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Evaluation of the Sysmex Xe-2100® Hematology Analyzer in Hospital Use

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The Sysmex XE-2100® (Sysmex Corp. Kobe, Japan) is a latest-generation hematology analyzer. Its optical and electrical measuring technology is improved by the addition of flux cytometry, fluorescence, and differential lysis. Its analytical performance in terms of precision, reproducibility, linearity, carryover, and time stability was found to be entirely satisfactory. In addition, the results of 500 complete blood counts and differentials correlated perfectly with those obtained by the Coulter STKS® (Beckman Coulter, Villapointe, France). The comparison of 500 leukocyte differential count results analyzed in parallel with optical microscopy and the XE-2100® were surprising, and favorable to the XE-2100®. This analyzer provides the user with an undeniable feeling of security concerning its reliability in detecting and identifying anomalies in the automated leukocyte differential count. With a sensitivity of 96%, a negative predictive value (NPV) of 98%, and a false-negative (FN) rate of 4%, the XE-2100® has perhaps reached the technological limits for a machine performing morphological recognition of normal and pathological blood cells. J. Clin. Lab. Anal. 17:113–123, 2003. © 2003 Wiley-Liss, Inc.

Key words: hematology analyzer; Sysmex XE-2100®; Coulter STKS®; performance evaluation

INTRODUCTION

The Sysmex XE-2100® multiparameter selective analyzer is innovative in its combined use of flow cytometry and fluorescence for the analytical differentiation of blood cells. The leukocyte differential count is established by simultaneously measuring the volume, structure, and fluorescence based on the quantity of ribosomal RNA and DNA in the cells, which in turn allows the quantification of immature myeloid cells. In addition, using this new concept based on fluorescence, the cell blood count (CBC) and white blood cell (WBC) differential count are enriched by the selective and specific analysis of erythroblasts, enabling precise leukocyte and lymphocyte counts. Moreover, platelets can be enumerated more precisely with this optical method, especially when microcytes or large platelets are present. Finally, the different levels of fluorescence intensity in the reticulocytes permit them to be distinguished at three stages of maturity.

The objective of this study was to evaluate the analytic performance of the XE-2100® by tests involving precision, linearity, carryover, time stability, and reproducibility. In addition, the results were compared by correlation studies with results obtained with the XE-2100® and the Coulter STKS®. Finally, by in-depth analysis of the qualitative flags provided by the two analyzers for the same leukocyte differential count, compared to the measurement of this differential using the benchmark method (optical microscopy), we sought to determine the sensitivity and specificity of the XE-2100®.

MATERIALS AND METHODS

Sysmex XE-2100® Measurement Principles

In the Sysmex XE-2100® method, all of the cells in a blood specimen are detected by flow cytometry before they are analyzed. A system of hydrodynamic focalization, which optimizes the precision of the count and avoids edge effects and coincidence errors, transfers the cells one by one into the measuring chamber. The

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analyzer uses two fundamental analytical methods: electrical and optical.

The electrical method combines two sources of electric current: low-frequency direct current, which measures impedance and provides information on cellular volume, and high-frequency alternating current (radiofrequency), which supplies information on cell structure and density.

In the optical method, the origin of the light source is a semiconductor laser. The cells that are stimulated are differentiated using three methods: 1) forward-scattered light, 2) side-scattered light (90°), and 3) fluorescent emission from cells previously marked with a fluorochrome (polymethine), which forms unstable complexes with the ribosomal RNA and the DNA.

Data on the analyzer operative characteristics for WBCs, WBC differential, red blood cells (RBCs), nucleated RBCs (NRBCs), reticulocytes, and platelet counts can be found in Refs. 1 and 2.

Table 1 summarizes in chart format the different techniques used for the parameters studied.

Specimens

Venous blood samples in collection tubes containing a tripotassium EDTA-type anticoagulant (Vacuette®, Greiner Labortechnik) were used throughout the evaluation for a period of 3 weeks. All of the specimens (from Nice University Hospital, Nice, France) were analyzed within 6 hr after blood collection, except for those used in the time stability tests.

More than 4,000 samples were studied in parallel on the XE-2100® and the STKS® by determining a complete blood count. In addition, 500 of the samples that generated no qualitative flag for the differential count were used for correlation studies. Analysis of the leukocyte differential count, combined with a systematic blood smear stained using the May Grünwald Giemsa procedure, was carried out for 500 randomly chosen specimens. These samples were taken from patients in the intensive care and clinical hematology units of Nice University Hospital.

Sysmex XE-2100® Analytical Performance

Precision studies

The objective of these tests was to determine whether the analyzer was capable of reproducing the same results for a given specimen when the analysis was done under standard conditions, that is, by the same technician, at the same time of the day, and with the same reagents for the count parameters. For specimen selection, specific criteria were chosen as follows:

- Leukocytes (four categories): $<1\times10^9$/L, 1×10^9/L to 4×10^9/L, 4×10^9/L to 10×10^9/L, and $>20\times10^9$/L.
- RBCs (three categories): hematocrit (Ht) <0.20 L/L, 0.37–0.42 L/L, and >0.50 L/L.
- Platelets (five categories): 10×10^9/L to 20×10^9/L, 20×10^9/L to 50×10^9/L, 50×10^9/L to 100×10^9/L, 150×10^9/L to 400×10^9/L, and $<400\times10^9$/L.

One specimen in each of the ranges (total of 12 samples) was tested a maximum of 20 consecutive times in manual mode on the XE-2100®. The mean, standard deviation (SD), and variation coefficient were calculated for each precision test.

Leukocyte and platelet linearity tests

These tests enabled validity thresholds to be established for the linear relationship that exists between theoretical and observed values.

