

# Evaluation of Leukocyte Differential Count Information From the CELL-DYN 3200 Hematology Analyzer

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## ABSTRACT

A new hematology analyzer, the CELL-DYN 3200, was evaluated in a tertiary care hospital laboratory with regard to precision and accuracy of the 5-part white blood cell differential provided and clinical sensitivity and specificity of the instrument flagging system. Short- and long-term precision was fully satisfactory in normal and abnormal nonflagged specimens. CELL-DYN 3200 values corresponded closely with those of reference microscopic 400-cell differentials: in normal samples, average bias did not exceed 1% for any cell type. Moreover, in abnormal nonflagged specimens, no case with gross discrepancy between CELL-DYN 3200 and microscopy results was observed; linear regression coefficients were 0.96, 0.95, 0.68, 0.95, and 0.57 for neutrophil, lymphocyte, monocyte, eosinophil, and basophil percentages, respectively. The instrument diagnostic efficiency was 88.5% for morphologic abnormalities only and 90.6% if both morphologic and distributional abnormalities were considered. False-negative results were largely confined to some cases with moderate elevation of immature granulocytes and band cells. Our evaluation suggests that the CELL-DYN 3200 will serve the needs for automated leukocyte differential counting in a tertiary care hospital or other setting with a high proportion of abnormal specimens. *Lab Hematol.* 1999;5:137-148.

**KEY WORDS:** Hematology automation ·  
Hematology analyzer evaluation ·  
Leukocyte differential · Flagging

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## INTRODUCTION

In routine care, laboratory hematologic diagnosis generally starts with a cellular blood count and a leukocyte differential count. The cellular blood count can be regarded as primarily a quantitative task; its automation has long been established [1]. In contrast, the leukocyte differential count essentially represents a qualitative procedure involving leukocyte classification and the diagnosis of cell abnormalities in each cell class. For leukocyte classification, in our laboratory in Germany we adopted a scheme used for external quality control of microscopic leukocyte differential count, which includes 18 cell types. In addition, an overview listed 53 qualitative abnormalities distinguishable by microscopic leukocyte examination [2]. Because no manufacturer of an automated hematology analyzer claims that the instrument can recognize this huge variety of cell types or morphologic abnormalities, the microscopic leukocyte differential count remains an essential part of laboratory diagnosis. However, because this technique is subjective, laborious, and imprecise under routine conditions, many laboratories try to combine the advantages of automated and microscopic testing. With this strategy, automated analysis is performed on all samples, whereas microscopic examination is restricted to samples with predefined features of analyzer testing. This procedure requires that instrument results be correct with regard to quantification of specific cell populations and that the presence of relevant pathology exceeding distributional changes is indicated in the results by flags or other means. The fulfillment of these requirements must be proved in field studies.

To facilitate and standardize such studies, guidelines have been published [2,3] and special attention given to the establishment of a standard for reference leukocyte differential counting [4]. Using these guidelines, valuable information regarding the performance of an analyzer can be obtained. Because there are clear differences (especially in clinical sensitivity) between the more laborious reference leukocyte differential and routine microscopic testing, this information does not directly relate to a comparison between the instrument and microscopy under routine conditions. This problem can be overcome by parallel evaluation of both procedures against the reference method; however, we are not aware of any study in which this approach was chosen.

TABLE 1. Flagging Messages of the CELL-DYN 3200 Analyzer

Parameter	Suspect Parameter Flags	Suspect Population Flags
Leukocyte count	WBC	NWBC (nonwhite blood cells) FWBC (fragile white blood cells) NRBC (nucleated red blood cells) RRBC (resistant red blood cells)
Leukocyte differential (DIFF)	DIFF (NLMEB*)	BAND (neutrophil band forms) IG (immature granulocytes) BLAST (blast cells) VARIANT LYM (variant lymphocytes)

\*Cell types affected: N, neutrophils; L, lymphocytes; M, monocytes; E, eosinophils; B, basophils.

Alternatively, some differences between reference and routine microscopy can be taken into account on the basis of statistical considerations. Assuming that the Poisson distribution fits best for both automated and microscopic leukocyte differentials [5], the statistic of the widely used 100-cell microscopic differential can be calculated.

In this study, the leukocyte differential count information from a new hematology analyzer, the CELL-DYN 3200 (CD 3200) (Abbott, Abbott Park, IL), was evaluated with regard to precision, accuracy, and clinical sensitivity and specificity.

## MATERIALS AND METHODS

Throughout the study, unless otherwise indicated, we adhered to the International Council for Standardization in Haematology guidelines for blood cell analyzer evaluation and the National Committee for Clinical Laboratory Standards (NCCLS) standard for reference leukocyte differentials [3,4]. Deviations from these guidelines included the choice of anticoagulant and the composition of samples.

### Blood Samples

Patient blood samples were obtained from the Oststadt-krankenhaus Hannover, a tertiary care hospital that belongs to the Medical School Hannover, Germany, and cares for a high proportion of critically ill patients, and the Department of Hematology of the Medical School Hannover. Of 387 selected blood specimens, 333 were drawn for routine hematologic analysis from adult inpatients of the Oststadt-krankenhaus Hannover and 39 samples, most with malignant hematologic abnormalities, were from the Medical School Hannover. In addition, 15 cord blood samples were examined. Analysis of accuracy and flagging performance relies on 382 samples only, because in 5 cases (all with white blood cell count  $<0.4 \times 10^9/L$ ) no 400-cell microscopic differential could be obtained. All samples were run in duplicate.

Venous blood was collected in Sarstedt monovettes (Sarstedt, Nümbrecht, Germany), with  $K_2$ -EDTA (1.2-2.0 mg/mL blood) serving as anticoagulant. All samples were stored at room temperature and measured within 4 hours after venipuncture.

### Instrument

The CD 3200 simultaneously determines a cellular blood count and a 5-part leukocyte differential count. Leukocyte identification

and differentiation are performed using multiangle polarized scatter separation. With this technique, which has been described elsewhere [6-8], scattered light is determined in the angle regions 0, 10, and 90 degrees. In addition, light depolarization serves for eosinophil identification. The basic analytical performance of the CD 3200 was evaluated by us on a reproduction version of the instrument; the results were published elsewhere [9]. Because development of the flagging algorithms was ongoing at the time of that evaluation, we report here the results of another study focusing on the leukocyte differential, which were obtained with a fully developed instrument (software version 1.3).

