White Blood Cell Counts
Reference Methodology

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KEYWORDS

- Automated hematology analyzer • Methodology • Leukocyte
- White blood cell count • Differential count • Laboratory instrumentation

KEY POINTS

- Numerous technologies are used to generate the white blood cell (WBC) differential including electrical impedance, radiofrequency (RF) conductivity, light scatter, cytochemistry, fluorescent labeling, monoclonal antibodies, and automated differential cell counters.
- Most current analyzers report at least a 5-part WBC differential including neutrophils, monocytes, lymphocytes, eosinophils, and basophils.
- It is important to recognize common sources of error in the automated differential, including low cell count, nucleated red blood cells (nRBCs), platelet clumps, and clotted specimens; basophil counts in particular are prone to error.
- Hematology analyzers generate flags on specimens with abnormalities requiring further investigation; these flags are based on criteria, which must be validated by individual laboratories.
- Depending on the specific analyzer, numerous WBC parameters may be reported including nRBC ratio, hematopoietic progenitor cells (HPCs), immature granulocytes (IGs), granularity index, and lymph index.

INTRODUCTION

Historically, WBC counts were performed manually. Skilled technologists are necessary to perform this labor-intensive evaluation. Although manual cell counts are still performed in some situations, modern hematology laboratories use automated hematology analyzers to perform cell counts. These instruments provide accurate, precise, low-cost differential counts with fast turnaround times. Technologies commonly used include electrical impedance volume, RF conductivity, laser light

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Abbreviations	
FITC	Fluorescein isothiocyanate
HPC	Hematopoietic progenitor cell
IG	Immature granulocyte
LUC	Large unstained cells
nRBC	Nucleated red blood cell
PE	Phycoerythrin
PE-Cy5	Phycoerythrin-cyanine 5
RF	Radiofrequency
WBC	White blood cell

scattering, and cytochemistry. In addition to the traditional 5-part differential of neutrophils, eosinophils, basophils, lymphocytes, and monocytes, with flags for abnormal cells, newer analyzers are better able to quantify abnormal and immature cell types including reactive lymphocytes, IGs, and nRBCs. Some instruments also report a granularity index, indicating toxic granulation of neutrophils. This article reviews the principles of these methodologies and possible sources of error, provides guidance for selecting flagging criteria, and discusses novel, clinically relevant WBC parameters provided by new instruments, including IG count and granularity index and the lymphocyte index.

THE WHITE BLOOD CELL COUNT

WBC count is the number of neutrophils, lymphocytes, monocytes, eosinophils, basophils, and immature or atypical cells present in 1 μL of blood. Leukocytosis, or elevation of the WBC, can be seen in a broad range of conditions, including both benign and malignant conditions. Elevation of the WBC requires accurate differential count and morphologic evaluation of the peripheral blood smear along with clinical information to determine the cause.[1,2] Leukopenia, or decrease of the WBC, can also be caused by several conditions and requires accurate differential and morphologic examination to determine which cell line is decreased and to assess whether rare atypical or abnormal cells are present.[3]

METHODS

Historically, the WBC and differential count were determined manually. Cell counts were typically performed using a hemocytometer, a ruled counting chamber. This technique is still routinely used for assessment of cerebrospinal fluid and body fluid specimens and may be available as a backup method or for validating or calibrating automated analyzers. The specimen is diluted in a solution that lyses erythrocytes. The diluted specimen is added to the hemocytometer, a glass slide with ruled chambers of known volume. The technologist then counts the cells on a microscope with a low-power lens. The types of cells are differentiated, and nRBCs are included in the count. The hemocytometer method is prone to error, and skilled technologists are required. Manual differential counts require examination of a stained peripheral blood smear, with enumeration of 100 to 200 WBCs by category. This method is operator dependent and relies on the ability of the technologist to accurately classify cells. In addition, cells may be unequally distributed on the slide. When large cells are pulled to the feather edge of the smear, they may be underrepresented in the area counted by the technologist. There is also an inherent statistical error because the total number of cells analyzed is low.[4]

Automation of the Differential

In the 1970s, attempts to automate the cell differential relied on image analysis. Optical density thresholding was applied to digital images of cells in order to classify the cell types. These instruments were slow, limiting the number of cells counted to 100 to 200, leading to the same statistical imprecision seen in manual counts. Suspect cells required review by technologists for correct identification. These instruments were not cost effective, and development of technologies based on liquid suspensions of cells rather than stained smears became predominant.

