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SEED HAEMATOLOGY

The blast cell – a diagnostic heavyweight

Causes and cytological manifestations

Blast cells are described as precursor cells with the ability to preserve themselves by dividing and to further differentiate. Under pathological conditions, blast cells can be mobilised from the bone marrow into the peripheral blood circulation. In adults, this represents an alarming finding that can indicate both reactive and malignant diseases such as leukaemia. Therefore the detection of blast cells in the peripheral blood is considered extremely important, and great responsibility is placed on the investigating laboratory. As well as information on the physiology, this article describes the possible causes of the release of blast cells into the blood, the characteristics by which they can be identified and how further diagnosis is carried out.

Development, maturation and regulation

Haematopoietic precursor cells develop from the pluripotent embryonic stem cells as a result of numerous development stages. In the bone marrow, these cells are referred to as blast cells ('blastós' is the Greek word for germ, bud, sprout or shoot). For their further development, they are committed to one specific line (erythropoiesis, granulopoiesis, monopoiesis, thrombopoiesis and lymphopoiesis). Asymmetrical replication, as shown in Fig. 1, allows blast cells to form both identical daughter cells (replication) and to differentiate to form mature blood cells.

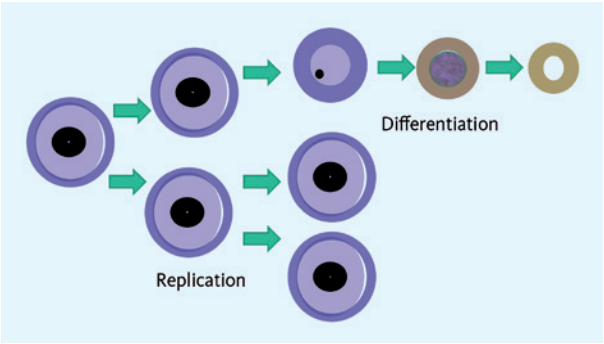

Fig. 1 *Asymmetrical replication (example erythropoiesis)*

A mature cell is developed after several differentiation stages, involving gradual condensation of the nuclear chromatin. While blast cells have a homogeneous chromatin, the nucleus shows chromatin clumping in the mature cells. The nucleus-plasma relation also drops (see Fig. 2)

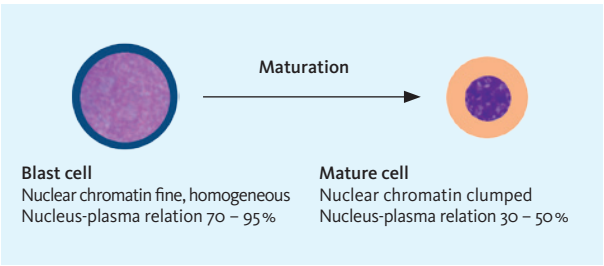

Fig. 2 *Schematic illustration: blast cell / mature cell*

Bone marrow barrier

Blast cells and other immature cells of haematopoiesis are captured in the bone marrow due to their size and adhesion properties, and do not enter the blood stream. This mechanism is referred to as the 'bone marrow barrier'. A disruption of this bone marrow barrier is associated with a leucoerythroblastic blood picture.

Definition of leucoerythroblastic blood picture
The peripheral blood shows a left shift of the granulopoiesis towards promyelocytes and myeloblasts and the presence of nucleated red blood cells.

Physiological blast cells

These are medium to large cells (14 – 18 µm*) with the specific characteristics of the nucleus and cytoplasm described in Table 1.

Table 1 *Diagnostic characteristics of physiological blast cells*

Nucleus	Cytoplasm
Shape: round/oval	Narrow (constituting 5 – 30 % of the cell)
Nucleus-plasma relation: 70 – 95 %	Basophilic
Nucleoli: one to several (may not be visible)	Not granulated **
Finely distributed nucleic chromatin, no clumping	

* *Exception: megakaryoblast 150 µm*
** *Leukaemic blast cells may be granulated*

With leukaemia, blast cells can have a significantly changed appearance. What all blast cells have in common is the finely and evenly distributed, light nuclear chromatin.