The CD 3200 uses 10 flags concerning leukocyte identification and differentiation (Table 1). Suspect parameter flags indicate that the instrument is not able to provide an accurate value for a parameter or a set of parameters, and suspect population flags hint as to the presence of abnormal cells in the samples. Direct morphologic equivalents exist for 1 of the 4 white blood cell count suspect population flags (the NRBC [nucleated red blood cells] flag) and for all differential suspect population flags (the BAND [band cells], IG [immature granulocytes], BLAST [blast cells], and VARIANT LYM [variant lymphocytes] flags). For the other flags, a firm link to a distinct morphologic abnormality cannot be established. In case of any flag, the manufacturer does not recommend the use of instrument results without further action; generally, the review of a stained smear is necessary.

### Precision

Short-term imprecision and long-term imprecision were analyzed as outlined in the NCCLS H20-A standard [4]. For determination of long-term imprecision, the control material CELL-DYN

TABLE 2. Hematologic Features of Patient Samples as Judged by Microscopic Examination

Feature	Number of Cases
Hematologically normal	59
Hematologically abnormal	328
Hematologically abnormal without instrument flag	232
Hematologically abnormal with instrument flag	96
Quantitative leukocyte abnormality (any of the following criteria)	127
Neutrophilia ( $\geq 9.0 \times 10^9/L$ and $>80\%$ )	63
Neutropenia ( $\leq 1.5 \times 10^9/L$ and $<10\%$ )	21
Lymphocytosis ( $\geq 3.5 \times 10^9/L$ and $>50\%$ )	17
Lymphopenia ( $\leq 1.0 \times 10^9/L$ and $<7\%$ )	26
Monocytosis ( $\geq 0.8 \times 10^9/L$ and $>10\%$ )	22
Eosinophilia ( $\geq 0.5 \times 10^9/L$ and $>7\%$ )	13
Qualitative leukocyte abnormality (any of the following criteria)	80
Band cells ( $\geq 0.9 \times 10^9/L$ and $>6\%$ )	10
Immature granulocytes* ( $\geq 0.1 \times 10^9/L$ and $>2\%$ )	34
Variant lymphocytes* ( $\geq 0.7 \times 10^9/L$ and $>2\%$ )	28
Blasts* ( $\geq 0.1 \times 10^9/L$ and $>2\%$ )	21
Nucleated red blood cells ( $\geq 0.02 \times 10^9/L$ and $>2\%$ )	27

\*Definitions differing from the H20-A standard. Immature granulocytes comprise promyelocytes, myelocytes, and metamyelocytes.

TABLE 3. Short-term Paired Imprecision of CELL-DYN 3200 Leukocyte Percentage Measurement\*

Cell Type	Parameter	All Samples	Sample Group		
			Normal Samples	Abnormal Samples Without Flag	Abnormal Samples With Flag
Neutrophils	Number of samples	387	59	232	96
	Mean value	62.3	60.5	70.7	43.1
	Coefficient of variation	1.3	1.1	0.9	2.8
	Mean difference	0.0	-0.1	0.0	0.2
	Minimum difference	-3.4	-1.9	-2.4	-3.4
Lymphocytes	Maximum difference	7.7	1.9	3.1	7.7
	Mean value	25.2	29.7	19.3	36.6
	Coefficient of variation	8.7	3.6	5.6	11.1
	Mean difference	0.2	0.5	0.4	-0.8
	Minimum difference	-38.5	-1.9	-4.0	-38.5
Monocytes	Maximum difference	16.0	4.3	6.7	16.0
	Mean value	8.5	6.4	6.9	13.9
	Coefficient of variation	22.1	12.2	13.8	24.8
	Mean difference	-0.4	-0.4	-0.4	-0.2
	Minimum difference	-33.3	-3.4	-5.9	-33.3
Eosinophils	Maximum difference	18.2	1.4	4.8	18.2
	Mean value	2.3	2.4	2.3	2.4
	Coefficient of variation	48.8	8.2	8.8	93.6
	Mean difference	0.1	0.0	0.0	0.3
	Minimum difference	-2.3	-0.6	-0.9	-2.3
Basophils	Maximum difference	30.8	0.8	1.0	30.8
	Mean value	1.7	1.0	0.9	4.0
	Coefficient of variation	39.8	17.7	19.7	32.4
	Mean difference	0.1	0.0	0.0	0.4
	Minimum difference	-2.8	-0.7	-1.0	-2.8
	Maximum difference	10.5	0.5	1.3	10.5

\*Data are given in %. Differences were calculated as run 2 - run 1.

3000 Control (Abbott) provided by the manufacturer was measured on each of 20 consecutive workdays. Separate analyses were performed on data from all specimens, from abnormal specimens with and without instrument flag, and from normal specimens (all cellular blood count and leukocyte differential count values within the laboratory reference ranges).

#### Accuracy

Accuracy was examined in accordance with the proposals made in the NCCLS standard H20-A [4]. Reference microscopy was performed by 2 experienced medical technologists. For the comparison of CD 3200 neutrophil percentages, the manual differential promyelocyte, myelocyte, metamyelocyte, and band cell and segmented neutrophil percentages were added. Similarly, with regard to CD 3200 lymphocyte estimates, the total of normal and variant lymphocytes by microscopy was determined. Again, separate analyses were done for different sample groups.

#### Clinical Sensitivity and Specificity

The NCCLS H20-A procedures were used. For a sample to be classified as morphologically abnormal by microscopic examination, one of the following requirements had to be fulfilled: (1) band

cells >6%; (2) variant lymphocytes >2%; (3) total of promyelocytes, myelocytes, and metamyelocytes >1%; or (4) total of all other abnormal cell types >1%. In addition, clinical sensitivity was analyzed considering the diagnostic capacity of routine 100-cell microscopic differentials. If the percentage of an abnormal cell type reaches 3%, the Poisson distribution gives a 95% probability of finding 1 of these abnormal cells in the 100 leukocytes examined. Therefore, special attention was given to samples containing at least 3% of an abnormal cell type.