Electrical Impedance

The first automated method for counting and differentiating cells using electrical impedance was patented in 1953 by Wallace H. Coulter, an electrical engineer, and his brother Joseph Coulter. The Coulter Corporation rapidly began producing semiautomated instruments for the analysis of peripheral blood specimens.[5] Since then, there have been several refinements and new methods to improve the accuracy of cell counts and differentials and to add additional reporting parameters. Modern analyzers use a combination of multiple techniques for cell counting and differentiation; however, the Coulter principle is still used in some manner by most analyzers.

The Coulter principle relies on electrical impedance to count and sort cells. Cells are nonconductive and produce measurable changes in electrical resistance in a conducting solution. To count and sort white cells, red blood cell lysing agents are added to the sample. Next, the specimen is diluted in an electrolyte solution, such as isotonic saline. This solution is conductive and also preserves cell size and shape. A low-voltage direct current is passed through the liquid. The cell suspension is drawn through an aperture positioned between the 2 electrodes. As cells pass through the aperture, changes in electrical resistance are measured as a voltage pulse. The number of pulses corresponds to the number of cells, and the height of each pulse is proportional to the volume of the cell. The data collected are plotted on a histogram showing the number of cells and their volumes. Thresholds can be set for exclusion of pulses above or below the desired amplitude range (Fig. 1).

Early automated instruments generated a 3-part differential based on cell size, because normal samples generally produce 3 distinct peaks on a histogram. The largest size group (>160 fL) includes mature and band neutrophils and eosinophils.
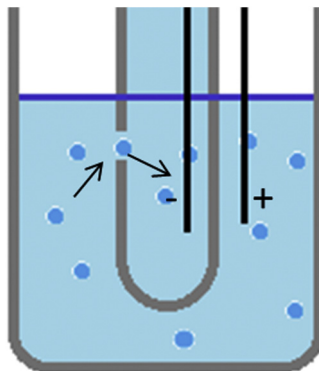

Fig. 1. Schematic diagram of Coulter principle. Cells are suspended in saline and drawn through an aperture, across which a current is flowing. As cells pass through, the current is disrupted, creating a pulse. The pulse amplitude is proportional to the size of the cell.

The intermediate size group (90–160 fL) includes monocytes, immature and mononuclear neutrophils, and eosinophils. The smallest size group (<90 fL) includes lymphocytes and basophils. nRBCs are also included in this group. Abnormal or immature cells and abnormally large populations of eosinophils obscure the distinction between these groups, resulting in inaccurate counts and error flags (Fig. 2).

Radiofrequency Conductivity

The principle of RF conductivity can be added to the Coulter principle to give more information about the internal constituents of cells, including nuclear size and density and chemical composition. A high electromagnetic alternating current is generated across the aperture. As cells pass through the aperture, this current penetrates the cell membrane. The resulting pulse amplitude depends on the cell's internal complexity. The electrical impedance and RF conductivity results are combined to classify the cell types. Cells with abnormal localization on the impedance versus RF plot generate flags and require additional review for subclassification.

Light Scattering

Laser light scattering techniques provide information about cell size and structure. These techniques are similar to those used in multiparameter flow cytometry. A flow cell detector is used to analyze light scattering produced as hemodynamically focused blood cells pass through a laser. Recording the number of times the laser is interrupted provides the cell count. The amount and angle of scatter is used to classify cells by size, refractive index, nuclear features, cytoplasmic granularity, and shape of the cell. Multiple angles of scatter are measured. Forward scatter, or 0°, corresponds to cell size. Side scatter of 10° corresponds to internal complexity. A scatter of 90° corresponds to cytoplasmic granularity. Eosinophils show a characteristic depolarized 90° scatter due refraction by their crystalline granules. In addition to classifying the 5 normal subtypes of WBCs, light scatter techniques give characteristic histogram findings for abnormal and immature cells. In addition to light scattering characteristics, WBCs exhibit characteristic autofluorescence when interrogated by the laser, which can further aid in classification (Fig. 3).