Blast cells in the peripheral blood, causes and cytological appearance

A shift of blast cells into the peripheral blood occurs physiologically only in neonates. The reason for this is the extramedullary haematopoiesis that still exists at the time of birth. In adults, the presence of blast cells in the peripheral blood is a serious finding. Essentially, it is important to differentiate between a reactive and a leukaemic appearance of blast cells. Examples are shown in Table 2. The extent of the influx of blast cells can be used to differentiate between a reactive and a malignant picture, as can the composition of the other cell populations. Blood count values and clinical data are also helpful.

Table 2 *Diagnostic reasons for the presence of blast cells in the peripheral blood*

Reactive	Malignant
Severe bacterial infections, sepsis	Acute leukaemias (AML, ALL, AUL)
Treatment with growth factors (G-CSF)	Myeloproliferative neoplasia (CML, PMF)
Regeneration after chemotherapy	Myelodysplastic syndromes (RAEB 1 and 2)
Viral infections (mononucleosis)	MDS/MPN overlap syndrome (CMML 1 and 2)
Bone marrow carcinosis	Aggressive lymphoma of the B cell and T cell lines

Blast cells using May-Gruenwald stain [7]

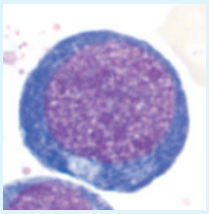

Image 1
Proerythroblast;
size 14 – 18 µm, nucleus-plasma relation 70 %, deeply basophilic cytoplasm, Golgi zone

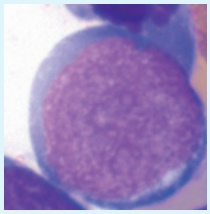

Image 2
Myeloblast;
size 14 – 16 µm, nucleus-plasma relation 80 %, light basophilic cytoplasm

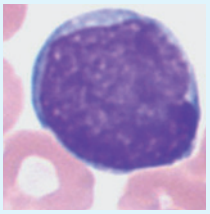

Image 3
Lymphoblast;
size 14 – 16 µm, nucleus-plasma relation 90 %, narrow cytoplasm medium basophilic

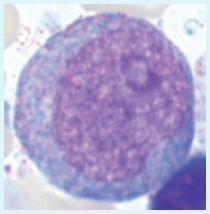

Image 4
Monoblast;
size 14 – 18 µm, nucleus-plasma relation 70 %, nucleic lobulation +/–, basophilic cytoplasm

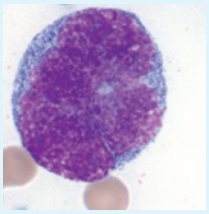

Image 5
Megakaryoblast;
size up to 150 µm, nucleus-plasma relation 80 %, deeply basophilic cytoplasm, vacuoles +/–

Fig. 3 *Physiological blast cell types*

Reactive

The proportion of blast cells detected in the peripheral blood in the case of a reactive event is comparatively low (< 5 %) and there tends to be a continuous left shift up to the myeloblast stage or a leucoerythroblastic blood picture as shown in Fig. 4.

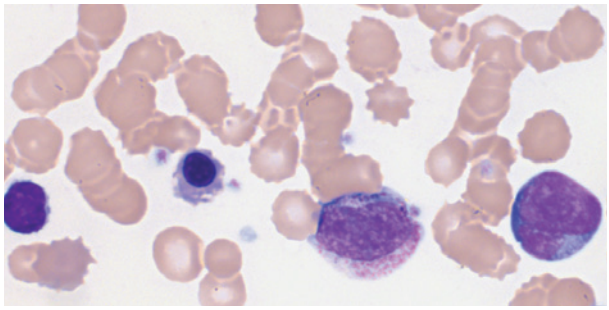

Fig. 4 *Leucoerythroblastic blood picture in pneumogenic sepsis*

There are also often reactive changes in the neutrophils, such as toxic granulation and vacuolisation. In the case of viral infections (e.g. mononucleosis), single blast cells may be released into the peripheral blood. These are lymphoblasts, corresponding to the T cell line, in immunophenotyping, more specifically T immunoblasts, and they are component parts of a generally reactive lymphocytic appearance.

