quality-of-life methodology to the scrupulously collected cost data allows determination of an expenditure for expected clinical impact to be determined. Again this provides a contextual framework for comparing this significant morbidity to other required clinical interventions by the health care system. For extreme cost outliers, like hemophilia with inhibitors, this is necessary both to justify the expenditures and to define strategies to increase positive clinical impact per monetary unit expended. Further, it may well justify expanded research into more aggressive and costly strategies for morbidity prevention in the hope that the up-front costs will ultimately diminish costly rehabilitative services later.

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The title is ascribed to Karl Marx 1875 from Critique of the Gotha Program; it was in quotes by Marx and may have originated with Louis Blanc (1811-1882) or Morelly (1840).


The evolution of hematopoietic stem cell transplantation for multiple sclerosis

Multiple sclerosis, commonly referred to as MS, is a disease that hematologists do not commonly encounter in their clinical practices. However, MS is the most common demyelinating disease and is characterized by focal destruction of myelin sheaths in the central nervous system accompanied by an inflammatory response. Clinically, MS may persist for more than 30 years with neurologic symptoms, which occur, remit, and recur. Symptoms of MS can be extremely debilitating and include impaired vision, decreased perception and position sense, ataxia, bladder dysfunction, muscle weakness, and paralysis. The exact cause of MS is unknown but current opinion is that it is an autoimmune disease, which is perhaps induced by a viral illness or environmental factors in genetically susceptible individuals. Typical treatments include several immune-based therapies such as corticosteroids, beta-interferons, cyclophosphamide, plasma exchange, azathioprine, and cyclophosphamide.

Similar to their application in hematologic malignancies, the dose-limiting toxicity of many immunosuppressive agents, such as cyclophosphamide, is hematologic. As such, there was significant clinical interest as to whether the administration of high doses of these agents with hematopoietic support would result in stabilization or improvement in MS and other autoimmune diseases such as rheumatoid arthritis. The first publications on autoimmune diseases treated with high-dose immunosuppressive agents with hematopoietic stem cell transplantation appeared only in late 1996. The number of patients with autoimmune diseases that received transplants has expanded rapidly such that more than 400 treated patients have been described and reported to the European League Against Rheumatism/European Group for Blood and Marrow Transplantation database. The largest number of these patients has the diagnosis of MS.

In this issue of Blood, 2 studies highlight the significant progress that has been made in the investigation of hematopoietic stem cell transplantation as treatment for MS. These 2 studies demonstrate that this treatment has evolved beyond anecdotal novelty to address several important issues such as unique toxicities with transplantation and, more importantly, the evaluation of which patients are most appropriate to be considered for this treatment. Nash and colleagues (page 2364) describe the results of a multi-institutional pilot study in which 26 patients with advanced MS received high-dose cyclophosphamide, total body irradiation, and antithymocyte globulin followed by CD34-selected autologous stem cell transplantation. This study points out that there are several complications with transplantation that are relatively unique to MS. These included flairs of disease with cytokine mobilization and relatively high incidences of bladder complications and engraftment syndrome. Burt and colleagues (page 2373) observed similar complications in their single-institution trial, which included 21 MS patients and used a similar immunosuppressive regimen with higher doses of radiation and omission of antithymocyte globulin. An important observation from this latter trial was the lack of efficacy in MS patients with more advanced neurologic progression, as defined by the expanded disability status scale (EDSS). Specifically, there was minimal to no evidence of disease stability in patients with EDSS scores greater than 6.0. The authors hypothesized that intensive immunosuppression may be of little or no benefit in patients late in their disease course, which is characterized more by axonal degeneration than by an active inflammatory process.

Both of these studies highlight the complexity of treating MS and the absolute necessity for a multidisciplinary approach for proper protocol execution. Their design, observations, and data interpretation provide both a detailed template and suggest appropriate research questions for future trials. These studies also suggest that hematopoietic stem cell transplantation has further evolved from a method to replace defective stem cells and administer high-dose cytotoxic therapy for cancer to an immunotherapeutic approach for nonmalignant diseases. As the number of patients with autoimmune disease far exceeds the number of patients with malignancy, it is not inconceivable that in the future the most common indication for hematopoietic stem cell transplantation will be for autoimmune diseases. As such, hematologists involved with transplantation are going to have to refamiliarize themselves with diseases that they have not had to particularly think about since medical school or residency. Similarly, several specialties may have to develop expertise in hematopoietic stem cell transplantation or possibly an entirely new specialty of hemat-immunotherapy will emerge.

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