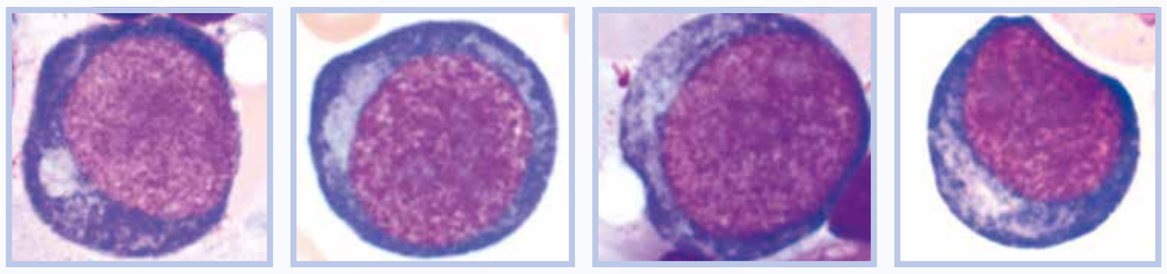
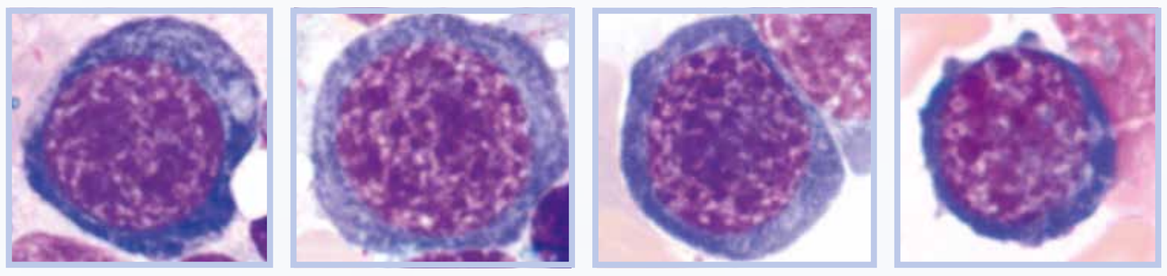
Erythropoiesis

