Harmonisation of full blood count reports, recommendations of the French-speaking cellular haematology group (GFHC)

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ABSTRACT

Aims To propose recommendations related to the presentation, content and formulation of full blood count analysis reports.

Methods Strong professional agreement among a group of experts from the French-Speaking Cellular Haematology Group (GFHC) was obtained.

Results The following two proposals emerged from the consensus: (1) stratification of comments into three parts upon the discovery of an anomaly in blood cell analysis and (2) selection and/or redefinition of the terms recommended for designating the cell types found in normal and pathological peripheral blood.

Conclusions The recommendations can help biologists who are currently undergoing the process of accreditation.

INTRODUCTION

The French-Speaking Cellular Haematology Group (GFHC) aimed to propose a harmonisation approach for professional practices. Two publications were dedicated to this effort; the first concerned complete blood count reference values[1] and the second presented blood film review criteria.[2] In the logical follow-up to this reflection, the GFHC wanted to address the question of the full blood count (FBC) reports by considering the presentation of the breakdown itself and the associated comments. There are several reasons for the current lack of standardisation, including the multitude of identified cell types, vocabulary evolution over time, modifications in the nomenclature and classifications, and the necessity of integrating new diagnostic tools. The need for harmonisation brings together concerns about the accreditation of French laboratories for medical analysis. The EN ISO 15189[3] standard reaffirms the medicalisation of biology by underlining the importance of the postanalysis step and the need for a clear, relevant final report. Recommendations must be distributed among all players in the healthcare system, regardless of their responsibilities and geographical location. Obtaining such a consensus and its application requires simplification; this is the principal concern of this work, which summarises a synthesis of the recommendations after obtaining strong professional agreement.

METHODS

A group of experts from the GFHC, representative of the diversity in France of medical analysis laboratories, was formed in June 2014 to reflect on its practices according to the EN ISO 15189 standard, the recommendations of the French HAS (High Health Administration) related to the FBC,[4] the proposals of the European Leukaemia Net (ELN) group[5] and the quality documents (procedures, operating methods and work instructions) that have been implemented in the laboratories. The group was organised to propose a general presentation of the report and comments formulated based on different pathological situations. The prerequisites were the requirements of the EN ISO 15189 standard (identity of the patient, prescriber, date and time of the sample, biological validation, etc) and performance of blood film examination according to a standardised procedure by authorised personnel. The goal of the work is not to provide an exhaustive description of the cell types, as contemplated by the morphologists of the European Leukemia Net (ELN) (library of available images on the site http://www.leukemia-net.org).[5] It involves recommendations, limited to the initial diagnostic situations, that are intended to have consensus for the use of French-speaking haematologists after they have been validated by clinical haematologists.

FBC REPORT: STRUCTURING AND REGULATORY ASPECTS

Composition of the FBC report

The FBC report must, according to the recommendations of the National Agency for Accreditation and Evaluation in Health (ANAES) in 1997,[4] contain the following at a minimum:

1. The values of the haemoglobin concentration, haematocrit, erythrocyte count and the principal erythrocyte parameters: mean cell volume, mean cell haemoglobin concentration and mean cell haemoglobin.
2. The leucocyte count and differential detailing in terms of the absolute value number of neutrophils, eosinophils, basophils, monocytes and lymphocytes. The percentages can be useful on occasion (% of blast cells and monocytes needed for the World Health Organization (WHO) classification of myeloid neoplasms). In the event of identifying abnormal cellular populations, the following categories can be employed according to

the circumstances: immature granulocytes, erythroblasts, blast cells, neoplastic cells or abnormal cells that are difficult to classify. However, the recommendation is to not multiply the cellular subtypes that are preferentially described in the associated comment.

3. The platelet count.

The use of international units is mandatory, with a goal of harmonisation, even if it is contrary to widespread practices, in particular for the haemoglobin concentration in France.

The reference values or intervals must be specified based on sex and age. The following two sources can be used: the values of the Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES), recognised according to strong professional agreement, such as threshold values that are most likely pathological, and those published more recently by the GFHC, corresponding to normal values (1, 4). In all circumstances, the result must be interpreted based on the clinical and/or physiological context (age, pregnancy, ethnicity, etc).

A microscopic review, when it is performed, must be clearly indicated in the report, including the morphological study of the three bloodlines.