Cytochemistry

Myeloperoxidase staining can be added to light scattering techniques to provide further information about levels of intracellular peroxidase enzyme. The cells are fixed and stained using a myeloperoxidase substrate. Absorbance of white light by the stained cells is proportional to the intensity of the peroxidase reaction. The
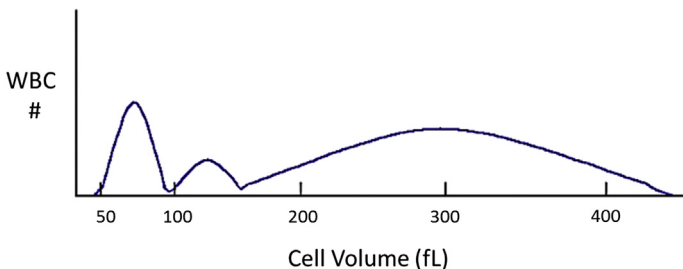

Fig. 2. Three-part differential. Cell volume is on the X-axis and the number of cells is on the Y-axis. The largest cells (>160 fL) include neutrophils and eosinophils. The intermediate cells (90–160 fL) include monocytes, immature neutrophils, and eosinophils. The smallest cells (<90 fL) include lymphocytes and basophils.
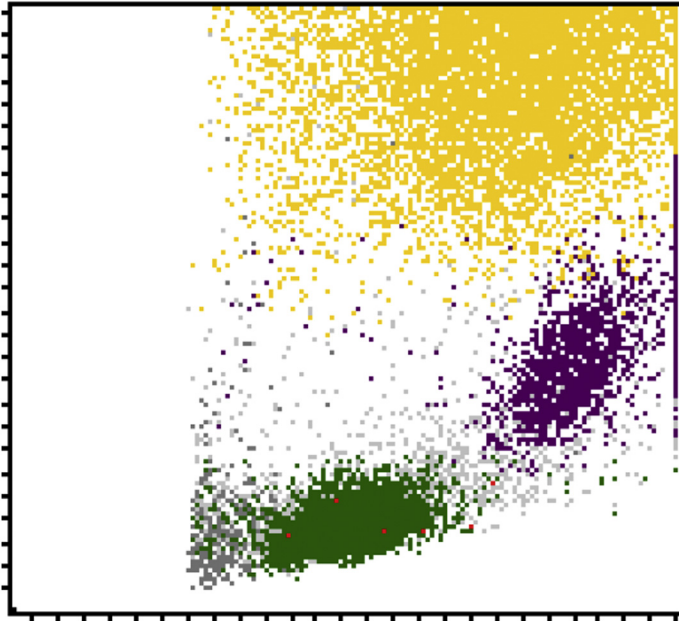
Fig. 3. This scattergram of peripheral blood forward versus side scatter shows 3 separate populations of cells, the lymphocytes (*green*), monocytes (*purple*), and granulocytes (*yellow*).

peroxidase-containing granulocytes, neutrophils, monocytes, and eosinophils give positive results, whereas lymphocytes and basophils give negative results. The cells are further subclassified by size. Large unstained cells (LUCs) may be present; this population includes activated lymphocytes, plasma cells, and blasts.

Fluorescent Labeling

Basic light scattering techniques can be augmented by the use of fluorescent dyes. These dyes stain certain cell structures. As the cells pass through the laser, the dyes emit specific wavelengths of light depending on the fluorochrome, which can be measured. RNA and DNA dyes, such as propidium iodide (PI) or polymethine dyes, are commonly used and can separate nRBCs and reticulocytes from WBCs and also give information about cell viability. PI binds to double-stranded DNA and cannot pass through the membrane of viable cells. If the cells fluoresce with PI, membrane compromise and nonviability are indicated. Cells are separated according to their side scatter and fluorescence emission characteristics to determine the cell type. Polymethine DNA staining is used in conjunction with side scatter characteristics to improve separation of populations of WBCs (**Fig. 4**).

