

# Introduction to the Leukemias

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## Abstract

Leukemias are malignant neoplasms of the blood forming tissues.<sup>1</sup> The bone marrow is the primary organ which produces red blood cells, white blood cells, and platelets, the final products of proliferation and differentiation of primitive cells capable of maturation into blood cells of all hematopoietic lineages. See Table 1 for normal values. This pool of pluripotent hematopoietic stem cells is constantly regenerating throughout life. The leukemias are malignant disorders resulting from defects of the stem cells at different stages of maturation, with subsequent clonal expansion of the myeloid (red cells, granulocytes, platelets) or lymphoid lineages. Leukemia often manifests itself when suppression of normal hematopoiesis results in anemia, infections, or hemorrhage.

## Figure 1

TABLE 1: NORMAL HEMATOPOIESIS\*

BONE MARROW		BLOOD PERIPHERAL	
Normal %	Cell Type	Cell Type	Normal %
0.3 - 5.0	Blast	Blast	0
1.8 - 8.0	Promyelocyte	Promyelocyte	0
5.0 - 20.0	Myelocyte	Myelocyte	0
13.0 - 32.0	Metamyelocyte	Metamyelocyte	0
7.0 - 30.0	Neutrophil	Neutrophil	42 - 66
0.5 - 4.0	Eosinophil	Eosinophil	1.0 - 4.0
0.0 - 0.7	Basophil	Basophil	0.0 - 1.0
3.0 - 17.0	Lymphocyte	Lymphocyte	24 - 44
0.0 - 2.0	Plasma Cell	Plasma Cell	0
0.5 - 5.0	Monocyte	Monocyte	1.0 - 6.0
0.1 - 2.0	Reticulocyte	Reticulocyte	0.0 - 1.0
1.0 - 8.0	Pronormoblast	Mature Red Blood Cell	
7.0 - 32.0	Normoblast	Mature Red Blood Cell	
	Megakaryocyte	Platelet	140-440 x109/L

\*Adapted from Hoffbrand AV, Pettit JE: Essential Haematology, 3rd edition, pp 1-11,244. London, Blackwell Scientific Publications, 1993.

The earliest documentation of leukemia was in 1827 by Velpean, but the entity was ignored until 20 years later when cited by Virchow, who was later credited with recognition of "weisses Blut" in 1847.<sup>2</sup> Arsenic oxide was the first substance used to treat leukemia, chronic myeloid leukemia (CML), and produced a complete, although transient,

remission. Later, radiotherapy was used. Leukemia was considered virtually incurable until the 1940s.<sup>2</sup> Today an arsenal of chemotherapy drugs exists, but current therapies are still not completely effective in treating various leukemias. Approximately 20,500 new cases of leukemia are diagnosed in adults and 2,500 new cases in children each year in the United States.<sup>3</sup>

Leukemias are classified into essentially <sup>4</sup> major types - acute myeloid (AML), acute lymphocytic (ALL), chronic myeloid (CML), and chronic lymphocytic (CLL), depending on which cell lines are involved. Acute vs. chronic is an historical distinction determined clinically by duration of survival. Paradoxically, with older chemotherapy regimens acute leukemias have been more curable. Acute leukemias are characterized by a maturation arrest resulting in accumulation of immature/undifferentiated, nonfunctional neoplastic cells, or blasts.<sup>4</sup> Chemotherapy eliminates the neoplastic clone, allowing reestablishment of normal hematopoiesis. In contrast, chronic leukemias are characterized by accumulation of a spectrum of differentiated cells.<sup>4</sup> Apoptosis, or programmed cell death, may also be defective leading to accumulation of mature cells. Therapy is directed at reducing the tumor burden, suppressing the defective clonal element, and returning the patient's life to normal for as long as possible. A better understanding of the different mechanisms causing each type of leukemia will lead to the development of more specific and effective therapy.

## References

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