Apart from the aforementioned parameters, the FBC report can include additional alternative parameters. Reticulocytes are not automatically part of the FBC. If applicable, they must be given as an absolute value and percentage. Possible 'research' parameters or those associated with specific technology can appear if they represent relevant information.

Structure of the comments accompanying an FBC anomaly

The comment is not automatic: it must provide meaningful, added value. Therefore, it is accepted that *normality is often not acknowledged. However, in some cases, the comment may emphasise the absence of relevant abnormalities (eg, in case of an isolated pancytopenia, the absence of abnormalities should be noted; see below).*

In addition, quantitative anomalies do not automatically justify a comment, but they can be highlighted within a provision of advice, if applicable (they can simply be underlined on the computer).

Any interference must be clearly mentioned to justify the fact that a determination is impossible. Table 1 proposes standardised comments that correspond to the most frequently found situations and specifies, according to the circumstances, whether quantitative values can be rendered.[6–9]

After microscopic examination, the comment is explained to highlight and/or specify an abnormal result in its initial state. The structure of the comment can be divided into three levels:

- Level 1: synthetic *morphological description* of the observed anomaly.
- Level 2: *interpretation* with possibly one (or two) diagnostic orientations.
- Level 3: *provision of advice* by suggesting the approach or investigations that are potentially useful for completing the diagnostic orientation or to document the hypotheses formulated in level 2.

According to the situation, the three levels are not automatic or mandatory. In a diagnostic situation, it is not always possible to advance hypotheses when the morphology is insufficiently contributory. The comment is thus limited to level 3 that, according to the situation, can go from a simple follow-up suggestion ('full blood count to monitor in…') to the recommendation of additional examinations or specialised advice. In urgent situations (inventoried in table 2), telephone contact (to track) is imperative for the physician.

Report recipient

The recipient of the FBC report is the physician; its composition must be evaluated and the first priority is the clinical relevance of the results. The morphological descriptions must be synthetic and limited to those that are truly contributory. The document must be legible and, particularly for electronic result reporting, have easily viewable comments. When the cytology allows, the diagnosis must be explicitly formulated to avoid erroneous diagnoses and multiplication of additional examinations.

Table 1 Proposals for comments associated with analytical interferences

Impact	Interference	Comment	Result achieved
Global	Coagulated sample	'Clotted sample, test impossible'	No
	Diluted sample	'Diluted sample, test impossible' or 'request for a new sample'	No
RBC	Agglutination of the RBC by auto antibodies	'Probable presence of cold agglutinins'	Yes, if MCHC is normalised after reaching 37°C
	Lipids interfering with the Hb measurement	'Lactescent plasma'	Yes for count of the RBC, MCV and Hct No for measured and constant Hb Possibility of rendering a calculated Hb from a MCHC measured according to the automated devices or Hb/constant after washing
	Haemolysis with under estimate of RBC	'Haemolysed sample'	Yes for MCV No for Hb, RBC count, Hct and constant
Leucocytes	Agglutination of neutrophils	'Leucoagglutination' desire for a sample in a citrate tube	Yes, if resolved after reaching 37°C
	Nucleated RBC	White blood cell count not including erythroblasts	Yes after correction if necessary (under a microscope or by automated device)
Platelets	Overestimate by counting cryoglobulin precipitates	'Suspicion of cryoglobulins' (or more affirmative if deposits observed on the smear test)	Yes, if resolved after reaching 37°C
	Platelet clumps Platelet satellitism	'Platelet clumps' in place of the value	**No** Possibility of rendering **as a comment** the value of the automated device with the mention that it is a value BY DEFAULT (notably in a context indicating surgery) State 'Platelet count normal' if this is clearly so
	Citrate tube count	'Approximate value given using a citrate tube'	Only after verification of the absence of aggregation AND if no value obtained in EDTA (does not give other blood count values)

Hb, haemoglobin concentration; Hct, haematocrit; MCHC, mean cell haemoglobin concentration; MCV, mean cell volume; RBC, red blood cells.

