

## Editorial

# How useful are haematology analyser flags?

In this issue Van der Meer and colleagues describe how flags generated by haematology analysers can lead to inconsistency and observer bias of morphological differentials (1). The authors of this paper are to be complimented with the simple but elegant design of the study, which yields results that are of major importance for daily practice in a clinical laboratory.

These authors prepared two sets of blood smears, containing increased fractions of band cells and atypical lymphocytes, respectively, and presented them twice to 30 morphologists. The first time there was no supplementary information provided, whereas two months later the same smears, which were differently coded, were each accompanied by the corresponding report from a haematology analyser. The reports included a full blood count with a five-part differential as well as alert flags for left shift, immature granulocytes or atypical lymphocytes. Not unexpectedly, the morphological review of the smears containing band neutrophils and immature granulocytes showed considerable inter-observer inconsistency in band count. Also, the intra-observer reproducibility between the first and second observations was rather low. Similarly, the inter-observer consistency in atypical lymphocyte recognition was poor. Moreover, the authors demonstrated that there was nearly complete lack of intra-observer agreement in atypical lymphocyte assessment between the two observations. In this particular case, they noted that the degree of intra-observer disagreement was highly correlated with the presence of analyser flags for atypical lymphocytes, meaning that the morphologists reported significant more atypical lymphocytes when assessing smears of samples that were flagged in the analyser report. To my knowledge the authors are the first to recognise that “analyser reports may induce observer bias in variant lymphocytes estimates” (1).

This conclusion is not only surprising but it is also a reason for concern. Most observers have no detailed knowledge why analysers generate alert flags and as a consequence it is difficult to appraise the value of a flag. When morphologists apparently are influenced by the presence or absence of an analyser flag this can be clinically misleading, like Van der Meer et al. have discussed. This raises the question how clinically useful analyser flags are.

Traditionally, many evaluation reports of haematology analysers include some sort of validation of left shift or immature granulocytes flags. In general the results show moderate to good agreement with left shift assessed morphologically in blood smears. However, until now very few studies have validated the flag directly as a function of clinical outcome, whereas

only such studies could answer the question posed above. For example, a recent study showed that although the automated immature cell count of an analyser correlated well with the manual differential, it was not associated with relevant clinical variables (2). Moreover, it has never convincingly been proven that left shift or band count is of any clinical value in detecting inflammation. On the contrary, **there is no place for the band count in detecting bacterial infection because the absolute neutrophil count is at least as sensitive (3) and probably more specific than the band count (4).** So, where every modern haematology analyser already offers a reliable absolute neutrophil count, why should we bother about manual band counts or the sensitivity of left shift and immature granulocytes flags? These parameters would only be necessary if it were proven that the immature granulocytes count would have true clinical relevance and at present, such evidence is non-existing.

The situation regarding the atypical lymphocyte flag is even more complicated, due to the fact that the morphology of atypical lymphocytes and their clinical relevance are ill defined. Moreover, there are very few validation studies on analyser flagging for atypical lymphocytes. Recently we demonstrated that the variant lymphocyte flag of a sophisticated haematology analyser had no additional diagnostic value over the absolute lymphocyte count (5). The finding by Van der Meer that analyser flagging of atypical lymphocytes particularly biased the observers in their morphological assessment, underscores that such flags should be used with caution.

Unfortunately, current practice in many laboratories is that any analyser flag is used as the trigger for morphological review of the blood smear, irrespective of whether the clinical utility of the flag has been demonstrated. This practice yields not only clinically misleading information, but it also implies inefficient use of valuable resources in health care. What we therefore need is that clinical laboratory scientists perform studies for collecting evidence-based data on the clinical utility of analyser flags. Then, manufacturers should provide the possibility that customers activate and deactivate analyser flags depending on evidence-based threshold settings. Finally, as clinical laboratory professionals we should stimulate our clinical colleagues in abandoning the practice of indiscriminately requesting full blood counts with differential counts. Actually, for most patients the standard report of any modern haematology analyser contains sufficient information for diagnosis and clinical monitoring. Morphological appraisal of a blood smear is only necessary in selected cases for discovering an abnormality that may not have been apparent from the ana-

lyser's results alone (6) and then the clinical question rather than an ill-defined analyser flag should trigger an expert morphologist to review the smear.

## References

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