Improved Flagging Rates on the Sysmex XE-5000 Compared With the XE-2100 Reduce the Number of Manual Film Reviews and Increase Laboratory Productivity

Carol J. Briggs, FIBMS,[1] Joachim Linssen, PhD,[2] Ian Longair,[1] and Samuel J. Machin, FRCP[1]

Abstract

Hematology analyzers generate suspect flags in the presence of abnormal cells. False-positive rates for flags are high on all analyzers. Sysmex, Kobe, Japan, has developed new software for its XE-5000 with improved algorithms for flagging blast cells, abnormal lymphocytes or lymphoblasts, and atypical lymphocytes.

This study evaluated the efficiency of these flags in 1,002 samples. The XE-5000 was compared with the XE-2100 (Sysmex) and microscopic examination of cell morphologic features.

On the XE-2100, the blast flag demonstrated 90 false-positives, 13 true-positives, and 3 false-negatives. The values on the XE-5000 were 27 false-positives, 14 true-positives, and 2 false-negatives. The abnormal lymphocyte/lymphoblast flag was assessed with the atypical lymphocyte flag. The XE-2100 showed 114 false-positives, 23 true-positives, and 20 false-negatives, and on the XE-5000, there were 45 false-positives, 22 true-positives, and 21 false-negatives.

This more specific flagging reduces the number of films that require manual review.

During recent years, there has been increasing demand for hematologic tests with clearly defined turnaround times and also within the context of cuts to laboratory budgets. Staff members represent the major expenditure, and, in many laboratories in which staff numbers have even been reduced, there is now more work for fewer laboratory scientists. Automated blood cell counters offer leukocyte, RBC, and platelet counts and a 5-part (some 6-part) leukocyte differential count. In addition, some instruments provide a nucleated RBC (NRBC) count. Hematology instrument differentials provide only limited information about cell morphologic features using various algorithms to generate abnormal cell flags and are often unable to reliably classify abnormal and immature cells. The usefulness of instrument-generated flags depends on their sensitivity and specificity.

The Sysmex XE-2100 (Sysmex, Kobe, Japan) was introduced in 1999. It is a widely used, fully automated hematology analyzer using direct current sheathed flow for the RBC count, hematocrit measurement, and impedance platelet count and fluorescence flow cytometry to provide a leukocyte differential, NRBC count, reticulocyte count, and optical fluorescent platelet count.[1] The leukocyte differential is measured using optical information (forward-scattered light, side-scattered light, and side fluorescence) to produce the differential (DIFF) scattergram. Information on immature cells is derived from the immature myeloid information (IMI) channel.

Software upgrades have been introduced, the first of which allows reliable automated counting of immature granulocytes (promyelocytes, myelocytes, and metamyelocytes) in the DIFF channel.[2] Another upgrade is the new automated method to quantitate reticulated platelets, expressed as the

immature platelet fraction. The immature platelet fraction is identified by flow cytometry with the use of a nucleic acid–specific dye in the reticulocyte/optical platelet channel. The clinical usefulness of this parameter has been established in the laboratory diagnosis of thrombocytopenia due to increased peripheral platelet destruction, particularly autoimmune thrombocytopenic purpura and thrombotic thrombocytopenic purpura,[3,4] and as a predictor of platelet recovery following hematopoietic progenitor cell transplantation.[5] The latest software to be introduced was for the measurement of the reticulocyte hemoglobin concentration. The reticulocyte hemoglobin is a measure of the forward scatter of stained reticulocytes and provides an indirect measure of the functional iron available for new RBC production during the previous 3 or 4 days. It also provides an early measure of the response to iron therapy, increasing within 2 to 4 days of the initiation of intravenous iron therapy.[6]

The most recently introduced analyzer from Sysmex is the XE-5000, launched in 2007. This instrument performs a CBC and differential in the same way as the XE-2100, but new parameters have been introduced, and it also has the ability to measure body fluids. The instrument measures the hemoglobin content of individual RBCs, calculates the percentages of hypochromic and hyperchromic RBCs, and quantifies the proportion of marginally sized erythrocytes. The availability of extended RBC parameters should allow earlier diagnosis of abnormal iron metabolism and the response to iron or folate supplementation.[7]

The sensitivity and specificity of flags for blasts, abnormal lymphocytes/lymphoblasts, and atypical lymphocytes on the XE-2100 have been reported previously,[8,9] and, generally, the results are similar to those for other instruments available.[10] These flags show good sensitivity but poorer specificity, which, in the routine laboratory, leads to the unnecessary examination of blood films.

A new set of algorithms for the detection of the presence of these cells, efficient multichannel messaging (eMM) software, was developed for the XE-5000 in October 2009. The software integrates the flagging areas from the DIFF and the IMI channels.

On the XE-2100 version for flagging in the IMI channel, it was possible to have an overlap between the blast and immature granulocyte flagging areas; however, because lymphocytes are not measured in this channel, there cannot be any overlap between blasts and atypical lymphocytes. In the DIFF channel, there is no overlap between blasts and immature granulocytes, but there is possible overlap between blasts and atypical lymphocytes. The XE-5000 eMM software was designed to improve the specificity of these flags.