Table 2 Urgent initial states revealed by the blood count that require immediate communication

Situation/blood disorder	Diagnosis	Treatment
Cytopaenias by themselves (in initial state)	Anaemia, neutropenia, thrombocytopenia under the threshold of greatest urgency*	Urgent communication (by telephone) to the prescriber and guidance counsellor of the patient regarding a specialised treatment
Haematological malignancy with aggressive course, notably	Acute leukaemias, particularly microgranular and classic promyelocytic AML Hyperleucocytic AML or ALL High hyperleucocytosis (>100×10^9/L in ALL, AML, CML, CLL, NHL, etc) Burkitt lymphoma Diffuse large B-cell lymphoma in leukaemia phase (including Richter syndrome)	
Thrombotic microangiopathy	HUS or Moschowitz syndrome with thrombocytopenia and mechanical haemolysis (schistocytes >1%)	
Haematozoa: malaria, babesiosis	Parasitic red blood cells	

*The definition of these thresholds is based on laboratory recruitment and the responsibility of each biologist.
ALL, acute lymphoid leukaemia; AML, acute myeloid leukaemia; CLL, chronic lymphocytic leukaemia; CML, chronic myeloid leukaemia; HUS, haemolytic uraemic syndrome; NHL, non-Hodgkin lymphoma.

Under French legislation, the patient is the owner and must, therefore, be the recipient of his/her results. Legally, it is possible that a patient suffering from a serious blood disorder learns about his/her diagnosis by mail. The EN ISO 15189 standard provides a slight difference on this point (5.9.1 note 1) as follows:

> Concerning the results for certain examinations (eg, certain genetic or infectious disease examinations), detail explanations by a physician are proved to be helpful for the correct understanding of the patient. It is appropriate for the laboratory to ensure that the results having serious implications not be communicated directly to the patient without adequate prior consideration.

This standard is a recommendation and not an obligation. On this point, the consensus of the group was established to recommend informing the physician beforehand of the diagnosis of a blood disorder by giving priority, if possible, to telephone contact (see above for the particular urgent situations where this contact is vital). In the event of non-disclosure of the diagnosis, a comment mentioning the need for a medical consultation is recommended.

PROPOSALS OF COMMENTS RELATED TO MORPHOLOGICAL ANALYSIS

Red blood cells

The erythrocytic morphological anomalies must only be reported if they have clinical significance. Table 3 proposes formulations in the most common or important situations and specifies the circumstances in which anomalies, even minor ones, on the film are significant.[10 11] As a general rule, an anomaly is only reported in level 1 if a diagnostic orientation can be provided in level 2. The description in level 1 is simple; it avoids terms that are too specialised or not very clear for the prescriber. The very general notions of *anisocytosis* or *poikilocytosis* most often lack semiological value and must not be used alone.

Platelets

Apart from reporting analytical interferences (*clumps*, *satellitism* and *fibrin*), comments regarding platelet morphology are very infrequent. Morphological platelet anomalies can be observed with certain chronic or acute myeloid blood disorders, but they are most often subdominant to more informative abnormalities of other bloodlines. *Platelet anisocytosis* can be reported in level 1 when it is significant and associated with more specific anomalies.

Platelet morphology merits comment (level 1) in the event of suspicion of a constitutional thrombocytopenia (level 2). The morphological study oriented by the mean platelet volume and, sometimes, by the presence of leucocytic abnormalities (pseudo Döhle bodies and myosin aggregates), will seek a marked abnormality in the size or appearance of the platelets. The *macroplatelet* is defined by augmentation in the size greater than half of a red blood cell and giant platelet by a size equivalent to a full red blood cell. The microplatelets correspond to elements in the range of 1 μm.

Neutrophils

Anomalies that may inspire a comment are detailed in table 4. Comments can be regarding a quantitative anomaly (severe neutropenia alone) and/or qualitative anomaly.

Lymphocytes

Lymphocytic morphology calls for comment in case of discovery of an absolute lymphocytosis (in particular, if greater than 5×10^9/L) and/or of an abnormal lymphoid subpopulation on the blood film.

Concerning the differential reports, it is recommended that *all lymphoid cells appear preferentially, including the abnormal elements, in the group of lymphocytes*. This consensus by the group is the following: (1) the poor reproducibility of the breakdown of the circulating lymphomatous cells and the reactive lymphoid cells, (2) the absence of clinical relevancy, in the majority of circumstances, of a precise quantification of these cells and (3) the interest for the clinician in quantitatively monitoring the total lymphocytosis.

