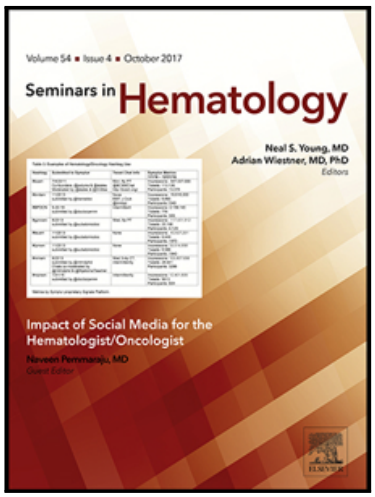

Sickle Cell Disease- Unanswered Questions and Future Directions in therapy

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Sickle Cell Disease- Unanswered Questions and Future Directions in therapy.

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Sickle cell disease was regarded as a "disease of childhood" less than 50 years ago in 1960 [1] and few children survived beyond their teens, while 25 years later, the Cooperative Study of Sickle Cell Disease reported a median age at death of 42 years for males and 48 years for females with HbSS and that 85% HbSS patients will survive to adulthood [2]. More recent studies confirmed that the majority of newborns (94 to 99%) in well-resourced countries will now survive to adulthood [3-6] but early mortality remains. Based on 2008 US population and SCD birth -cohort, the mean age of death for was 39 years in 2006, and that, only 35% of the cohort would be alive at age 45 years [7]. In a medium-resourced setting, follow-up of the Jamaican HbSS cohort commenced in June 1973, for up to periods of 43 years, showed that 55.2% have so far survived to 40 years [8]. Some studies show higher median survival estimates, but were not based upon birth cohorts [9, 10]. Nonetheless, there is clearly an improvement in survival in sickle cell disease, and while these estimates have to be viewed with a great deal of caution, the life expectancy of patients with SCD is still shortened by more than 20 to 30 years compared to the general population. Much more, however, remains to be done for the vast majority of affected patients who are born in low-income regions within Africa and India. To this day, as many as 90% of the affected children born in sub-Saharan Africa die, usually undiagnosed, before they reach their 5th birthday [11].

Since unravelling of its genetic basis at the molecular level half a century, sickle cell disease arguably launched the whole field of human molecular genetics and molecular medicine, but sadly, the translation of such knowledge into treatments has been much too slow. This issue summarizes some of the unanswered questions and the future directions on developing new therapies on sickle cell disease. Recent years have seen major advances on several fronts with concerted efforts to discover and develop new drugs targeting the root cause of HbS polymerization [12] (*Targeting HbS polymerization – Frank Ferrano)* and drugs targeting pathways downstream of sickling, aimed at preventing the complications of SCA [13] (*Deepa Manwani)*. Inhibition of HbS polymerization via therapeutic induction of HbF has been pursued