BY JOHN RICHERT, MD

B cells and MS

Research points to new treatments for MS

Many readers of **InsideMS** have become accustomed to reading about T cells. They have heard about their postulated role in causing MS, and how various current and newer therapies in the pipeline block destructive T-cell functions.

B cells, another arm of our body's immune system, have been somewhat neglected. But B cells are now gaining prominence in our thinking about MS, both in terms of the cause of the disease and in terms of new therapies.

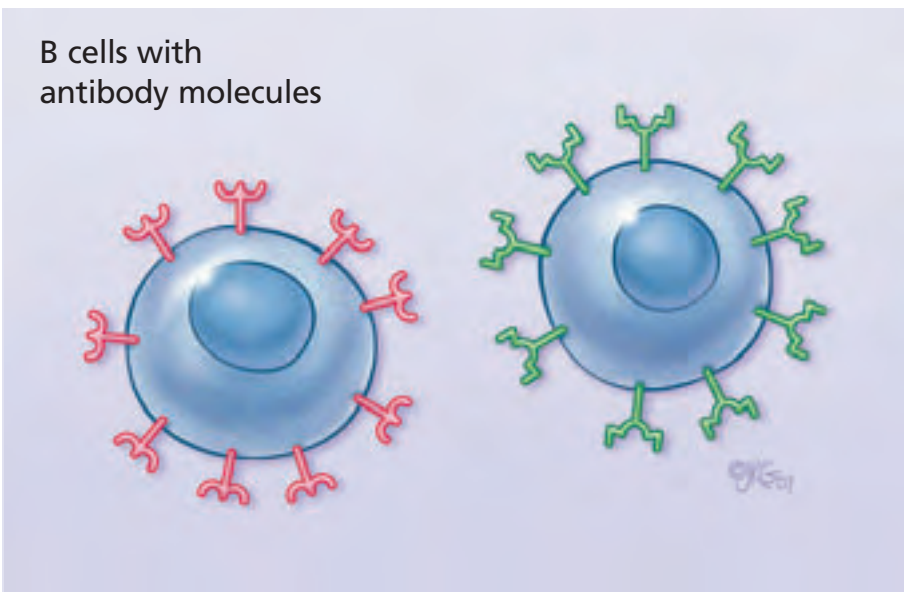
The Ts and the Bs

Let's start with what they are. T cells are so named because they take their major steps to maturity in the thymus gland (in the chest). Mature T cells carry out a variety of immune functions, including killing virus-infected cells and launching inflammatory reactions. Some T cells also help other immune system cells; this subtype is called "helper T cells."

B cells received their name initially because their maturation process was first successfully studied in chickens, in the "bursa of Fabricius." It's a bit easier to remember that, in humans, this maturation occurs in the bone marrow.

Antibody action

B cells typically carry antibody (also known as "immunoglobulin") on



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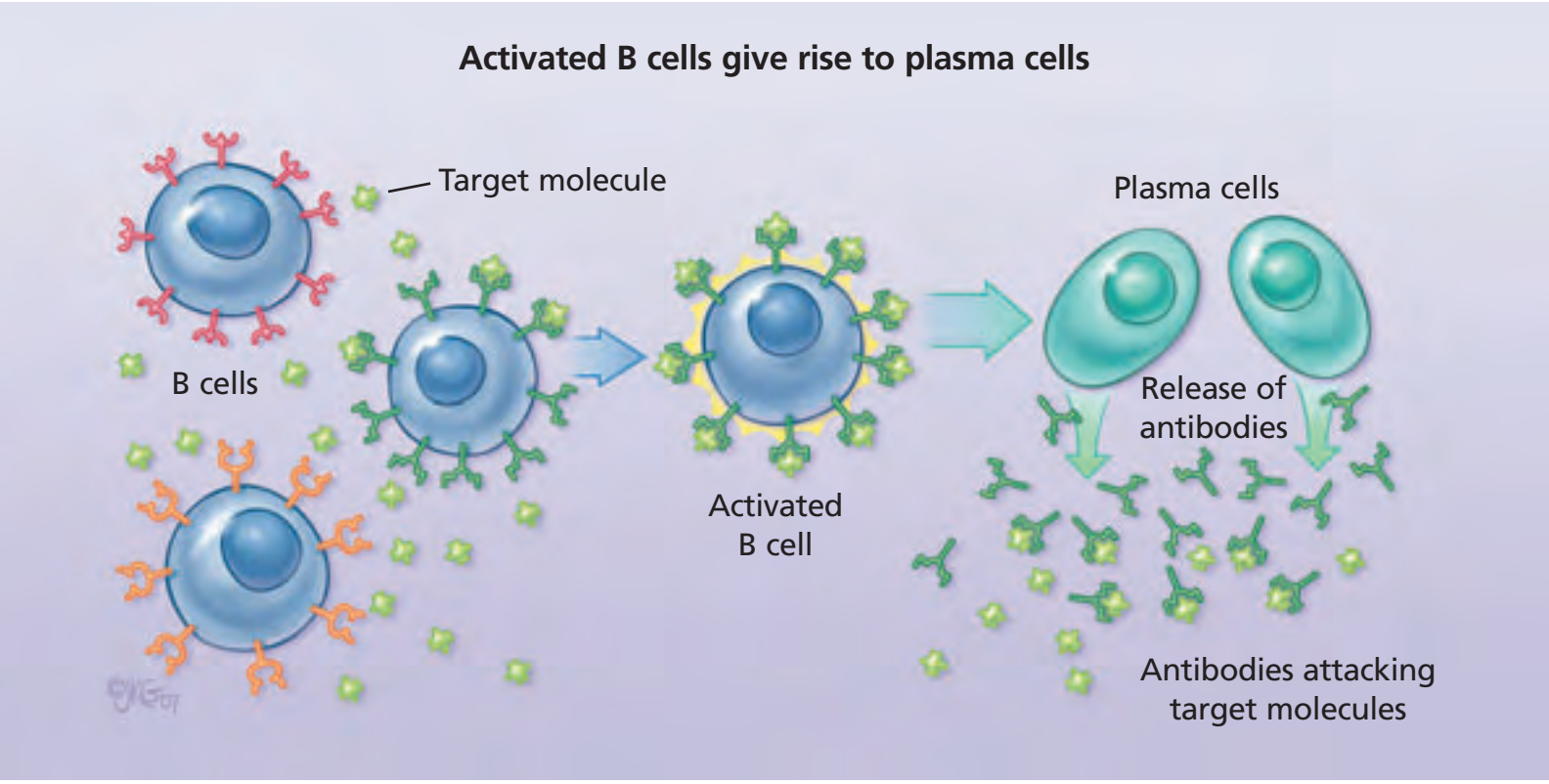

