For WBC differentials, report in absolute numbers

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Feature Story
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Historically, leukocyte (white blood cell) differentials have been reported in proportional (percentage) numbers, probably because only manual smear methods were available initially for WBC differential analysis. Currently, WBC differentials are performed primarily on automated hematology analyzers, with these instruments providing the proportional differential as well as absolute counts for the various WBC types, including neutrophils, lymphocytes, monocytes, eosinophils, and basophils. In addition, these instruments can be interfaced with the laboratory information system; the differential counts are easily transferred across the interface to the laboratory and hospital information systems.

The CAP provides proficiency testing for automated analyzer reporting of the leukocyte (WBC) differential. On the most recent CAP automated instrument Surveys in 2009, 94.8 percent of participants reported WBC differential results as a percentage and 5.6 percent reported absolute numbers, including a small percentage of laboratories that reported both. While these proficiency testing results may not entirely reflect current practice, it appears that many laboratories in the United States are continuing to report WBC differentials as a proportion rather than as an absolute number.

Unfortunately, for clinical interpretation, these WBC proportions must be converted to absolute numbers by multiplying the percentage of a given WBC type (for example, neutrophils) by the overall WBC count. There is potential for error if this conversion is performed outside the laboratory by the clinical services. Generally, clinically relevant WBC elevations ("cytoses") and declines ("cytopenias") are defined by their absolute numbers, not by their relative proportions. Based on this, current recommendations, including those of the CAP Hematology and Clinical Microscopy Resource Committee and the Clinical and Laboratory Standards Institute, state that the absolute count is the preferred reporting method for the WBC differential.

While generally not necessary for clinical assessment, the percentage result could also be reported in conjunction with the absolute value if so desired. Of note, classification of various hematopoietic neoplasms, including acute leukemias, myelodysplastic syndromes, myeloproliferative neoplasms, and myelodysplastic/myeloproliferative overlap disorders, depends on the proportion (percentage) of blasts present. In these situations it may also be appropriate to denote the blast percentage within an interpretive comment.

Let's take a brief look at how alterations in WBC absolute differentials may aid diagnosis and clinical decision making:

Absolute neutrophil count (ANC). The functional ANC includes the absolute number of segmented neutrophils and bands.

Neutrophilia (>6.8 × 10^9/L for adults in our laboratory) is associated with infections, a variety of inflammatory disorders, cytokine therapy, and some myeloid neoplasms. Neutropenia (<1.8 × 10^9/L for adults in our laboratory) can be seen with various medications, including chemotherapy, toxins, bone marrow replacement (for example, metastatic tumor, granulomas), myelodysplastic syndromes, autoimmune disorders, and congenital disorders. Generally, the degree of neutropenia defines the patient’s risk of infection.

For example, an ANC less than 0.5 × 10^9/L is associated with a significantly increased propensity for serious infection; a patient with this degree of neutropenia and a fever most often requires parenteral antibiotics. Patients with an ANC of 0.5–1.0 × 10^9/L have some propensity for infection but often can be managed as an outpatient.

Absolute lymphocyte count. Lymphocytosis (>3.4 × 10^9/L for adults in our laboratory) may be noted in a variety of disorders, including infections, in particular viral infections, autoimmune diseases, and lymphoproliferative disorders.

For example, a diagnosis of chronic lymphocytic leukemia requires a clonal lymphocytosis of 5.0 × 10^9/L for at least three months (in the absence of extramedullary disease).

Absolute monocyte count. Monocytosis (>0.8 × 10^9/L for adults in our laboratory) may be seen with chronic myelomonocytic leukemia (CML), acute myeloid leukemias, chronic infections, autoimmune disorders, cytokine therapy, carcinoma, and as a response to neutropenia.

For example, one criterion necessary for a diagnosis of CML is an absolute monocyte count of 1.0 × 10^9/L.

Absolute eosinophil count. Eosinophilia (>0.4 × 10^9/L for adults in our laboratory) can occur with allergic or atopic disease, infectious disorders (including parasites), medications, immunologic reactions, skin disorders, pulmonary syndromes, rheumatologic diseases, myeloproliferative neoplasms, and secondary to other malignancies.

