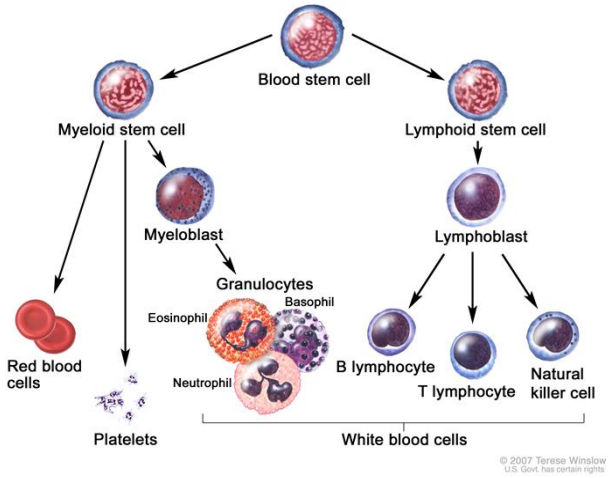
Qure
Center for Complete Care
Blood Diseases, Cancer, Stem Cell Transplantation

Acute Promyelocytic Leukemia

What is Acute promyelocytic leukemia (APL)?

APL is a cancer of the blood in which the bone marrow makes too many immature promyelocytes (a kind of white blood cell). Blood is made in the bone marrow where white blood cells pass through various stages as they mature in the marrow. In APL there is a genetic defect in a rogue cancer cell, which causes it to multiply and fill up the bone marrow with immature cancerous white blood cells (blasts). This prevents normal white cells, red cells and platelets from being formed, leading to anemia and easy bleeding. The bleeding is worsened by substances in the APL blasts, so it is extremely important to start treatment urgently.



What are the signs of APL?

- Easy bruising or bleeding.
- Petechiae (dark-red spots under the skin).
- Weakness, feeling tired, or looking pale.
- Loss of appetite.

What causes APL?

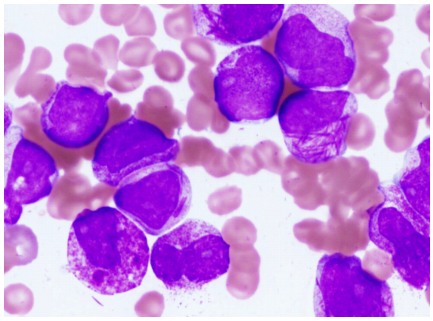
Although we know the genetic defect usually present in APL blasts, we do not know what causes this. Commonly there is nothing in the environment or diet, and it is not inherited so other family members should not be at risk. It is also not infectious so it cannot be passed onto other family members or neighbors.

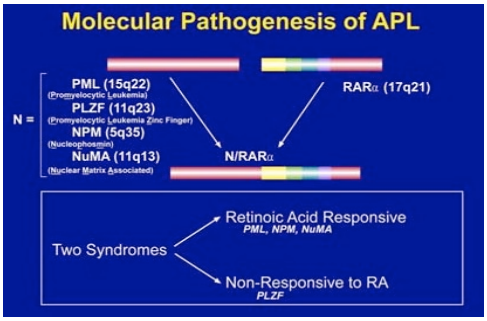
How is APL diagnosed?

We may suspect the diagnosis from the blood count but the tests described below will confirm it

- **Physical exam and history:** An exam of the body to check or signs of disease,
- **Blood tests:** such as complete blood count (CBC) tells the number and type of each blood cell, and blood chemistry and clotting studies help in initial care and to avoid complications.

- **Bone marrow aspiration and biopsy:** Removal of liquid bone marrow and a small piece of bone by inserting a needle into the hipbone while sedated provides material for a pathologist to look at under a microscope to confirm the diagnosis. APL blasts have a distinct appearance with large bright red granules/rods as seen below **(FAB Classification M3)**.
- Additional tests include flow cytometry to look at markers on the surface of leukemia cells, and genetic testing of APL blasts for the defect ***PML/RARA***. Almost all patients will have it in their blasts and ***PML/RARA*** levels can be monitored in blood or marrow to see if the leukemia has cleared completely.