Two specimens were selected: one with leukocytes $>50\times10^9$/L, and one with platelets $>800\times10^9$/L. Two dilution ranges (1/2, 1/4, 1/8, 1/20, 1/50, 1/100) were carried out in a diluent (Cell Pack®, Sysmex) for the same sample. Each range (containing seven points, including the pure specimen) was tested three consecutive times in manual mode on the XE-2100®. The relationship between the values of the range measured and the values of the theoretical range was studied by determining the correlation coefficient and the regression line equation using the least-squares method. The

TABLE 1. Techniques used according to cell type Sysmex XE-2100®

Cell type	Forward scattered light	Side scattered light	Fluorescence	Radio frequency	Impedance
WBCs/Basophils	Yes	Yes	No	No	No
Differentials	Yes	Yes	Yes	No	No
Immatures	No	No	No	Yes	Yes
NRBCS	Yes	No	Yes	No	No
Reticulocytes	Yes	No	Yes	No	No
Red blood cells	No	No	No	No	Yes
Platelets	No	No	No	No	Yes
Optical PLTs	Yes	No	Yes	No	No

significance of the difference between these two ranges was analyzed by the paired Student's *t*-test (3).

Carryover studies

The objective of these tests was to analyze the influence the high value of a count parameter might have on subsequent counts.

The possibility of intraspecimen carryover was studied for the leukocytes and platelets.

To carry out this test, four samples were chosen: one with WBCs $>20\times10^9$/L, one with WBCs $<1\times10^9$/L, one with platelets $>1{,}000\times10^9$/L, and one with platelets $<10\times10^9$/L. Each specimen with a high value was tested three consecutive times in manual mode, followed immediately by three tests of its equivalent with a low value. The same procedure was carried out in this way for a maximum of five times in succession. For each series, the carryover percentage was calculated using the following equation:

$$\frac{|L1-L3|}{H3-L3}\times100$$

L1 = value of the low specimen in the first test for the parameter studied, L3 = value of the low specimen in the third test for the parameter studied, and H3 = value of the high specimen in the third test for the parameter studied.

Time stability tests

These tests studied the adverse effects on the CBC and differential parameters resulting from the time stability of the specimens.

Ten samples were stored at room temperature, and 10 were kept at 4°C.

The CBC + differential count for all of the subjects was reanalyzed 12, 24, 48, and 72 hr after the first test on the analyzer, in automatic mode.

Reproducibility tests

These tests determined the ability of the analyzer to reproduce the same results for the parameters of a count for a specimen when the specimen was analyzed several times during the course of a day. The specimens were selected according to the following criteria:

- Leukocytes (three categories): 1×10^9/L to 4×10^9/L, 4×10^9/L to 10×10^9/L, and $>20\times10^9$/L.
- Erythrocytes (three categories): Ht <0.20 L/L, 0.37–0.42 L/L, and >0.50 L/L.
- Platelets (five categories): 10×10^9/L to 20×10^9/L, 20×10^9/L to 50×10^9/L, 50×10^9/L to 100×10^9/L, 150×10^9/L to 400×10^9/L, and $>400\times10^9$/L.

This procedure was carried out a maximum of 20 times in the same day in automatic mode on the XE-2100®. For each reproducibility test, the mean, SD, and variation coefficient were calculated.

Correlation Studies

Our objective in these studies was to compare, parameter by parameter, the results from the Sysmex XE-2100® and the Coulter STKS® CBC + differentials.

A total of 500 CBC + differential counts were chosen that showed no sign of qualitative flags on the two hematology analyzers. The comparison was based on the number of RBCs, leukocytes, and platelets. Within the RBC population, the hemoglobin (Hb) and Ht rates, the mean cell volume (MCV), the mean cell Hb concentration (MCHC) and content (MCH), and the red cell distribution indices (RDW-CV) were compared. Finally, the absolute values of the neutrophils, eosinophils, and basophils, as well as the lymphocytes and monocytes, were compared. For each parameter, the correlation coefficient and the regression line equation were determined using the least-squares method. The difference between these two analyzers was examined by use of a paired Student's *t*-test.

Analysis of the Leukocyte Differential Count

To conduct a relevant study of the leukocytic differential results provided by the two analyzers, an optical microscopy was performed. A count of up to 400 WBCs was performed, and 500 smears stained using the May Grünwald Giemsa technique were analyzed. The 500 samples were randomly chosen from patients in the intensive care and hematology departments of Nice University Hospital. These patients had normal or reactive hematologic profiles, or known various hematological disorders.

For the Sysmex XE-2100®, we focused on the following qualitative flags:

– "Immature Gran": immature granulocytes (IGs).
– "Abn Lymph/L-Blast": abnormal lymphocytes/lymphoblasts.
– "Blasts": blasts.
– "Atypical Lympho": atypical lymphocytes.
– "PLT Clumps," "PLT Clumps (S)": platelet clumps.
– "NRBC": nucleated red blood cells.

For the Coulter STKS®, the following qualitative flags were examined:

– "R*" on the leukocytes, WBC distribution anomaly.
– "Imm Gran/Band 2": IGss.
– "Blasts": blasts.

– ''Variant lymphs'': atypical lymphocytes.
– ''Platelet clumps'': platelet clumps.
– ''NRBCs'': nucleated red blood cells.

Each differential not given by the two analyzers was considered to be pathological. The positivity threshold for the leukocytic elements not usually present in the differential count was set at $\geq 1\%$ with regard to the benchmark method.