TABLE 4. Long-term Imprecision of CELL-DYN 3200 Leukocyte Percentages

Cell Type	Mean Value (%)	Coefficient of Variation (%)
Neutrophils	66.4	1.6
Lymphocytes	17.9	6.6
Monocytes	9.3	11.1
Eosinophils	3.9	10.0
Basophils	2.5	22.4

**TABLE 5. Accuracy of CELL-DYN 3200 Leukocyte Percentage Measurement With 400-Cell Microscopic Differentials Serving as Reference Method\***

Cell Type	Parameter	All Samples	Sample Group		
			Normal Samples	Abnormal Samples Without Flag	Abnormal Samples With Flag
Neutrophils	Number of samples	382	59	232	91
	Mean (microscopy) (%)	64.6	60.7	72.8	46.0
	Range (microscopy) (%)	0.0-93.8	49.5-73.3	28.0-93.8	0.0-93.8
	Mean (CELL-DYN 3200) (%)	62.9	60.5	70.7	44.3
	Mean difference (%)	-1.7	-0.2	-2.1	-1.7
	Minimum difference (%)	-54.4	-8.0	-15.9	-54.4
	Maximum difference (%)	22.9	10.6	13.2	22.9
	SD of difference (%)	5.7	3.6	3.6	9.8
	Passing/Bablok	$0.97x + 0.61$	$1.11x - 7.14$	$0.99x - 1.38$	$0.97x + 0.90$
<i>r</i>	0.97	0.81	0.96	0.96	
Lymphocytes	Mean (microscopy) (%)	23.6	30.0	18.2	33.0
	Range (microscopy) (%)	0.0-99.0	20.5-42.3	2.3-64.3	0.0-99.0
	Mean (CELL-DYN 3200) (%)	24.6	29.4	19.0	35.6
	Mean difference (%)	1.0	-0.6	0.8	2.5
	Minimum difference (%)	-34.2	-7.9	-12.5	-34.2
	Maximum difference (%)	70.7	7.9	14.0	70.7
	SD of difference (%)	8.5	3.4	3.3	16.5
	Passing/Bablok	$0.94x + 1.57$	$1.02x - 1.15$	$0.96x + 1.49$	$0.94x + 1.37$
	<i>r</i>	0.89	0.81	0.95	0.85
Monocytes	Mean (microscopy) (%)	6.5	6.4	6.5	6.8
	Range (microscopy) (%)	0.0-38.8	3.5-10.0	1.3-18.3	0.0-38.8
	Mean (CELL-DYN 3200) (%)	8.7	6.6	7.1	14.2
	Mean difference (%)	2.2	0.2	0.6	7.4
	Minimum difference (%)	-8.4	-2.5	-5.8	-8.4
	Maximum difference (%)	80.7	3.6	8.6	80.7
	SD of difference (%)	8.5	1.4	2.1	16.0
	Passing/Bablok	$1.10x - 0.00$	$1.20x - 0.94$	$0.91x + 0.98$	$1.78x - 1.76$
	<i>r</i>	0.41	0.62	0.68	0.41
Eosinophils	Mean (microscopy) (%)	2.0	2.1	1.9	2.0
	Range (microscopy) (%)	0.0-23.3	0.3-5.5	0.0-18.0	0.0-23.3
	Mean (CELL-DYN 3200) (%)	2.2	2.4	2.3	2.0
	Mean difference (%)	0.3	0.3	0.3	0.0
	Minimum difference (%)	-10.7	-1.4	-2.0	-10.7
	Maximum difference (%)	5.4	3.0	5.4	4.8
	SD of difference (%)	1.1	0.8	0.9	1.6
	Passing/Bablok	$1.10x + 0.12$	$1.14x + 0.02$	$1.11x + 0.12$	$1.07x + 0.07$
	<i>r</i>	0.93	0.86	0.95	0.93
Basophils	Mean (microscopy) (%)	0.5	0.8	0.5	0.4
	Range (microscopy) (%)	0.0-6.5	0.0-2.0	0.0-3.5	0.0-6.5
	Mean (CELL-DYN 3200) (%)	1.6	1.0	0.9	3.9
	Mean difference (%)	1.1	0.3	0.4	3.5
	Minimum difference (%)	-5.5	-1.2	-1.7	-5.5
	Maximum difference (%)	51.7	1.1	1.8	51.7
	SD of difference (%)	4.0	0.5	0.5	7.7
	Passing/Bablok	$1.40x + 0.36$	$0.54x + 0.66$	$0.95x + 0.38$	No result
	<i>r</i>	-0.02	0.32	0.57	-0.05

\*Results of the method comparison according to Passing and Bablok are given as  $y = (\text{slope})x + / - \text{intercept}$ , where  $y = \text{CELL-DYN 3200 values}$  and  $x = \text{microscopy values}$ ; SD, standard deviation;  $r$ , linear regression coefficient.