Haematological neoplasia

A lot of haematological neoplasias are associated with blast cells' appearance in the peripheral blood. The underlying damage to clonal stem cells can result in an absence of cell maturation, with a subsequent influx of blast cells. The proportion of blast cells can vary greatly, as can the number of white blood cells, manifesting in either leucopenia or excessive leucocytosis. The highest proportion of blast cells is exhibited in acute leukaemia. The proportion of blast cells in the blood and/or bone marrow defined for acute leukaemia is 20 % according to the WHO classification 2008 [8]. As well as an increase in blast cells and low numbers of mature white blood cells still present, the intermediate forms are often absent in patients with acute leukaemia (leukaemic hiatus). Morphological details, such as Auer rods, prove the origin of the blast populations from the myeloid cell line. An example of blast cells from an acute myeloid leukaemia (AML) is shown in Fig. 5.

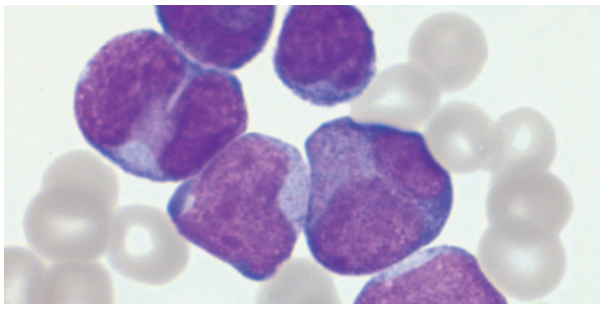

Fig. 5 *Blast cells in the peripheral blood in AML*

Acute promyelocytic leukaemia with the presence of faggot cells (FAB type M3/M3V), as shown in Fig. 6, is of particular clinical importance. In this specific type, associated with chromosomal translocation t(15;17), a prompt diagnosis is of key importance due to coagulation complications and the need for a special therapy.

If cell morphology indicates haematological neoplasia, a defined step-wise haematological diagnostic analysis is carried out for further differentiation.

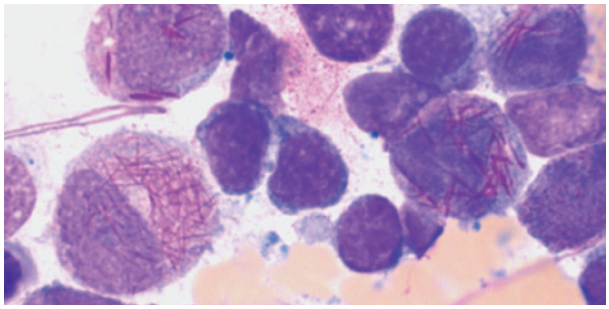

Fig. 6 *AML M3 faggot cells, bone marrow*

Blast cell differentiation by a step-wise diagnostic approach

The **cytology** from the blood and bone marrow with the quantification of the blast cells is the starting point for a step-wise haematological diagnostic approach. Myeloid characteristics by which blast cells are differentiated, such as Auer rods or granules, are used to distinguish between a myeloid and lymphatic form of leukaemia.

Cytochemical stains, such as peroxidase (POX), are used for further classification of myeloid cells, and alpha-naphthyl acetate esterase (NAE) is used to detect monocytes and their precursor cells.

