ICSH Recommendations for the Standardization of Nomenclature and Grading of Peripheral Blood Cell Morphological Features

Stefanie L. McFadden
ICSH Morphology Panel Co-Chair
Issues – lack of

- Consistent terminology
- Consistent definitions
- Consistent reporting
- Consistent grading

This is often the case
- Between Countries
- Between States/Counties/Provinces
- Between Cities
- Within Cities
- Within the same hospital system
Value to Physicians

- Need consistent terminology
- Need consistent methods of reporting and grading

- Physicians need dependable/reproducible **information** in order to better treat patients
Why is this important

- Changes over the years:
  - Consolidation of facilities
  - Hub and Spoke Laboratories
  - Core Laboratories
  - Health Care System with multiple hospital laboratories
    - Within the same town
    - Within the same state
    - Across different states
    - Across different countries
Current Status – Wide Variation

- Various literature
- Local regional publications from national societies:
  - College of American Pathologists (CAP)
  - United Kingdom National External Quality Assessment Service (UKNEQAS)
  - Japanese Society for Laboratory Hematology
  - Royal College of Pathologists of Australasia Quality Assessment Programs (RCPA QAP)
Global Consensus

- Need recognized for a global consensus guideline dealing with cell morphology.

- The aim of this ICSH committee is to provide a guideline for the nomenclature and the grading of red cell, white cell and platelet abnormalities.
Investigation Method

- An international group of morphology experts was sought from Europe, America, Australasia and Asia.
  - Pathologists, hematologists and scientists with blood film morphology expertise

- Initial Survey on blood film morphology and grading

- Survey results were discussed at a full day meeting in New Orleans USA (May 2011)
  - Outcome: Recommendations and further investigation
Features of paper

Standardization of Peripheral Blood Cells for Red Blood Cells, White Blood Cells and Platelets

- Cell Nomenclature with morphology descriptors
- Association of the cell name with the image number on the two websites for easier reference
- Morphology Grading
Cell Nomenclature / Morphology

- Consensus terminology
- Alternative terminology (when applicable)
- Description of cell morphology
- Medical Relevance
- Table for common Red Cell Synonyms
Analyzer Grading

- Encourage the use of grading some cell morphology using analyzer parameters
  - Higher level of accuracy and precision compared with observer use of the optical light microscope

- Examples for Red Cell Size
  - Mean cell volume (MCV) for microcytosis and macrocytosis
  - Mean cell hemoglobin (MCH) for hypochromia and hyperchromia
Analyzer Grading

- It is important for the laboratory to establish policies to review peripheral blood smears for abnormalities when the full blood count (FBC) data contain test results that indicate pathologies which must be investigated.

- Example for Review Policy:
  - MCV < 70 Review by manual microscopy
  - MCV > 110 Review by manual microscopy
Grading of Morphological Features

- Provide the clinician with **useful information** regarding the status of any abnormality in the peripheral blood.

- Morphology grading table contains a two-tiered grading system
  - 2+ (moderate)
  - 3+ (many)

- 1+ (few/rare) is reserved only for schistocytes, as the observation even in small numbers is clinically significant.

- Each laboratory or laboratory system should have policies in place to ensure the **consistent application of the grading criteria**.
### Morphology Grading Table

