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Sensitivity for the Detection of Leukemic Cells

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In a recent article, Cranendonk et al. [1] reach a conclusion that is at odds with the clinical experience and experimental results of many other investigators [2–5]. They state that automated flow cytochemistry (Hemalog-D; Technicon, Tarrytown, N.Y.) is not reliable for the detection of even large amounts of lymphoblasts. This conclusion is not warranted by their own data. They formulated the following hypothesis, ‘Is it possible to recognize a leukemic relapse earlier with the aid of the HD (Hemalog) than with MDC (manual differential count)?’ In response, the authors give the number of blood counts with and without an elevated % LUC (large unstained cell) correlated with the presence or absence of lymphoblasts on the manual differential.

Cranendonk et al. [1] assume that the recognition of lymphoblasts on a manual smear is an infallible test result or at least a gold standard for the recognition of early relapse of ALL. Under this assumption, from their data the sensitivity is 64% and the specificity is 82% for increased % LUC correlating with lymphoblasts [6]. To demonstrate the importance of the assumption that the manual differential represents truth let us invert the logical problem and consider % LUC as the gold standard and the presence of lymphoblasts to be a test under investigation. From the same data we calculate that the presence of lymphoblasts gives only a 19% sensitivity, but a high 97% specificity for correlating with increased % LUC.

New laboratory tests are too often looked at only in terms of comparison to the older tests that they may potentially replace. The fallacy of using this type of comparison is that one must a priori decide that one test represents truth. Given this assumption, the only possible outcome is that the new test is only as good as (assuming perfect correlation), or otherwise, is inferior to the old test. To correctly compare the performance of two test strategies in diagnosing a disease, one must compare the test results directly to the presence or absence of the disease.

For the monitoring of patients with leukemia, nobody advocates the complete abandonment of the blood smear. Instead, a synthesis of automated flow cytochemistry (a method which is highly sensitive for the detection of potential leukemic cells), and expert morphological review of positive specimens (a method highly specific for confirming the presence of leukemic cells) offers the optimum use of these data. This later conclusion is the experience of many published reports of users of automated flow cytochemistry and other forms of flow cytometry.

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Automated Cytochemistry in Acute Leukemia

We wish to make several remarks about the paper by Cranendonk et al.: Evaluation of the use of the Hemalog D in acute lymphoblastic leukemia and disseminated non-Hodgkin's lymphoma in children [*Acta haemat.* 71: 18–24 (1984)], which deals with automated cytochemistry performances in acute leukaemias. The subject, indeed, is not a worthless one: automated leukocyte differential devices, in fact, are more and more diffused among hematology laboratories, so that the awareness of their qualities and defects deserves considerable interest. In that paper, the authors report their results concerning Hemalog D differential counts in 79 children with acute lymphoblastic leukemia (ALL) and 18 children with disseminated non-Hodgkin's lymphoma; only 25 of them, however, were studied since the onset of their disease. The authors generalize their conclusions, claiming that the Hemalog D seems inadequate in diagnosis and follow-up of leukemic patients. Over the last 4 years we have been able to analyze a large number of leukemic blood samples with the Hemalog D [1, 3]. We would like to report very briefly our experience, which is indeed quite different.

As far as reliability and accuracy are concerned, the Hemalog D appears entirely capable of detecting and signaling pathological samples: with one exception, in 43 cases of acute leukemia adequate flags (increase in LUCs or HPX, abnormal Remainder, LR or LPX warnings) were constantly provided, allowing an immediate microscope check. The only exception was represented by a patient with acute promyelocytic leukemia, in which no alarm signals were reported in the printout: the peroxidase display plot, however, was clearly abnormal, and the association with pseudo-eosinophilia, marked leukocytosis, decreased hemoglobin and platelet count would have pointed out that sample as abnormal in any case.