Table 3 *Progenitor markers*

Progenitor markers	Cells that express the antigen
CD34	Haematopoietic precursor cells, capillary endothelial cells
HLA-DR	Progenitor cells of all lines, especially myeloblasts
CD117	Haematopoietic precursor cells
CD10	B cell and T cell precursor cells, stromal cells of the bone marrow
TdT	Lymphatic progenitor cell marker, especially of the T cell line

Immunophenotyping is a key component of the step-wise diagnostic approach. This allows antigens to be detected on the cell surface or in the cell cytoplasm. Progenitor markers (Table 3) are of key importance for detecting blast cells, which are expressed as precursor cells at a defined time. As these mature, the antigens are lost and are replaced by other markers. In combination with line-specific markers, which are only expressed by one specific cell line (e. g. CD19 for B cells), the blast cells can be accurately classified in terms of their maturity and cell lines.

Cytogenetics / molecular genetics represent another important diagnostic tool. By combining various methods, chromosomal aberrations that are relevant for therapeutic and prognostic reasons can be detected at a cytogenetic or molecular biological level. As part of a comprehensive investigation to record all changes (aberrations) in the genome, a karyogram is produced, which separates all chromosome pairs. The fluorescence in situ hybridization (FISH) and the polymerase chain reaction (PCR) are used to selectively detect specific mutations.

At the end of these step-wise diagnostic investigations, a final assessment should be made, taking into account all methods, to deliver an integrated finding.

Concluding remarks

Methodology developments in haematological diagnostics now allows the disease types to be much more accurately diagnosed and classified than was possible in the times of FAB classification.

This does not, however, in any way reduce the importance of morphology, as this remains the initial method, allowing a prompt and reliable filter and gatekeeping function/setting of the further course. The abnormal blood smears are filtered by the laboratory staff in the central or specialist haematology laboratory, and the pathological findings are passed on, so that the haematological step-wise diagnostics can be set in motion. Added to this is the need for an integrated finding, taking into account all applied diagnostic methods.

Blast cells in picture and text

An overview of the physiologically and pathologically occurring blast cells is shown on the Sysmex blast cell poster and the complementing chart, which were developed in cooperation with the Clinic of Oncology/Haematology and Stem Cell Transplantation at the University Hospital of Aachen (Fig. 7). You are welcome to request a copy from your local Sysmex representative.

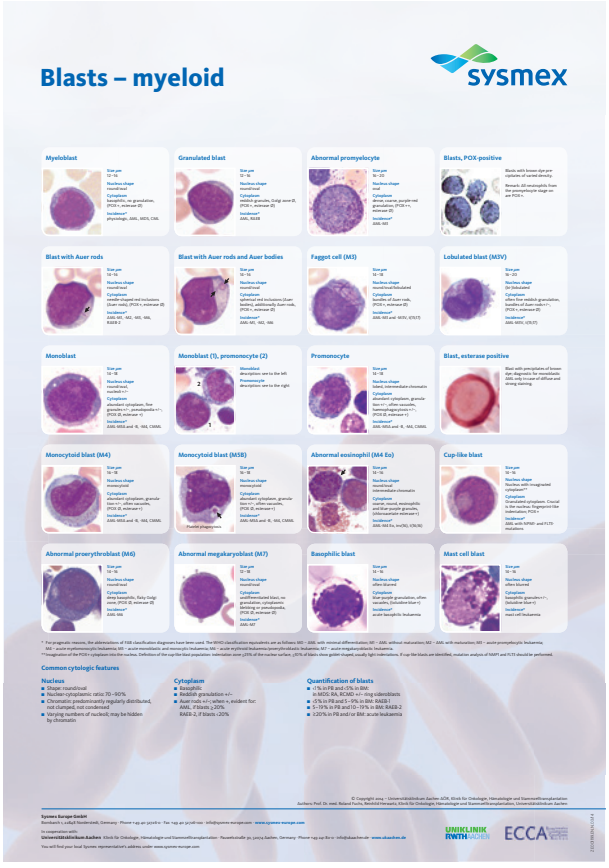

Fig. 7 *Overview of various physiological and pathological blast cells available as a wall poster or A4 chart from your Sysmex representative*

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