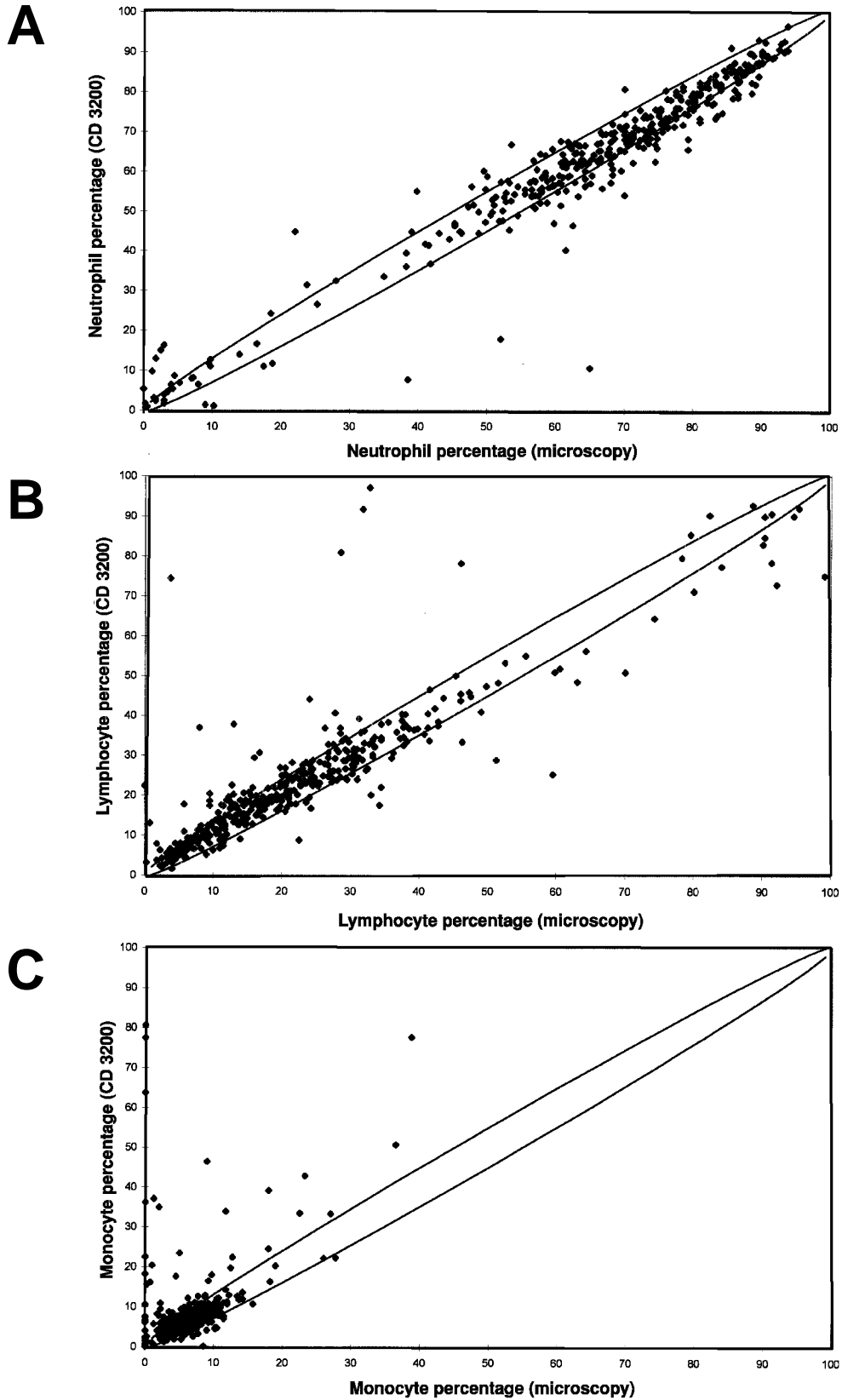


FIGURE 1. CELL-DYN 3200 accuracy (all specimens). Neutrophil (A), lymphocyte (B), monocyte (C), eosinophil (D), and basophil (E) percentage results of the CELL-DYN 3200 analyzer were compared with 400-cell microscopic differentials. All specimens were included. Solid lines show the 95% confidence limits. Continued on next page.

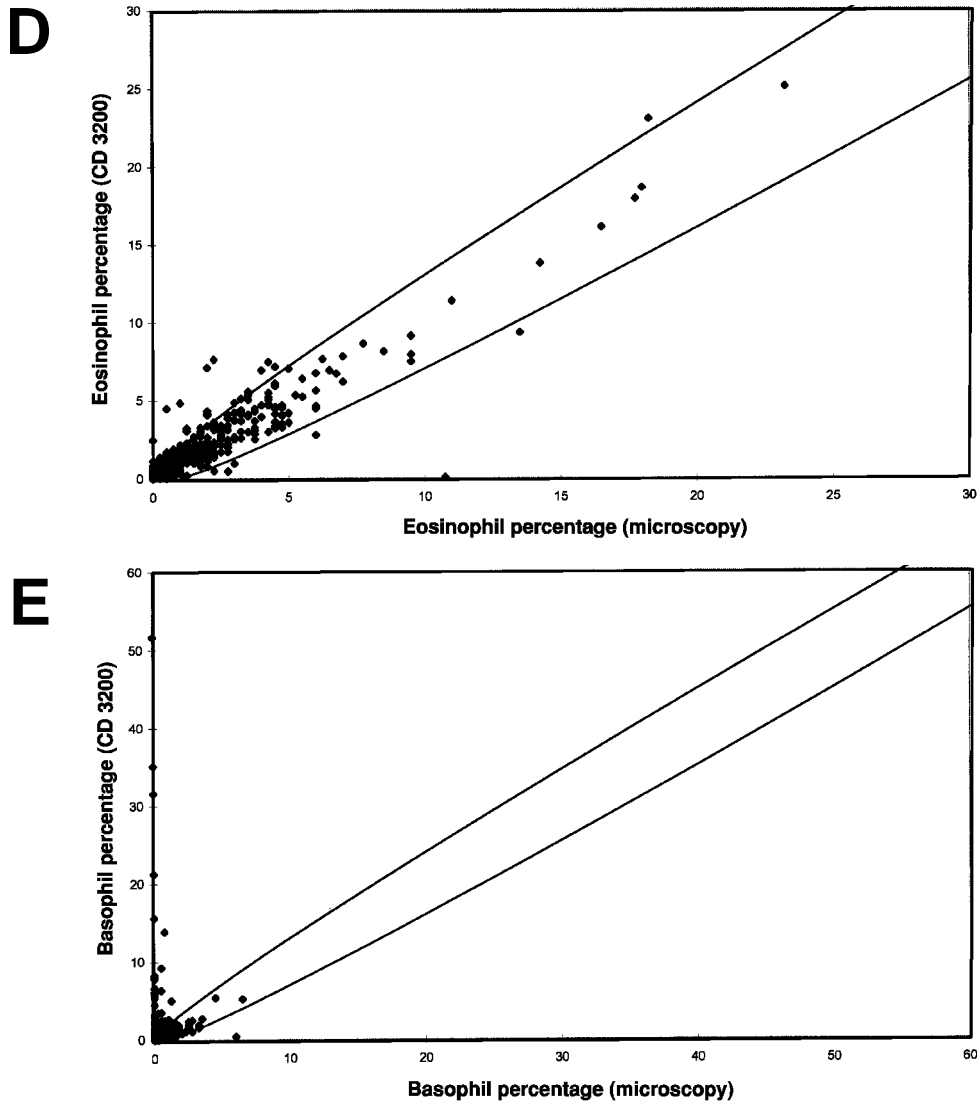


FIGURE 1 continued. CELL-DYN 3200 accuracy (all specimens). Neutrophil (A), lymphocyte (B), monocyte (C), eosinophil (D), and basophil (E) percentage results of the CELL-DYN 3200 analyzer were compared with 400-cell microscopic differentials. All specimens were included. Solid lines show the 95% confidence limits.

#### *Statistical Analysis*

In addition to the procedures outlined in the NCCLS H20-A standard, the biometrical method proposed by Passing and Bablok [10] was used for method comparison.

## RESULTS

#### *Sample Composition*

The patient samples examined comprised 59 hematologically normal and 328 hematologically abnormal specimens. The hematologically abnormal samples comprised 127 and 80 specimens with quantitative and qualitative leukocyte abnormalities, respectively; the remaining abnormal specimens showed quantitative

deviations of cellular blood count parameters. Zero normal and 96 abnormal samples were flagged by the CD 3200. With regard to the characteristic leukocyte differential count findings described in the H20-A standard, at least 10 specimens with any of the leukocyte abnormalities were included in the study. The details are summarized in Table 2.

