Given the fact that the immunodominant human minor H antigens are encoded by dimorphic genes, potential donors can be screened for the expression of both major and minor H antigens. Perhaps even more intriguing is the possibility that precursor CTLs derived from multiparous female donors can be developed into therapeutics against tumor cells that express specific minor H antigens. Skeptics, stay tuned! Studies of minor H antigens in mice and men have much to offer to our understanding of basic and clinical human immunology.

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Myocardial iron measurements by MRI: getting to the heart of the matter

Cardiac toxicity from transfusional iron overload is the most common cause of death in young adults with thalassemia major. Noninvasive assessment of the degree of cardiac iron deposition would be a great advance in the field. In a first for North American thalassemia patients, Wood and colleagues (page 1934) report in this issue on the prevalence of myocardial iron overload, using a magnetic resonance imaging (MRI) technique known as T2* (stated as "T2 star"). For this method, which was pioneered by Pennell and colleagues[1] in London, patients are subjected to a brief measurement in an MRI scanner. The parameter T2*, calculated from a special gradient spin echo series, is inversely related to iron deposition, so that lower values suggest too much iron. The lower limit of T2* in patients without iron overload is 20 ms. Many patients with transfusional iron overload have lower levels.

Because the time course to develop myocardial iron overload over many years is poorly understood, Wood et al chose a young cohort, prior to the age of onset of typical thalassemia cardiac problems. Among patients ranging in age from 7 to 26 years, they found that 8 of 10 subjects who received transfusions for more than 13 years had abnormally low T2*, whereas 0 of 9 patients who received transfusions for less than 13 years had abnormal values. In the thalassemia group, 2 of the 8 patients with abnormal T2* had abnormal ejection fractions.

As a control group, the authors settled on a group of sickle cell disease patients receiving chronic transfusions and matched with the thalassemia subjects for age, sex, and hepatic iron concentration. There was no attempt to match for duration of transfusions, and indeed the sickle cell patients proved to have received transfusions for fewer years on the average, so that the overall higher T2* and absence of heart disease among the sickle cell patients in the study is not necessarily surprising. As the authors discuss, their number of sickle cell subjects who received transfusions for more than 13 years is much too small to be able to conclude that cardiac complications are less common among sickle cell patients who received a high number of transfusions.

It is a telling point in this study that hepatic iron concentration was not correlated with T2* measurements and that ferritin levels had only a weak correlation. This underscores the clinical fact that these measures do not predict very well who will get heart disease from transfusions and who will not.

Does T2* directly reflect cardiac iron burden well enough to assess response to therapy and to guide future treatments? This is a controversial point. A recent study purporting that this is so, with regard to cardiac iron chelation by oral agent deferiprone,[2] engendered some criticism.[3] Suffice it to say that *if* T2* is to be used in this fashion, more careful studies of populations as done by Wood et al and of individuals with longitudinal follow-up will be necessary to teach us how to use the measurement.

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