This aim of this study was to evaluate the efficiency of these flags by examining the results from the XE-2100 and XE-5000 on a routine daily workload. The ideal result would

be an increase in specificity, fewer false-positives, and no loss of sensitivity or decrease in true-positives.

Materials and Methods

Sample Selection and Study Design

For the study, 1,002 adult patient residual K_2EDTA samples were randomly selected from University College London Hospital Haematology laboratory (London, England) after all routine testing had been completed. Samples were selected at different times of the day and on different days of the week during a 3-month period to try to mimic 1 day's workload. University College London Hospital receives a high proportion of abnormal samples as a tertiary reference center.

Samples were analyzed on the XE-2100 and the XE-5000 in CBC and DIFF mode. Most XE-5000 instruments automatically report the NRBC count for all samples; however, some models have NRBC counts as a selectable test to save on NRBC reagent, and the count is performed in response to the NRBC flag. The XE-5000 used in this evaluation did not routinely report NRBCs in every CBC and differential; when an NRBC flag was triggered, samples were rerun in NRBC mode to enumerate the NRBCs and correct the WBC count and differential. If the reticulocyte (RETIC) action message appeared, samples were rerun in the RETIC mode, not only to count reticulocytes, but also in case an optical fluorescent platelet count, instead of impedance, was needed. The number of reruns on each instrument was recorded.

Two blood films were made and stained on all samples using the Sysmex SP100 slide maker. Blood films were examined for leukocyte morphologic features by 2 experienced observers (C.J.B. and I.L.), a third if there was disagreement between the first 2 results. Observers were not aware at that time of the instruments' results. Lymphocytes were classified as normal or abnormal. Abnormal lymphocytes included atypical (likely associated with viral infection), plasmacytoid, or malignant (lymphocytes with coarse nuclear chromatin, nuclear clefts, prolymphocytes, plasma cells, or smear cells). Abnormal lymphocytes and atypical lymphoid cells are heterogeneous populations; even very experienced observers cannot always be sure to which category they belong. Although there are 2 flags for abnormal and atypical lymphocytes on the Sysmex instruments, these 2 flags were assessed together and counted as true-positive if either flag was triggered in the presence of atypical or abnormal lymphocytes.

Despite the fact that only the blast cell, abnormal lymphocyte/lymphoblast, and atypical lymphocyte flags have been changed for the XE-5000, for this study, any sample with an abnormal cell flag or incomplete differential results was

considered to need a manual blood film review. Quantitative flags alone or numeric results outside the reference range were not considered to need a manual review. This approach allowed the assessment of the changes in flagging on the total number of blood films made in the laboratory on a typical working day.

Principle of Leukocyte Differential on the XE-2100 and XE-5000

The optical system on both XE instruments uses a stable red diode laser producing a light beam of 633 nm wavelength and a polymethine-based fluorescent dye. When the laser beam collides with a stained cell, 3 signals are produced: forward-scattered light, providing information on cell size; side-scattered light, providing information on internal cell structure; and side fluorescence, providing information on DNA and RNA content. The light scatter signals are detected by photo diodes and the fluorescence signal by a photomultiplier via a dichroic mirror. In the DIFF scattergram ❚Image 1❚, side fluorescence is on the y-axis and side-scattered light on the x-axis. In a healthy person, cluster analysis reveals cell ghosts, lymphocytes, monocytes, eosinophils, combined neutrophil and basophil populations, and, if present, immature granulocytes, which are the sum of metamyelocytes, myelocytes, and promyelocytes (Image 1).

The basophil count is derived in the WBC/BASO channel in which basophils are resistant to the reagent system and retain their size and shape, forming a cluster of larger cells distinct from other nonbasophil nucleated cells whose membranes are perforated and cytoplasm is lost.

In the IMI channel, a combination of radio frequency and impedance, direct current resistance methods are used in conjunction with special reagents. Immature WBCs contain less lipid than do mature cells. In the presence of special lysing reagents, mature cells are disrupted, their granules are eluted, and only their nuclei remain. Immature cells of the myeloid series behave in a different way: before the intracellular components are eluted, the lysing reagent enters the cells and binds to the membrane and granules, thus fixing the cells and differentiating them from mature cells. The effect of the lysing reagent differs with each type of immature cell, allowing quantitative differentiation ❚Image 2❚.

