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Criteria for Blood Smear Review

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After reading this article, the reader should be able to understand the who, what, where, when, and why of a blood smear review. Hematology exam 0201 questions and answer forms are located after the "Your Lab Focus" section, p. 387.

- Blood smear review is defined as a microscopic examination of an appropriately prepared and stained blood smear by a qualified hematomorphologist.
- Blood smear review can serve as a quality control tool or as a means to assess competency of the technical staff.

Complete blood count (CBC) and white cell differential (diff) are the 2 most frequently performed hematologic tests in the clinical laboratories. Automated hematology analyzers, when appropriately calibrated, generate reliable results for both of these tests on many blood specimens. The results of a significant proportion of specimens are flagged by the analyzers, however, and require confirmation by other techniques. One of these techniques is the microscopic examination of blood smear, generally known as "manual diff." The number of manual diffs performed daily by clinical hematology laboratories of many tertiary care medical centers is quite large. Quality control of the CBC and automated diff is made easy and practical by the availability of commercial reference materials. In contrast, for the manual diff, a common means of quality control is the review of selected blood smears by a qualified individual.[1-3] This type of review meets the accreditation requirement of the Commission on Laboratory Accreditation (CLA) of the College of American Pathologists (CAP). The Commission on Laboratory Accreditation of the CAP requires each laboratory to have a list of criteria specific for blood smears that must be reviewed.[4] In this article, the authors discuss the issue of blood smear review and provide a list of review criteria which may be used as a guide by hematology laboratories.

What Is a Blood Smear Review?

Blood smear review, for the purpose of this article, is defined as a thorough and careful microscopic examination of an appropriately prepared and stained blood smear by a qualified hematomorphologist. After verifying the quality of the smear and stain, the reviewer will examine the smear for clinically significant findings. All abnormalities should be noted, suspected as well as unsuspected, blood cells-related or otherwise. A complete examination should include observation under both low (x100) and high magnification (x500 and/or x1000).

The morphology of all cellular elements is reviewed in addition to verification of the results obtained for the CBC and differential. The end product is the confirmation or revision of the CBC and diff results. Additionally for new cases, a written report should be generated by a laboratory physician providing interpretation of hematologic and other available pertinent laboratory and clinical findings. Manual diff and blood smear review, while similar to each other, do differ in certain aspects.

A manual diff does not include interpretation by a laboratory physician, whereas blood smear review does, especially for new cases. Manual diffs are usually performed on specimens that are either flagged by the automated analyzer or reveal significant abnormalities in the CBC or automated diff results; whereas blood smear reviews are performed only on cases selected mainly for clinically significant findings in the CBC and/or manual diff. A manual diff, which is classified as a high complexity test by the federal government, may be performed by an associate degree holder with an appropriate clinical laboratory training; whereas the blood smear review, according to the CLA of the CAP, must be performed by a hematomorphologist.

What Purpose Does the Blood Smear Review Serve?

Besides meeting accreditation requirement, review of blood smears by a well-trained and experienced hematomorphologist serves several functions that are essential to patient care. It serves as a quality control/quality assurance (QC/QA) tool for CBC, diff, and reticulocyte count results. It can be used to assess competency of the technical staff performing manual diffs. Blood smear review allows appropriate interpretation of CBC and manual diff data with other available laboratory findings and clinical information. Such an interpretation may provide a definite diagnosis or suggest a strategy for additional work-up of the case in an efficient and cost-effective manner. Finally, it serves as an excellent hematology teaching resource for training students and staff, and in the continuing education of technical staff.

Proposed criteria for blood smear review (for adults)

T1

Criteria		Initial Smears	Follow-up Smears
CBC			
WBC (x 10^9/L or 10^3/µL)	>30	yes	no
HGB (g/dL)	< 6 or >18	yes	no
MCV (fL or cmm)	< 75 or >105	yes	no
MCHC (g/dL or %)	> 36	yes	no
PLT (x 10^9/L or 10^3/µL)	< 50 or > 999	yes	no
Differential			
Lymphocyte # (x 10^9/L or 10^3/µL)	> 4.0	yes	no
Monocyte # (x 10^9/L or 10^3/µL)	> 2.0	yes	no
Eosinophil # (x 10^9/L or 10^3/µL)	> 1.0	yes	no
Basophil (%)	> 4	yes	yes
Atypical lymph (%)	> 10	yes	yes
Blasts (%)	any	yes	yes
Promyelocytes (%)	> 3	yes	yes
Myelocytes (%)	> 5	yes	yes
Metamyelocytes (%)	> 10	yes	yes
Other abnormal or unidentifyable cells	any	yes	yes
NRBC (# per 100 WBC)	> 2	yes	no
Organisms	any	yes	yes
Significant morphological abnormality of RBC, WBC, and/or PLT*		yes	no
Blood Smear Review requested by clinician		yes	yes