Monoclonal Antibodies

New analyzers offer the use of fluorochrome-conjugated monoclonal antibodies to expand the information given in the cell differential. The Cell-DYN Sapphire (Abbot Diagnostics, Abbot Park, IL, USA), for example, can be used as a 3-color flow cytometer using the fluorescein isothiocyanate, phycoerythrin (PE), and PE-cyanine 5 fluorochromes. The most common panel uses CD3-, CD4-, and CD8-conjugated monoclonal antibodies to specify T-cell subsets and can report CD4 and CD8 cell counts.
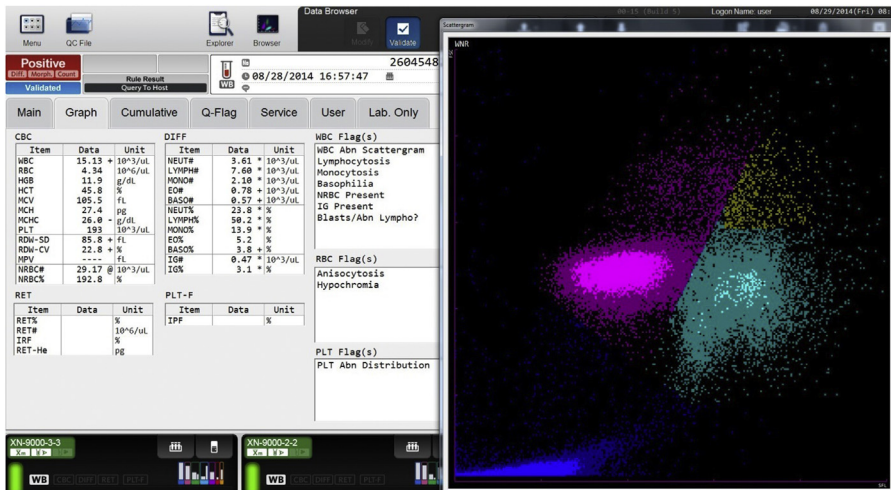
Fig. 4. Sysmex XN-9000 WNR channel. The WNR (White and Nucleated Reds) channel on the Sysmex XN-9000 differentiates cells based on fluorescent intensity and size. The cell membranes are perforated, and the nucleic acids are labeled with a fluorescent marker. The basophil population is yellow, nucleated red blood cells are pink, and other white blood cells are light blue. Debris is dark blue. This sample shows increased nucleated red blood cells.

Automated Differential Cell Counters

In cases in which abnormalities are seen on the automated differential, morphologic review by a trained technologist or pathologist is required for accurate classification. Automated digital image analysis platforms have been developed to facilitate this process. These platforms review stained blood smears and classify WBCs. Images of the cells with the assigned classifications are displayed on a monitor on which a trained technologist can quickly review the cell morphology and confirm or change the classifications. The CellaVision DM9600 automated microscope platforms (CellaVision Inc, Durham, NC, USA) can classify WBCs into 12 different categories: band neutrophils, segmented neutrophils, eosinophils, basophils, monocytes, lymphocytes, promyelocytes, myelocytes, metamyelocytes, blast cells, variant lymphocytes, and plasma cells. The technologist can further subclassify cells into additional categories. Compared with manual methods, these platforms show excellent correlation in normal cases, although accuracy is decreased in the monocyte and basophil categories. In cases with hematologic disease, accurate classification of abnormal cell types is decreased.[6]

Roche Diagnostics (Hoffmann-La Roche, Basel, Switzerland) is currently developing a platform (Cobas m 511 Bloodhound) that uses computer imaging to generate all complete blood cell count (CBC) and differential parameters. This platform generates a 5-part differential using multispectral imaging to classify cells by size, shape, color, and optical density. Abnormal cell types are reviewed by a technologist and assigned to the appropriate categories.

Automated Sampling Modes

Historically, the preparation of samples for analysis required hands-on aliquoting, mixing, and reagent addition by a technologist. Beginning in the 1980s, automated sampling modes were added to analyzers. Samples are aspirated from closed tubes, and mixing and reagent dispension occurs within the analyzer. The instrument includes

monitors to evaluate for clots and correct volumes. The addition of barcode readers improves sample identification. Algorithms can be created to initiate additional testing based on initial results, such as the addition of reticulocyte counts in a patient with anemia. Automated slide makers are available that prepare and stain blood smears when laboratory-programmed parameters, such as the presence of abnormal cells, are met. These improvements decrease hands-on time for technologists and improve throughput and efficiency.

SOURCES OF ERROR

There are several common causes of inaccurate automated WBC counts and differentials.[7] Most instruments are sensitive in detecting large populations of abnormal cells; however, when the percentage of abnormal cells drops below 5%, counts may become inaccurate and cells may not be detected. The WBC may be spuriously increased in specimens with increased nRBCs or when many unlysed red blood cells are present. Giant platelets and platelet clumps can also cause an increase in the WBC count, usually classified as a high percentage of lymphocytes. Cryoglobulin and monoclonal protein may also cause a spurious increase because of red blood cell clumping.[8] Most instruments flag the WBC when there is significant interference in the low end of the WBC size region because of these conditions. Apparent decrease in the WBC count may be seen in clotted specimens, when many smudge cells are present, and in patients with uremia.