Abnormal Cell Flags

Abnormal cells have characteristics different from those of normal cells, such as cell size, nuclear size, and granule content. In the presence of abnormal cells, most instruments will generate an "abnormal" cell or "suspect" flag. The instrument detects the "cloud" (as seen in Image 1) for a particular cell population as having an abnormal size or
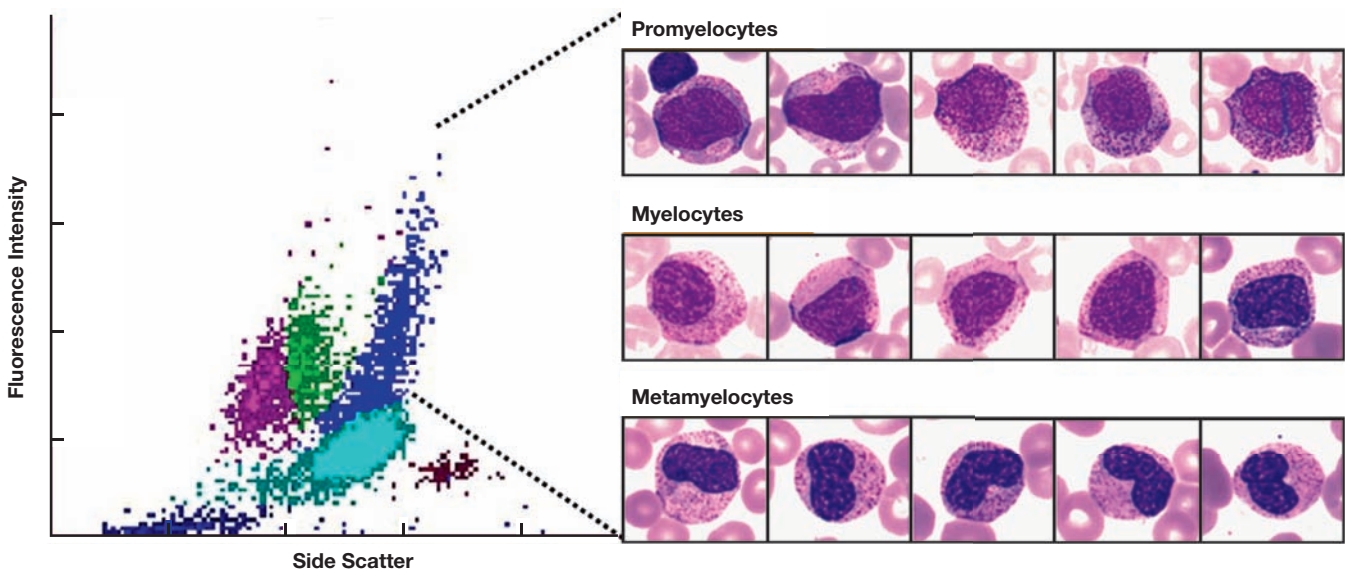

❚Image 1❚ Sysmex differential (DIFF) channel scatterplot. Different leukocyte types have different locations in the scattergram. Fluorescence is depicted on the y-axis and side-scattered light on the x-axis. The blue dots close to the x-axis are cell ghosts; the turquoise clusters, neutrophils and basophils; pink dots, lymphocytes; green dots, monocytes; and orange dots, eosinophils. Immature granulocytes show higher fluorescence than neutrophils and are represented by blue dots appearing above the neutrophils with the earliest cells, promyelocytes, demonstrating the highest fluorescence; more mature cells, metamyelocytes, are in the area closest to the neutrophil cluster.
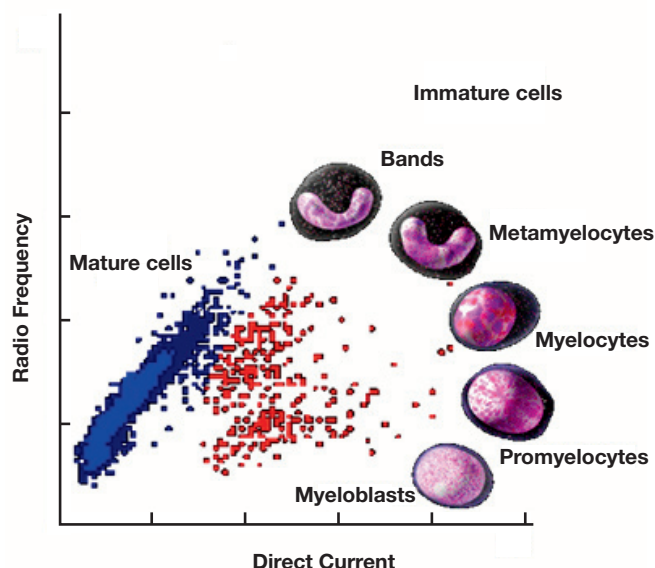
Image 2 Sysmex immature myeloid information channel with direct current resistance on the x-axis and radio frequency on the y-axis. Mature WBCs are completely lysed and shrunken by the reagent and are located in the blue cluster. The effect of the lysing reagent is different on immature myeloid cells; they are not completely lysed, allowing for their quantitative differentiation from mature cells. The red dots represent immature myeloid cells. In a normal scattergram there are very few or no red events.

shape by cluster analysis. The instrument will also detect events outside the normal cell population areas. The flags are generated by combining pattern abnormalities from the DIFF and IMI channels.

The areas of abnormal WBCs in the DIFF and IMI scatterplots are shown in **Image 3**.