**Significant morphologic abnormalities:*

RBC (red blood cells):

Anisocytosis ≥ 3+, Poikilocytosis ≥ 3+, Hypochromasia ≥ 3+, Polychromasia ≥ 3+

Basophilic stippling ≥ 3+, Elliptocytes ≥ 3+, Stomatocytes ≥ 3+

Microcytes ≥ 2+, Macrocytes ≥ 2+, Target cells ≥ 2+, Rouleaux ≥ 2+

Tear drop cells ≥ 1+, Schistocytes ≥ 1+, Spherocytes ≥ 1+, Acanthocytes ≥ 1+

Sickle cells any, Howell jolly bodies any, Pappenheimer bodies any, agglutination any

WBC (white blood cells):

Dohle bodies ≥ 3+, Hyposegmented neutrophils ≥ 2+,

Hypersegmented neutrophils ≥ 1+

Hypogranular granulocytes any, Auer rods any

PLT (platelets):

Giant platelets ≥ 2+, platelet satellitosis ≥ 1+

Who Should Specify the Criteria for Review?

A standard set of criteria developed by a professional organization such as the CAP is perhaps what the clinical laboratories would like to have. Although feasible, such a set of criteria may not be workable in its entirety for all laboratories. It would have to be based solely on the clinical significance of abnormal CBC and diff findings and could serve only as a recommended guide. Until such a set of criteria becomes available, laboratory professionals need to rely upon their own knowledge, experience, and judgment in developing the list of criteria most suited to the needs of the patient population as well as to the concerns of the clinicians, and to the level of expertise of the technical staff at their institution.

Proposed manual diff delta values for selecting follow-up blood smears for review

T2

Manual Diff Parameter	Result Value (%)	Delta Value (#)
Neutrophils	NA	NA
Bands	30	20
Lymphocytes	NA	NA
Monocytes	20	20
Eosinophils	20	20
Basophils	10 4	10 4
Atypical Lymphocytes	20 10	15 10
Metamyelocytes	20 10	20 10
Myelocytes	20 5	10 5
Promyelocytes	10 3	10 4
Blasts	20 10 5	20 10 5
Plasma Cells	20 10 5	20 10 5
NRBC* (per 100 WBC)	100 75 50 25	50 25 20 15

**Nucleated red blood cells*

Explanation for Delta Values Set-up in Laboratory Information System, using the example of NRBC in Table 2:

A delta value represents the degree of change from the latest previous result. The degree of change could be in absolute # or as a fraction in percentage. Furthermore the degree of change could be set at different levels for different levels of results of any given test parameter. In the NRBC example in Table 2, the delta check function will look for a change in absolute terms of 15 if the NRBC result is below 25 (0 to 24 per 100 WBC). In other words, if the current result for NRBC is 21 and the previous result for NRBC is 5, ie, a difference of 16 (21 minus 5), a delta failure will occur and can be set to generate a reflex order for smear review. In the same example, if the result for NRBC is 25 or more but less than 50, the delta check function will look for a change in absolute terms of 20. Since delta checks looks for a change irrespective of its direction (increase or decrease), some of the smears for review will have normal diff results.

A laboratory physician, preferably a hematopathologist, is the person most suited to specify the criteria for blood smear review. However, input from the clinical staff and other qualified laboratory professionals, such as a doctoral scientist, supervisor, or senior technologist(s) should also be utilized.

What Factors Should Form the Basis for Review Criteria?

Clinical significance of the abnormal CBC and/or manual diff findings is the major determining factor in deciding which blood smears need review. Nonetheless, several other factors often contribute to such a decision. These factors may vary among institutions, but often include some or all of the following: (i) the patient population served, (ii) concerns of clinicians, particularly those pertaining to specific patient populations (eg, hematology/oncology patients), (iii) the training and experience of the laboratory physician(s), (iv) the workload of the laboratory physician(s), (v) the availability of the additional supervisory staff, (vi) the training and experience of the additional supervisory staff, (vii) the training and experience of the technical staff performing CBCs and manual diffs, (viii) the workload of the staff in the hematology laboratory, (ix) the possibility of subtle changes in the blood smear, which may be missed even by skilled laboratory personnel, (x) initial vs follow-up blood smear(s), and (xi) teaching/educational considerations.