The use of optical microscopy enabled us to determine the percentages of the normal and pathological differentials (i.e., the true negatives (TNs) and true positives (TPs)). For each analyzer, the rejection rates corresponding to the ratio of the number of differentials with flags and the number of specimens examined expressed as a percentage were determined. The significance of the difference in rejection rates was examined using the χ^2 test. Then the number of false positives (FPs—the number of differentials with flags that were normal on optical microscopy) and the number of false negatives (FNs–the number of differentials that had no flags but were pathological on optical microscopy) were calculated. The sensitivity, or the proportion of positive results found by the analyzers among the truly pathological differentials, was determined by the ratio TP/TP + FN. The specificity, or the proportion of negative results found by the analyzers among the truly normal differentials, was calculated using the ratio TN/TN + FP. Finally, the positive (PPV) and negative (NPV) predictive values were determined by the ratios TP/TP + FP and TN/TN + FN, respectively. These values correspond to the capacity of an analyzer to provide a truly positive result compared to all the pathological differentials, or a truly negative result compared to all the normal differentials. All of the results are expressed as a percentage. In addition, the sensitivity, specificity, and PPVs and NPVs were also studied for each of these flags. When two or more flags were found to coexist, the nature of the flag retained as a priority was chosen using the following rule: blasts > [atypical or abnormal lymphocytes or lymphoblasts] > IGss > others [NRBC, platelet clumps, WBC distribution anomaly]. The set [atypical or abnormal lymphocytes or lymphoblasts] is represented by the global ''atypical lymphocytes'' flag for both systems.

RESULTS

Analytical Performances

Precision studies

Considering that the maximum acceptable variation coefficient was 5%, the Sysmex XE-2100® precision test showed excellent results for the parameters analyzed, except for the low values for WBCs ($< 1 \times 10^9$/L) and platelets (10×10^9/L to 20×10^9/L) (Tables 2–4).

The precision threshold of the analyzer corresponded to these lower threshold values.

Leukocyte and platelet linearity tests

For each sample (WBC average = 358.69×10^9/L, platelet average = $1{,}468.00 \times 10^9$/L), two ranges of identical dilutions were prepared. The linearity tests were performed on these four ranges. The results were excellent and showed positive correlations. The correlation coefficients found between the theoretical and observed values for the leukocytes and platelets were > 0.99 (Figs. 1 and 2).

Carryover studies

The carryover study procedure was carried out four times in succession. A specimen with a high WBC value (average = 42.68×10^9/L) and another with a low WBC value (average = 0.27×10^9/L) were employed. The average of the carryover percentages was 0.05%.

For the platelets, two samples (one with a high value (average = $1{,}702.33 \times 10^9$/L), and one with a low value (average = 4.33×10^9/L)) were chosen for this test.

TABLE 2. Precision tests on the leukocytes (10^9/L) Sysmex XE-2100®

WBC range	Mean	SD	Variation coefficient
WBC < 1	0.51	0.04	6.91
1 < WBC < 4	2.58	0.07	2.81
4 < WBC < 10	8.29	0.09	1.10
WBC > 20	34.60	0.40	1.16

TABLE 3. Precision tests on the hematocrit (L/L) Sysmex XE-2100®

Hematocrit range	Mean	SD	Variation coefficient
Ht < 0.20	0.176	0.002	1.004
0.37 < Ht < 0.42	0.409	0.002	0.515
Ht > 0.50	0.531	0.003	0.507

TABLE 4. Precision tests on the platelets (10^9/L) Sysmex XE-2100®

Platelet range	Mean	SD	Variation coefficient
10 < PLT < 20	12.81	1.52	11.83
20 < PLT < 50	24.88	1.22	4.90
50 < PLT < 100	62.00	2.10	3.39
150 < PLT < 400	262.60	5.34	2.04
PLT > 400	588.29	9.18	1.56

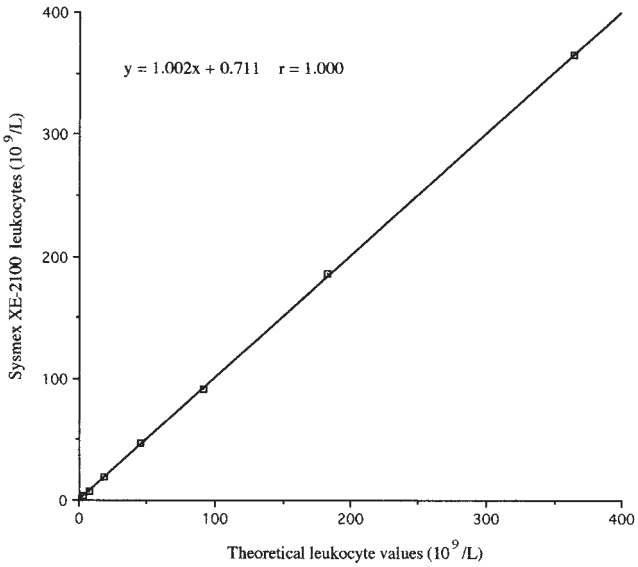

Fig. 1. Sysmex XE-2100® leukocyte linearity test.

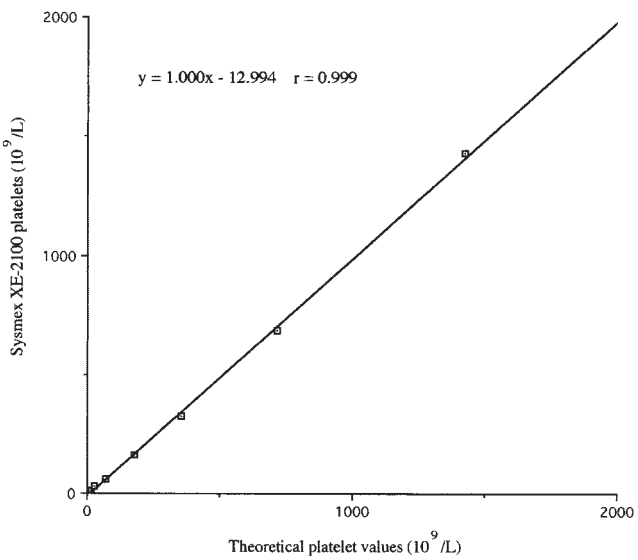

Fig. 2. Sysmex XE-2100® platelet linearity test.

