Here it is again, late August….hot, dry, ragweed levels increasing, the occasional leaf dropping from a tree, and yes, kids heading back to school (that is of course, for those of us who have yet to move towards year-round school). As kids readjust to life back in the classroom, teachers often serve up a quick and easy writing assignment on "How I Spent my Summer Vacation." Well, taking their lead, I figured I'd tell you a little about how I spent the summer of 2013; specifically the week of July 21-26, at Camp Sunshine on the north shore of Lake Sebago, Maine.

As a scientist attending Camp, most of my time is spent in the scientific/clinical sessions which often run from around 9AM each morning to around 3 PM in the afternoon, with a break for lunch. This lunch break, along with other meals at Camp Sunshine, is often a highlight for many of us working in the DBA field because this is a time we get to meet the patients and families affected by Diamond Blackfan anemia. These interactions are inspirational, motivating us as we head back to the trenches in our labs and clinics.

One of the most anticipated talks in this year's scientific session was a talk by Dr. Lawrence Wolfe from Cohen Children's Medical Center in New York. The anticipation for most was likely a mixture of awe and trepidation. Dr. Wolfe is a world-renown expert on iron with an emphasis on the clinical effects of iron overload and their management. Thus, the awe! The trepidation comes from the fact that Dr. Wolfe is very passionate about his work and exceedingly blunt about the effects of not taking iron overload seriously in a transfusion-dependent DBA patient. His talk was entitled "Iron: Can't live without enough of it, Can't live with too much of it." This title sets the stage for an uncompromisingly forthright discourse on the how's and why's through which iron accumulates in the body with each transfusion and the ravages this iron can wreak on critical organs like the liver, pancreas, pituitary and heart. Fortunately, Dr. Wolfe's talk has a "good news" component which is that iron overload can and is being managed through chelation therapy. But this good news is nevertheless qualified by admonishments regarding the hard work required by patients, parents, and physicians to effectively manage iron overload.

During his talk, Dr. Wolfe mentioned the importance of effective iron management prior to hematopoietic stem cell transplantation for DBA. This point was also emphasized by Dr. Adrianna Vlachos in her talk on hematopoietic transplantation in DBA based on data from the DBA Registry. The concept of effective iron management prior to transplant improving outcomes seems to fly in the face of an article published in June by Trottier *et al* in *Blood* "Association of iron overload with hematopoietic stem cell transplantation outcomes: a prospective cohort study using R2 MRI measured liver iron content" [1].

The key points of this article listed by the authors:

- We found no association between iron-overload and survival or complications in allogeneic transplant recipients at 1-year post-transplant
- Future studies should use liver iron content to define iron-overload instead of ferritin in this population.

So what's the story here? Who's right? Well, it turns out that both groups are likely correct except that they are studying quite different patient populations. When queried about this point Dr. Jeffrey Lipton mentioned that the mean liver iron content in the patient population in the *Blood* study was 4.3 mg/g, where when considering the DBA population, the liver iron contents can be considerably higher. He also mentions that the Trottier study only includes a one-year follow up, and monitoring outcomes over longer periods of time would be ideal.

So what is the mean liver iron content observed in DBA patients? Surprisingly, there isn't a whole lot of information published on this topic and as can be seen in Dr. Wolfe's slide 29 where values for DBA are often inferred or grouped with data on more prevalent diseases like thalassemia or sickle cell disease. This dearth of data on DBA appears to be changing with the recent publication in the American Journal of Hematology from the laboratory of Dr. Thomas Coates, UCLA [2]. The paper's title is "Tissue Iron Evaluation in Chronically Transfused Children Shows Significant Levels of Iron Loading at a Very Young Age." The following is a statement directly from their abstract "Median liver iron concentrations in patients less than 3.5 years old were 14 and 13 mg/g dry weight in thalassemia major and Diamond Blackfan Anemia patients, respectively." These data make it clear, iron loading occurs at a young age and the levels attained in patients with diseases like Diamond Blackfan anemia and Thalassemia are considerably higher that the values derived from the patient population in the Trottier *et al* study. Importantly, Dr. Vlachos and Lipton try and bring patients' iron levels down to the 3-7 mg/g range, and as close as possible to 3 mg/g prior to transplant, thus near the levels where outcomes were measured in the Trottier paper. They also support phlebotomy post-transplant if necessary to bring liver iron content to normal range.

I think the foregoing discussion stresses the importance of iron management in chronically transfused DBA patients while at the same time indicating that certain features of iron loading and distribution within the body may be distinct for anemias like DBA making this an area in significant need of further study.

Anyone wishing to see the PowerPoint of Dr. Wolfe's talk can access it through the link below:
http://dbafoundation.org/families/camp-sunshine/

For more information on how I spent the summer of 2013, please go to NSA file 379518.322.SFR

[1] B.J. Trottier, L.J. Burns, T.E. Defor, S. Cooley, N.S. Majhail, Association of iron-overload with allogeneic hematopoietic cell transplantation outcomes: a prospective cohort study using R2 MRI measured liver iron content, Blood, (2013).
[2] V. Berdoukas, A. Nord, S. Carson, M. Puliyel, T. Hofstra, J. Wood, T.D. Coates, Tissue iron evaluation in chronically transfused children shows significant levels of iron loading at a very young age, American journal of hematology, (2013).