Regarding the nomenclature, the group sought the most consensual and pragmatic formula. It led to conclusions of the ELN by distinguishing among the following three situations: the presence of lymphocytes that are morphologically suggestive of a reactive situation (with or without a real mononucleosis syndrome), lymphocytic anomalies that may suggest the diagnosis of a lymphoid neoplasm and non-specific lymphocytes of an indeterminate nature (table 5).

Lymphocytes/lymphoid cells in favour of a reactive origin (with or without mononucleosis syndrome)

An absolute lymphocytosis may or may not exist.

Mononucleosis syndrome is defined by the existence of more than 50% lymphocytes on the leucocyte count, including more

Table 3 Proposals of comments regarding the principal red blood cell abnormalities (in their initial state)

Red blood cell abnormality	Mention even if rarely observed	Level 1 comment (associated abnormality (ies))	Level 2 comment	Level 3 comment
Schistocytosis	Yes	Provide a deduction (threshold at 1%), differential diagnosis with non-specific fragments	Orientation towards a thrombotic microangiopathy	**Urgent** treatment in a specialised environment
Sickle cells	Yes	Sickles cells alone (with or without HJ bodies) or associated with appearances, suggesting an associated haemoglobin C	Drepanocytic syndrome	Study of the haemoglobin
Spherocytosis	Yes	Spherocytes only or associated with those that are 'mushroom' shaped	Constitutional or autoimmune haemolytic anaemia according to the context	Haemolysis markers and Coombs test Then, EMA/Ektacytometry test if suspicion of hereditary spherocytosis
Haemoglobin crystals	Yes	To be described, presence of haemoglobin C crystals	Haemoglobin anomaly (including haemoglobin C)	Study of the haemoglobin
Red blood cell ghosts: hemighosts	Yes	Semiquantitative evaluation	*G6PD* deficiency	Search for an oxidative stress, enzyme assays
Dacryocytosis	Yes	Leucoerythroblastosis and dacryocytes	Orientation towards a primitive myelofibrosis	*JAK2 V617F, MPL, CALR* mutations Indication of a bone marrow examination
Howell-Jolly bodies	Yes	Anomalies associated with asplaenia: poikilocytosis, acanthocytes, etc	Anatomic or functional asplaenia	According to the context (prophylaxis of encapsulated germ infections)
Microcytosis Hypochromia Target red blood cells	No	Microcytosis with anisocytosis and marked hypochromia Microcytosis without anisocytosis, with±target red blood cells	Orientation towards an iron deficiency Orientation towards a thalassaemic syndrome	Ferritinaemia, inflammatory assessment Study of the haemoglobin
Macrocytosis	No	Includes neutrophils with hypersegmented nuclei Includes dysplastic neutrophils (variable)	Orientation towards a vitamin deficiency Orientation towards a myelodysplastic syndrome	Measurement of vitamin B_{12} and folate levels Eliminate hyper-reticulocytosis Discuss the recommendation of a bone marrow examination
Acanthocytes	No	Isolated or associated (echinocytes)	Constitutional membrane anomaly or associated with a liver disease	Hepatic assessment, haemolysis assessment if associated anaemia, ektacytometry
Rouleaux	No	Search for abnormal lymphoid or plasma cells	Poly or monoclonal hypergammaglobulinaemia Severe anaemia	Electrophoresis of serum proteins if no associated severe anaemia CRP

Table 4 Proposal for standard comments associated with neutrophil abnormalities (in the initial state)

	Situation under the microscope	Level 1 comment	Level 2 comment	Level 3 comment
Quantitative abnormality	Neutrophils $<0.5\times10^9$/L	Severe neutropenia Report of abnormal cells (blast cells, hairy cells, etc) if applicable	According to the context	According to the context Urgent communication with the prescriber
Qualitative abnormality	Reactional abnormalities associated with severe infections: degranulation by strands, hypergranulation, vacuolisation, Döhle bodies	Reactional anomalies of neutrophils	In favour of sepsis	None
	Anomalies associated with myelodysplastic syndromes: hyposegmented neutrophils, homogeneous hypo/agranulation, (secondary cases apart from a medicinal origin) Anomalies associated with deficient dysmyelopoiesis	Dysplastic neutrophils Hypersegmented neutrophils (+ macrocytosis)	In favour of a myelodysplastic syndrome In favour of a (deficient) megaloblastic dysmyelopoiesis	Potential discussion of advice for a bone marrow examination Vitamin measurement
	Pseudo-Döhle bodies (not including reactional and regenerative situations)	To be reported if associated with a macroplatelet thrombocytopenia	In favour of a constitutional thrombocytopenia	'*MYH9* syndrome' type anomaly
	Constitutional anomalies	Pelger–Huet type, Chediak type	Suggesting the corresponding hypothesis	None

