WHAT YOU NEED TO KNOW

You or your loved one has been diagnosed with a type of blood cancer. You may experience side effects from the therapy you receive. Cytokine release syndrome (CRS) is a side effect that can happen after some forms of immunotherapy treatment. It may cause your immune system to respond too aggressively. How can you manage it?

This fact sheet will help you:

• Learn about immunotherapy, cytokines, and cytokine release syndrome
• Understand the symptoms, causes, and tests involved
• Know how to manage this side effect and optimize your health and well-being
• Prepare a list of questions to ask your healthcare team
Cytokines, your immune system, and immunotherapy

<table>
<thead>
<tr>
<th>Cytokines</th>
<th>Cytokines are proteins that act as messengers between cells in your body. They play a variety of roles, including helping your immune system respond to disease. They tell your immune system to do its job.</th>
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</thead>
<tbody>
<tr>
<td>Your immune system</td>
<td>The immune system is your body’s primary defense against infection and cancer. It recognizes the difference between cells that naturally belong in your body and cells that are foreign and toxic (antigens). An antigen can be from the environment, like bacteria or a virus. An antigen can also be made inside your body, such as a cancer cell. Having a foreign cell in your body causes your immune system to identify, target, and eliminate the cell.</td>
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<tr>
<td>Immunotherapy</td>
<td>Immunotherapy is a type of cancer treatment that improves your immune system’s ability to detect and attack cancer cells. Doctors and researchers are learning to manage the immune system to destroy cancer cells. This approach is effective for certain blood cancers, but not all blood cancers can be treated with immunotherapy.</td>
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**Cytokine release syndrome**

CRS can happen as a side effect of some immunotherapy treatments.

**About CRS**

- CRS is sometimes called a “cytokine storm”
- It can happen when your immune system responds too aggressively to immunotherapy treatment (such as CAR T cell therapy) or as a result of infection
- CRS involves an excess of cytokines, where a large number are released into the blood quickly and the blood becomes toxic
- Cytokine release is usually helpful, but too many can be toxic

**Symptoms of CRS**

Your reaction to CRS can be mild or moderate, or it can be severe or even life-threatening. The symptoms may vary, depending on which part of your body is affected. You will need treatment as soon as possible.

Symptoms can include:

- Fever and chills
- Cough and shortness of breath
- Low blood pressure
- Joint and muscle pain
- Headache and fatigue
- Nausea and vomiting
- Confusion and dizziness
- Difficulty swallowing
- Skin rash and swelling

CRS can be divided into four grades (1 to 4), depending on how severe your symptoms are. The higher the number, the more serious the CRS is.

**Causes of CRS**

CRS related to blood cancer can be caused by:

- Your immunotherapy treatment (such as bispecific antibodies, checkpoint inhibitors and CAR T cell therapy)
- An infection
Diagnosis of CRS

Cytokine release syndrome is a complication of an underlying condition. You may need to have tests done to confirm treatment. These are some of the tests your healthcare provider may need to run.

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<thead>
<tr>
<th>Name of test</th>
<th>Description</th>
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<tr>
<td>Medical history and physical exam</td>
<td>The doctor reviews past illnesses, injuries, and symptoms. They examine your lungs, heart, and other organs.</td>
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<tr>
<td>Blood tests</td>
<td>Blood tests confirm your need for treatment and the extent of your disease.</td>
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<tr>
<td>Complete blood count</td>
<td>This test measures the number of red blood cells, white blood cells, and platelets in a sample of your blood to find out if the counts are high or low.</td>
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<tr>
<td>Imaging tests</td>
<td>A computed tomography (CT) scan uses a computer linked to an X-ray machine to make a series of detailed pictures of areas inside your body.</td>
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<td></td>
<td>Magnetic resonance imaging (MRI) uses magnetic fields and radio waves to create images of your body's organs and tissues.</td>
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<td></td>
<td>An X-ray creates pictures of the structures inside your body, especially the bones.</td>
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Managing side effects

Learning about side effects helps you know what to expect and how to manage them. If the cause is cancer treatment, your doctor may recommend using smaller doses in your treatment. Recovery depends on the cause of CRS and how severe it is. Many people recover in around 1 to 2 weeks.
Treatment to manage CRS

The treatment for CRS depends on the cause, the symptoms, and your needs. Symptoms can become dangerous quickly, so you need to be treated as soon as possible.

Types of treatment

- Medication to relieve fever and reduce inflammation
- Intravenous fluids (IV) to help your body recover from low blood pressure
- Oxygen or ventilation to help with shortness of breath
- Other medications, depending on your symptoms

Track your side effects with the LLS Health Manager App

bloodcancers.ca/health-manager-app

Managing your side effects is an important part of cancer care. Tracking your medication, side effects, and food and nutrition intake allows you to share the information easily with your doctor to identify patterns and strategies.
Questions to ask your healthcare team

- Is cytokine release syndrome a possible side effect of my treatment?
- What symptoms should I watch for?
- What can I expect with CRS?
- What can I do to manage or prevent this side effect?
- When and how should I contact you if I have CRS symptoms?
- Can you reduce the medication dosage of my treatment if I start to have side effects?