CHRONIC LYMPHOCYTIC leukemia (CLL) is a form of blood cell cancer that can impact healthy B-cell production, which may increase the risk of infection. Patients with CLL are often treated with intravenous immune globulin (IVIG) replacement therapy in conjunction with other forms of treatment. In fact, CLL is one of the few U.S. Food and Drug Administration (FDA)-approved indications for Gammagard SD, an IVIG therapy.

Understanding CLL

Leukemia is cancer that originates in blood-forming tissue characterized by the uncontrolled growth of blood cells that are produced in the bone marrow. In healthy bone marrow, blood stem cells mature over time and become either myeloid stem cells or lymphoid stem cells. Lymphoid stem cells transform into lymphoblast cells and then either B lymphocytes, T lymphocytes or natural killer cells. B lymphocytes bind to antigens, and with the help of T lymphocytes, transform into plasma cells that secrete antibodies to destroy antigens. Key to protecting individuals from bacterial infections, this humoral immunity is impaired in patients with leukemia. In the bone marrow of patients with leukemia, cancerous blood cells form and, in essence, crowd out the healthy blood cells, interfering with their normal function.

There are several types of leukemia (Table 1) categorized according to which blood cells are affected, and whether the disease is acute or chronic. While leukemia occurs in both adults and children, the most common type — CLL, a white blood cell cancer — occurs mostly in adults. In fact, more than 75 percent of people newly diagnosed with CLL are over the age of 50, and men make up the majority. CLL can occur in teenagers and, occasionally, in children, but it is rare.

In CLL, there is an overproduction of lymphocytes that never fully mature and, thus, do not function as they should. In addition, these cells remain viable and multiply, whereas normal lymphocytes die. The result is impaired antibody production, leaving the person at risk for infection.

CLL is usually one of the slower progressing types of leukemia, and many

<table>
<thead>
<tr>
<th>Type</th>
<th>Cells Affected</th>
</tr>
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<tbody>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>Overproduction of lymphoblasts</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>Abnormal production of myeloblasts</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>Overproduction of lymphocytes</td>
</tr>
<tr>
<td>Chronic myelogenous leukemia</td>
<td>Overproduction of white cells</td>
</tr>
</tbody>
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Table 1. Types of Leukemia

Source: www.cancer.gov/types/leukemia/hp/cll-treatment-pdq#link/_10_toc
people don’t experience symptoms for quite some time. In fact, the first sign of CLL may be an increased white blood count during routine blood work. Symptoms usually begin with frequent infections and/or fever, night sweats, fatigue and enlarged yet painless lymph nodes. There can also be pain in the left upper abdomen that may be due to an enlarged spleen.

If CLL is suspected, testing will include blood work and, possibly, a bone marrow biopsy. The test results are used to stage CLL, most commonly using the Rai staging system (Figure 1). Once the stage of CLL is confirmed, treatment can be determined. Treatment can range from routine monitoring for changes in blood values to chemotherapy, targeted drug therapy and bone marrow transplant. In the earlier stages, since CLL is typically slow to progress, observation may be all that is required. Indeed, it has been shown that early initiation of chemotherapy fails to show benefit in CLL; instead, it may increase mortality.

**How IVIG Helps to Prevent Infections**

Some people with CLL don’t produce enough antibodies (immunoglobulins, or IgG) to fight infection, which can lead to repeated lung and/or sinus infections. Therefore, CLL patients are monitored for signs and symptoms of infection, and IgG levels can be checked with a blood test to determine whether IVIG therapy should be started.

The initiation of treatment with IVIG therapy differs from clinician to clinician. While some cancer centers and hematology/oncology physicians will wait until IgG levels drop below a certain range, some initiate treatment with or without low levels to prevent infections. IVIG therapy is often given once a month at first, but may be needed less often based on antibody levels.

Research has shown that IVIG is effective in preventing infections in CLL patients. In a 2009 meta-analysis of nine trials, researchers assessed treatment of CLL and multiple myeloma patients with polyclonal IVIG versus a control group with primary outcomes of all-cause mortality and major infections. They found that while no survival benefit could be demonstrated, there was a significant decrease in the occurrence of major infections and a significant reduction in clinically documented infections.1

Another crossover study found that low-dose IVIG therapy was just as effective as high-dose IVIG therapy. In the study, 42 CLL patients with hypogammaglobulinemia (IgG levels less than 600 mg/dL) and/or a history of at least one episode of severe infection in the six months preceding inclusion in the study were randomly allocated to receive either an infusion of 300 mg/kg IVIG every four weeks for six months or no treatment. They were then switched to observation or IVIG for another 12 months, and then received IVIG or no therapy for an additional six months. Results showed a significantly lower incidence of infectious episodes during IVIG prophylaxis in 30 patients who completed the six-month period of either observation or IVIG therapy, as well as the 17 patients who completed 12 months of either observation or IVIG prophylaxis.2

### A Preventive Treatment

Lack of proper B cell function is one reason why CLL patients experience frequent infections, which is one of many complications of the disease. While not all physicians recommend IVIG therapy to prevent these infections, it has been shown to be a successful preventive treatment.3

**References**