#### *Precision*

In normal samples, CD 3200 short-term imprecision coefficients of variation varied between 1.1% for neutrophils and 17.7% for basophils. In abnormal specimens without instrument-generated flags, only moderately higher short-term imprecision was determined. However, CD 3200 measurements of flagged samples

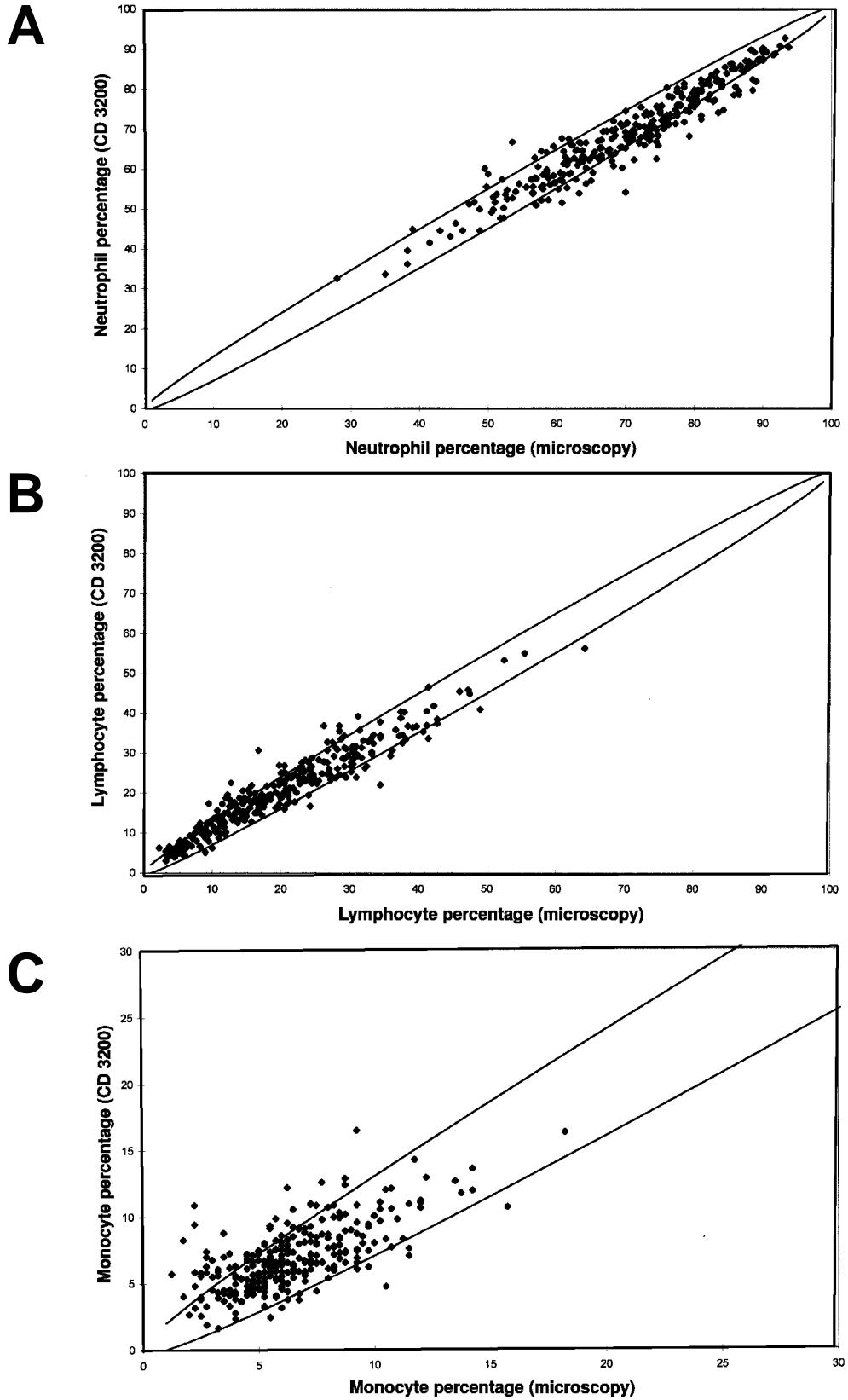


FIGURE 2. CELL-DYN 3200 accuracy (nonflagged specimens). Neutrophil (A), lymphocyte (B), monocyte (C), eosinophil (D), and basophil (E) percentage results of the CELL-DYN 3200 analyzer were compared with 400-cell microscopic differentials. Analysis was restricted to specimens without instrument-generated leukocyte flags. Solid lines show the 95% confidence limits. Continued on next page.