their surfaces. Antibody molecules are extremely diverse and very specific. Antibody that binds to measles virus is different from antibody that binds to mumps virus. Both are different from antibody that binds to myelin basic protein, and so on. Each B cell makes only one type of antibody, so a huge number of B cells is required to recognize the host of infectious targets that we encounter throughout our lives.

When a B cell encounters its target molecule (let's say it's a measles virus protein), it is stimulated to do a variety of things, one of which is to differentiate into a different type of cell, called a "plasma cell." The antibody molecules on the surface of a B cell serve as "receptors" that detect when the target molecule (that measles protein) is in the vicinity. Plasma cells do more than detect. They **secrete** anti-measles antibody molecules that circulate throughout the body and attack that measles protein wherever it is found.

Antibodies may also attack the body's own tissues. In a disease called myasthenia gravis, for example, antibody

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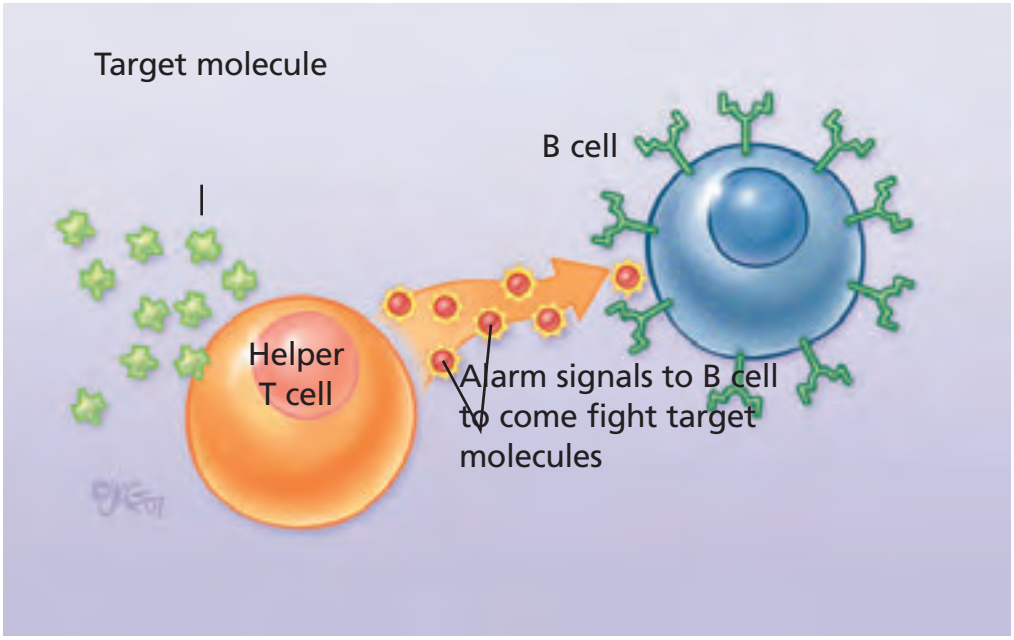
attacks muscle cells and causes weakness. The role of antibodies in MS is not yet known. However, it has been known for decades that abnormal collections of antibodies, known as "oligoclonal bands," are found in the spinal fluid of



more than 90% of people with MS. Do these antibodies play a role in damaging the nervous system in MS? Or are they a byproduct of MS damage? We don't yet know the answers.

A new drug opens new questions

Questions about antibodies have new importance today because, for the first time, a drug has been developed that depletes B cells from the circulation. It is called **rituximab** (Rituxan®) and it is being studied in patients with most types of MS—including secondary-progressive and primary-progressive. A phase II trial in relapsing-remitting MS and a phase II/III trial in primary-progressive MS are in progress.

There is even more at stake. A definitive phase III trial of rituximab, in addition to potentially identifying a new therapy, may help us learn more about the MS disease process. A successful trial would imply that B cells and antibodies do play a role in the destructive process in MS. That understanding would lead investigators to seek more therapies that intervene in the B cell-mediated process and spur intensified efforts to find the answers about MS that B cells and antibodies may give us.

The National MS Society is already funding research in this area. Studies underway include investigations of:

- the disease-causing abilities of antibodies found in the oligoclonal bands in the spinal fluid of people with MS
- the factors that cause B cells to be recruited to the brain and spinal cord
- the potential predictive value of antibody patterns in people at high risk for developing clinically definite MS.

There is a high likelihood that both B cells and T cells play critical roles in the development of MS, and that both will provide new therapeutic targets for the MS treatments of the future. ■

More information about B cell research currently funded by the Society can be found at **nationalmssociety.org/BCell**.

Dr. John Richert is executive vice president for our Research and Clinical Programs.