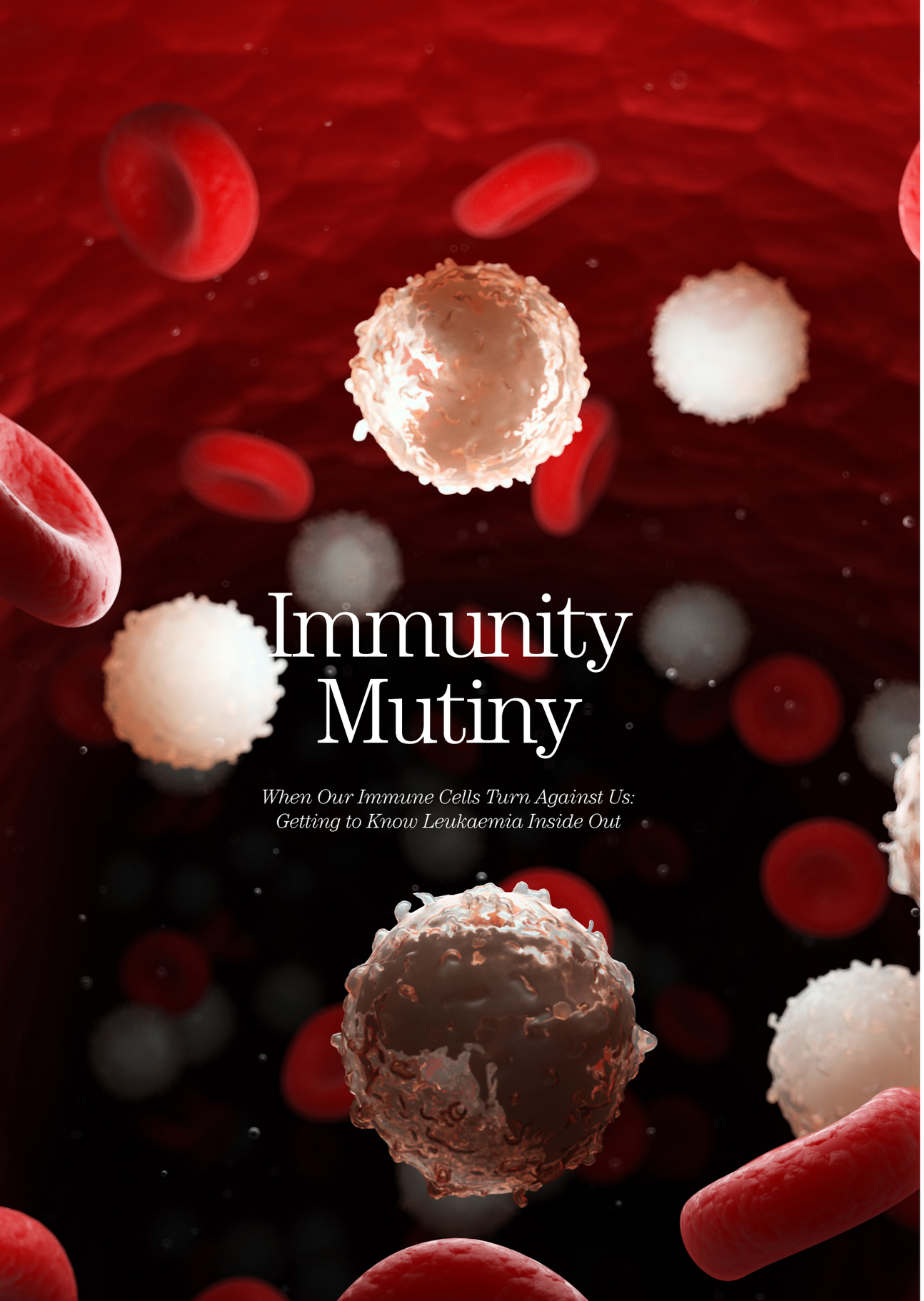


Immunity Mutiny

When Our Immune Cells Turn Against Us: Getting to Know Leukaemia Inside Out

The word "leukaemia" literally means excessive abnormal white blood cells in the blood. It is a broad term given to a group of blood cancers affecting white blood cells. In leukaemia, the body's white blood cells are produced in excess with abnormal function. Leukaemia is often a highly deadly condition if left untreated. However, with modern treatments, many forms of leukaemia can be highly curable. Let me walk you through the basics of leukaemia as well as the latest advancements in the treatment of leukaemia.