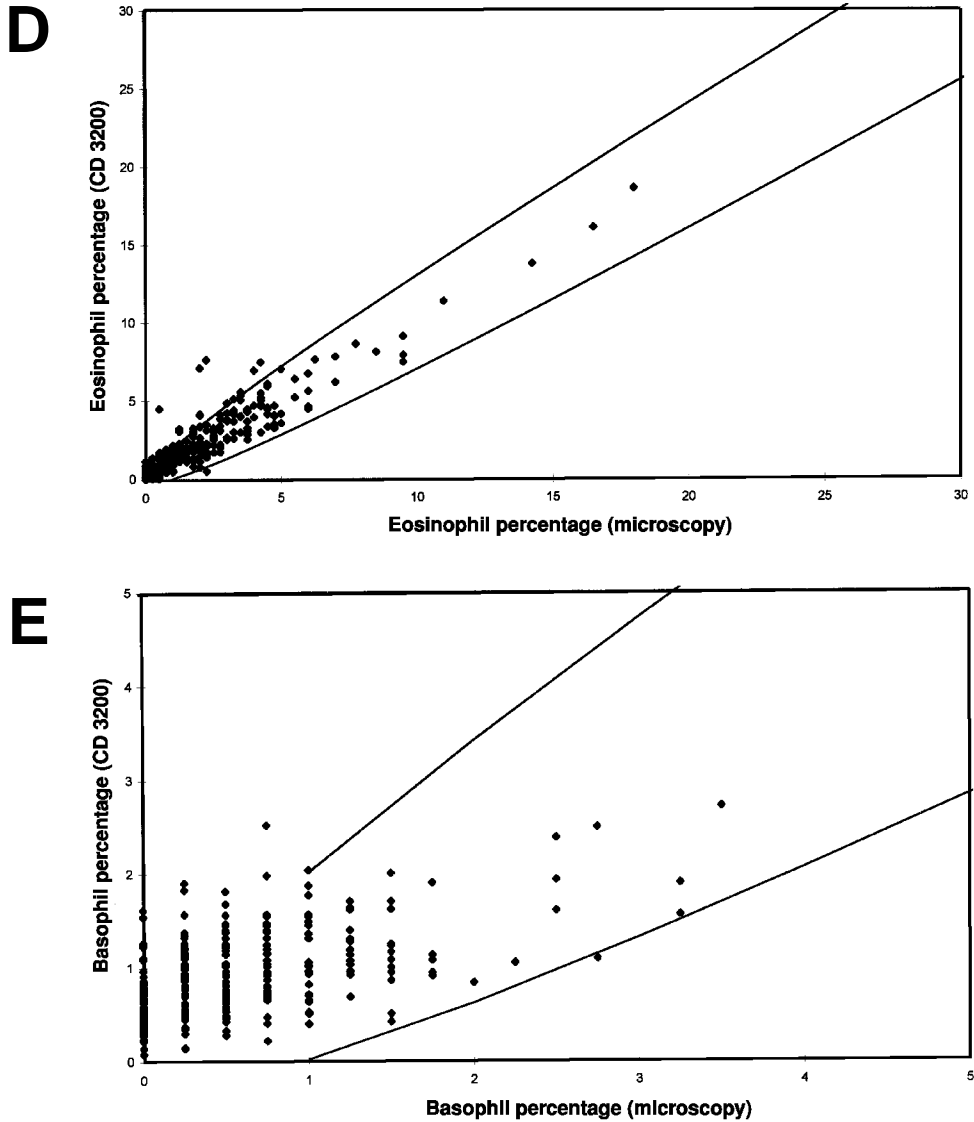


FIGURE 2 continued. CELL-DYN 3200 accuracy (nonflagged specimens). Neutrophil (A), lymphocyte (B), monocyte (C), eosinophil (D), and basophil (E) percentage results of the CELL-DYN 3200 analyzer were compared with 400-cell microscopic differentials. Analysis was restricted to specimens without instrument-generated leukocyte flags. Solid lines show the 95% confidence limits.

were clearly less precise, with coefficients of variation generally 2 to 3 times higher than in the normal sample group. Run-to-run imprecision bias plots (not shown) revealed 6 samples (all flagged) with gross imprecision of cell type percentages. Two of these samples were leukopenic (white blood cell counts  $0.04 \times 10^9/L$  and  $0.33 \times 10^9/L$ ), with chance effects exerting a strong influence on measured percentages. In the other 4 cases, irregularly positioned blasts (on microscopical examination shown to be made up of 88.5%-100% leukocytes) led to an arbitrary separation of cell types. Long-term imprecision coefficients of variation varied from 1.6% for neutrophils to 22.4% for basophils. Short- and long-term imprecision results are summarized in Table 3 and Table 4, respectively.

#### *Accuracy*

Accuracy of the CD 3200 analyzer depended largely, again, on the type of specimen used. CD 3200 results generally compared well with those of reference microscopy in both normal samples and abnormal samples without instrument-generated flags. In normal samples, mean values of CD 3200 and microscopic results were nearly identical, and standard deviations of differences varied between 0.5% (basophils) and 3.6% (neutrophils). In abnormal nonflagged samples, similarly low inaccuracy was determined, although maximal deviations were somewhat higher. In contrast, a substantial proportion of flagged samples showed gross discrepancies between CD 3200 results and microscopy. However, even with