Nucleated red blood cells

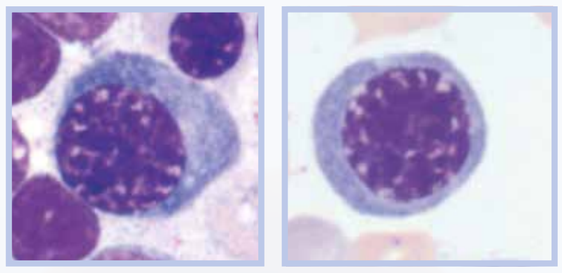
Proerythroblast



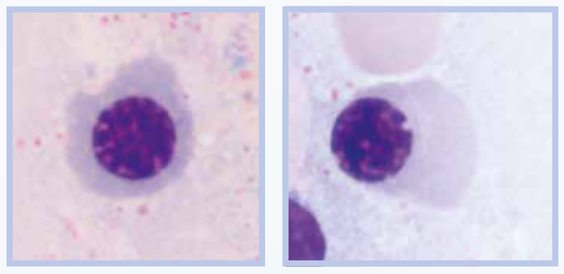
Basophilic erythroblast



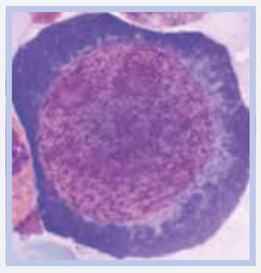
Polychromatic erythroblast



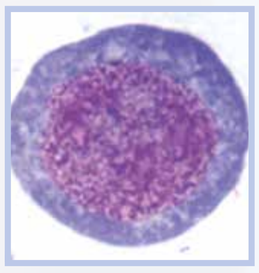
Orthochromatic erythroblast



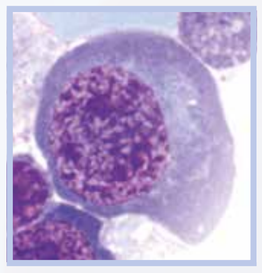
Promegaloblast



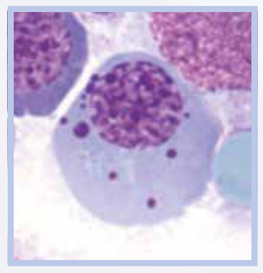
Basophilic megaloblast



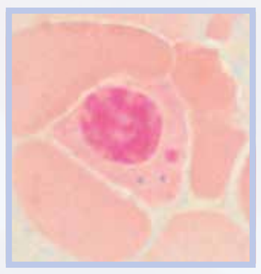
Polychromatic megaloblast



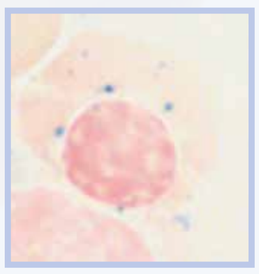
Orthochromatic megaloblast



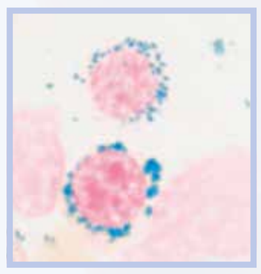
Sideroblast, physiological



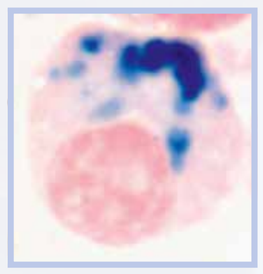
Sideroblast, pathological



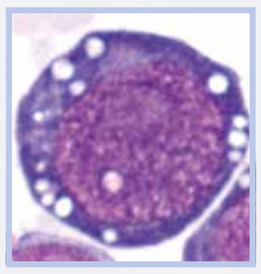
Ring sideroblast



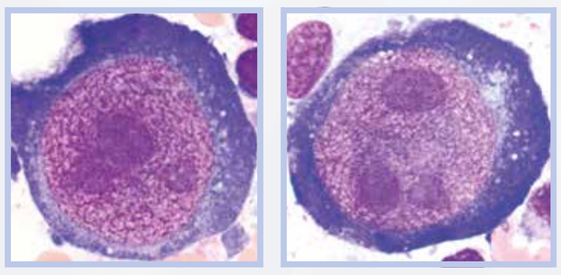
Siderotic plasma cell



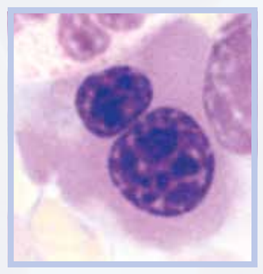
Vacuolated proerythroblast



Macro-proerythroblasts, infected with parvovirus B19

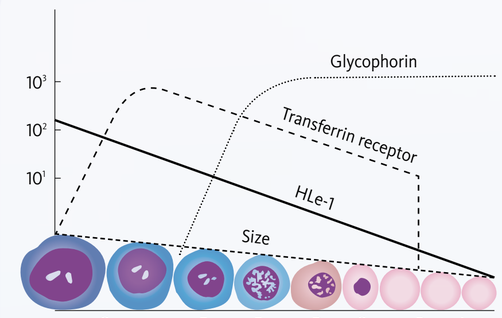


Binuclear erythroblast, CDA



Physiology

The red cell line develops from a pluripotent stem cell. With adults under physiological conditions, this development takes place exclusively in the bone marrow. Stimulated by erythropoietin, the stem cells develop via progenitors, which are not identifiable using MGG staining, into proerythroblasts, which are the first red blood cell precursors recognizable by panoptic staining.



A: mature red cell; B: reticulocyte; C: orthochromatic erythroblast; D: polychromatic erythroblast; E: basophilic erythroblast; F: proerythroblast; G: undifferentiated blast

Proerythroblast

Blast-like cell. Size 14 – 18 µm. Nucleus-cytoplasm ratio (N:C ratio) 80 %. Chromatin slightly clumped with one or more prominent nucleoli, slightly more dense than that of a myeloblast. Cytoplasm dark blue, agranular, often with perinuclear halo, which repesents the Golgi apparatus.