Table 5 Proposals for standard comments associated with lymphocyte abnormalities (initial or new state in a known patient)

State		Level 1 comment	Level 2 comment	Level 3 comment
Lymphocytic morphology in favour of a reactional state (ELN: 'atypical reactive')	1. With mononucleosis syndrome (>50% of lymphocytes and >10% of basophilic lymphocytes) All categories: basophilic lymphocytes, large granular lymphocytes, plasma cells, apoptotic cells are counted with the lymphocytes and not separately 2. Without mononucleosis syndrome	Not automatic (to potentially recommend a slight difference such as a differential containing several plasma cells in certain viral infections) Not automatic	'Mononucleosis syndrome' None	Not automatic
Lymphocytic morphology in favour of a lymphoid neoplasm (ELN: 'atypical suspect neoplastic')	All lymphocytic cells or cells with near lymphocyte morphology are counted in the lymphocytes	Succinct description: size, chromatin, nuclear contours, cytoplasm (granules, villi), smudge cells Semi-quantitative* or quantitative evaluation if customisable cell (Hairy cell, prolymphocyte, etc.) or if threshold WHO†	'Cytological appearance compatible with: (one to two hypotheses)' Or 'Leukaemic stage of non-classifiable lymphoid neoplasm' by specifying the size (small or large cells)	Immunophenotyping +/– karyotype and molecular biology Urgent communication if large cells
Indeterminate lymphocytosis (ELN: 'uncertain nature')	Commonplace morphology Or excess of LGL Or presence of binucleated Ly	Potential succinct description	Not automatic, except certain circumstances by specifying that the reactional or malignant nature cannot be established	According to the context, recommendation of a simple follow-up or immunophenotyping

*In the form of a scale, out of 100 lymphoid cells: <20%, from 20% to 50% and more than 50%.
†Sézary syndrome, plasma cell leukaemia, T-cell or NK-cell large granular lymphocyte leukaemia.
ELN, European Leukaemia Net.

than 10% basophilic lymphocytes. Although not consensual, the term basophilic lymphocyte remains practical and is largely used to designate the large lymphoid cells that are observed during mononucleosis syndromes and related situations, regardless of the immunoblastic or plasmacytoid appearance according to the circumstances. However, we advise against the use of the term 'activated lymphocytes' (which implies a functional instead of morphological character). It is not recommended to individualise the basophilic lymphocytes, plasmacytoid lymphocytes, large granular lymphocytes or lymphocytes in apoptosis; rather, it is advised that these elements be combined within the overall category of lymphocytes. As a level 1 comment (not mandatory), the cytologist may mention that the 'presence of polymorphous basophilic lymphocytes' is often expected by the clinician or underline a slight difference (such as predominantly plasmacytoid reaction in certain viral infections). A level 2 comment will most often be sufficient; we conclude with 'mononucleosis syndrome'. Level 3 is not automatic.

If in doubt about the reactive or neoplastic nature of large cells, especially in the absence of lymphocyte-associated polymorphism, prudence must be exercised. Such situations should be considered as the third type that is, ELN 'uncertain nature' lymphocytosis (see below): the level 1 comment can mention the 'presence of large lymphoid cells for which the reactive or neoplastic nature cannot be specified and must be interpreted based on the clinical context'. The level 3 comment can mention 'recommending specialised advice' or 'recommending immunophenotyping'.

