The article by Matiello et al1 regarding a relapse of neuromyelitis optica (NMO) after autologous hematopoietic stem cell transplantation highlights the need to further understand the role of the immune system in this disease. Immunosuppressive therapeutics targeting B and T cells are used to prevent disabling relapses in NMO.2 Rituximab is a monoclonal anti-CD20 antibody that is reported to be effective in NMO.3 Alemtuzumab is a monoclonal anti-CD52 antibody with preliminary phase II data in multiple sclerosis, but not in NMO.4 Here we describe a patient with 20 relapses in 5 years despite sequential treatment with 4 immunomodulatory therapeutics in combination with corticosteroids and plasma exchange for relapses. She appeared to paradoxically worsen, with profound weakness, after B cell depletion with rituximab and developed tumefactive cerebral lesions after alemtuzumab.

Report of a Case. A 40-year-old African American woman presented with optic neuritis 5 years prior, with recovery of visual acuity to 20/20 after intravenous methylprednisolone (IVMP) (Figure). Three months later, dys-
esthesias in 4 extremities, mild sensory ataxia, and urinary incontinence developed. Cervical-spine magnetic resonance imaging revealed longitudinally extensive transverse myelitis and serum was positive for NMO-IgG antibodies (1:1920). Treatment included IVMP for this relapse. Treatment with azathioprine and daily prednisone were added. Azathioprine treatment was adjusted to lymphocyte counts of 500,000 to 1,000,000/mm³. She relapsed 2 months later, and had 5 total episodes of transverse myelitis in the first year; each episode was treated with IVMP. Azathioprine treatment was discontinued and 1000 mg of mycophenolate mofetil twice per day with daily prednisone was used for 18 months. She experienced 4 additional sensory and bladder relapses, unaccompanied by urinary tract infection. Findings of motor testing were normal during the first 3 years.

Owing to continued disease activity, rituximab was administered. Beginning 5 months after rituximab treatment, and with a confirmed count of 0 CD19⁺ cells, she experienced 4 additional relapses over 5 months, stabilizing after each. However, these culminated in persistent paraplegia.

Nine months following rituximab treatment, B cells began to return (CD19⁺ cell count, 9/mm³; reference range, 79-545). Fourth-line treatment options were discussed owing to concern for quadriplegia and respiratory compromise. Mitoxantrone was not chosen owing to dose limitations and risks of cardiotoxicity and malignancy. Cyclophosphamide was not used owing to risk of infection among other adverse effects. Alemtuzumab was selected to suppress mononuclear immune system cells and because it is well tolerated, with promising early results in relapsing multiple sclerosis. She received 12 mg/kg/d of intravenous alemtuzumab for 5 days, with 5 days of IVMP.

Six weeks following alemtuzumab, a relapse manifested by worsening dyesthesias culminated in apnea and intubation. Magnetic resonance imaging showed an expansile, contrast-enhancing, longitudinally extensive transverse myelitis. Her CD4 count was 30 cells/mm³ (reference range, 393-1607). She received plasma exchange and was extubated. Four months after beginning treatment with alemtuzumab, aphasia, dysarthria, lethargy, and moderate right arm weakness developed. Brain magnetic resonance imaging revealed a 3 cm³ lesion. The thoracic cord demonstrated an enhancing expansile T2 lesion. Brain biopsy, performed to exclude opportunistic infection and malignancy, confirmed a demyelinating process. The CD4 count was 133 cells/mm³, and the CD19 count was 115 cells/mm³. During the next 5 months, the patient had 2 confirmed relapses and received IVMP. Mycophenolate and low-dose prednisone were added, with no further clinical relapse after 6 months’ follow-up. She currently resides in a nursing facility, transfers with a lift, and cannot feed herself.

Comment. This case, together with the article by Matiello et al, may be instructive, as NMO disease activity continued despite marked suppression of cellular immunity. Plasma cells are the primary source of antibodies, but CD20 is not expressed by plasma cells, and CD52 is only expressed by a fraction of plasma cells. Failure to eliminate anti-aquaporin 4 antibodies may be the reason for lack of therapeutic success in each case.

