MS Consult

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Monitoring for Infection in MS Patients

Q How do you monitor for infection in patients with multiple sclerosis who take disease-modifying therapies?

The answer to this question is "it depends"—on several factors, including current and previous use of disease-modifying therapies (DMTs), concomitant medications, comorbidities, vaccination history, presence of John Cunningham virus (JCV) antibodies (in the case of natalizumab use), and prior or current use of immunosuppressive therapies.

There are many FDA-approved DMTs for multiple sclerosis (MS). Each has a different rate of infection occurring in clinical trials and varying requirements and/or recommendations for safety monitoring. The package inserts for each DMT offer some guidance for clinicians.

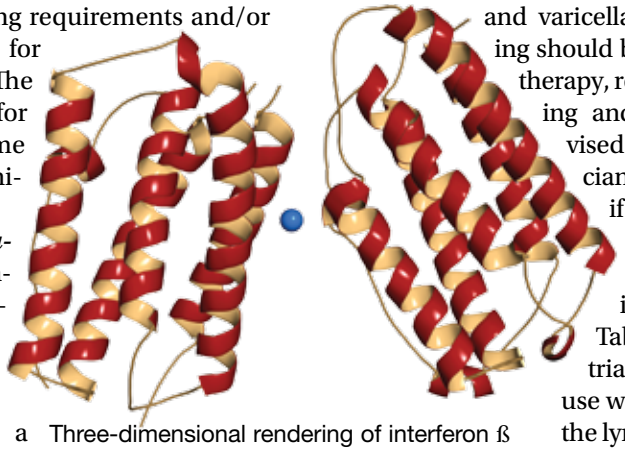
Injectable therapies. For two interferon therapies—interferon ß-1b SC and interferon ß-1a—it is recommended to order a complete blood count (CBC), blood chemistry, and liver function tests (LFTs) at baseline, then again at one, three, and six months, and then at clinician discretion thereafter.[1,2] For peginterferon ß-1a, ordering a CBC, basic chemistry, and LFTs, at the clinician's discretion, is advised.[3] The package insert for interferon ß-1a IM does not offer specific recommendations for routine safety monitoring.[4]

The package insert for glatiramer acetate offers no recommendations for routine safety monitoring.[5]

In patients for whom two or more DMTs have failed to work, the monoclonal antibody daclizumab may be indicated. Compared to placebo and active comparator, this drug was associated with a higher risk for infection in clinical trials. The most commonly observed types were upper respiratory, urinary tract, and viral infections. There are no recommendations for CBC monitoring with daclizumab, but monthly LFTs are required due to increased risk for hepatic injury.[6]

Oral DMTs. Patients taking fingolimod, teriflunomide, and dimethyl fumarate have increased risk for infection; as a result, there are more safety monitoring recommendations for these medications.[7-9]

Prior to starting therapy with fingolimod, baseline CBC, blood chemistries, and varicella antibody testing should be done. During therapy, routine CBC testing and LFTs are advised at the clinician's discretion *or* if the patient exhibits signs and symptoms of infection (see Table). In clinical trials, fingolimod use was interrupted if the lymphocyte count was sustained at < 200. In rare cases, progressive multifocal leukoencephalopathy (PML) has occurred—so the patient's age, JCV antibody status, prior use of immunosuppressant therapy, and length of fingolimod treatment should be taken into consideration.[7]



Three-dimensional rendering of interferon ß protein, used to treat multiple sclerosis.

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Patients starting teriflunomide should have baseline LFTs and CBC and tuberculosis (TB) testing (either skin or serum), with subsequent monthly LFTs for the first six months on treatment. Some patients may experience neutropenia, thrombocytopenia, and lymphopenia. As a result, patients

may have an increased risk for infection. Safety monitoring is at the clinician's discretion.[8]

For patients initiating dimethyl fumarate, a baseline CBC is recommended, to be repeated every six to 12 months thereafter, and/or as clinically indicated. Since lymphopenia may occur, consider interruption of dimethyl fumarate in patients with lymphocyte counts < 0.5 persisting for more than six months. Rare cases of PML have also occurred; at the first suggestive sign or symptom, dimethyl fumarate should be withheld and appropriate diagnostic testing should be completed.[9]

Infusion therapies. There are four infusion therapies available for MS treatment. Mitoxantrone, though not commonly used, is still available for relapsing and secondary progressive forms of MS. Common infections seen in clinical trials include upper respiratory, urinary tract, and sinus infections. A CBC, including platelets, should be obtained prior to each course of mitoxantrone and again if signs and symptoms of infection develop.[10]

Natalizumab is an integrin receptor antagonist administered in monthly IV infusions. Patients receiving natalizumab may have increased risk for urinary tract infections, lower respiratory infections, gastroenteritis, vaginitis, and herpes infections. These risks should be monitored at the clinician's discretion. There have been several cases of PML associated with natalizumab; risk factors include duration of therapy, prior use of immunosuppressants, and presence of JCV antibodies.[11]

Alemtuzumab is a CD52-directed monoclonal antibody indicated in patients with relapsing forms of MS who have had an inadequate response to at least two DMTs. In clinical trials, subjects had a higher risk for nasopharyngitis, urinary tract infections, upper respiratory infections, sinusitis, herpetic infections, influenza, and bronchitis. Due to the increased risk for infection and secondary autoimmunities, patients are required to have monthly CBC testing, LFTs, and urinalysis for up to 48 months after their last infusion.[12]

TABLE

Signs and Symptoms of Infection Warranting Evaluation

Arthralgia	Malaise
Chills	Myalgia
Dysuria	Nausea
Fever	Vomiting
Headache	

Lastly, ocrelizumab is a CD20-directed cytolytic antibody for the treatment of relapsing and progressive forms of MS. In clinical trials, there was a higher incidence of upper and lower respiratory infections, skin infections, and herpes-related infections. Prior to initiating ocrelizumab, hepatitis B virus screening should be completed. There are no specific recommendations for routine monitoring during therapy, although providers should monitor patients clinically for any signs and symptoms of infection.[13]

A word of caution: The common signs and symptoms of infection are listed in the Table. If these symptoms are present in your patient, consider ordering diagnostic testing to evaluate for infection.