The average of the carryover percentages calculated over five tests was 0.04%.

The carryover percentages found were very satisfactory. The interspecimen carryover was practically nonexistent.

Time stability tests

These tests took place over a period of 4 days. All specimens stored at room temperature (average of 25°C) showed an increase in MCV from 12 hr (minimum of 4 U), shown by a rise in the Ht and a reduction in the MCHC. This phenomenon continued over time. Also, from 12 hr on, additional flags were registered for samples that had shown a qualitative flag from the beginning. From the 24th hr onward, qualitative flags were registered for samples that did not initially have any qualitative flag. Quantitatively, the counts for RBCs, WBCs, and platelets did not undergo any modification.

Storage at 0°C allowed stability to be obtained over time for the blood count parameters, in particular for the MCV. After 72 hr, the increase of MCV, of 2 U on average, affected the erythrocytic constants very little. The appearance of qualitative flags was noted in 40% of the cases after 24 hr, in 50% of the cases after 48 hr, and in 100% of the cases after 72 hr.

Reproducibility tests

In the precision study, the maximum limit selected for the variation coefficient was 5%. All of the results were excellent, with the exception of the platelet values, which were 10×10^9/L to 20×10^9/L (Tables 5–7). For a platelet value $< 20 \times 10^9$/L, the Sysmex XE-2100® did not provide reproducible results.

Correlation Studies

For each parameter studied, there existed a positive correlation between the Sysmex XE-2100® and the

TABLE 5. Reproducibility tests on the leukocytes (10^9/L) Sysmex XE-2100®

WBC range	Mean	SD	Variation coefficient
1 < WBC < 4	3.32	0.06	1.68
4 < WBC < 10	7.62	0.17	2.27
WBC > 20	23.77	0.18	0.77

TABLE 6. Reproducibility tests on the hematocrit (L/L) Sysmex XE-2100®

Hematocrit range	Mean	SD	Variation coefficient
Ht < 0.20	0.185	0.002	0.851
0.37 < Ht < 0.42	0.412	0.003	0.708
Ht > 0.50	0.543	0.003	0.625

TABLE 7. Reproducibility tests on the platelets (10^9/L) Sysmex XE-2100®

Platelet range	Mean	SD	Variation coefficient
10 < PLT < 20	16.64	1.15	6.91
20 < PLT < 50	41.29	1.59	3.85
50 < PLT < 100	70.80	1.74	2.46
150 < PLT < 400	345.73	3.58	1.03
PLT > 400	629.36	8.77	1.39

Coulter STKS® (Figs. 3–6). This correlation was very strong for the majority of the parameters ($r > 0.9$). For the basophils and the MCHC, the positive correlations found were less strong but were 95% significant. The linear relation between the two analyzers was given in the regression line equation for each parameter. The probabilities associated with the paired Student's *t*-test were calculated (Table 8).

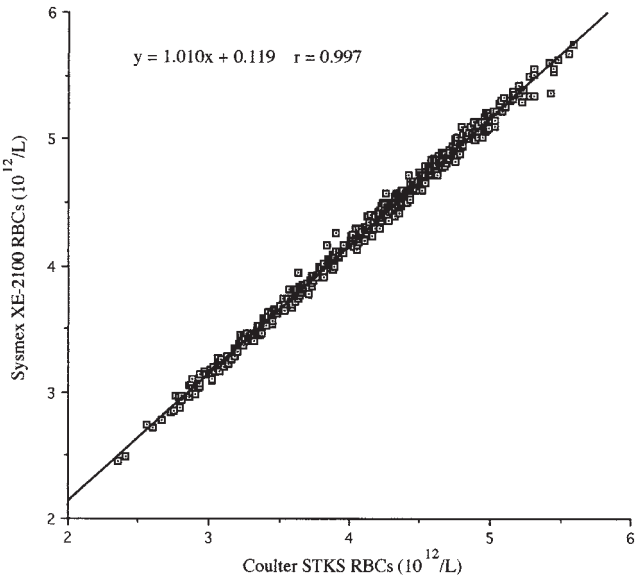

Fig. 3. Correlation of the Sysmex XE-2100® and Coulter STKS® RBC counts (n = 500).

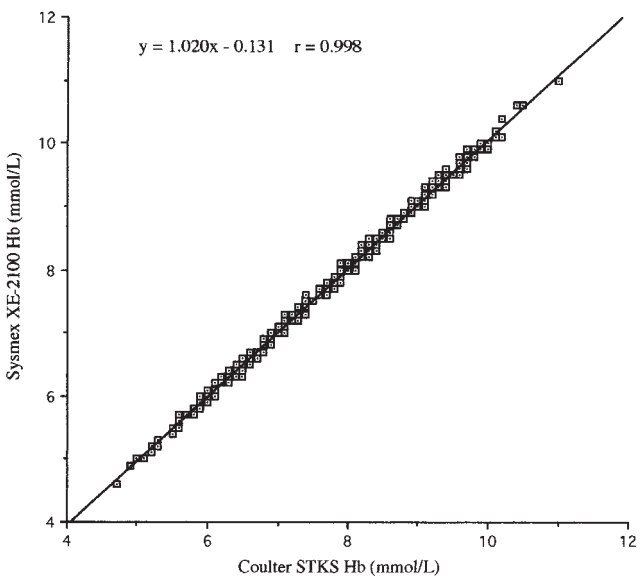

Fig. 4. Correlation of the Sysmex XE-2100® and Coulter STKS® Hb values (n = 500).