The New Blast Cell Flag Algorithm

The blast cell flag is given when number of cells in the IMI channel blast area exceeds a preset trigger limit *and* when more cells in the IMI channel immature granulocyte area are detected than in their signature position in the DIFF channel. This information is then combined with the number of cells in the DIFF channel blast area **Image 4A**, which must exceed the trigger limit *and* be more than in the DIFF channel atypical lymphocyte area.

The New Abnormal Lymphocyte/Lymphoblast Flag Algorithm

For this flag to be triggered, the blast flag is not present (no cells in IMI blast area) *and* the number of cells on the lymphocytes and monocytes border **Image 4B** is more than normal (Image 1) and exceeds the trigger limit. The trigger limit varies depending on the total WBCs *or if* the number of cells in the DIFF channel blast areas (Images 4A and 4B) exceeds the trigger limit *and* is more than in the DIFF channel atypical lymphocyte area combined with absence of cells in the IMI channel blast area.
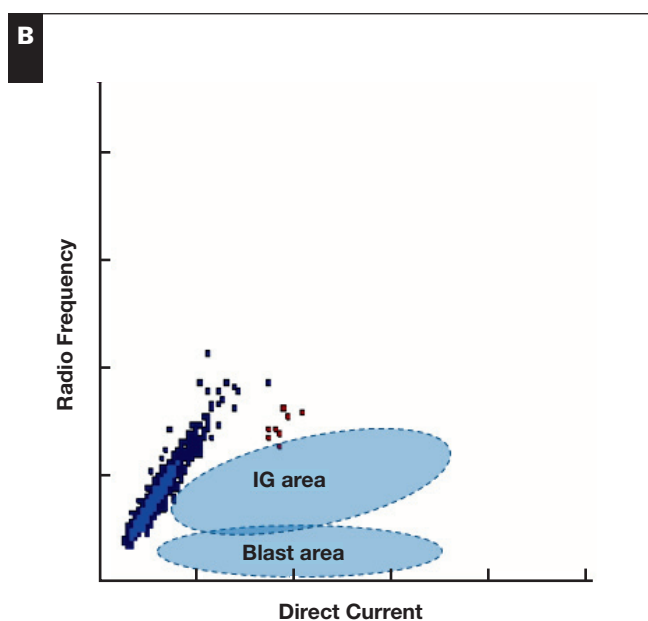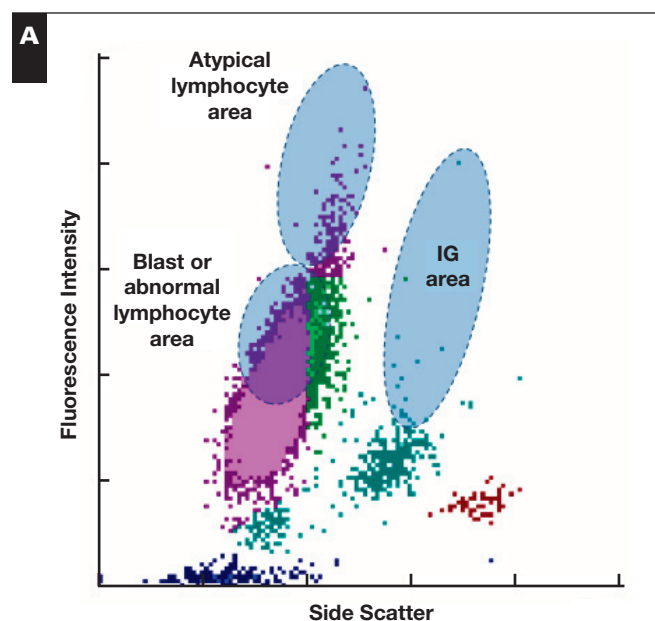

Image 3 **A**, Schematic representation of the Sysmex differential channel scatterplot showing abnormal cell locations. **B**, Schematic representation of the Sysmex immature myeloid information channel scatterplot showing immature myeloid cell locations. IG, immature granulocyte.

The New Atypical Lymphocyte Flag Algorithm

This flag means that the high-fluorescent lymphocyte count is more than 1% of the total lymphocyte count ❚Image 4C❚ *and* the number of cells in the DIFF channel atypical lymphocyte area exceeds the trigger limit *and* the number of cells in the DIFF channel atypical lymphocyte area exceeds those in the DIFF channel blast area (Image 4A). Under these conditions, high-fluorescent lymphocytes have been proven to be activated B lymphocytes or plasma cells,[11] resulting in high specificity and sensitivity for screening for plasma cells with the atypical lymphocyte flag.[12]

Statistical Methods

The rates of efficiency for the blast cell and abnormal/atypical lymphocyte flags were compared statistically by using the McNemar test on S-PLUS, version 6.1 (Insightful, Palo Alto, CA).