Symptoms of PML include progressive unilateral weakness, clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. At the first sign or symptom suggestive of PML, the DMT should be discontinued and diagnostic testing performed.

Providers may contact the manufacturer directly for further guidance on DMT surveillance and treatment protocols. **—CK**

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The ACA and Multiple Sclerosis

Q How has the Affordable Care Act affected people living with multiple sclerosis—an Americans with Disabilities Act recognized disease?

The Affordable Care Act (ACA) has been a source of controversy since it became law in 2010. Perhaps some of the tension surrounding it stems from misunderstanding; however, it is clear that individual experiences and/or perceptions flavor the ongoing debate. Rather than perpetuate the contention, we'd simply like to outline some of the ways in which patients with multiple sclerosis (MS) *have* benefited from the ACA—and what we must do to ensure continued quality and affordability of care in the event of changes to the law.

Living with MS in the United States is costly. According to the National Multiple Sclerosis Society, average annual costs—both direct and indirect (ie, lost wages)—are about $69,000. Health care costs account for more than half of this total (about $39,000). Total costs for all people in the US living with MS are estimated at $28 billion per year.[1]

In 2016, according to the US Census Bureau, almost 13% of Americans lived below the federal poverty level, and 6% of Americans reported "deep poverty"—defined as household income below 50% of the poverty threshold for that year.[2] It has been reported that while at least 90% of people living with MS are insured, 70% are struggling to pay for health care. In fact, 30% put off seeking care because of costs; one consequence is delay in filling prescriptions.[3]

The burden of expense for our MS patients is considerable. Here's how the ACA has impacted our patients by attempting to minimize the devastating cost.

Guaranteed Health Insurance Coverage for Pre-existing Conditions. When the ACA became law in March 2010, there were three main goals: making affordable health insurance available to more people, expanding the Medicaid program to cover all adults with income below 138% of the federal poverty level, and supporting innovative medical care delivery methods to lower the cost of health care.[4]

Following the ACA's full implementation in 2014, private health insurance companies were prevented from refusing coverage to those with pre-existing conditions, such as MS. This was a game changer, since patients, regardless of their MS diagnosis, were now guaranteed individual insurance. Furthermore, they could not be charged increased premiums based on their prior medical history.[5]

Preventive Services Covered Without Cost-sharing. Under the ACA, health plans generally must provide preventive services, such as those rated A or B by the US Preventive Services Task Force. This includes routine immunizations for both adults and children, which represents a cost savings to patients living with MS. Another advantage is that women, including those living with MS, have access to sexually transmitted infection screenings, breastfeeding support and supplies, domestic violence screening, and contraceptives.[6]

Improved Coverage Through Medicare. The ACA mandated improvement in coverage with Medicare Part D benefits. In addition to the preventive care benefits noted above, which apply to Medicare recipients as well, the ACA reduced federal payments to Medicare Advantage plans over time and provided bonus payments to plans with high quality ratings.[7]

Further changes in Medicare spending included the creation of a 15-person, by-appointment board (known as the Independent Payment Advisory Board) tasked with identifying ways to "modify benefits,

eligibility, premiums, or taxes," which will hopefully continue to optimize the cost of care for patients living with MS and utilizing Medicare.[7]

Cost Savings With Medicaid Expansion. Medicaid expansion was enacted to keep patients with a costly illness, such as MS, from financial destitution because of their condition. As of January 2018, 32 states and the District of Columbia have seen expansion of their programs.[8] In those states, people with a household income below 138% of the poverty level (less than $27,000 for a family of three) can now qualify for Medicaid. States that have *not* expanded coverage include Idaho, Wyoming, Utah, South Dakota, Nebraska, Kansas, Oklahoma, Texas, Missouri, Wisconsin, Tennessee, Mississippi, Alabama, Georgia, Virginia, North Carolina, South Carolina, and Florida.[8] The expansion of Medicaid helps MS patients by shrinking the ever-present gap that still prevents some from qualifying for the additional financial assistance they need due to their chronic illness.

One thing we have learned is that MS patients may not realize they have access to some of these services—particularly preventive care—or they may hesitate to obtain services due to a lack of clarity on whether they are covered. Health care providers can remind patients that they may qualify for "unrealized services," which could provide value and optimize general preventive care. MS patients with Medicare and Medicaid, for example, may not know that they have access to colorectal cancer screenings via a waived deductible.[6]

Since last year, there has been vigorous discussion about repealing, replacing, or otherwise amending the ACA. While a political discussion is beyond the bounds of this column, we do need to be aware of how changes to the ACA would affect patients with MS.

Optimizing wellness and prevention and providing access to care to patients with a costly disease, such as MS, is important. In addition to ensuring ongoing access to affordable services, we need to do more to improve mental health access and reduce the cost of needed medications. We also need to close the insurance gap in all 50 states. Continued dialogue will be necessary to help government leaders understand the cost impact of MS (and other diseases), in order to keep our country moving in a positive direction that optimizes wellness and health care reform. **—ALD**

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International Organization of Multiple Sclerosis Nurses (IOMSN) is the first and only international organization focusing solely on the needs and goals of nurses involved with the care, education, research, and advocacy for multiple sclerosis and related autoimmune disorders of the central nervous system. For more information on IOMSN, visit www.iomsn.org.

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