What Review Criteria Are Currently Used?

A Medline literature search and review of the pertinent hematology and clinical pathology books revealed few references that outline specific criteria for blood smear review by pathologists or other qualified laboratory professionals.

The laboratory at the authors' place of work currently uses 2 sets of criteria for blood smear review, 1 for

initial smears and the other for follow-up smears. The interpretation of laboratory findings, though a major objective of the blood smear review, is understandably most important on initial smears. The follow-up smears of a given patient may require interpretation, but only in case of significant change(s) in laboratory findings and/or clinical condition. The set of review criteria for initial smears is based on clinically significant findings of both the CBC and differential. The review criteria for follow-up smears, for the purposes of QC/QA and competency evaluation, are based solely on clinically significant findings of the differential [T1]. Furthermore, the criteria for review of follow-up smears may be based on either the actual results [T1] or changes in results flagged by delta checks of selected manual diff parameters [T2]. The selection of the proposed delta values outlined in T2 was guided by 3 factors, (a) clinical significance of change in results of individual parameters, (b) inherent imprecision of manual diff results,[5] and (c) authors' personal experience with the use of different delta values over time. Irrespective of the set of criteria employed, good QC/QA practice requires that a few smears with normal manual diff results are also routinely reviewed in addition to the smears selected for abnormal findings. Both sets of criteria, as outlined in T1 and T2, meet this QC/QA requirement of reviewing a few smears with normal diff results. Based on the criteria in T1, it is not uncommon to occasionally get smears for review which have abnormal CBC finding(s) but normal diff results. Similarly, the criteria in T2 also regularly flag some smears for review with normal diff results because the delta-check failure can occur with either an increase or decrease in results over the predefined level. Both sets of criteria for follow-up smears have yielded an approximately equal number of total slides for review. Our laboratory is currently using the criteria outlined in T1 for adults. One modification (MCV <70 or >110) has been made to suit our patient population and our workload. For newborn babies up to the age of 1 week, the HGB, MCV, and NRBC criteria are changed to <14 or >26; <90 or >130; and >30 per 100 WBC, respectively. The lymphocyte criteria for children up to the age of 6 is set at 8 x 10^9/L. For reasons of availability and clinical significance, absolute numbers rather than relative percentages are utilized for lymphocytes, monocytes, and eosinophils. On the other hand, relative percentage rather than absolute number of basophils was included because of an undesirable false positive rate for basophils. For patient populations that come frequently to the hospital for care or check-up, such as those with chronic disorders, blood smear review by a pathologist is performed only once per year unless a clinically significant change from the previous review is noted.

Who Should Perform the Blood Smear Review?

Blood smear review for the purpose of quality assurance and competency assessment, while meeting accreditation requirement, may be performed by a laboratory professional qualified as a hematomorphologist. Such a laboratory professional could be a pathologist, supervisor, or senior technologist, who, in the judgment of either the Laboratory Director or the Director of the Hematology Laboratory, has demonstrated expertise in blood cell morphology and quality assurance. However, for the purpose of interpretation of laboratory findings to help clinicians diagnose and monitor their patients in an optimal and cost-effective way, an appropriately trained and/or experienced laboratory physician or doctoral scientist, preferably a hematopathologist, is desirable.

How Often Should Smears be Reviewed for QC?

As a matter of good professional practice and to meet requirements of accrediting/regulatory agencies, the QC/QA of manual diff should be performed daily on a fraction of smears encompassing work performed during all 3 shifts. To our knowledge, there is no rule indicating the number of smears to be reviewed daily for the sole purpose of QC/QA. However, based on our experience with using the sets of criteria illustrated in T1 and T2, a 600 bed tertiary care center with a daily workload of approximately 700 CBCs and 185 manual diffs would review approximately 8% (range of 5% to 10%) of blood smears daily. Initial and follow-up smears with significant change(s) from previous results requiring interpretation by a laboratory physician represent approximately 3% (range of 2% to 5%) of all blood smears. The remaining 5% represent an adequate number for QC/QA of manual diffs. Reviews performed on initial or follow-up smears by qualified personnel can automatically serve the purpose of staff competency assessment provided appropriate documentation is kept. Such documentation should reveal that over a period of time (usually 1 year) the competency of all personnel involved in performing manual diffs has been verified and appropriate corrective action has been taken, when necessary. The use of smears selected for review, particularly the initial smears, for the training of pathology residents, hematopathology fellows, medical students, medical technology students, and others, serves as a useful teaching and continuing education resource.

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