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5. Bichuetti DB, Lobato de Oliveira EM, Oliveira DM, Amorim de Souza N, Gab-
comments and opinions

The Th1/Th2 Paradigm in Guillain-Barré Syndrome

N yati and colleagues1 described a cohort of 65 patients with Guillain-Barré syndrome (GBS) with characteristic lymphocyte cytokine expression profiles in response to Campylobacter jejuni outer membrane protein stimulation. While their findings followed the T helper (Th) 1/Th2 paradigm, they should be interpreted with caution before robust conclusions are drawn.

Guillain-Barré syndrome is a heterogeneous disease entity with several clinical subtypes including acute inflammatory demyelinating polyneuropathy (AIDP) and the axonal variants.2 The latter is closely associated with C. jejuni infection.3 Given the different etiologies and clinical features, we would like to know if the authors performed stratified analyses, eg, AIDP vs axonal variants. Although an association between C. jejuni infection and AIDP has been proposed, we wonder whether the characteristic responses of lymphocytes are antigen specific. Unless they can provide more evidence, eg, C. jejuni–specific antibodies or GM1 antibodies supporting an over-whelming ratio of C. jejuni infection in the studied cohort, further stratified analysis seems a necessity.

The Th1/Th2 paradigm has also been used to explain the dynamic immune responses against infections. A Th1-oriented response is related to an acute-phase reaction to pathogens, while a Th2-oriented response is related to the elimination of antigens and recovery of diseases.4 In this regard, the findings might be confounded by the host immune responses against infections, which usually precedes the onset of GBS.

Since the cytokine expression patterns in the acute and recovery phases were opposite, we are also interested in the inflexion point of this dynamic change. One potential way is to correlate the cytokine levels with the severity and clinical course of the disease. A dynamic curve of cytokine expression levels relative to the clinical course of the disease. A dynamic curve of cytokine expression levels relative to the clinical course of the disease. A dynamic curve of cytokine expression levels relative to the clinical course of the disease. A dynamic curve of cytokine expression levels relative to the clinical course of the disease. A dynamic curve of cytokine expression levels relative to the clinical course of the disease. A dynamic curve of cytokine expression levels relative to the clinical course of the disease. A dynamic curve of cytokine expression levels relative to the clinical course of the disease.

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In reply

We appreciate the comments raised by Zhang and Li regarding our article1 presenting an overview of Th1/Th2 response to C. jejuni antigen in patients in the progressive and recovery phases of GBS. Campylobacter jejuni infection is identified as a major triggering agent of GBS. Several studies also confirmed the association between C. jejuni and axonal subtypes of GBS.2 Although there are conflicting reports, both subtypes, demyelinating (AIDP) and axonal, can follow C. jejuni infection. We had earlier reported the stratified analyses that showed C. jejuni (26%) was the most common preceding infection in our GBS cohort and had more frequent association with the axonal subtype than demyelinating subtype (41% vs 6%; P < .001). Further, antiganglioside antibodies were detected more frequently in patients with GBS than controls (81% vs 10%; P < .001), and a higher proportion of axonal cases had anti-GM1 antibodies than patients with AIDP (IgG: 65% vs 32%; P = .004 and IgM: 46% vs 29%; P = .05).

Besides microbial factors, host susceptibility also plays an important role in the development of the disease because only 1 in 1000 patients who are exposed to C. jejuni infection develop GBS.3 Several lines of evidence point out the importance of host factors in the development and pathogenesis of GBS. First, GM1 gangliosidike epitopes are also present in C. jejuni strains isolated from diarrheal patients, yet they do not develop antiganglioside antibodies. Second, GBS is rarely found in 2 people within the same family, even within the same village. Finally, although C. jejuni lipopolysaccharides may exhibit mimicry with gangliosides, why do some people develop a particular form of GBS? Geographic variations and different immunogenetic backgrounds may account for different clinical and serologic manifestations of the disease in different parts of the world. In our study, we observed Th1-like response in patients in the progressive phase of GBS; the recovery phase of GBS was associated with a Th2-like cytokine profile.4 We performed the study only at 2 time points (progressive and recovery phases); therefore, the exact inflexion point of this cytokine dynamic change cannot be commented on because it needs everyday and/or more frequent observation and sample collection. However, study in animal models showed that most proinflammatory cytokines (interferon γ, interleukin 1β, tumor necrosis factor, and interleukin 6) reached their peaks on or before 14 days after immunization with myelin antigens, whereas anti-inflammatory cytokines (transforming growth factor β1 and interleukin 4) were observed after 14 days and associated with recovery from the disease.5 The correlation of the cytokine levels with sever-