

## What is chronic myelogenous leukemia?

Chronic myelogenous leukemia (CML; also known as chronic myeloid leukemia or chronic granulocytic leukemia) is a cancer of the blood system in which too many white blood cells (WBCs) are made in the bone marrow. In the early stages of CML (the chronic phase), these excess WBCs mature normally. In contrast, excess WBCs in late CML (the accelerated and acute phases) do not mature.

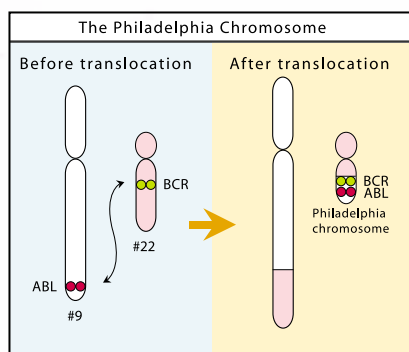
## Who gets CML?

The American Cancer Society estimates that 4,300 new cases of chronic myelogenous leukemia will be diagnosed in the United States this year. CML usually occurs in people in their 40s and beyond, although it can occur in younger patients.

## What causes CML?

In almost everyone with CML, the genetic material (chromosomes) in the leukemia cells has an abnormal feature called the Philadelphia chromosome.

The Philadelphia chromosome results from a mutation called a translocation (two chromosomes break, then parts from each chromosome switch places). In CML, the translocation occurs between chromosomes 9 and 22 (human DNA is packaged in 23 pairs of chromosomes) and produces a new, abnormal gene called BCR-ABL. This abnormal gene produces Bcr-Abl tyrosine kinase, an abnormal protein that causes the excess WBCs typical of CML.



The Philadelphia chromosome is an acquired mutation – that is, a person is not born with it and it is not passed on to their children. Exactly why the Philadelphia chromosome forms is unknown in most cases, although exposure to ionizing radiations (such as during the atomic bomb explosions in Japan) has been shown to cause CML.

## What are the symptoms of CML?

In chronic phase CML many people have no symptoms. When symptoms are present, they are often nonspecific and can include signs such as weakness, fatigue, weight loss and fever. These symptoms occur because the leukemia WBCs are replacing normal bone marrow cells.

## How is CML diagnosed?

About half of CML cases are detected when a person visits a doctor for a routine checkup or blood test.

In people with symptoms, a doctor may order blood tests to examine the different kinds of blood cells present. If the results of the blood test are not normal, the doctor may order more blood tests and a bone marrow exam (or aspiration) may also be done. During the exam, a needle is inserted into the hipbone and a small amount of bone marrow is withdrawn. The bone marrow sample is then examined by chromosome and/or molecular techniques for the presence of the Philadelphia chromosome. Presence of this abnormality is required for a definitive diagnosis of CML.

## What are the phases of CML?

CML is divided into three phases depending on the maturity of the leukemia WBCs.

### CHRONIC PHASE

There are mostly mature leukemia WBCs in the blood and bone marrow and there may be no symptoms of leukemia. This phase lasts from several months to several years, with an average duration of five years.

### ACCELERATED PHASE

There are some immature leukemia WBCs in the blood and bone marrow (between 5 percent and 30 percent). Patients may have fever, poor appetite and weight loss. The leukemia cells may have new chromosome changes, in addition to the Philadelphia chromosome.

### ACUTE PHASE

Also called blast phase or blast crisis. In this phase, there are mostly immature WBCs in the blood and bone marrow (more than 30 percent). Symptoms such as anemia and recurring infections are typical.

## How is CML treated?

Treatment options for people with CML depend on the phase of their disease, age and the availability of a potential donor for a bone marrow or blood cell transplant. Only treatment options for chronic phase CML are discussed below.

There are four chemotherapies used in the treatment of chronic phase CML, the newest of which is Gleevec® (imatinib mesylate, Novartis\*), an oral therapy that is believed to interfere with the action of the abnormal Bcr-Abl tyrosine kinase in CML white blood cells.

Immune therapy with interferon alpha (a regulator of the immune system) can also be used to treat chronic phase CML and is sometimes combined with chemotherapy.

Bone marrow transplantation is generally limited to patients younger than 55 years old who have a suitable donor (about 10 percent of CML patients).

\*[www.novartis.com](http://www.novartis.com)