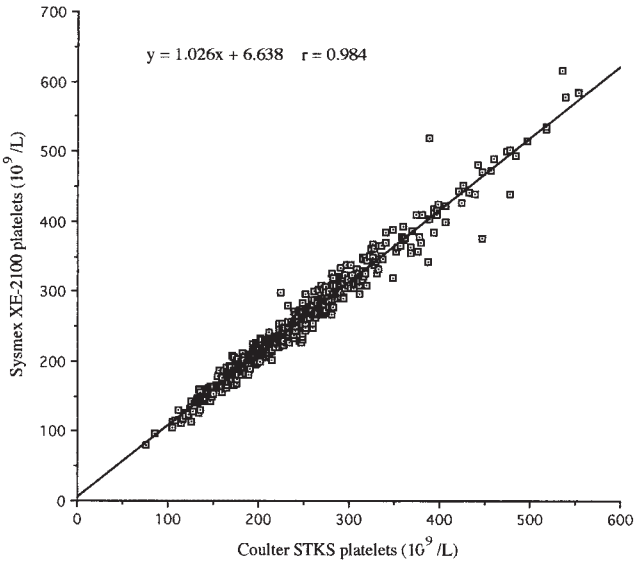

Fig. 5. Correlation of the Sysmex XE-2100® and Coulter STKS® platelet counts (n = 500).

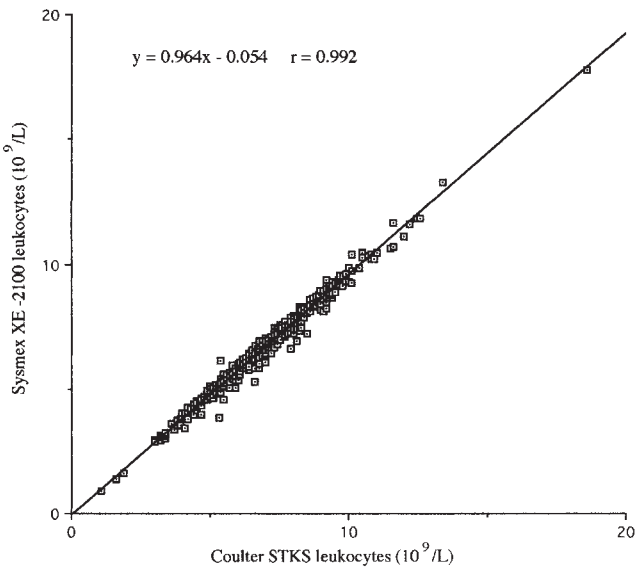

Fig. 6. Correlation of the Sysmex XE-2100® and Coulter STKS® leukocyte counts (n = 500).

Analysis of the Leukocyte Differential Count

The results of the 500 leukocyte differential counts analyzed by optical microscopy were compared with those from the Sysmex XE-2100® and the Coulter STKS®. This comparison enabled us to determine the sensitivity, specificity, and PPVs and NPVs for the two hematology analyzers.

The sensitivity of the triggering of flags influences the rejection rate and, consequently, the financial costs of

TABLE 8. Sysmex XE-2100® and Coulter STKS® Correlations

Parameter n = 500	Regression line equation	r = correlation coefficient	*P* = probability associated with paired Student's *t*-test
Red blood cells	y = 1.010x + 0.119	0.997	<0.01
Hemoglobin	y = 1.020x−0.131	0.998	<0.01
Hematocrit	y = 0.995x + 0.024	0.989	<0.01
MCV	y = 0.893x + 8.252	0.943	<0.01
MCHC	y = 1.050x−1.415	0.546	<0.01
MCH	y = 0.936x + 0.055	0.973	<0.01
RDW-CV	y = 0.923x + 1.480	0.961	<0.01
Platelets	y = 1.026x + 6.638	0.984	<0.01
Leukocytes	y = 0.964x−0.054	0.992	<0.01
Neutrophils	y = 0.965x + 0.042	0.993	<0.01
Eosinophils	y = 0.906x + 0.010	0.965	<0.01
Basophils	y = 0.302x + 0.028	0.558	0.20
Lymphocytes	y = 0.994x + 0.007	0.988	0.57
Monocytes	y = 0.715x−0.003	0.943	<0.01

the CBC + differential count. The rejection rate of the Sysmex XE-2100® was 42% (211/500), and that of the Coulter STKS® was 28% (139/500) (Fig. 7). The difference between the two rates was highly significant in the χ^2 test. As the rate of pathological differentials determined by the benchmark method was 29% (147/500), the sensitivity of anomaly detection was 96% for the XE-2100® and 67% for the STKS®. As the rate of normal differentials determined by the benchmark method was 71% (353/500), the specificity was 80% for the XE-2100® and 89% for the STKS®. In terms of the PPVs for a differential with a flag, it was 67% for the XE-2100® as opposed to 71% for the STKS®. For the NPV, the XE-2100® was more effective: 98% for the XE-2100® vs. 87% for the STKS® (Table 9).

