Earlier this year new guidelines on CLL were published by the IWCLL[1]. I have to admit that despite being consulted about the paper before publication a change has slipped through that I did not notice – and it is a very controversial change. Previously the threshold for diagnosis was a lymphocyte count of 5000 per cu mm. This has been changed to a B lymphocyte count of 5000. The proportion of lymphocytes that are B cells is extremely variable, so in order to reach a B cell count of 5000 a person might need to have an absolute lymphocyte count of greater than 10,000.

This needs to be seen in the context of the diagnosis of monoclonal B lymphocytosis (MBL) in which the individual has circulating lymphocytes exactly like CLL cells, but the absolute lymphocyte count is less than 5000. Under the new definition what would previously have been called CLL would now be called MBL unless that total B-lymphocyte count is greater than 5000. A lot of patients who have been told that they have been told that they have CLL would suddenly have their diagnosis corrected to MBL. It has been estimated that 40% of patients with stage 0 CLL in fact have MBL.

There are real problems with this. First, it means that flow cytometry becomes essential for diagnosis and also for follow up. This is much more expensive than a simple cbc. Second, patients will fluctuate between MBL and CLL on successive visits to their doctor. Third, MBL turns into CLL at the rate of1% per year, so it does not mean that follow-up can be omitted. Fourth, a paper from Andy Rawstron in the NEJM earlier this year[2] suggested that a threshold of 2000 B cells was necessary for MBL to progress – patients with lower levels were very unlikely to do so.

To some extent this new definition satisfies the problem that Victor Hoffbrand and I raised earlier this year[3], namely that patients were being told that they had leukemia, yet they would never need treatment for it, though even with the new definition that will still be the case for some patients (though for fewer than before).

I guess the major problem that I have with this change is that it has been made without the benefit of evidence to guide it, merely on the gut-instinct of the authors.

1. Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Döhner H, Hillmen P, Keating MJ, Montserrat E, Rai KR, Kipps TJ; International Workshop on Chronic Lymphocytic Leukemia. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute-Working Group 1996 guidelines. Blood. 2008;111:5446-56.
2. Rawstron AC, Bennett FL, O'Connor SJ, Kwok M, Fenton JA, Plummer M, de Tute R, Owen RG, Richards SJ, Jack AS, Hillmen P. Monoclonal B-cell lymphocytosis and chronic lymphocytic leukemia. N Engl J Med. 2008;359:575-83.
3. Victor Hoffbrand A, Hamblin TJ. Is "leukemia" an appropriate label for all patients who meet the diagnostic criteria of chronic lymphocytic leukemia? Leuk Res. 2007; 31:273-5.