Results

❚Table 1❚ shows the total number of abnormal cell flags seen on each instrument. The XE-5000 had 185 fewer abnormal cell flags than the XE-2100, which would lead to
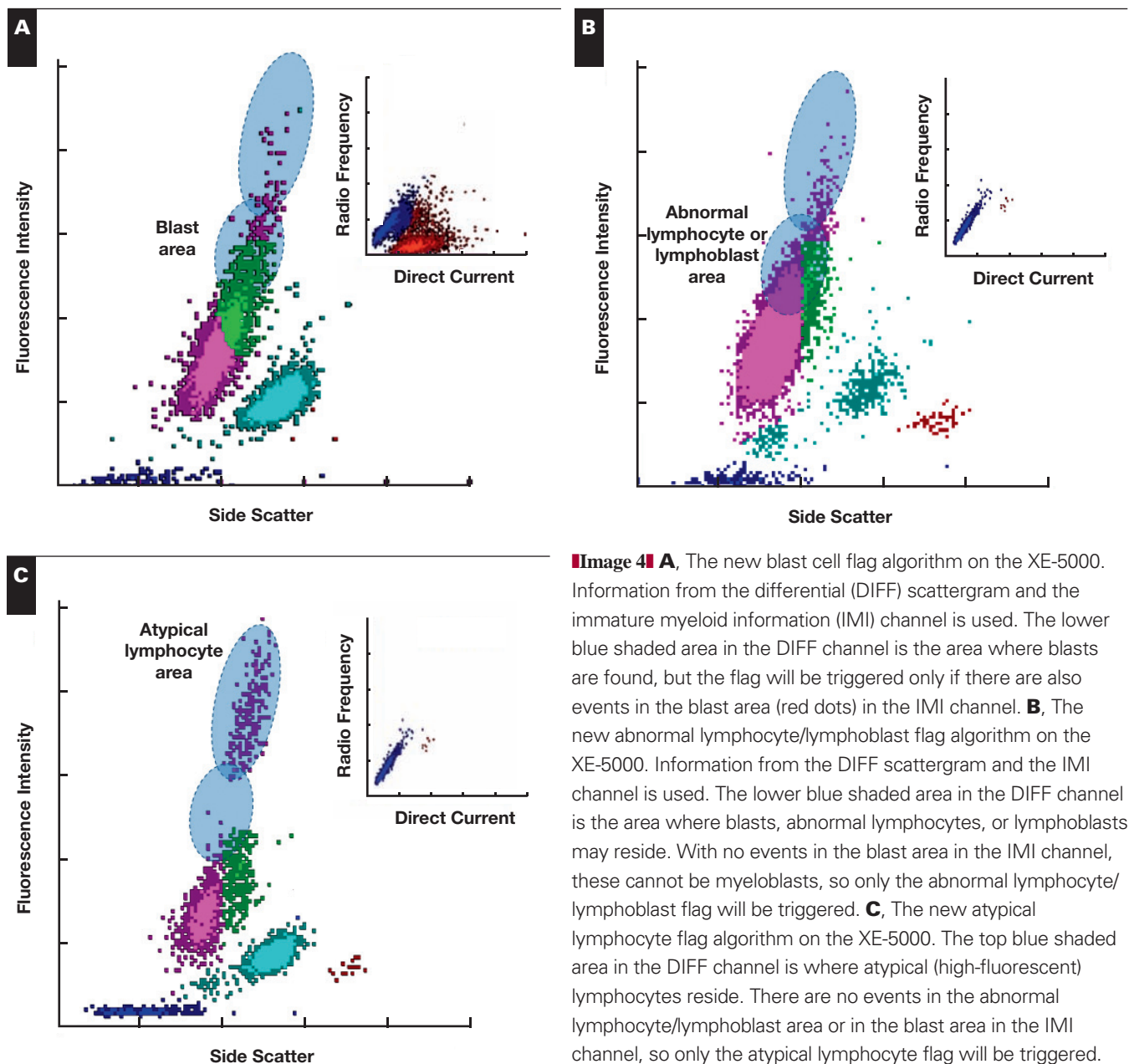

❚Image 4❚ **A**, The new blast cell flag algorithm on the XE-5000. Information from the differential (DIFF) scattergram and the immature myeloid information (IMI) channel is used. The lower blue shaded area in the DIFF channel is the area where blasts are found, but the flag will be triggered only if there are also events in the blast area (red dots) in the IMI channel. **B**, The new abnormal lymphocyte/lymphoblast flag algorithm on the XE-5000. Information from the DIFF scattergram and the IMI channel is used. The lower blue shaded area in the DIFF channel is the area where blasts, abnormal lymphocytes, or lymphoblasts may reside. With no events in the blast area in the IMI channel, these cannot be myeloblasts, so only the abnormal lymphocyte/lymphoblast flag will be triggered. **C**, The new atypical lymphocyte flag algorithm on the XE-5000. The top blue shaded area in the DIFF channel is where atypical (high-fluorescent) lymphocytes reside. There are no events in the abnormal lymphocyte/lymphoblast area or in the blast area in the IMI channel, so only the atypical lymphocyte flag will be triggered.