With regard to the relevance of the results of the automatic differential, we noted that out of 353 differentials that were normal in optical microscopy, the XE-2100® signaled 70 differentials (20%) to be excessive (FPs) vs. 40 differentials (11%) for the STKS®. In contrast, for the 147 differentials that were indeed pathological, the XE-2100® did not generate a flag (FNs) for six differentials (4%) and the STKS® ignored 48 (33%) pathological differentials (Table 10).

The type and frequency of detection errors that resulted from fault or excess were analyzed. Figure 8 shows that for the XE-2100®, three factors of almost equal frequency (corresponding to atypical lymphocytes (35%), IGs (31%), and other flags (NRBCs, platelet clumps, and WBC distribution anomaly) (31%) were responsible for the errors caused by excess. For the STKS®, the causal factor was the IG flag (64%) (Fig. 8). For the FNs, it was principally IGs that were not detected; the XE-2100® was in error 49% of the time and the STKS® was in error 88% of the time. It should be noted that in the present study, neither of the two analyzers ever generated flags for circulating blasts (Fig. 9). The results shown in Fig. 10 confirm that on a day-to-day basis, circulating IGs were the most frequently occurring anomaly. In our study, IGs represented 75% of the pathological differentials. The IG flag was displayed in only 53% of the cases for the XE-2100® and in 51% for the STKS®. On the other hand, the flag for blasts was overused for the two analyzers.

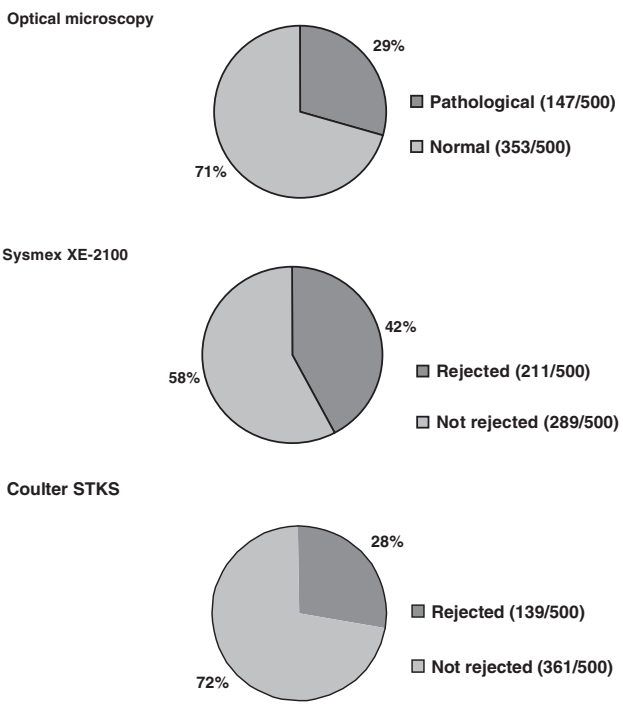

Fig. 7. Numbers of Sysmex XE-2100® and Coulter STKS® pathological differentials.

TABLE 9. Results of the leukocyte differential count evaluation

Number of differentials analyzed = 500	Optical microscopy	Sysmex XE-2100®	Coulter STKS®
Number of pathological differentials	147	211	139
Number of normal differentials	353	289	361
Number of false positives		70	40
Number of false negatives		6	48
Sensitivity in %		96	67
Specificity in %		80	89
Positive predictive value in %		67	71
Negative predictive value in %		98	87

TABLE 10. Breakdown of the leukocyte differential count

Number of differentials analyzed = 500	Pathological		Normal	
Optical microscopy	147		353	
Analyzer	TP	FN	TN	FP
Sysmex XE-2100	141	6	283	70
Sysmex XE-2100 in %	96	4	80	20
Coulter STKS	99	48	313	40
Coulter STKS in %	67	33	89	11

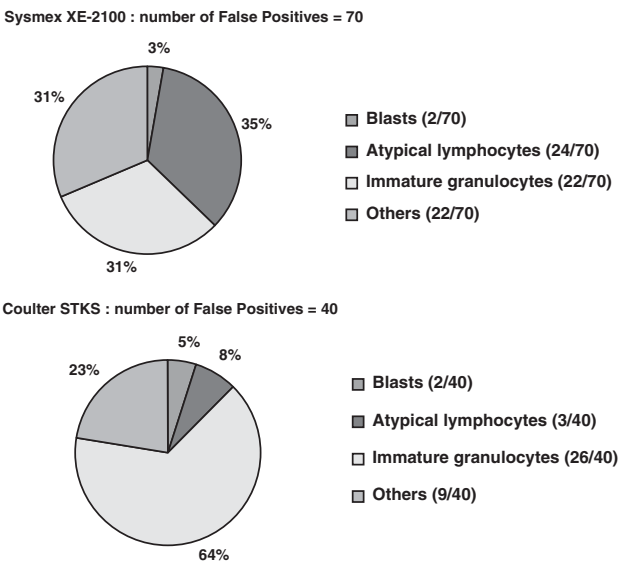

Fig. 8. Types of Sysmex XE-2100® and Coulter STKS® false positives.