FUNCTION AND PRODUCTION OF WHITE BLOOD CELLS

White blood cells are produced in the bone marrow. They protect us from infection and help us fight infections by recognising and destroying foreign objects that enter the body, including bacteria, viruses and even cancer cells.

Leukemia happens when genetic changes occur in white blood cells. This causes the white blood cells to divide and reproduce rapidly. The abnormal white blood cells replace the healthy space in the bone marrow and affect the normal function of the blood system. As a result, patients often develop and present with symptoms like anaemia (tiredness), easy bruising and bleeding. There is also an increased risk of infections.

Leukaemia can be grouped into two categories: acute and chronic leukaemia. Acute leukaemia tends to be more aggressive, affecting the early cell types in the bone marrow, and is often rapidly fatal without treatment. Chronic leukaemia is often more slow-growing as the disease affects the more mature blood cells in the bone marrow.

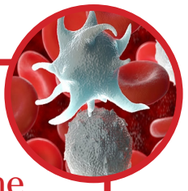
DIAGNOSIS OF LEUKAEMIA

The suspicion of leukaemia is often raised when a patient presents with high (or sometimes very low) total white blood cell count. Examination of a drop of the patient's blood under the microscope (called a peripheral blood film) may reveal the presence of abnormal white blood cells. A bone marrow biopsy assessment is usually performed to confirm the diagnosis.

A bone marrow aspiration and biopsy are a simple and safe procedure. It is usually performed by the bedside or at an outpatient clinic. The samples from the bone marrow are sent for a panel of tests which often includes tests looking at the genes (cytogenetic analysis) as well as a more novel form of tests to look at specific commonly occurring mutations in leukaemia (next generation sequencing). The tests are important to establish the prognosis of leukaemia patients and may sometimes help to guide the use of targeted therapies.

ACUTE LEUKAEMIA

There are two main subtypes of acute leukaemia – Acute Myeloid Leukaemia (AML) and Acute Lymphoblastic Leukaemia (ALL). The latter is further subclassified into B-ALL and T-ALL. Acute leukaemia is invariably fatal within 3-4 months if no prompt and appropriate treatment is given.



> With a growing understanding of the molecular genetics in leukaemia, an increasing number of newer targeted agents are entering the early phase of clinical trials. We can expect to see more novel targeted therapies being introduced as mainstream treatments for leukaemia in the very near future.

The treatment of acute leukaemia often involves upfront high intensity chemotherapy (known as induction chemotherapy). With induction chemotherapy, 70-80% of patients would achieve a complete remission. This is usually followed by 3 to 4 more cycles of chemotherapy to clear any residual leukaemia. Some patients with high risk leukaemia may require an allogeneic stem cell transplant (bone marrow transplantation) to reduce the risk of relapse and improve the chances of long-term survival.

Intensive chemotherapy is often not well tolerated by older patients (>60 years). More recently, an increasing number of novel targeted therapies and immunotherapies have become available for the treatment of acute leukaemia. These newer therapies are generally less toxic compared to conventional chemotherapy. Hence, they provide some good treatment options for patients who are less fit for intensive chemotherapy.

CHRONIC LEUKAEMIA

Chronic leukaemia is a less aggressive form of blood cancer, and patients are often diagnosed incidentally during routine health screenings. Some cases may present with symptoms of anaemia such as fatigue and reduced effort tolerance, or a more general complaint such as loss of weight and appetite. A few cases may present with extremely high white blood cell count. The latter is often life-threatening and requires urgent treatment.

The white blood cells in chronic leukaemia are usually of mature form but dysfunctional. As a result of excessive production of abnormal white blood cells in the bone marrow, a normal production of healthy blood cells is compromised. When red blood cell production is compromised, patients can become anaemic. When normal white blood cell

production is compromised, our defence against infections will be affected. Patients could present with recurrent fever and infection. An increase in bleeding tendency, such as prolonged gum bleeding and easy bruising, are due to reduced platelet production.