▌**Table 1**▌
Total Number of Flags Generated by Both Instruments, Number of Blood Films That Would Have Been Made in the Laboratory, Number of Samples That Needed to Be Rerun, and Number of Differential Vote-Outs for Each Instrument

	XE-2100	XE-5000
Total No. of samples analyzed	1,002	1,002
Total No. of flags	525	340
No. (%) of blood films	243 (24.3)	138 (13.8)
No. of rerun samples*	75	86
No. (%) of reruns that gave additional clinical information†	49 (65)	55 (64)
No. of vote-outs‡		
Neutrophils	27	24
Lymphocytes	25	23
Monocytes	20	17
Eosinophils	9	9
Basophils	10	11
Immature granulocytes	27	25

* Rerun because of an nucleated RBC (NRBC) flag or the reticulocyte (RETIC) action message.
† Reruns that gave additional clinical in formation are those with NRBCs present or an optical platelet count reported as measured in the RETIC channel.
‡ Instrument did not report the leukocyte differential cell count.

a reduction in blood film reviews from 24.3% to 13.8% of samples analyzed in the laboratory.

The number of differential vote-outs, where the instrument does not report a differential count in the presence of abnormal cells, was similar for both instruments (9.1% on the XE-5000 and 8.4% on the XE-2100); however, on both instruments, all voted-out differentials can be seen in the WBC research screen.

The XE-5000 required the rerunning of slightly more samples because of more NRBC flags on first analysis on the XE-5000 than on the XE-2100. The number of justified reruns, ie, NRBCs were present in the sample or an optical platelet count from the RETIC channel was reported, was almost the same for both instruments, 65% (49/75) for the XE-2100 and 64% (55/86) for the XE-5000.

▌**Table 2**▌ shows the flagging performance for blasts, abnormal lymphocytes/lymphoblasts with atypical lymphocytes, left shift, NRBCs, and platelet clumps. The eMM software, version 00-06, only has new algorithms for the blast cell, abnormal lymphocyte/lymphoblast, and atypical lymphocyte flags, but the other flags were assessed to determine how many manual blood film reviews would be performed on a daily basis in the routine laboratory using either instrument.

It is interesting that the XE-5000 tended to give more false-positives for NRBCs, 37 compared with 27 on the XE-2100. This finding means that extra samples are rerun in the NRBC mode on the XE-5000, but does not necessarily mean that these samples would need manual review. There were fewer false-positive platelet clump flags on the XE-5000, but this flag did not perform efficiently on either analyzer.

▌**Table 2**▌
Clinical Usefulness and Efficiency of Abnormal Cells Flags on the XE-2100 and XE-5000 for 1,002 Samples

Flag	XE-2100	XE-5000
Blasts		
TP	13	14
TN	896	959
FP	90	27
FN	3	2
Sensitivity (%)	81.2	87.5
Specificity (%)	90.8	97.2
Efficiency (%)	90.7	97.1†
Abnormal lymphocytes or lymphoblasts/atypical lymphocytes		
TP	23	22
TN	845	914
FP	114	45
FN	20	21
Sensitivity (%)	53.5	51.2
Specificity (%)	88.1	95.3
Efficiency (%)	86.6	93.4†
Left shift		
TP	32	28
TN	910	929
FP	24	15
FN	36	30
Sensitivity (%)	47.1	35.7
Specificity (%)	97.4	98.4
Efficiency (%)	94.0	95.5
Nucleated RBCs		
TP	20	22
TN	945	936
FP	27	37
FN	10	7
Sensitivity (%)	66.7	75.8
Specificity (%)	97.2	96.2
Efficiency (%)	96.3	95.6
Platelet clumps		
TP	1	1
TN	960	976
FP	31	16
FN	10	9
Sensitivity (%)	9.1	10.0
Specificity (%)	96.9	98.4
Efficiency (%)	95.9	97.5

FN, false-negative; FP, false-positive; TN, true-negative; TP, true-positive.
* Values are given as number of samples unless otherwise indicated.
† $P < .001$.

Although the immature granulocyte count is derived from the DIFF channel, if there is an abnormal cell pattern, a suspect immature granulocyte flag is generated but the count is still reported. Each laboratory should have a defined protocol on how to deal with samples generating this flag, but for this evaluation, a stained peripheral blood film was examined. On the XE-2100, this flag was seen 66 times (6.6% of samples) and on the XE-5000, 50 times (5.0% of samples). All samples that were positive for immature granulocytes on the blood film were also positive by both instruments, and all samples with an automated immature granulocyte count of 3% or more were positive on the blood film, unless the WBC count was less than 500/µL (0.5×10^9/L).

The red cell fragment flag was not sensitive on either instrument: 33 blood films demonstrated fragments on the

© American Society for Clinical Pathology

blood film, but the XE-2100 flagged only 7 of these samples, and the XE-5000 flagged 3. Neither instrument showed any false-positives. There is a fragmented red cell count available on both instruments on the RBC research screen,[13] but this was not assessed in this evaluation.