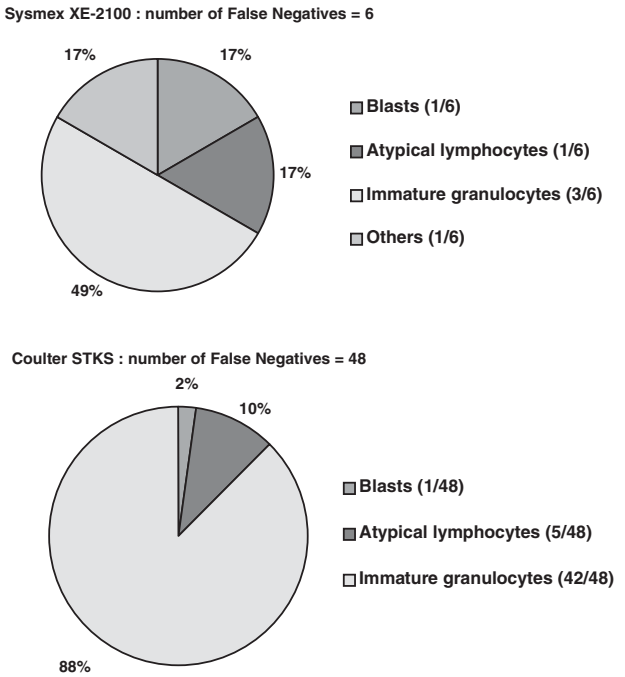

Fig. 9. Types of Sysmex XE-2100® and Coulter STKS® false negatives.

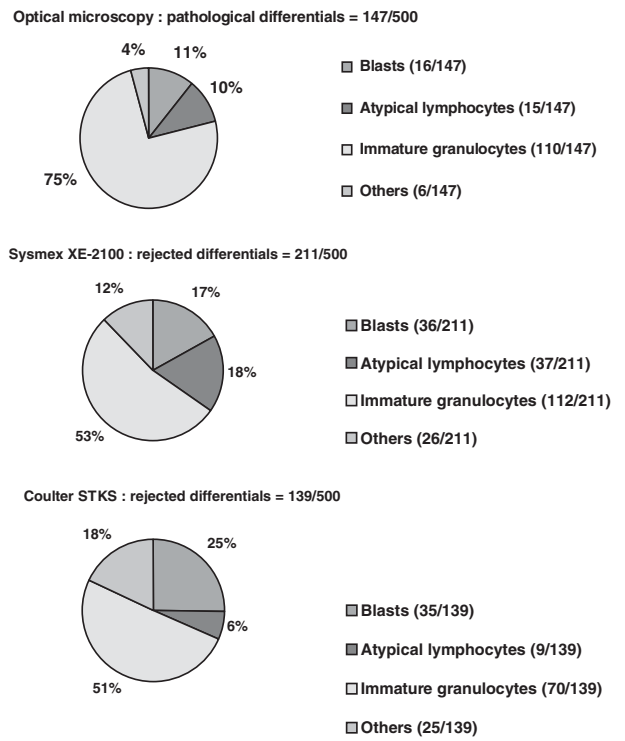

Fig. 10. Type and frequency of leukocyte differential count anomalies.

The last part of the evaluation was devoted to assigning values to the sensitivity and specificity, and the PPVs and NPVs for the two analyzers' major flags for the presence of blasts, atypical lymphocytes, and circulating IGs (Table 11). The relevance of the XE-2100® flags for these three types of atypical cells was excellent. The sensitivities and specificities were >90%. In terms of PPV for these three types of pathologies, the XE-2100® was no more successful than the STKS® for

TABLE 11. Flag Epidemiological Parameters For Sysmex XE-2100® and Coulter STKS®

	Sensitivity in %		Specificity in %		Positive predictive value in %		Negative predictive value in %	
Flag type	Sysmex XE-2100®	Coulter STKS®	Sysmex XE-2100®	Coulter STKS®	Sysmex XE-2100®	Coulter STKS®	Sysmex XE-2100®	Coulter STKS®
Blasts	93.3	93.7	95.5	95.9	38.9	42.9	99.8	99.8
Atypical lymphocytes	91.7	44.4	94.7	99.0	29.7	44.4	99.8	99.0
Immature granulocytes	96.7	48.1	94.4	92.6	79.5	55.7	99.2	90.2
Others	80.0	100.0	95.6	96.0	15.4	20.0	99.8	100.0

the blasts and the atypical lymphocytes. On the other hand, for the IGs, the PPV of 79.5% obtained by the XE-2100® was distinctly higher than that of the STKS® (55.7%). For the NPVs, the two analyzers obtained excellent scores, both exceeding 90%.

DISCUSSION

Quantitative Analytical Aspects of the Sysmex XE-2100®

In order to determine the analytical performance and the advantages and limits of the Sysmex XE-2100®, we followed the evaluation protocol proposed by the International Committee for Standardization in Haematology (ICSH) (4).

Precision tests showed excellent results, except for the leukocyte low values ($<1 \times 10^9$/L) and platelet low values (10×10^9/L to 20×10^9/L). The same precision problems have been encountered with other analyzers currently on the market, such as the Abbott Cell-Dyn 4000® (5) and the Sysmex SE 9500® (6). These weak concentrations in WBCs and platelets constitute the limits beyond which no current analyzer is capable of counting with reproducibility. In contrast to the Cobas Vega ABX®, the variation coefficient for platelet values of 50×10^9/L to 100×10^9/L for the Sysmex XE-2100® is very good (7.70% vs. 3.39%) (7).

The reproducibility tests also yielded excellent results, except for the platelet rates of 10×10^9/L to 20×10^9/L. The same situation is encountered with the Bayer Advia 120® (8), the Abbott Cell-Dyn 4000® (5), and the Sysmex SE 9500® (6). On the other hand, for platelet values of 20×10^9/L to 50×10^9/L, the Sysmex XE-2100® has a variation coefficient that is entirely acceptable (3.85%), unlike the Sysmex SE 9500® (6) and the Bayer Advia 120® (8) (6.62% and 7%, respectively).

To compensate for the underperformance of the Sysmex XE-2100®, we propose the use of a measuring chamber control with optical microscopy (particularly phase contrast microscopy) for every leukopenia $<1 \times 10^9$/L and every thrombocytopenia $<20 \times 10^9$/L.