Lymphocytes/lymphoid cells suggesting the existence of a lymphoid neoplasm

The level 1 comment can constitute a succinct description of the following: (1) the cell size (in reference to that of a red blood cell), nucleus with a study of the chromatin texture (dense, intermediate or fine), nuclear contour (regular or irregular), presence or absence of the nucleolus/nucleoli, cytoplasm (villi, granules, etc) and the presence or absence of bare nuclei (with their semi-quantification). This description is accompanied by a semi-quantitative estimate of the pathological population of <20%, from 20% to 50% or more than 50% of the lymphocytes. However, if the cells are easily identifiable (hairy cells, prolymphocytes, binucleated lymphocytes, etc), they should be noted in the comment and without subtracting the cells from the total lymphocytosis count, with a more precise result (as an absolute value and a percentage) determined using a breakdown performed on 100 lymphoid cells. If there is a diagnostic threshold recommended by the Organisation Mondiale de la Santé (OMS) (for Sézary syndrome, plasmacytic leukaemia or granular lymphocyte leukaemias),[6] the absolute value should be calculated using the combined total of leucocytes. Level 2 can be formulated as follows: 'Cytological appearance compatible with [the suggested diagnosis]', with, in case of doubt, a maximum of two hypotheses. If a precise diagnosis cannot be proposed, a more general category can be suggested, such as the 'lymphoma blood dissemination stage', by trying to specify 'small mature cells' or 'large cells'. In general, level 3 formulates a recommendation for additional examinations (lymphocytic immunophenotyping, potentially cytogenetic or molecular biology).

Lymphocytosis of a non-specific appearance and/or indeterminate nature

Certain lymphocytosis, notably moderate ($<10\times10^9$/L), presents with a common morphological appearance, preventing a precise aetiological orientation, or has an appearance for which the benign or malignant nature is uncertain, such as with the expansion of large granular lymphocytes or the presence of binucleated lymphocytes. In these situations, the comment includes a level 1 comment underlining the excessive mature lymphocytosis and observed appearance, no level 2 comment and a level 3 comment recommending a simple follow-up ('full blood count to control in…') or an immediate diagnostic approach (immunophenotyping recommended), according to the situation.

Particular circumstances among children

Apart from mononucleosis syndromes or related situations and lymphocytosis with small lymphocytes, which is suggestive of certain acute viral infections or whooping cough, a comment regarding the lymphocytes is justified in two particular paediatric situations:[7–10] (1) in children <1-year-old, lymphopenia with lymphocytes count under 3×10^9/L is potentially indicative of an immunodeficiency and justifies underlining the numerical result with the comment 'lymphopenia to monitor later on' and (2) morphological anomalies suggestive of a storage disease (vacuolated lymphocytes or Gasser cells) can lead to a recommendation in level 3 of the corresponding biochemistry examinations.

Eosinophils and basophils

A very excessive eosinophilia can represent a risk of serious short-term complications and therefore justify a comment emphasising its serious nature, and direct notification should be performed via a phone call. Outside of these situations, an eosinophilia or basophilia are only noted in level 1 if other associated anomalies are suggestive of a myeloproliferative syndrome or of circulating lymphomatous cells. Eosinophil or basophil qualitative anomalies can be reported during certain myelodysplastic syndromes. They are of very limited semiological value.

Monocytes

An isolated monocytosis is frequent, very often reactive and does not justify inclusion of an automatic comment. In the event of a comment, level 1 underlines the chronic nature of the monocytosis or its association with a myelaemia, a dysgranulopoiesis, dysplastic monocytes or the presence of immature cells (promonocytes, monoblasts and blast cells). Among children, we are also searching for dacryocytes and basophils with rough sparse granules (which are suggestive when they are associated with juvenile myelomonocytic leukaemia). In level 2, the diagnostic orientation can be directed towards a chronic or juvenile, myelomonocytic leukaemia or an acute monocytic component leukaemia. In level 3 and in the absence of a more suggestive context, the provision of advice is limited to a follow-up recommendation: 'monocytosis to monitor later on'.

Plasma cells

A reactive plasmacytosis must not be subject to a separate breakdown because the situation is understood as the presence of reactive lymphocytes. Separate breakdown of plasma cells is only recommended if there is a suspicion of malignant plasmacytic pathology. The level 1 comment allows for description of a certain monomorphism and plasmacytic anomalies that are suggestive of malignancy as follows: augmented size, fine chromatin, irregular nucleus, nucleolus and disappearance of the archoplasm. It is associated with a level 2 comment suggesting the suspicion of myeloma or plasmacytic leukaemia and a level 3 comment indicating the need for a bone marrow examination and serum protein study.