One sample with red cell autoagglutination was included in the study, and both instruments correctly flagged the abnormality. There were no false-positives.

The efficiency of the flagging for blasts and abnormal or atypical lymphocytes was significantly better ($P < .001$) on the XE-5000 compared with the XE-2100. One sample was false-negative for the blast flag on both instruments. This sample was from a patient with acute myeloid leukemia undergoing chemotherapy, and the WBC count was only 690/µL (0.69×10^9/L). There were 2 more false-negatives on the XE-2100 and 1 on the XE-5000. Overall, the number of false-positives was greatly reduced on the XE-5000, 27 compared with 90 on the XE-2100, without any loss of sensitivity. This result was also true for the abnormal/atypical lymphocyte flag: The number of false-positives was reduced to 45 on the XE-5000 from 114 on the XE-2100, and both instruments showed similar numbers of false-negatives and true-positives. Of the false-positives, 17 were the same samples on both instruments and were from patients with various diagnoses and WBC and lymphocyte counts.

Discussion

Examination of blood films is not only labor-intensive, but it is also requires highly trained staff. The impact of a wrong diagnosis necessitates that experienced staff be present in the laboratory 24 hours a day. However, manual cell classification is subjective, with significant interobserver and intraobserver variation,[14] and any count is also subject to significant statistical variance.[15]

With continuing pressure on laboratory resources and the need for faster turnaround times, it is essential to reduce the number of manual blood film reviews and manual differential counts. A film is reviewed to provide information additional to or missing from the analyzer report or to confirm results provided by the analyzer. The challenge is to reduce the number of blood films examined without missing important diagnostic information. In 20% to 25% of CBCs with differentials, leukocyte-related abnormal cell flags are generated, which means a manual microscopic review on a stained blood smear may be required.[16,17] However, depending on the clinical population and local guidelines for making blood films, film review rates range from 10% to 50% in different laboratories.[17,18] More than 80% of manual film reviews are triggered by hematology analyzer flags[16]; however, more than 62% of reviews undertaken in the routine laboratory are due to false-positive flags.[17]

The objective for the laboratory is to reduce the number of samples needing further action as far as possible without endangering patients by reporting false or misleading results, especially false-negative results. Any analyzer that decreases the number of false-positive flags without losing sensitivity will increase laboratory efficiency.

The flagging efficiency of the XE-2100 has been published,[8,9] and, generally, the results are similar to those for other instruments available. The XE-2100 blast flag has been reported as the most sensitive when compared with the Abbott CELL-DYN Sapphire (Abbott Diagnostics, Santa Clara, CA), the Siemens Advia 120 (Siemens Diagnostics, Tarrytown, NY), and the Beckman Coulter LH 750 (Beckman Coulter, Miami, FL).[10]

The efficiency evaluation of the XE-2100 and XE-5000 was obtained by assessment of the number of blood films made in the laboratory owing to the presence of abnormal cell flags. This approach allows a simple means of determining how efficient the instrument is in detecting true abnormalities and how inefficient it is in generating false flags.

Our findings indicate that the use of the XE-5000 in the routine laboratory would reduce the number of manual film reviews triggered by abnormal cell flags from about 24% on the XE-2100 to about 14% on the XE-5000. With a daily workload of about 1,000 samples, this difference represents a reduction of 105 blood films. Nearly all of this reduction is from fewer false-positive blast cell and abnormal/atypical lymphocyte flags. High sensitivity of blast cell detection in routine hematology analyzers is important for the diagnosis and follow-up of hematologic malignancies. There were 3 false-negatives on the XE-5000 and 2 on the XE-2100. These samples were from patients with leukopenia, and it has been reported that flagging sensitivities are reduced with low WBC counts.[8]

Many instruments available only have 1 flag for the presence of abnormal or atypical lymphocytes, but the Sysmex instruments have 2, the abnormal lymphocyte/lymphoblast and atypical lymphocyte flags. In this study, as in a previous evaluation,[9] these flags were assessed together. Morphologic definitions of atypical or abnormal lymphocytes are highly variable and would make the assessment of the individual flags problematic. If abnormal or atypical lymphocytes were seen in the blood film, the presence of either one of the flags constituted a true-positive. There was a reduction in the number of false-positive flags on the XE-5000, 4.5% compared with 11.4% on the XE-2100. There was no loss of sensitivity, with both instruments showing similar numbers of false-negatives, which were mostly the same samples on both instruments from patients with various diagnoses and lymphocyte counts.

Despite the fact that the eMM software only has new algorithms for blast cell, abnormal lymphocyte/lymphoblast,

and atypical lymphocyte flags, some differences were noted for NRBC flag, with the XE-5000 giving slightly more false-positives, which would mean more reruns for the NRBC count but not necessarily more manual film reviews.

The platelet clump flag did not perform well on either analyzer.