The linearity study was very convincing. The paired Student's *t*-test produced probabilities that exceeded the threshold for statistical significance (0.05). Thus, there was no significant difference between the theoretical values and the observed values. As such, we recommend that samples not be diluted up to the values of the specimens analyzed for the test (300×10^9/L for leukocytes and $1{,}400 \times 10^9$/L for platelets).

The almost complete absence of intersample carryover is a valuable feature, especially for laboratories working with samples from diverse sources such as emergency rooms, cancer and hematology clinics, and intensive care units. A high level of leukocytes or platelets in one specimen does not call the results from the specimen previously tested by the analyzer into question.

The results of the time stability tests confirm the need to keep the blood at 4°C to maintain the stability of the differential count parameters (5,6,8,9). The quantitative aspect is thus stored up to 72 hr, and qualitative drifts are possible after 24 hr.

On the quantitative side, all the correlations were positive and significant, even though the correlation coefficients for basophils and MCHCs ($r = 0.558$ and 0.546, respectively) were not as good as the others. All calculated probabilities associated with the paired Student's *t*-test were <0.01, except for the lymphocytes ($P = 0.57$) and basophils ($P = 0.20$). With those two exceptions, there was a highly significant difference between the two analyzers for all the parameters for the CBC + differentials, which can be explained by the very dissimilar technologies of these two devices. The quantifications of the lymphocytes and basophils by the Sysmex XE-2100® and the Coulter STKS® were not statistically significantly different. For those two types of cells, the analyzers provided identical feedback even though the counting technologies were dissimilar. A recent study of 544 specimens (1), in which results from optical microscopy were compared to those from the Sysmex XE-2100®, showed a good correlation for the polynuclear basophils ($r = 0.756$) and an excellent correlation for the lymphocytes ($r = 0.922$). Briggs et

al. (2) also found that the NRBC count was highly correlated (r = 0.97) with the manual reference count. For platelet counts $< 100 \times 10^9$/L, the optical method showed excellent correlation with the reference flow cytometry (r = 0.97). The optical and impedance platelet counts were also well correlated (r = 0.89) (2). However, the precision of the impedance method was somewhat better than that of the optical method (10).

Analytic Aspects of the Sysmex XE-2100® Leukocyte Differential Count

The XE-2100® is currently the top-of-the-line analyzer on the market. Its performance in terms of the leukocyte differential count was eagerly anticipated, given the new technological approach announced by the Sysmex company.

In our comparative study, the proportion of truly pathological differentials was 29%. For the same samples, the XE-2100® counted 42% of differentials with flags; almost every second differential was considered pathological. This rejection rate can be explained by a very high flag-triggering sensitivity. This hypersensitivity is shown in the results by a lower PPV compared to that for the STKS® (67% vs. 71%), and in practice, it increases the number of manual checks required due to an increased rate of FPs. These errors in excess are not due to the IG flag (as is the case for the STKS® (64%)), but are shared among the three principal flags (other than blasts) (Fig. 8). The specificity of the XE-2100® is satisfactory, although it is lower than that of the STKS® (80% vs. 89%, respectively). Moreover, Ruzicka et al. (1) found that the efficiency rates of flagging for the presence of $\geq 1\%$ abnormal WBCs were 83% for the XE-2100®.

Roche, the French distributor of the Sysmex brand, has produced software for the analytic management of results, called the MPL system. When connected to the XE-2100®, this system acts as a mediator between the analyzers and the laboratory information system. Because appropriate parameters were set up for the algorithm used to validate the CBC + differential results, the rejection rate of the XE-2100® fell from 42% to 19% in our laboratory. We recommend that future users of the XE-2100® purchase such a filtering system to reduce the cost of having a technician verify the differentials with flags.

The XE-2100® represents a direct and major improvement in terms of the security and credibility of the differential results, as shown by its very high NPV rate (98%). This rate also remains very high for each type of major flag (Table 11). Of the current analyzers evaluated in our laboratory (5–8), the XE-2100® was the only one that provided an exceptionally low (4%) FN rate, with sensitivities and specificities >90% for major flags for the automatic differential (blasts, atypical lymphocytes, and IGs). However, even considering its exceptional FN rate, microscopeless cytology with the XE-2100® still has room for improvement. While the consequences of errors due to excess are less dramatic than errors due to a fault, the biologist is still required to intervene. The advantage of adding a complete blood count validation algorithm, such as the MPL system, is that these errors can then be managed in an effective way.

CONCLUSIONS

The XE-2100® is Sysmex's top-of-the-line hematology analyzer. Its performance and ease of use were surprising, especially because the Sysmex brand had not attained this level of success in the past. Although its analytic performance (precision, reproducibility, linearity, and carryover) did not differentiate it from other analyzers currently on the market, the results for the leukocyte differential count were certainly remarkable. The advantage lies in the use of fluorescence together with flow cytometry in the differential classification of blood cells. According to our evaluation, no other device has obtained such a respectable NPV (98%) in determining the differentials. The level of FNs is so low (4%) that it almost equals the diagnostic efficiency of an experienced cytologist.

The XE-2100® is a fully functional analyzer: the circulating NRBC count is subtracted automatically from the leukocytes, and the reticulocytes are classified according to their stage of maturity. The analyzer introduces new parameters for erythrocytic anisocytosis and platelet indices. It expresses the IG rate as both a percentage and an absolute number. Its throughput of 150 CBC + differentials per hour is particularly impressive.

The XE-2100® is the first analyzer on the market to offer an exceptional quality/price ratio. When used together with validation software, it delivers performance worthy of a true top-of-the-line analyzer.

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