Abnormalities of WBCs can also cause interference with other CBC parameters. A high WBC can result in a spuriously high red blood cell count and hemoglobin and hematocrit levels. Other red blood cell parameters, including the mean corpuscular volume and mean corpuscular hemoglobin, may also be affected. When WBCs are fragmented or damaged, they may falsely elevate the platelet count.[9]

Depending on the technologies used to generate the differential count, many platforms show lower correlation with manual differentials and increased between-platform variability in the counts of monocytes and basophils in particular. Neutrophil and monocyte counts may be decreased in specimens with delayed processing.[10] Platforms that use the LUC category may include normal monocytes in that group, resulting in a lower monocyte count.[11] Basophil counts performed by automated instruments are notoriously inaccurate.[12] This inaccuracy may be due in part to the low numbers of these cells in normal specimens. Most platforms rely on differential lysing agents to identify basophils, as these cells are resistant to lysis. Abnormal cells may be resistant to lysis and counted in this category. Platforms using light scattering to classify basophils, such as the CELL-DYN Sapphire, require tight gating to exclude lymphocytes from the basophil count and may underestimate the basophil percentage.[13]

REPORTING AND FLAGGING

Several parameters are used to define CBC abnormalities that require further attention, such as morphologic evaluation by a technologist or pathologist. These flags may be instrument or user defined. Most instrument manufacturers recommend thresholds, which must be validated by individual laboratories. Criteria must be selected that minimize the amount of manual blood smear review required while also minimizing the release of erroneous results. Setting the thresholds for flags requires careful consideration of the patient population being tested (Fig. 5).[14]

Suspect flags note the presence of abnormal populations of cells that cannot be accurately subclassified, resulting in an inaccurate differential. Common named flags
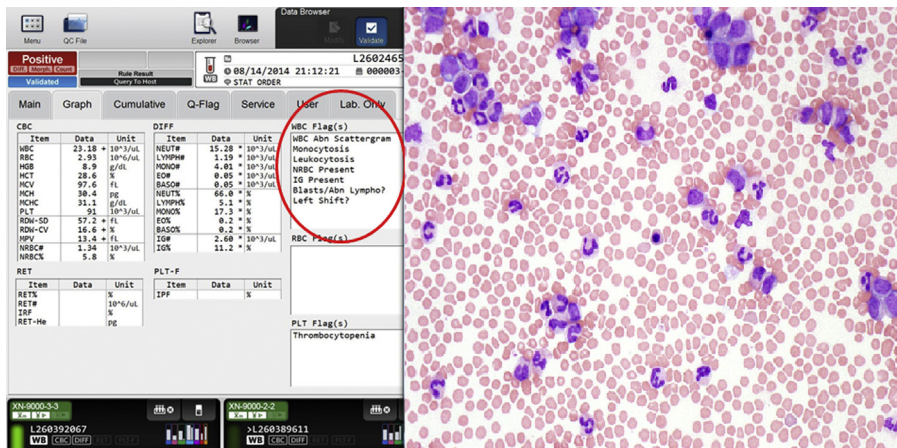
Fig. 5. WBC sample flags on a patient with chronic myelogenous leukemia. The CBC shows leukocytosis with anemia and thrombocytopenia. Immature granulocytes, blasts, and nucleated red blood cells are present on the peripheral smear.

include nRBC, clump (for platelet clumps), blast, IG, bands, left shift, and atypical lymphocyte. Suspect flags may be generated in several situations. nRBCs or platelet clumps or giant platelets may be present in the lowest forward/side scatter region for lymphocytes, resulting in an increased lymphocyte count. This will result in a clump or nRBC flag. Large mononuclear cells may be present at the monocyte/neutrophil interface or may show high 90° light scatter, resulting in a blast flag. Large cells may be seen in the lymphoid region or at the lymphocyte/monocyte interface, giving an atypical lymph or blast flag. The neutrophils may show abnormal forward or side scatter because of the presence of IGs, resulting in an IG or bands flag. When suspect flags are generated, a peripheral blood smear review by a medical technologist or, in certain cases, a pathologist, is required to validate the differential count and further define the abnormality. Studies have demonstrated that although specific flags tend to be poor predictors of the presence of specific abnormalities, the presence of a flag does correlate with the existence of any abnormality. For example, a differential flagged with atypical lymphocyte may show blasts on peripheral blood smear review.[15]

WHITE BLOOD CELL PARAMETERS

Although some small, portable analyzers still report a 3-part WBC differential including small lymphocytes and basophils, intermediate monocytes and mononuclear cells, and large neutrophils and eosinophils, modern analyzers report at least a 5-part differential with neutrophils, monocytes, eosinophils, basophils, and lymphocytes (Fig. 6). The monocyte and basophil counts are typically the least accurate and tend to underestimate the actual percentage of cells. Most analyzers also report additional parameters, which can help to identify atypical populations of cells or aid in diagnosis of certain conditions (Table 1). Inclusion of these parameters in laboratory algorithms can help to reduce the number of samples requiring manual slide review (Fig. 6, Table 2).

