



Cooley's Anemia FOUNDATION

Leading the Fight Against Thalassemia

Cause of Death in Patients with Thalassemia in the US

Accumulating levels of iron in the body generated from hundreds of blood transfusions, together with increased absorption of iron from the diet, cause critical organs and glands in patients with thalassemia to experience serious iron-induced toxicity and early death. Several publications provide evidence that the heart is unquestionably the most critical organ affected by iron jeopardizing survival of thalassemia patients. 36% of patients between the ages of 15 and 18 showed detectable cardiac iron.¹

The risk of cardiac disease increases as patient's age, as revealed in a study in the New England Journal of Medicine that examined cardiac disease-free survival during treatment with desferrioxamine in 97 thalassemia patients. For the full cohort, the estimated survival without cardiac disease was 80 percent after 5 years of chelation therapy, 65 percent after 10 years and only 55 percent after 15 years.² At the New York Academy of Sciences, Seventh Symposium on Thalassemia,³ the causes of death reported in 240 thalassemia major patients in Italy born between 1960-1984 were:

- Cardiac disease 171 (71%)
- Infections 28 (12%)
- Liver 15 (6%)
- Other causes 26 (11%)

A recent review of information available to the Cooley's Anemia Foundation shows that 11% of its 724 registered patients (77 total) died over the time period January 1999 – July 31, 2008. The data demonstrate that heart disease in these young patients remains the leading cause by far.

¹The most recent of these articles is by Wood JC, Origa R, Agus A, Matta G, Coates TD and Galanello R; Onset of Cardiac iron loading in pediatric patients with thalassemia major. *Haematologica* 2008 93(6) 917 – 920. Doi:10.3324/haematol.12513

² Borgna-Pignatti C, Rugolotto S, DeStefano P, Zhao H, Cappellini MD, Del Vecchio GC, et al. Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. *Haematologica* 2004;89:1187-93

³ Borgna-Pignatti C, Rugolotto S, Piga, A, DiGregorio F, Gamberi M.R., Sabato V, Melevendi C, Cappellini MD, Verlato G; Survival and Disease Complications in Thalassemia Major. *Annals of the New York Academy of Sciences*, Volume 850, 1998

- 54% of the reported causes of death were due to cardiac failure (42 total). The median age at time of death for patients who died of cardiac failure was 31.6 years (range 18 to 55 years).
- Infection was the second most frequent cause of death with 5 deaths. The median age of death for patients who died of infection was 22.6 (range 3 – 39 years).

The Journal of Cardiovascular Magnetic Resonance recently published a report entitled "Improved survival of thalassemia major in the UK and relation to T2* cardiovascular magnetic resonance." This paper concludes that "since 1999, there has been a marked improvement in survival in thalassaemia in the UK, which has been mainly driven by a reduction in deaths due to cardiac iron overload." The paper also indicates that one of the reasons for this improvement in survival is due to the use of the oral chelator deferiprone.

The Cooley's Anemia Foundation believes that the physicians and patients in the United States are in need of more chelating options and that deferiprone should be among the options readily available in the United States. We encourage the U.S. Food and Drug Administration to take into consideration the urgent need for specific, individual therapeutic options when treating thalassemia and that without expanded options, the patient population cannot receive treatment that will produce optimal outcomes.