This Week's Citation Classic™
CC/NUMBER 47
NOVEMBER 19, 1984

**Bennett J M, Catovsky D, Daniel M T, Flandrin G, Galton D A G, Gralnick H R & Sultan C.** Proposals for the classification of the acute leukaemias.
*Brit. J. Haematol.* 33:451-8, 1976. [Univ. Rochester Cancer Ctr., Univ. Rochester Sch. Med. and Dentistry, NY; MRC Leukaemia Unit, Royal Postgrad. Med. Sch., London, England; Inst. Recherchés sur les Leucémies et les Maladies du Sang, Hôp. Saint-Louis, Paris; Serv. Central Hématol.-Immunol., Hôp. Henry Mondor, Creteil, France; and Hematol. Serv., NIH, Bethesda, MD]

Based on an extensive study of blood and marrow films of over 200 cases of acute leukemia, seven French, American, and British hematologists (the FAB group) defined nine subgroups of leukemic morphologic variants. The originally proposed nomenclature (M1-M6 and L1-L3) has been adopted widely by numerous treatment groups. In addition, significant, nonrandom chromosome alterations (rearrangements, translocations) have been found to be associated with several of the defined FAB cell types. [Cited over 890 times, this is the most-cited paper ever published in this journal.]

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August 14, 1984

"In 1974, G. Flandrin and I were discussing cytochemical staining of leukemia cells, and we realized that precise description of leukemic types of both acute myeloid and lymphoblastic leukemias were lacking. Further interactions with another hematologist, C. Sultan, prompted a decision to assemble a group of dedicated morphologists to discuss differences in concepts and practice in the diagnosis of the acute leukemias. The group's interest focused primarily on pathogenesis of the leukemias but also on therapeutic questions, particularly the availability to groups worldwide of a system to render data from different sources comparable. To achieve this goal, every effort was made to define each leukemia subtype as unambiguously as possible. Two extensive working meetings were held during 1974 and 1975, in which 150 cases of acute leukemia were reviewed and points of disagreement resolved. A uniformity of 85 percent agreement was achieved on a fresh set of slides, and the classification was published in 1976.

"The hematology community worldwide responded favorably. It became apparent, however, that there remained some areas of imprecision in both the myeloid and lymphoid classification schemas, which necessitated revisions. Subsequently, two additional papers appeared that described a variant type of promyelocytic leukemia and a scoring system for the two types of acute lymphoblastic leukemia (ALL)—L1, L2.[1,2] More recently, the FAB group has classified a very different group of hematologic disorders that include conditions variously described as preleukemia or subacute leukemia.[3] Five categories of 'myelodysplastic' syndromes were described, with significant differences in survival and leukemic evolution observed by us and others.

"Although it appears unlikely that substantial survival differences will be found between the major FAB myeloid subtypes, there is evidence that hypergranular promyelocytic leukemia (FAB M3) is associated with prolonged remission duration and acute monocytic leukemia (AML: FAB M5) with a short response duration and a high likelihood of central nervous system leukemia.[4] Of potentially greater importance is the association of certain myeloid subtypes with nonrandom chromosome abnormalities: FAB M2 (AML with maturation) with t(8:21) in 20 percent of cases; FAB M4Eo (acute myelomonocytic leukemia with eosinophilia) with C16 inversion; FAB M3 with t(15:17); and FAB M5 with chromosome 11 abnormalities.

"Concerning ALL in children, numerous groups have confirmed the prevalence of the L1 subtype over L2 and L3, whereas in adults there are more L2 cases, particularly in patients over age 30.[2] Moreover, patients with L2 morphology have a significantly shorter survival than those with L1, and those with L3 ('Burkitt cell' or B-cell ALL) have the worst survival (less than one year).[5] The only consistent chromosome abnormality associated with FAB lymphoid subtypes has been the translocation in FAB L3 of the c-myc gene locus translocated from chromosome 8 to the immunoglobulin gene locus on chromosome 14.[6]

"A decade ago, the FAB members could not predict the ultimate significance of our leukemia classification proposals. Intuitively, we believed that precise definitions of morphologic subtypes of the acute leukemias and myelodysplastic syndromes, incorporating understandable terms and excellent photomicrographs, would be of value to researchers. Overall, the acceptance of the 'proposals' indicates that the provision of an international classification provides a basis for useful discussion and comparative research. Certainly, we have not been without our critics, and their comments have led to appropriate responses and clarifications."

1. **Bennett J M, Catovsky D, Daniel M T, Flandrin G, Galton D A G, Gralnick H R & Sultan C.** A variant form of hypergranular promyelocytic leukemia (M3). *Ann. Intern. Med.* 92:261, 1980.
2. ----------. The morphological classification of acute lymphoblastic leukaemia. Concordance among observers and clinical correlations. *Brit. J. Haematol.* 47:553-61, 1981.
3. ----------. Proposals for the classification of the myelodysplastic syndromes. *Brit. J. Haematol.* 51:189-99, 1982.
4. **Bennett J M & Begg C B.** Eastern Cooperative Oncology Group study of the cytochemistry of adult acute myeloid leukemia by correlation of subtypes with response and survival. *Cancer Res.* 41:4833-7, 1981.
5. **Bloomfield C D.** The lymphocyte in clinical medicine: classification and prognosis of acute lymphoblastic leukemia. (Sell K W & Mill W V, eds.) *The lymphocyte*. New York: Liss, 1981. p. 167-83.
6. **Rowley J D.** Human oncogene locations and chromosome aberrations. *Nature* 301:290-1, 1983.

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