Is APL curable?

APL is a subtype of Acute myeloid leukemia (AML), but is very different because it is very sensitive to some highly effective targeted treatments. Long-term cure rates are 80% or higher, with little or no long-term effects. APL is rare with only 5000 cases per year diagnosed in the whole of India, so it is important to be treated by experts familiar with this condition.

What are the risk Groups in APL?

Risk groups are used to plan treatment, and there are only two risk groups in APL:

- **Standard (low) risk**: initial white cell count $\leq$10,000/mm^3 accounts for 2/3 of patients
- **High risk**: initial white cell count >10,000/mm^3 accounts for 1/3 of patients

Your doctor will use information gathered at diagnosis and in the first month of treatment to accurately determine your further treatment. This includes the gene changes in the leukemia cells, and how quickly the leukemia is cleared from the bone marrow.

What is the treatment for APL?

Overall cure rates with modern day treatment are excellent and bone marrow transplant or radiation are usually **not** indicated. The medications used in APL specifically target the APL blasts which reduces the risk of side effects. **Nevertheless all people who receive cancer treatment are at risk of having side effects, some of which are mild but others of which can be life-threatening** In addition to killing tumor cells, chemotherapy can damage normal tissue. Side effects usually get better when the medication is stopped but sometimes last a long time or never go away. Common side effects include nausea, vomiting, hair loss, low blood counts and fatigue (tiredness). It is important to remember that the treatment given is essential for cure, and most patients will have very few of the side effects listed.

During early induction we often transfuse blood products such as fresh frozen plasma (FFP) as well as platelets to reduce the risk of bleeding. In APL the main chemotherapy drugs given are:

- **All-*trans*-retinoic acid [ATRA]** is given by mouth daily, often started before the diagnosis is fully confirmed. ATRA causes the leukemic blasts to mature so the risk of bleeding is eliminated. Sometimes it works too well, which leads to high white counts and shortness of breath ("differentiation syndrome") needing steroid treatment.
- **Arsenic trioxide [ATO]** is given by IV daily and acts in a similar fashion with similar side-effects, but can also cause heart rhythm changes, liver and nerve toxicity.
- **Idarubicin** is a chemotherapy drug used for other leukemias, and is given IV on alternate days for high risk patients only, in order to help them go into remission.

Induction

In this initial stage of treatment our goal is to remove all visible signs of leukemia and allow normal blood cells to be restored (*remission).* A special bone marrow test is done on day 28 of induction to look for the PML/RARA marker and is known as **MRD test.** If the MRD test remains positive on day 29 induction may be extended longer.

Consolidation

Patients receive 4 cycles of ATO (5 days per week for 4 weeks, repeated after a 4 week gap) and 7 cycles of ATRA (2 weeks repeated after a 2 week gap) as consolidation to kill any remaining leukemia cells. This treatment may be modified if MRD testing shows disease persistence/ progression. Maintenance therapy is no longer routine, but may be given to high-risk patients

What dietary and other precautions should I take?

Chemotherapy suppresses the immune system so infections are a concern. We place diet and activity restrictions for the first month of treatment, and often for the first 6-7 months, especially for young children. We prohibit any street/outside food and recommend home food be thoroughly cooked. No special foods will help with cure but we ban vitamin or nutritional supplements that might interfere with chemotherapy. Visits to movie theaters, malls, weddings, or other crowded places and plane, bus or railway travel are all banned. You should contact your doctor *immediately* if in spite of these precautions you develop a fever >100.4F, diarrhea, cough, vomiting, abdominal pain, headaches or feel unwell.

What happens after completion of therapy?

We will continue to monitor your blood for MRD at regular intervals to check for any risk of relapse. Your doctor will discuss with you what other follow up tests might be needed.