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A Programme for Post-Graduate Training and Quality Control in Blood Cell Morphology

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Summary: The programme presented can be considered as a combination of permanent education with quality control carried out on a regional level. The selection procedure of blood smears for distribution will be discussed. The sensitivity and specificity are tested of many frequently occurring haematological abnormalities.

Ein Programm für Post-Graduierten-Training und Qualitätskontrolle in der Blutzellmorphologie

Zusammenfassung: Das beschriebene Programm wird auf regionaler Ebene durchgeführt und kann als Kombination von permanenter Fortbildung und Qualitätskontrolle betrachtet werden. Das Auswahlverfahren für die Blutausstriche zum Versand wird erörtert. Empfindlichkeit und Spezifität häufig vorkommender hämatologischer Abnormitäten werden geprüft.

Introduction

Examination of the morphological characteristics of the various cell lines in peripheral blood may be very useful in the diagnosis of a variety of illnesses (1).

The subjective and qualitative nature of morphological analyses by microscopy is the major source of disagreement between laboratory technologists. This may diminish the value of results in the laboratory.

Only continuing education in haematological morphology may improve individual performance (2).

Therefore, starting in 1975 refresher courses in blood cell morphology have been organized periodically for laboratory technologists of seven regional hospitals by a Clinical Haematology Group in our hospital.

Consequently a regional quality control programme was developed in 1981 in order to test and maintain formerly acquired knowledge.

The organisation of the regional quality control programme is described. To know which topics demand more attention the sensitivity and specificity of thirty haematological characteristics present in four or more of the forty-eight blood smears distributed were determined.

Materials

Conventional spread blood smears for the programme are prepared from venous blood without anticoagulants from patients with characteristic haematological abnormalities. Chemically clean 26 × 76 mm glass slides and spreading slides with smooth edges are used. The smears are allowed to dry and half the number stained using an automated staining apparatus (Shandon Elliott, Shandon Scientific Co. Ltd, London, England). The staining was performed according to the *May Grünwald-Giemsa* method at pH 6.8. The stain solutions were purchased from E. Merck (Darmstadt, West Germany).

Several regional clinical laboratories contributed in delivering blood smears of interesting patients. These slides were stained in these laboratories according comparable but manual staining techniques.

The material gathered is suitable for our quality control programme provided that:

1. the haematological diagnosis of the patient is final and based on additional examination (e. g. from bone marrow)
2. the blood smears are representative.

Each smear is checked by microscope for the absence of misleading artefacts. We aim for the greatest possible variety of syndromes. In table 1 the diagnoses of fortyeight specimens are reviewed.

Tab. 1. Review of diagnoses of fortyeight distributed specimens.

Diagnosis	n
Acute lymphoblastic leukaemia	4
Chronic lymphocytic leukaemia	3
Acute myeloid leukaemia	5
Chronic myeloid leukaemia	4
Erythroleukaemia	1
Leukaemic malignant lymphoma	3
Multiple myeloma	2
Iron deficiency anaemia	4
Megaloblastic anaemia	5
Thalassaemia	1
Sickle cell anaemia	1
Malaria	4
Infectious mononucleosis	2
"Toxic" changes	8
Post splenectomy condition	2
Pelger-Huët anomaly	1
LE cell slides	2
No abnormalities	1

Determination of sensitivity and specificity

In each of the fortyeight smears it was determined which quantitative and/or qualitative haematologic characteristics were present in such a way as to be of clinical importance and as such ought to be recognized by the technologists.

For characteristics present in four or more of the fortyeight distributed blood smears the sensitivity and specificity were determined by applying the following formulae.

$$\text{The sensitivity of a specific characteristic} = \frac{A}{(A + C)} \times 100\%$$

$$\text{The specifity of a specific characteristic} = \frac{D}{(B + D)} \times 100\%$$

		Characteristic present (according to the lecturer and diagnostically confirmed)	
		yes	no
Statement characteristic by the technologists	yes	A	B
	no	C	D

A = number of (correct) positive statements in specimens which do contain the characteristic,

B = number of (incorrect) positive statements in specimens which do not contain the characteristic,

C = number of (incorrect) negative statements in specimens which do contain the characteristic,

D = number of (correct) negative statements in specimens which do not contain the characteristic.

Methods

Organisation

Once every six weeks stained blood smears from two patients and a reply-form with relevant clinical and laboratory data were distributed to the seven clinical laboratories participating. If useful a non-stained slide was enclosed for a complementary cytological staining.