Laboratory productivity is inversely related to the number of manual film reviews,[16] the higher the manual review rates, the lower the productivity. Using the XE-5000 with eMM software in the routine hematology laboratory reduces the number of manual blood film reviews needed and so increases workflow efficiency and improves turnaround times by speeding up sample processing. In the future, it is hoped that more abnormal cells, especially blast cells, will be accurately quantitated by hematology analyzers rather than their possible presence being indicated by a flag.

References

1. Briggs C, Harrison P, Grant D, et al. New quantitative parameters on a recently introduced automated blood cell counter: the XE-2100. *Clin Lab Haematol.* 2000;22:345-350.
2. Briggs C, Kunka S, Fujimoto H, et al. Evaluation of immature granulocyte counts by the XE-IG master: upgraded software for the XE-2100 automated hematology analyzer. *Lab Hematol.* 2003;9:117-124.
3. Briggs C, Hart D, Kunka S, et al. Assessment of an immature platelet fraction (IPF) in peripheral thrombocytopenia. *Br J Haematol.* 2004;126:93-99.
4. Pons I, Monteagudo M, Lucchetti G, et al. Correlation between immature platelet fraction and reticulated platelets: usefulness in the etiology diagnosis of thrombocytopenia. *Eur J Haematol.* 2010;85:158-163.
5. Zucker ML, Murphy CA, Rachel JM, et al. Immature platelet fraction as a predictor of platelet recovery following hematopoietic progenitor cell transplantation. *Lab Hematol.* 2006;12:125-130.
6. Brugnara C. Use of reticulocyte cellular indices in the diagnosis and treatment of haematological disorders. *Int J Clin Lab Res.* 1998;28:1-11.
7. Urrechaga E, Borque L, Escanero JF. Potential utility of the new Sysmex XE 5000 red blood cell extended parameters in the study of disorders of iron metabolism. *Clin Chem Lab Med.* 2009;47:411-416.
8. Ruzicka K, Veitl M, Thalhammer-Scherrer R, et al. The new hematology analyzer Sysmex XE-2100: performance evaluation of a novel white blood cell differential technology. *Arch Pathol Lab Med.* 2001;125:391-396.
9. Stamminger G, Auch D, Diem H, et al. Performance of the XE-2100 leucocyte differential. *Clin Lab Haematol.* 2002;24:271-280.
10. Kang S, Kim HK, Ham CK, et al. Comparison of four hematology analyzers, CELL-DYN Sapphire, ADVIA 120, Coulter LH 750 and Sysmex XE-2100, in terms of clinical usefulness. *Int J Lab Hematol.* 2008;30:480-486.
11. Linssen J, Jennissen V, Hildmann J, et al. Identification and quantification of high fluorescence-stained lymphocytes as antibody synthesizing/secreting cells using the automated routine hematology analyzer XE-2100. *Cytometry B Clin Cytom.* 2007;72B:157-166.
12. Linssen J, Jennissen V. Identification of high fluorescence-stained lymphocytes (HFL) count on the XE-5000 with efficient multichannel messaging (eMM) as antibody synthesizing, c.q. plasma cells. *Sysmex J Int.* 2009;19:1-8.
13. Jiang M, Saigo K, Kumagai S, et al. Quantification of red blood cell fragmentation by automated haematology analyser XE-2100. *Clin Lab Haematol.* 2001;23:167-172.
14. Koepke JA, Dotson MA, Shifmann MA. A critical evaluation of the manual/visual differential leukocyte counting method. *Blood Cells.* 1985;11:173-186.
15. Rumke CL. Statistical reflections on finding atypical cells. *Blood Cells.* 1985;11:141-144.
16. Novis DA, Walsh M, Wilkinson D, et al. Laboratory productivity and the rate of manual peripheral blood smear review: a College of American Pathologists Q-Probes study of 95,141 complete blood count determinations performed in 263 institutions. *Arch Pathol Lab Med.* 2006;130:596-601.
17. Barnes PW, McFadden SL, Machin SJ, et al. The International Consensus Group for Hematology Review: suggested criteria for action following automated CBC and WBC differential analysis. *Lab Hematol.* 2005;11:83-90.
18. Briggs C, Longair I, Slavik M, et al. Can automated blood film analysis replace the manual differential? an evaluation of the CellaVision DM96 automated image analysis system. *Int J Lab Hematol.* 2009;31:48-60.

ThinPrep® Processors
Meeting the Demands of Your Lab

THINPREP® GENESIS™ PROCESSOR
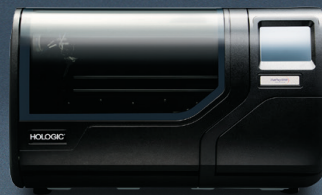
THINPREP® 5000 PROCESSOR

THINPREP® 5000 AUTOLOADER

ThinPrep® processors are versatile and scalable solutions for laboratories of all volumes.

The portfolio offers reliable, best-in-class systems that help cytology labs automate their processes — decreasing the need for hands-on labor and increasing laboratory efficiencies.

Explore the portfolio

ThinPrep®