Nucleated red blood cells

If the scanner does not specifically count the erythroblasts, it is imperative to provide the real value of the leucocytes, not that of the total nucleated cells, regardless of the rate of circulating erythroblasts. Outside the first week of life (where their rate must not exceed 5×10^9/L on day 1 and 1×10^9/L on day 8), the presence of circulating erythroblasts is always associated with a pathological situation. An isolated erythroblastosis or one associated with erythrocytic anomalies, suggestive of a strong regeneration, may be subject to a provision of advice for performing a reticulocyte count and the search for other haemolysis markers. In addition, a level 1 comment is desirable if there is suspicion of a blood disorder or of medullary involvement (metastases), which is notably the case in the event of an association with a circulating blasts or immature granulocytes (see the relevant paragraphs).

Circulating immature granulocytes/leucoerythroblastic reaction

During a first visit, we recommend a detailed breakdown of promyelocytes, myelocytes and metamyelocytes. Thereafter, an occurrence of immature granulocytes that has been verified (known) as reactive and without associated malignant cells can be rendered without differentiating the subcategories. Due to the difficulty in a precise breakdown, it is not usual in France to individualise the 'band cells', the intermediate stage between metamyelocyte and mature neutrophils corresponding to the neutrophils with non-segmented nuclei, reported by Anglo-Saxon authors as being associated with sepsis. The presence of circulating immature granulocytes or of a leucoerythroblastic reaction will be subject in particular to a comment in the event of suspicion of malignant pathology (table 6).

Blast cells

It is recommended to preferentially reserve the term 'blast cells' in a FBC to situations corresponding to haematopoietic precursor pathologies (acute leukaemias, myelodysplastic syndromes and myeloproliferative syndromes). The group recommends not using the terms 'immature cells', 'undifferentiated cells', 'stem cells' and 'progenitors', which imply a functional meaning that cannot be determined from morphology alone.

The presence of blast cells on the blood film, even in small numbers, requires the following: (1) knowing the clinical context (suspicion of blood disorder or follow-up of a known pathology and in this instance, the period since the last chemotherapy and potential growth factor consumption) and (2) attentively studying the morphology of the blast cells in the search for malignancy criteria: nuclear atypical shapes (irregular contours, 'cup-like' nucleus appearance)[11] or cytoplasmic abnormalities (Auer bodies, pseudo-Chediak granules, etc). In the event of morphological heterogeneity, all leukaemic cells are considered under the name 'blast cells'.

In the level 1 comment, we describe the blast cells themselves. The signs of myeloid differentiation (granular or monocytic) are important to note with 'blast cells of a probable myeloid origin' versus 'morphologically undifferentiated blast cells', in addition to mature cells in the event of anomalies (potential dysplasia of the granular cells, associated nucleated red blood cells, etc). The reporting of Auer bodies (single or in bundles) is essential for diagnostic orientation. Level 2 allows for the formulation of a diagnostic hypothesis that can be general ('suspicion of acute leukaemia, myelodysplastic syndrome/acute myeloblastic leukaemia') or more precise according to the circumstances (in a vital manner in the most urgent circumstances; see table 2). However, among adults, we advise against the use of the term 'lymphoblast' based solely on morphology due to the eventuality of acute myeloblastic leukaemia with minimal differentiation or leukaemia of ambiguous lineage. Among children, we recognise that a typical morphology enables formulation of the lymphoblastic hypothesis: 'lymphoid morphology blast cells'. Level 3 explicitly defines the action to take, such as a

Table 6 Proposals for standard comments associated with myelaemia and erythromyelaemia (in the initial state)

	Microscopic state	Level 1	Level 2	Level 3
Circulating immature granulocytic cells	Important, well-balanced, associated with basophilia, eosinophilia	None	Appearance suggesting a CML (specify the stage, most often chronic)	Bone marrow examination (to establish the stage) Highlighting the t(9;22) and/or the *BCR-ABL* rearrangement
	Chronic monocytosis	Dysgranulopoiesis	Suggesting a CMML	Establish the chronic nature Discussion of a bone marrow examination
Leucoerythroblastic reaction	With dacryocytes	Circulating erythroblasts and immature granulocytic cells +dacryocytes	None	According to the clinical orientation, discussion of a bone marrow examination or molecular analysis

CML, chronic myeloid leukaemia; CMML, chronic myelomonocytic leukaemia.

myelogram in general and/or an immunophenotyping, and, above all, the urgent necessity for a specialised treatment.