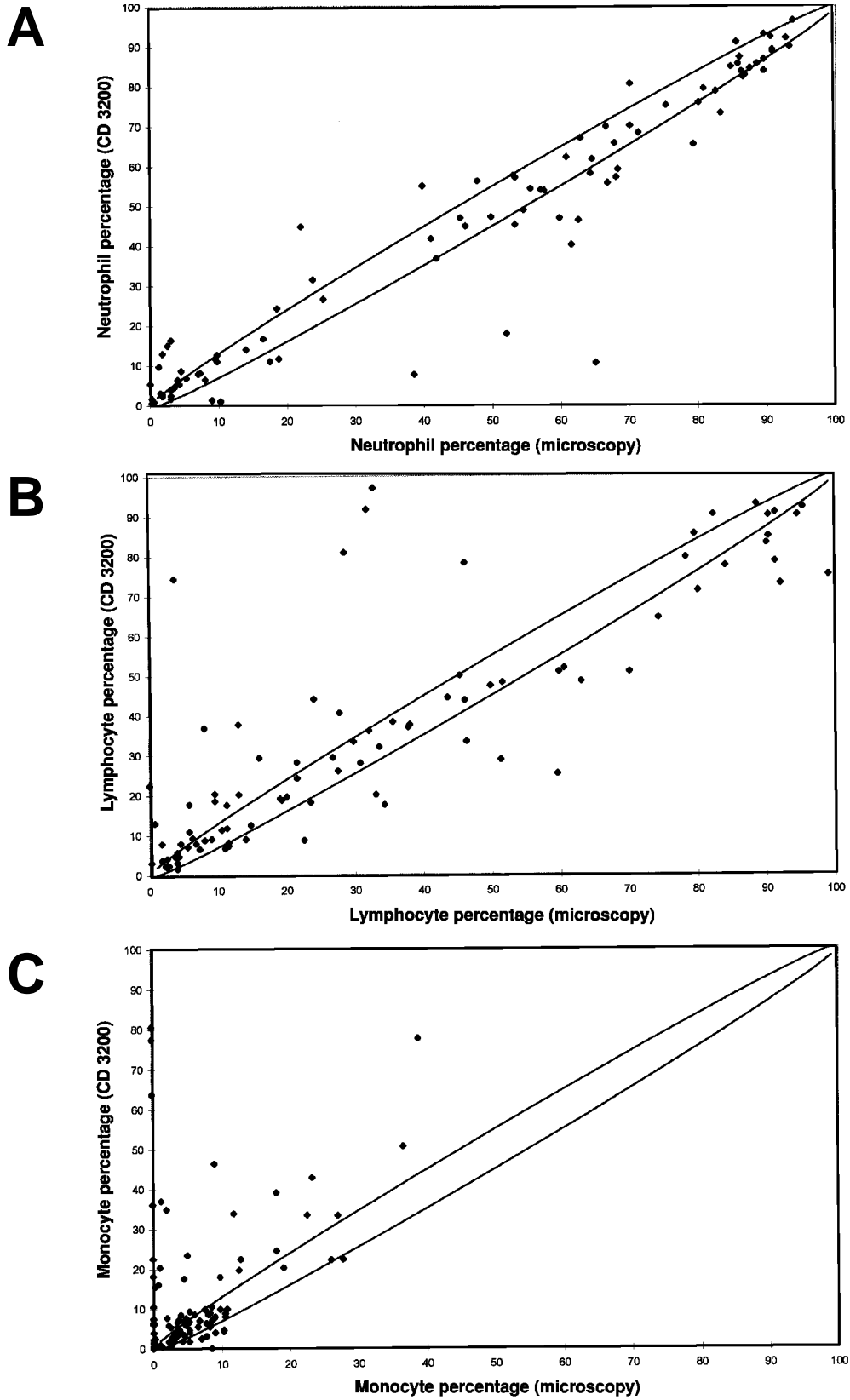


FIGURE 3. CELL-DYN 3200 accuracy (flagged specimens). Neutrophil (A), lymphocyte (B), monocyte (C), eosinophil (D), and basophil (E) percentage results of the CELL-DYN 3200 analyzer were compared with 400-cell microscopic differentials. Analysis was restricted to specimens with instrument-generated leukocyte flags. Solid lines show the 95% confidence limits. Continued on next page.

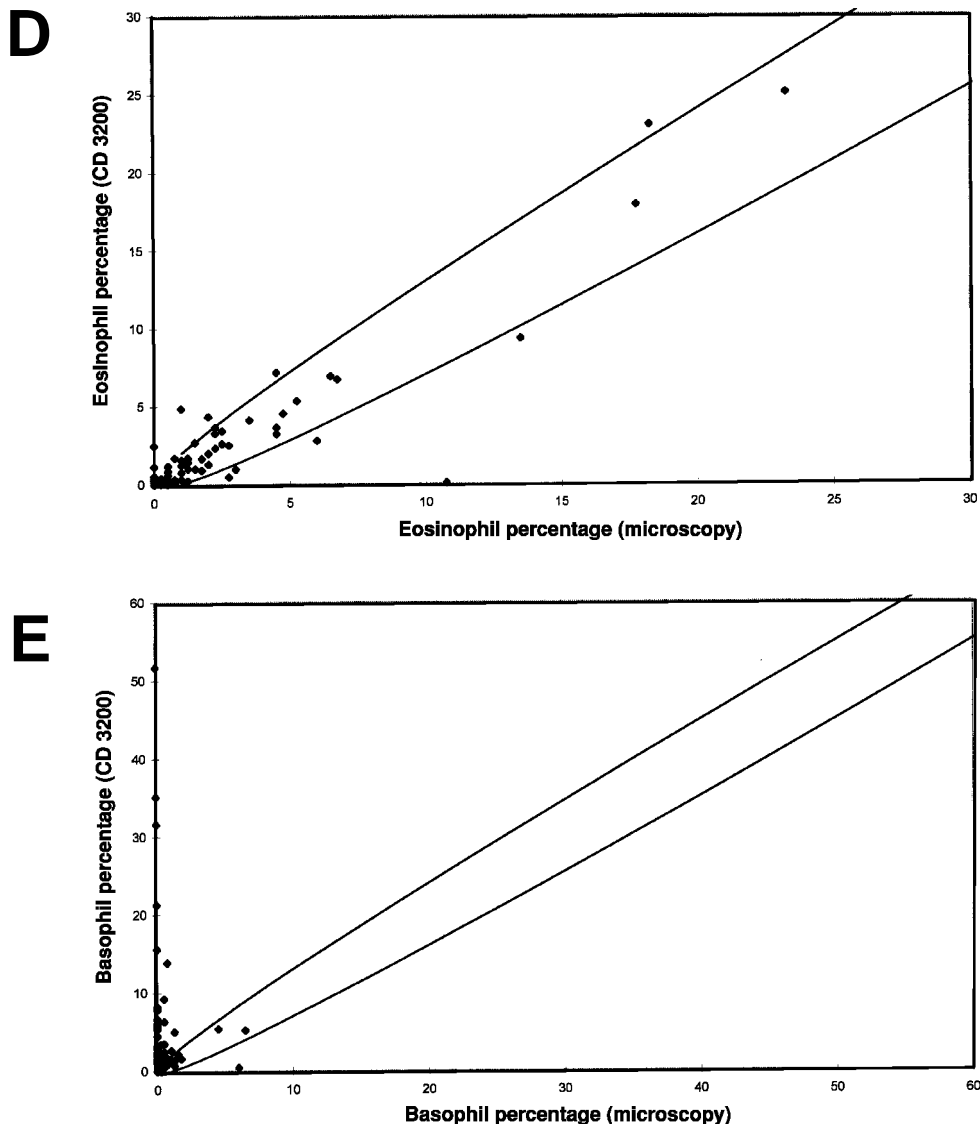


FIGURE 3 continued. CELL-DYN 3200 accuracy (flagged specimens). Neutrophil (A), lymphocyte (B), monocyte (C), eosinophil (D), and basophil (E) percentage results of the CELL-DYN 3200 analyzer were compared with 400-cell microscopic differentials. Analysis was restricted to specimens with instrument-generated leukocyte flags. Solid lines show the 95% confidence limits.

this specimen-type method, comparison analysis according to the method of Passing and Bablok revealed that neutrophil, lymphocyte, and eosinophil percentages of the CD 3200 generally reflect microscopic values. Accuracy results are shown in Table 5 and depicted in Figures 1, 2, and 3 for all specimens, nonflagged specimens, and flagged specimens, respectively.

#### *Clinical Sensitivity and Specificity*

Of the 382 samples, 93 were classified as morphologically abnormal by microscopic examination. In 70 of these samples, CD 3200 results were marked with a leukocyte flag. The other 23 specimens were nonflagged, resulting in a false-negative ratio of 24.7%

(Table 6). In 21 of 268 samples without morphologic abnormality as assessed by microscopy, a leukocyte flag was generated by the instrument; thus, false-positive ratio and efficiency (overall agreement) were 7.3% and 88.5%, respectively. Efficiency increased to 90.6% and false-negative ratio decreased to 6.0% if both morphologic and distributional abnormalities were considered.

