

Title: Modulation of Iron Deposition in Sickle Cell Disease and Other Hemoglobinopathies (Survey Study)

IRB# 2010-019

Principal Investigator: Elliott Vichinsky, MD

Synopsis:

A consortium of expert hematology centers in the US, Canada, and UK recruited a large population of heavily iron overloaded Sickle Cell (SCD) and Thalassemia (TM) patients to participate in a natural history study to compare the frequencies of iron-related organ injury in these two disease populations. Using statistical analyses, the Multi Center Study of Iron Overload established that endocrinopathies and in particular, gonadal failure, were seen predominately in TM and related to duration of transfusion. However, preliminary studies have identified a striking absence of cardiac iron deposition in heavily iron overloaded patients with SCD that contrasts with other transfusion iron overloaded patients. In these pilot studies, SCD patients were only matched with TM patients for current levels of body iron. The distribution of iron to the heart and pituitary is likely to depend not only on levels of total body iron at the time of study but more importantly on the lifetime duration of exposure to iron overload including the age when regular transfusions were initiated. In order to clarify the mechanisms that account for the apparent lack of iron deposition in the heart and pituitary of SCD patients, we will need to identify SCD and TM patients with similar total body iron and similar duration of chronic transfusion and age of initiating regular transfusion.

The purpose of the current study is to identify up to 100 patients from 10 centers with either SCD, TM, and DBA, 10-20 years of transfusion exposure (0.2-0.6 mg Fe/kg/day), at least 6 annual ferritin levels greater than 2500, and age of initiation of regular transfusion before age 10 who meet eligibility criteria for future studies of iron deposition.

A detailed iron burden, transfusion and chelation history will be obtained from chart review or from participant recall if the participant initiated transfusion and chelation at another institution and records are not available for review. Iron burden data will include: (1) documentation of liver iron from biopsy, SQUID or MRI including laboratory performing assay, whether liver biopsy was processed as fresh tissue or extracted from paraffin, and (2) average annual ferritin values available in the medical record will be recorded.

Transfusion data will include: (1) age at onset of regular transfusions, (2) years of chronic transfusion therapy (defined as 0.2-0.6 mg Fe/kg/day if number of units transfused and individual unit hematocrit (HCT) and volume available; or average HCT and volume available; or estimated as number of simple blood units transfused x 200 mg Fe per unit), and (4) pre-transfusion Hb calculated as average of all assessments for each year.

A general medical history will be obtained and any exclusion criteria for future study participation will be identified. Chelation data will include: (1) age at onset of chelation, (2) estimated annual chelation exposure defined as sporadic, 2-4 days/week, or 5+ days per week chelation, (3) record of the number of days or nights of chelation use per week in the last 14 days, (4) listing of all chelation drugs previously used including dose and time period.

Study Coordinators at each site will fill out data collection forms and provide source documentation. Forms will be mailed to CHRCO, the data coordinating center. Data will be entered into a Microsoft Access database and exported to SAS. Descriptive statistics summarizing the the number of patients, age, gender, years of transfusion, iron exposure, and chelation exposure will be provided for each patient population.