For example, one criterion required for a diagnosis of chronic eosinophilic leukemia is an absolute eosinophil count 1.5 × 10^9/L.

Absolute basophil count. Basophilia (>0.1 × 10^9/L for adults in our laboratory) may be associated with myeloproliferative neoplasms, hypersensitivity reactions, hypothyroidism, iron deficiency, and renal disease.

Here are a few case examples:

Case 1: Mr. Jones is a 54-year-old man with a fever and fatigue. The CBC shows a WBC of 2.0 × 10^9/L with the following differential:

- Neutrophils 40% (40–70%)
- Lymphocytes 50% (15–45%)
- Monocytes 10% (0–12%)
- Eosinophils 0% (0–7%)
- Basophils 0% (0–2%)

Based on review of this proportional differential and its associated reference range, one could conclude the patient has lymphocytosis (albeit relative) and pursue diagnostic considerations based on this result. Many of us have been witness to clinical conversations similar to this. If these differential results are converted to absolute values, the following data would be more appropriately evaluated:

- Neutrophils $0.80 \times 10^9/L$ (1.8–6.8 $\times 10^9/L$)
- Lymphocytes $1.00 \times 10^9/L$ (1.0–3.4 $\times 10^9/L$)
- Monocytes $0.20 \times 10^9/L$ (0.2–0.8 $\times 10^9/L$)
- Eosinophils $0.00 \times 10^9/L$ (0.0–0.4 $\times 10^9/L$)
- Basophils $0.00 \times 10^9/L$ (0.0–0.1 $\times 10^9/L$)

Now we can easily recognize that the patient has a moderate neutropenia and may be at risk of infection. In addition, we now focus our diagnostic considerations on the causes of neutropenia. We also recognize that the patient does not have a true lymphocytosis, as the absolute lymphocyte count is at the lower end of the reference range.

Case 2: Ms. Smith is a 62-year-old woman with a history of rheumatoid arthritis who presents with a two-month history of increasing fatigue. The CBC shows a WBC of $80.0 \times 10^9/L$ with the following differential:

- Neutrophils 70% (40–70%)
- Immature granulocytes 20% (none)
- Lymphocytes 4% (15–45%)
- Monocytes 1% (0–12%)
- Eosinophils 4% (0–7%)
- Basophils 1% (0–2%)

Based on the proportional differential, we can see that immature granulocytes are increased and lymphocytes are proportionally decreased. In comparison, the differential in absolute numbers shows the following:

- Neutrophils $56.00 \times 10^9/L$ (1.8–6.8 $\times 10^9/L$)
- Immature granulocytes $16.00 \times 10^9/L$ (none)
- Lymphocytes $3.20 \times 10^9/L$ (1.0–3.4 $\times 10^9/L$)
- Monocytes $0.80 \times 10^9/L$ (0.2–0.8 $\times 10^9/L$)
- Eosinophils $3.20 \times 10^9/L$ (0.0–0.4 $\times 10^9/L$)
- Basophils $0.80 \times 10^9/L$ (0.0–0.1 $\times 10^9/L$)

Now we can easily recognize that the patient has neutrophilia with left shift, eosinophilia, and basophilia. This constellation of findings raises concern for a myeloproliferative neoplasm, such as chronic myelogenous leukemia, since reactive neutrophilia usually is not accompanied by eosinophilia and basophilia.

As these cases illustrate, the proportional differential with corresponding reference ranges may not accurately reflect clinically relevant WBC alterations in the patient. Since most "cytoses" and "cytopenias" are defined by the absolute number of a type of WBC, the CAP Hematology and Clinical Microscopy Resource Committee recommends reporting the WBC differential results in absolute numbers rather than in percentages, including results on proficiency tests. For most laboratories, the proficiency test information reported to the Centers for Medicare and Medicaid Services to meet CLIA regulatory requirements will remain unchanged since reporting of cell identification results from photopages is still appropriate for any laboratory that checks automated differentials by manual smear review. If manual methods are not used, laboratories can elect to have automated differential results reported to the CMS as absolute numbers or percentages.

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