TREATMENT PARADIGM OF CHRONIC LEUKAEMIA

Conventional chemotherapy is no longer the standard of care for most chronic leukaemia cases. For example, in the case of Chronic Lymphocytic Leukaemia (CLL) which is one of the most common forms of leukaemia, upfront chemotherapy has been almost completely replaced by targeted therapy agents. These newer agents have significantly changed the landscape of treatment. For example, an oral targeted agent known as Ibrutinib, has tripled the CLL survival rate compared to conventional therapy (Chlorambucil).

The treatment paradigm of another common form of chronic leukaemia known as Chronic Myeloid Leukaemia (CML) has also totally shifted. Treatment of CML is largely based on oral targeted drug therapy, which has improved the 10-years overall survival rate from 45% to more than 80%. Excitingly, there are now several newer and more potent versions of the oral targeted therapy which are available. These novel targeted agents are extremely effective, with favourable toxicity profiles even for older patients.

IS LEUKAEMIA CURABLE?

The short answer is a big "Yes". There are certain subtypes of leukaemia that are more difficult to treat than others, and the long-term outcome or prognosis of an acute leukaemia subtype is largely dependent on the underlying genetic mutations. Those with adverse genetic risk have lower cure rate (i.e. 20% long term cure) compared with favourable risk (which has 60-80% chance of cure). Those with adverse risk will need a stem cell transplant to increase the likelihood of cure. In chronic leukaemia, the long-term survival rate is in excess of 60% with newer therapy. Many of these patients will need to be on long-term targeted therapy to suppress the leukaemia cells. Some of these patients who remain in deep remission may be taken off therapy with close monitoring.

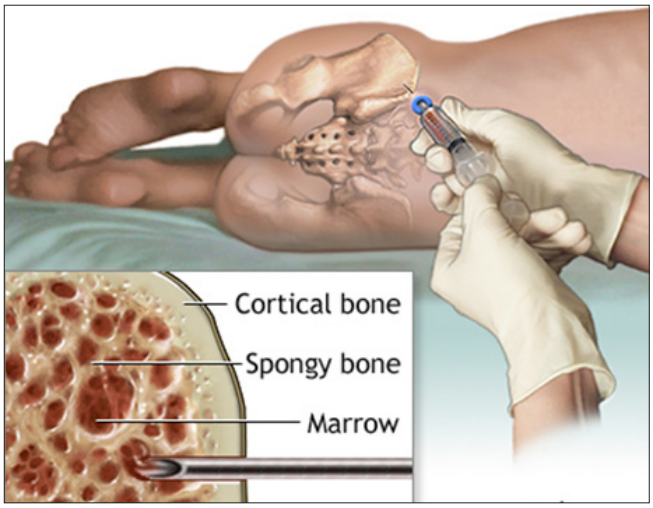
FAQS ABOUT LEUKAEMIA

Included below are some commonly asked questions that many people have about leukaemia.

- **WHY DO I GET LEUKAEMIA?**
  Leukaemia can happen to anyone. In most cases, no identifiable cause can be found. Some of the known risk factors are exposure to carcinogenic agents such as radiation, cigarette smoke, benzene, previous chemotherapy, etc. However, most people with exposure to these agents never develop leukaemia.

- **WHAT CAN I DO TO STOP MYSELF FROM GETTING LEUKAEMIA?**
  There is nothing specific you can do to definitely prevent yourself from getting leukaemia. However, living a healthy lifestyle which includes having a balanced diet, maintaining an ideal body weight, regular exercise, ensuring that you get enough sleep, and avoiding processed food (among others) may maintain you in good health and reduce your risk of illness.

- **DOES IT RUN IN THE FAMILY?**
  Most leukaemia cases do not present a family history of the disease. However, a strong family history of cancer may increase one's risk of contracting any cancer, including leukaemia.



AGE OF TARGETED THERAPY

With a growing understanding of the molecular genetics in leukaemia, an increasing number of newer targeted agents are entering the early phase of clinical trials. We can expect to see more novel targeted therapies being introduced as mainstream treatments for leukaemia in the very near future. We may be witnessing the dawn of a new chemotherapy-free age for the treatment of leukaemia in time to come. PRIME

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