Nucleated Red Blood Cells

Enumeration of nRBCs is important because high levels may artificially increase the WBC count. nRBCs are found in the peripheral blood in numerous benign and
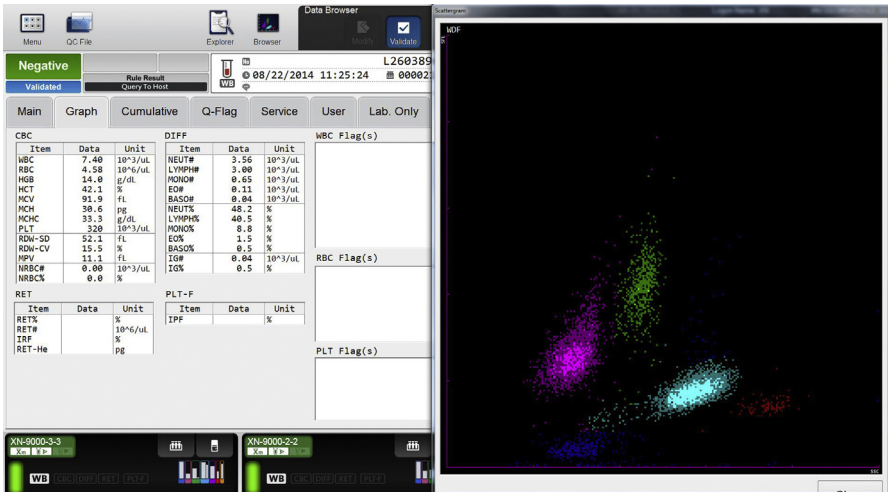
Fig. 6. A normal WBC differential from the Sysmex XN-9000 instrument. The scattergram on the right displays side scatter on the X-axis and side fluorescent intensity on the Y-axis. Monocytes (*green*) show the highest fluorescent intensity, followed by lymphocytes (*pink*), neutrophils and basophils (*light blue*), and eosinophils (*red*). Debris is colored dark blue.

malignant conditions including the neonatal period, with hemolysis, blood loss, sepsis, hematologic malignancy, and bone marrow involvement by other neoplasms. Depending on the technology used, nRBCs may be included in the lymphocyte category or present as a flag for interference in this region. More sophisticated analyzers now report nRBC as a separate category. nRBC can be identified by impedance and light scattering characteristics and high fluorescent intensity. DNA dyes can also be used. nRBCs are reported as a ratio of nRBC to WBC.[16]

Large Unstained Cells

The LUC category includes reactive lymphocytes, plasma cells, blasts, and other abnormal cells. This category is usually defined by light scatter characteristics in conjunction with myeloperoxidase activity and includes cells in the large cell area normally occupied by monocytes and neutrophils that do not exhibit peroxidase activity. In patients with decreased myeloperoxidase activity, the neutrophils will be included in the LUC population. Specimens with LUC counts require manual review of a peripheral blood smear for correct classification of these cells.

Hematopoietic Progenitor Cells

A combination of methods can be used to enumerate the percentage of HPCs. Side scatter and forward scatter characteristics can identify large cells with large nuclei. Differential lysing agents, which lyse mature cells with high membrane lipid content while preserving immature cells, may be used. DNA, RNA, and histone dyes may also be used. In addition to their use in patients with hematologic malignancy and other abnormal states, these counts can potentially be used in stem cell harvesting.[17] Typically, a flow cytometry assay for CD34 is performed to estimate the number of HPCs before leukapheresis for specimen collection. This can be time consuming and requires special equipment and trained personnel. Studies in pediatric populations have shown that the peripheral blood HPC count correlates well with CD34 flow assay, although there seems to be greater variability in adult patients particularly