The observation of circulating blast cells is possible outside of malignant blood disorders. The rare blast cells observed by chance and in isolation (physiologically present at a rate of 1–5/μL) are not highlighted. In addition, the few lymphoid elements of intermediate maturity are often observed among young children and classified with the lymphocytes. At the early state of aplastic postchemotherapy medullary regeneration, the presence of some circulating blast cells can be observed, corresponding to the blood flow of normal immature precursors. Monitoring of the FBC at 24/48 hours allows us to ascertain the actual end of the aplasia with, normally, the disappearance of these 'regeneration' blast cells.

Morphologically unclassifiable cells/abnormal cells

In certain circumstances, the morphological criteria do not allow us to define the bloodline and stage of differentiation of abnormal circulating cells, which is notably the case for leukaemic phases of large cell lymphomas and acute leukaemia without morphological differentiation. The use of the categories 'morphologically unclassifiable cells' or 'abnormal cells' is therefore possible but must be accompanied by a level 1 comment, thus allowing for succinct description of the elements. There is no need for a level 2 comment. A level 3 comment should be made; this comment should recommend the examinations to perform to characterise the non-classified cells, notably immunophenotyping.

Bicytopaenias/pancytopaenia

In the first occurrence, they are potentially indicative of a medullary insufficiency and must therefore lead to a search for abnormal cells. It appears justified in this situation to specify the potentially negative character of the search with a level 1 comment: 'Absence of morphologically detectable pathological cells'.

DISCUSSION

Concerned about the central role of medical advice recently redefined by the EN ISO 15189 standard, the GFHC group wanted to formulate simple recommendations that promote proper communication with the prescriber, who is the main interlocutor. The information must be clinically relevant and clear, specifying the potential degree of urgency and, whenever possible for a 'new' patient, suggesting an approach with the goal of guiding the diagnosis ('provision of advice', as defined by the standard).

To ensure a good sense of the morphological examination, the work of the cytologist is based on several checkpoints that are denoted by counters flags during automated analysis. This approach does not need to automatically appear in the examination report. The absence of potentially expected morphological signs in a given situation is almost always implied and not formulated, and the comments essentially reflect positive results.

The necessary consensus about the terms to use to designate the most common or important cell types has been the subject of discussions and constitutes, without a doubt, an important aspect of our approach. Concerns about clarity and simplicity dictated the choices. Terms that are too vague or that describe a functional rather than morphological character ('activated lymphocytes') were thus discarded for the benefit of a very simplified classification of lymphocytes in three entities that correspond to the consensus of the ELN, except for the term 'atypical', which is implied by its use in France. In the same manner, the recommendation in favour of an overall report for lymphoid cells, without individualisation of the pathological types in the breakdown, can be a matter of debate. However, it addresses the first concern of clinical simplicity and relevance of the result for the FBC. The same applies to the acceptance of the term 'blast' in a purely morphological sense without presupposition of the benign or malignant nature of the cells, even if the presupposition can modify some practices. This approach implies contact with the prescriber to avoid any poor interpretation of the presence of these blast cells (malignant vs benign). Ideally, this contact should be direct (via telephone) and tracked.

In return, the simplification of the classification of the cells and anomalies requires that whenever possible, they should be associated with a comment about the meaning of their presence, suggesting the best possible diagnostic hypothesis, which is a piece of advice regarding the approach to follow. This stratification of comments into three levels (description, diagnosis hypothesis and provision of advice) formed the basis for reflection and the suggestions proposed here.

CONCLUSION

The conclusions of the group constitute the 'recommendations of the GFHC' that were derived from proposals that have garnered strong professional agreement. We wanted them to be applicable to all private practice laboratories, general hospitals and university hospitals, regardless of the prescribers considered, whether general practitioners or specialists and private or public practice. However, they do not have a binding nature, that is, each biologist remains free to decide whether to follow them, and they may be subject to evolution according to new European or international consensuses. Aimed at improving the standardisation of the postanalytic stage in cellular haematology, they can help biologists who are currently undergoing the process of accreditation.

Take home messages

- An full blood count (FBC) analysis report should be of direct clinical relevance for the physician.
- A comment is needed when the FBC analysis reveals a relevant anomaly of potential clinical interest.
- This comment should be stratified into three parts: a short morphological description, interpretation and provision of advice.
- The terms used to designate the cell types and morphological abnormalities should follow the ICSH and European Leukaemia Net recommendations.

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