<table>
<thead>
<tr>
<th>Cell Name</th>
<th>Few/1+</th>
<th>Mod/2+, %</th>
<th>Many/3+, %</th>
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</thead>
<tbody>
<tr>
<td>RBC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anisocytosis</td>
<td>N/A</td>
<td>11–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Macrocytes</td>
<td>N/A</td>
<td>11–20</td>
<td>&gt;20</td>
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<tr>
<td>Oval macrocytes</td>
<td>N/A</td>
<td>2–5</td>
<td>&gt;5</td>
</tr>
<tr>
<td>Microcytes</td>
<td>N/A</td>
<td>11–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Hypochromic cells</td>
<td>N/A</td>
<td>11–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Polychromasia</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Acanthocytes</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Bite cells</td>
<td>N/A</td>
<td>1–2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Blister cells</td>
<td>N/A</td>
<td>1–2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Echinocytes</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Elliptocytes</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Irregularly contracted cells</td>
<td>N/A</td>
<td>1–2</td>
<td>&gt;2</td>
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<tr>
<td>Ovalocytes</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Schistocytes</td>
<td>&lt;1 %</td>
<td>1–2</td>
<td>&gt;2</td>
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<tr>
<td>Sickles cells</td>
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<td>1–2</td>
<td>&gt;2</td>
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<tr>
<td>Spherocytes</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Stomatocytes</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
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<tr>
<td>Target cells</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
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<tr>
<td>Teardrop cells</td>
<td>N/A</td>
<td>5–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Basophilic stippling</td>
<td>N/A</td>
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<td>&gt;20</td>
</tr>
<tr>
<td>Howell-Jolly bodies</td>
<td>N/A</td>
<td>2–3</td>
<td>&gt;3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cell Name</th>
<th>Few/1+</th>
<th>Mod/2+, %</th>
<th>Many/3+, %</th>
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</thead>
<tbody>
<tr>
<td>WBC</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Döhle bodies</td>
<td>N/A</td>
<td>2–4</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Vacuolation (neutrophil)</td>
<td>N/A</td>
<td>4–8</td>
<td>&gt;8</td>
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<tr>
<td>Hypogranulation (neutrophil)</td>
<td>N/A</td>
<td>4–8</td>
<td>&gt;8</td>
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<tr>
<td>Hypergranulation (neutrophil)</td>
<td>N/A</td>
<td>4–8</td>
<td>&gt;8</td>
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<tr>
<td>Platelets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giant Platelets</td>
<td>N/A</td>
<td>11–20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Nomenclature</td>
<td>Synonym</td>
<td>Common clinical conditions associated with</td>
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<td>-------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Acanthocyte</td>
<td>acanthoid cell, astrocyte, burr cell, prickle cell, pyknocyte, star cell, spur cell, thorn cell</td>
<td>Liver disease, vitamin E deficiency, postsplenectomy, abetalipoproteinaemia, McLeod RBC phenotype</td>
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<tr>
<td>Basophilic stippling</td>
<td>punctate basophilia</td>
<td>Lead poisoning, haemoglobinopathies, thalassaemia, abnormal haem synthesis, G6PD deficiency</td>
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<tr>
<td>Bite cell</td>
<td>keratocytes</td>
<td>Oxidative haemolysis, G6PD deficiency</td>
<td></td>
</tr>
<tr>
<td>Blister cell</td>
<td>puddle cell, eccentrocyte</td>
<td>Liver and renal disease, pyruvate kinase deficiency, storage artefact</td>
<td></td>
</tr>
<tr>
<td>Echinocyte</td>
<td>berry cell, burr cell, crenated cell, mulberry cell, poikilocyte, pyknocyte, spiculated cell, spur cell, sputnik cell, star cell</td>
<td>Hereditary elliptocytosis, iron deficiency</td>
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</tr>
<tr>
<td>Elliptocyte</td>
<td>bacillary cell, cigar or rod shaped cell, ovalocyte, pencil cell</td>
<td>Hyposplenism, postsplenectomy, haemolytic anaemia, megaloblastic anaemia</td>
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</tr>
<tr>
<td>Howell-Jolly body</td>
<td></td>
<td>Iron deficiency, thalassaemia, G6PD deficiency, haemoglobinopathies</td>
<td></td>
</tr>
<tr>
<td>Hypochromic cell</td>
<td>anulocyte, pessary form, ring form</td>
<td>B12/folate deficiency, liver disease, MDS</td>
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</tr>
<tr>
<td>Irregularly contracted cell</td>
<td></td>
<td>Iron deficiency, thalassaemia, Hereditary elliptocytosis, iron deficiency</td>
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</tr>
<tr>
<td>Macrococyte</td>
<td>macronormocyte, megalocyte</td>
<td>Sideroblastic anaemia, haemoglobinopathies, hyposplenism</td>
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</tr>
<tr>
<td>Microcyte</td>
<td>micronormocyte</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovalocyte</td>
<td>bacillary cell, cigar or rod shaped cell, elliptocyte</td>
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<td></td>
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<tr>
<td>Pappenheimer bodies</td>
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Images Repository

- www.morphology.mmu.ac.uk
- www.icsih.org
Morphology Images

Supplementary images: ICSH Recommendations for Peripheral Blood Cell Morphology

http://www.morphology.mmu.ac.uk/

ICS什 Cell Images

ICS什 Recommendations for the Standardization of Peripheral Blood Cell Morphology, Nomenclature and Grading

Image Set of typical morphological forms

International Council for Standardization in Haematology
### PUBLISHED STANDARDS

<table>
<thead>
<tr>
<th>Publication Date</th>
<th>File Download</th>
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<td>2015</td>
<td><strong>Download</strong></td>
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<td>2015</td>
<td><strong>Download</strong></td>
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- **ICSH guidelines for the laboratory diagnosis of nonimmune hereditary red cell membrane disorders.**
- **Supporting Information**
- **ICSH recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features.**
ORIGINAL ARTICLE

ICSHE recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features

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Stomatocytes

- Supplementary image S10

- Stomatocytes are uni-concave, cup-shaped red blood cells that appear on a stained blood film with a slit-like area of central pallor.