Table 1
Methodologies and parameters of manufacturer instruments

Manufacturer	Selected Instruments	Methodologies	Parameters
Beckman Coulter (Beckman Coulter, Inc., Brea, CA, USA)	DxH 800 LH780 LH750	Electrical impedance RF conductivity Laser light scattering Flow cytometry	WBC count 5-part differential
Sysmex (Sysmex America, Inc, Lincolnshire, IL, USA)	XE-2100 XE-5000	Electrical impedance RF conductivity Laser light scattering Fluorescence detection	WBC count • Immature granulocytes • Blasts Granularity index
Siemens (Siemens AG, Berlin, Germany)	Advia 2120 Advia 120	Cytochemistry Laser light scattering Fluorescence detection	WBC count • Large unstained cells
Abbott (Abbott Laboratories, North Chicago, IL, USA)	Cell-DYN 4000 Sapphire CD 3500 CD3700	Electrical impedance Fluorescence detection Laser light scattering Monoclonal antibodies	WBC count Leukocyte viability • Blasts • Atypical lymphocytes • Immature granulocytes
Mindray (Mindray Medical International Limited, Shenzhen, China)	BC-6800 BC-5800	Laser light scattering Fluorescence detection	WBC count • Immature granulocytes • High-fluorescence cells[a]
Horiba (Horiba Ltd, Kyoto, Japan)	Pentra DF Nexus	Electrical impedance Light scatter Cytochemistry	WBC count • Atypical lymphocytes • Large immature cells • Immature monocytes • Immature granulocytes • Immature lymphocytes

[a] High-fluorescence cells are blasts and atypical lymphocytes.

at low HPC counts. When the count is greater than 30 HPC/μL, however, the HPC count can be used to justify collection.

Immature Granulocytes

The IG fraction includes promyelocytes, myelocytes, and metamyelocytes. Bands and blasts are not included. These cells are increased in infection, inflammation, malignancy, necrosis, trauma, steroid use, and pregnancy, among other diseases. IG counts are available on many newer instruments and have been suggested as a marker for infection and sepsis. The Sysmex XE-2100 Automated Hematology System (Sysmex America, Inc, Lincolnshire, IL, USA), for example, uses light scattering and fluorescence to identify granulocytes with a larger nuclear volume, consistent with immature cells (Fig. 7).[18]

There has been particular interest in using IG counts to discriminate between sepsis and other noninfectious inflammatory conditions, particularly in patients in intensive care units and in pediatric and neonatal patients. Rapid diagnosis of sepsis in these

Table 2
Selected white blood cell parameters and clinical utility

nRBCs	Ratio of nRBCs to WBCs	Diagnosis of anemia, hematologic malignancy, and other disease states
Large unstained cells	Reactive lymphocytes, plasma cells, blasts, other abnormal cells	Diagnosis of hematologic malignancy and other disease states
Hematopoietic progenitor cells	Myeloblasts	Quantification for stem cell harvest, diagnosis of hematologic malignancy and other disease states
Immature granulocytes	Promyelocytes, myelocytes, metamyelocytes	Diagnosis of bacterial infection and sepsis in pediatric and critically ill patients
Granularity index	Degree of neutrophil granulation (hypogranular vs toxic granulation)	Diagnosis of dysplasia, bacterial infection
Lymph index	Reactive lymphocytes	Diagnosis of viral infection

patient groups can be difficult; however, early diagnosis is vital to guide life-saving interventions. Several studies have shown that a significantly increased IG count is specific for infection in patients in intensive care units; however, the sensitivity is lower.[19] Studies attempting to relate IG level to severity of disease and morbidity and mortality have not clearly demonstrated a correlation.[20] The findings are less clear in neonatal populations, however, because healthy neonates have high IG counts.[21] Further characterization of normal IG counts in this age range is required. In addition to infection, this parameter is also being evaluated for a possible role in identifying patients with myelodysplastic syndromes and myocardial infarction, among other conditions.
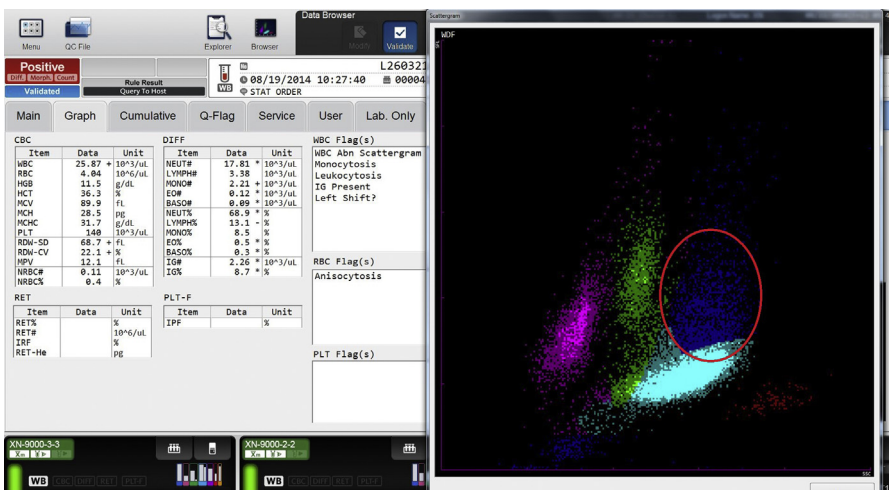