Special attention was given to samples containing at least 3% (band cells >6%) of any abnormal cell type. Eleven of these samples were measured by the CD 3200 without instrument-generated leukocyte flags (Table 7). The abnormalities observed were increased band cells (in 4 cases, maximum value 14.25%), immature granulocytes (in 5 cases, maximum value 8.25%), variant lym-

**TABLE 6. Clinical Sensitivity and Specificity of the CELL-DYN 3200 Analyzer in Comparison to 400-Cell Microscopic Differentials**

Parameter	Result (%)
Morphologic abnormalities only	
Efficiency (agreement)	88.5
Sensitivity	75.3
False-negative ratio	24.7
Specificity	92.7
False-positive ratio	7.3
Morphologic and distributional abnormalities combined	
Efficiency (agreement)	90.6
Sensitivity	94.0
False-negative ratio	6.0
Specificity	82.8
False-positive ratio	17.2

phocytes (in 1 case with 14.75% Sézary cells), and nucleated red blood cells (in 1 case with 10.75 nucleated red blood cells/100 leukocytes, red blood cell abnormality marked by the CD 3200).

## DISCUSSION

A principle of laboratory medicine says that a new technique should possess analytical and technical quality at least as high as the method it is thought to replace. Concerning automated versus microscopic leukocyte differential counting, the advantages of sophisticated hematologic instruments are undeniable, especially with regard to precision and turnaround time. At present, instrument-generated leukocyte differential counts cannot replace microscopy, because no analyzer is able to identify the variety of morphologic abnormalities possibly encountered in blood films. However, automated and microscopic methods can be combined in diagnostic strategies. Here, we report a field

study examining the ability of the CD 3200, a hematologic analyzer recently introduced into the market, to work as an efficient tool in such strategies.

The precision results of the CD 3200 compare well with those of other modern hematology analyzers. Generally, similar values have been obtained with Coulter STKS and MAXM (Coulter Corporation, Miami, FL) [11-15], Bayer Diagnostics H-1 and H-2 (Bayer, Tarrytown, NY) [11-13], Sysmex NE-8000 and SE-9000 (Sysmex, Kobe, Japan) [12,16], ABX Cobas Argos (ABX/Roche, Montpellier, France) [17], and Abbott CELL-DYN 3000 instruments [12]. CD 3200 monocyte percentage coefficients of variation tended to be somewhat higher than those reported in studies of other analyzers, whereas imprecision of eosinophil and basophil percentages was slightly lower. However, these differences can possibly be explained by variation in sample composition and precision testing techniques and are probably of no relevance in routine diagnosis. In our study, CD 3200 precision was satisfactory for both normal samples and nonflagged abnormal samples. Major imprecision was restricted to a minority of highly abnormal samples with gross deviations of white blood cell count and leukocyte composition.

Regarding accuracy, in the nonflagged specimen group, CD 3200 and microscopical leukocyte differential count results were closely correlated. Average bias was small for all cell types, the differences between instrument and microscopy values were within the statistical confidence limits in most samples, and no specimen with gross discrepancies could be identified. In contrast, analysis of flagged samples gave another picture; systematic bias and a considerable proportion of results clearly deviating from reference microscopy were observed.

For our study, we selected specimens with nonmalignant and malignant hematologic abnormalities to challenge the CD 3200 with a large variety of samples known to cause problems in automated leukocyte differential counting. It should therefore be made clear that our data set does not represent a sample composition likely to be encountered outside of specialized hematology units. Although comparisons with other studies are thereby made somewhat more difficult, the accuracy of CD 3200 measurements as

**TABLE 7. False-Negative CELL-DYN 3200 Results in Samples With Major Morphologic Abnormalities\***

Study Number	Microscopic Differential Abnormality	Comment
E004	14.75% variant lymphocytes, 0.75/100 NRBC	Sézary cells, 64.25% total lymphocytes, WBC = $9.4 \times 10^9/L$
G003	5% myelocytes, 3.25% metamyelocytes, 0.25% variant lymphocytes	WBC = $19.0 \times 10^9/L$
U007	14.25% band cells	
U040	6.25% band cells	
U110	9.75% band cells	WBC = $34.9 \times 10^9/L$
U112	3.75% myelocytes, 2% metamyelocytes, 0.25% variant lymphocytes	
V044	0.25% myelocytes, 0.25% metamyelocytes, 7.5% band cells, 0.25/100 NRBC	
V070	4.75% myelocytes, 1.25% metamyelocytes, 0.75% variant lymphocytes	WBC = $12.4 \times 10^9/L$
V097	2.25% myelocytes, 1.75% metamyelocytes, 0.75% variant lymphocytes	
W005	0.25% promyelocytes, 4.25% myelocytes, 1% metamyelocytes	WBC = $23.2 \times 10^9/L$
X017	0.25% metamyelocytes, 0.75% variant lymphocytes, 10.75/100 NRBC	WBC = $17.7 \times 10^9/L$ , cord blood sample, red blood cell abnormality indicated by CELL-DYN 3200

\*NRBC indicates nucleated red blood cells; WBC, white blood cells.

assessed by systematic bias, standard deviation of differences to reference microscopy, and regression coefficients largely corresponds to that described for other hematology analyzers, including Coulter STKS [11,18-20], Bayer Diagnostic H-1 [11,20,21], Sysmex NE-8000 and SE-9000 [20-22], ABX Cobas Argos [17], and Abbott CELL-DYN 3000 and CELL-DYN 3500 instruments [12,23,24].

Compared to reference microscopy, efficiency of CD 3200 testing was 88.5% when morphologic abnormalities only were considered and 90.6% when both morphologic and distributional abnormalities were taken into account. Similar diagnostic efficiencies have been found in some instrument evaluations [14,20], but most studies report lower values [12,13,19,23,25]. Discrepancies regarding sample composition and the definition of reference (microscopically) abnormal samples are difficult to exclude as causes for differences between independent studies; however, our efficiency data were obtained with a large proportion of samples showing leukocyte abnormalities, and we used a wide definition of reference (microscopical) abnormality, including some specimens that cannot reliably be recognized as abnormal by routine microscopy. These factors must be considered, too, when interpreting the morphologic false-negative ratio of 24.7%, which is somewhat above the average of other instrument evaluations. However, 12 of 23 false-negative results relate to minor abnormalities not reliably recognized by routine microscopy, and, in 4 other specimens, the main abnormality was a moderate increase of band cells, which are routinely quantified in our laboratory but were not included in many other studies. Moreover, our false-negative results included 1 case of Sézary syndrome, standing out by its high lymphocyte percentage and absolute count, and a cord blood sample with elevated nucleated red blood cells, which was indicated by a CD 3200 red blood cell flag. Therefore, false-negative CD 3200 results, possibly relevant under routine conditions, were confined to some cases with left shift, as assessed by moderate rises of immature granulocyte or band cell percentages.

In conclusion, this evaluation showed that the CD 3200 provides a precise and accurate 5-part white blood cell differential and that its diagnostic efficiency and flagging performance correspond to those of other modern hematology analyzers.

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