- In South East Asian ovalocytosis, the stomatocytes may have two stomas per cell which may be longitudinal, transverse, V or Y shaped.

- The recommendation is to grade stomatocytes.
WBC Differential

- WBC differential counts can be performed by automated analyzers or manual microscopic visual examination of a blood film.

- Automated analyzers count many more cells than the manual 100 or 200 cells. Therefore, more precise information can be gathered.

- It is recommended that the automated analyzer WBC differential count be reported in patients with normal cell populations in the absence of analyzer flags or abnormal cell populations that cannot be reliably differentiated and classified by automated instruments.

- The automated differential may also be reported after viewing a blood film due to flags or other indicators where the automated values are found to be accurate.
Normal cell development & morphology

- **Metamyelocyte**

  - The Metamyelocyte is smaller than the myelocyte with an indented or kidney-shaped nucleus.

  - Nucleoli are not observed. The cytoplasm is usually clearly pink and contains granules that are clearly differentiated as neutrophilic, eosinophilic or basophilic.

  - Immature granulocytes (promyelocytes, myelocytes and metamyelocytes) are not usually seen in normal peripheral blood.
Band Neutrophil

- Band neutrophils are 10–14 μm in diameter and have a nucleus that is non-segmented or has rudimentary lobes that are connected by a thick band rather than a thread. Cytoplasm is abundant, pink and contains many small violet-pink neutrophilic or secondary granules distributed evenly throughout the cell.

- Many laboratories do not report band neutrophils on adult patients or children due to inter-observer variation in band neutrophic classification. This is a well recognized and acceptable practice.

- It is recommended that band neutrophils be counted as segmented neutrophils in the differential. Appropriate comments may be made if increased numbers are seen in the blood film.
Monoblast

- Supplementary image S25.

- Monoblasts are larger than myeloblasts (20-30 lm), with a round/oval nucleus, fine chromatin and one or two prominent nucleoli. The cytoplasm is basophilic and usually lacks granules.

- The recommendation is to count these as blasts and describe them in the film report with a suitable interpretive comment.
Monoblasts

J. Burthem, M. Brerton

Acute monoblastic leukaemia - monoblasts and promonocytes
Platelets

- Platelet size is of diagnostic significance particularly when considered in relation to the platelet count.

- A normal platelet measures 1.5–3 lm in diameter.

- **Large platelets** measure 3–7 lm (roughly the diameter of a normal sized red cell)

- **Giant platelets** are larger than normal sized red cells at 10–20 lm in diameter and are flagged by automated analyzers.

- **In a normal person, usually less than 5% of the platelets appear large.**

- It is recommended that **giant platelets be graded.**

- A comment about the platelet count and the presence of small, large and/or giant platelets can be made with an additional interpretive film comment if appropriate.
Summary

- Recommendations deal with the need for a global standard in naming, grading and reporting abnormal cells or morphological abnormalities which are observed at the time of the PB film review and manual differential count.

- Primary goal is to produce clear guidelines for scientists who perform analysis of hematology samples.

- The ICSH Guideline reporting system may not fit all laboratories, thus, there should be some degree of flexibility in the way laboratories report. This may to some extent be dictated by the limitations of the different Laboratory Information Systems and middleware in use.

- However, one reporting system should be in use for that laboratory / networked laboratory system to ensure consistent information for the physicians and other care givers.
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<thead>
<tr>
<th>Name</th>
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<tbody>
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<td>Amphia Hospital, Breda, Netherlands</td>
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Images

- Compilation of the Images:
  - John Burthem
  - Michelle Brereton
    - Central Manchester and Manchester Children’s University Hospital, UK

- Images Provided by
  - John Burthem
  - Michelle Brereton
  - Gina Zini
  - Gillian Rozenberg*

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Thank You!