Fig. 7. Scattergram from a patient with immature granulocytes. The immature granulocyte population is dark blue. These cells have higher fluorescent intensity and greater mean volume than the mature granulocytes, shown in light blue.

Granularity Index

In situations in which neutrophil production is stimulated, circulating neutrophils exhibit toxic changes including distinct azurophilic granules in the cytoplasm. Hypogranularity is a dysplastic feature seen in myelodysplastic syndromes and other myeloid malignancies. Morphologic determination of neutrophilic granulation can be highly subjective, particularly in the case of toxic granulation. Using side scatter characteristics, analyzers such as the Sysmex XE-2100 can give a measurement of the granularity of neutrophil cytoplasm. This parameter has been shown to correlate with the grade of toxic granulation or hypogranularity, as determined by morphologic evaluation. Studies have shown that the granularity index increases along with C-reactive protein levels in infection.[22] A low granularity index, particularly in conjunction with other CBC abnormalities such as anemia, platelet distribution width, and standard deviation of red blood cell distribution width, is specific but not sensitive for dysplasia and can help identify specimens for manual slide review.[23] A combination of the granularity index, IG count, and hematopoietic precursor cell count may be even more useful.

Lymph Index

The lymph index relies on impedance, RF, and light scattering to define morphologically distinct populations of lymphocytes. Impedance gives information for cell volume, RF about cytoplasmic chemical composition and nuclear volume, and light scattering about cytoplasmic granularity and nuclear structure. The lymphocyte index is defined as the lymphocyte volume times the lymphocyte volume standard deviation divided by the lymphocyte conductivity. In viral infections, the lymphocyte population shows increased large cells, an increased range of sizes of lymphocytes (lymphocyte volume standard deviation), and decreased conductivity, resulting in an increased lymphocyte index. This may be useful in distinguishing viral from bacterial infection, which is associated with a lower lymphocyte index (Fig. 8).[24]
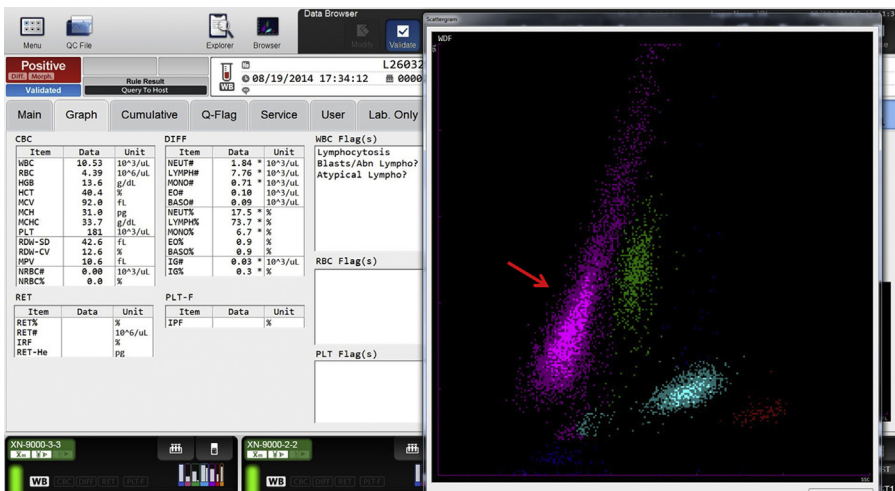

Fig. 8. This report is from a patient with Epstein-Barr virus infection. There is lymphocytosis, and the scattergram shows an abnormal lymphocyte pattern (*pink*) with a greater range of size and fluorescent intensity than the normal pattern.

SUMMARY

Automated hematology analyzers can now use a combination of different technologies to increase the information provided with CBC and differential testing. Understanding the abilities and limits of these instruments is necessary for appropriate triage and reporting of specimens. New parameters can allow for improvement of manual smear review algorithms and aid in diagnosis of benign and malignant conditions.

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