At first the individual technologists made a differential count of the leukocytes and an estimation of the morphology of erythrocytes, nucleated cells and thrombocytes. Subsequently they tried to reach consensus by discussion. A well-founded conclusion was also required. The completed reply-form was returned.

The participating clinical laboratories received a review of the results of the lecturer and of all participants as well as the lecturer's explanation about singularities and comments on mistakes.

Thereafter the technologists had a second chance to examine the smears to notice which singularities they may have misinterpreted.

About twice a year the most interesting specimens are discussed together with aid of a video-microscope.

Results

The results are reproduced in table 2 and 3 and will be discussed in the following section.

Discussion

In our opinion periodic refresher courses in blood cell morphology for technologists in clinical laboratories are necessary in order to keep their knowledge up to date or to extend their knowledge. Actually, the factor "experience" in examining blood cells is of great importance, just as it is in all other kinds of morphological diagnostics. Rare syndromes have to be presented regularly.

As training is linked to quality control this programme deviates noticeably from national programme for external quality control of blood cell morphology in Finland (2), Canada (3), West-Germany (4) and the U. S. A. (5).

Tab. 2. Sensitivity and specificity of quantitative and qualitative characteristics of nucleated cells.

Nucleated cells	Number of smears with characteristic	Sensitivity (%)	Specificity (%)
Myeloblasts	10	79	98
Promyelocytes	9	56	98
Myelocytes	9	67	91
Metamyelocytes	11	65	96
Promyelocytes, myelocytes and metamyelocytes combined	16	80	98
Band cells	17	76	91
Eosinophilic granulocytes	5	89	100
Lymphoblasts	6	64	97
Plasma cells	4	64	98
Monocytes	5	77	96
Döhle bodies	13	46	89
Toxic granulation	15	78	75
Hypersegmentation	10	50	98
Giant neutrophils	5	17	99
(Pseudo) *Pelger-Huët*	5	20	100
Normoblasts	20	61	91
Karyorrhexis	6	21	98

Tab. 3. Sensitivity and specificity of quantitative and qualitative characteristics of erythrocytes.

Erythrocytes	Number of smears with characteristic	Sensitivity (%)	Specificity (%)
Megalocytes	6	33	99
Macrocytosis	6	55	88
Microcytosis	4	39	95
Anisocytosis	27	62	48
Hypochromia	7	57	88
Polychromia	4	43	76
Elliptocytes; ovalocytes	9	46	97
Fragmentocytes	8	13	99
Echinocytes	5	17	98
Target cells	6	33	98
Howell-Jolly bodies	10	64	96
Cabot rings	5	11	99
Basophilic stippling	23	57	67
Poikilocytosis	9	52	89

As the number of participants is limited the lecturer is able to comment on individual mistakes.

This quality control and teaching programme offers an excellent opportunity to test uniformity within a particular laboratory and between laboratories. In our experience this programme results in increasing interest in blood cell morphology. This is concluded from individual contact with the technologists and from the fact that cytochemical staining techniques have been introduced in some laboratories.

Usually laboratory technologists do not describe their opinion in a presumptative diagnosis. However in this quality control programme they are required to do so because the group discussions of differential diagnoses have useful educational aspects. From the conclusive diagnosis it sometimes becomes clear whether or not one has noticed or missed for instance malignant transformation of cells.

In the laboratories involved the blood smears were examined very thoroughly. The resulting sensitivity and specificity may therefore not reliably illustrate the real situation in every day routine. They indicate, however, which subjects should be paid extra attention during refresher courses. Finally we comment on the observations by technologists:

- A "shift to the left" in granulocytes is nearly always observed. The distinction between promyelocytes, myelocytes and metamyelocytes is not always made correctly.
- Small lymphoblasts are often not recognized.
- *Döhle* bodies are often not distinguished from granules in granulocytes and are often misinterpreted as toxic granulation.
- Qualitative changes in granulocytes — e. g. hypersegmentation, giant cells and changes connected to (pseudo) *Pelger-Huët* anomaly, are often not noticed.
- The term anisocytosis is often used, while microcytes or macrocytes occur together with normal erythrocytes.
- The sensitivity and specificity of the term hypochromia is low.
- There is a low sensitivity for abnormal forms in erythrocytes. For inclusions in erythrocytes the sensitivity is variable. The specificity of basophilic stippling is low.

We may conclude that the organisation of a regional quality control programme for blood cell morphology is useful and well feasible. Extra attention should be paid to an uniform nomenclature and to the gradation of qualitative abnormalities.

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