Erythroblast

Smaller than the proerythroblasts. Nuclear chromatin heterogeneous with condensed or clumped DNA. Generally erythroblasts (E) are separated into three maturation stages. Similarities: decrease in cell and nucleus size, chromatin more and more unevenly distributed and darker stained. Differences: colour of the cytoplasm changing from blue (RNA) to red (haemoglobin). By this colour, erythroblasts are divided into **basophilic** E (blue), N:C ratio 70 – 80 %, **polychromatic** E (mixed colour: blue-grey/red), N:C ratio 30 – 50 %, and **orthochromatic** E (pink-orange), N:C ratio approx. 30 %. Orthochromatic erythroblasts are the last maturation stage and the nucleus undergoes pyknotic degeneration.
During the following four days RNA remnants are degraded. As long as this anuclear cell still contains retiform RNA structures it is called **reticulocyte**. After the **reticulocyte**, the cell becomes a mature red blood cell (erythrocyte) with a life span of 120 days. Its diameter is about 7 µm, which equals the nucleus size of a small lymphocyte. The central pallor makes up about one third of the total cell surface.

Pathological forms of nucleated red blood cells

Megaloblasts

They develop during a vitamin B12 or folate deficiency, both being essential for DNA synthesis. As a consequence pathological cells are formed, larger in size and with signs of nuclear and cytoplasmic maturation asynchronism.
Based on their size, the cells are named promegaloblast, megaloblast and megalocyte. Especially in the maturation stage of the megaloblast the nucleic structure is noticeably clumped. Orthochromatic megaloblasts demonstrate an unproportioned nucleus-cytoplasm ratio in favour of the cytoplasm. Due to impaired DNA synthesis they often show nucleus fragments or bizarre karyorrhexis figures. Reticulocytes are always decreased. Megalocytes are large oval red blood cells, which lack the central pallor. Often megaloblasts are associated with hypersegmented neutrophils, giant band cells and hyperlobulated megakaryocytes. The latter are present only in the bone marrow.

Proerythroblasts, siderotic plasma cells with chronic ethylism

Characteristic is an eye-catching vacuolisation of proerythroblasts, potentially also of basophilic erythroblasts. Else this phenomenon is only observed with MDS, acute leukaemia and copper deficiency.
Plasma cell siderosis describes a heterotopic, cytoplasmic accumulation of iron in the shape of ferritin lysosomes and haemosiderin in plasma cells. Using MGG staining, the iron can be identified as a coarsely clumped, blackish precipitate randomly distributed within the cytoplasm. With Prussian blue staining the iron presents as blue-black clumped precipitates.
Iron incorporation takes place via transferrin receptors of altered plasma cells. Ethylism-induced plasma cell siderosis is not associated with iron overload. Plasma cell siderosis can be also found with haemochromatosis, severe haemosiderosis and multiple myeloma.

Proerythroblasts with parvovirus B19 infection

The virus has a tropism towards erythropoietic precursors, invades their nuclei and causes proerythroblast enlargement followed by apoptosis and failure of erythropoietic regeneration, leading to the absence of erythroblasts in the bone marrow. Distinctive feature: giant proerythroblasts with unusually large, nucleoli-like virus inclusions in the nuclei. Clinically an aplastic anaemia in the sense of a pure red cell aplasia can be recognized, with a strong decrease or absence of reticulocytes.

Ring sideroblasts

Iron granules (siderosomes) arranged like a string of pearls, making up > 1/3 of the nucleus size. Ring sideroblasts develop due to damages to the enzyme cascade of the haem synthesis inside those mitochondria that are located close to the nucleic membrane. Reasons are manifold: genetic, toxic or neoplastic. Occurrence: MDS, AML – especially AML-M6, chronic toxic effects (alcohol, benzene, lead poisoning), copper deficiency anaemia, tuberculostatics (isoniazid, pyrazinamide, cycloserine), congenital sideroblastic anaemia. In bone marrow histology specimens, ring sideroblasts cannot be observed since ferritin is eluted during the decalcification process

Abbreviations: CDA – congenital dyserythropoietic anaemia, May-Grünwald-Giemsa – MGG, RNA – ribonucleic acid, DNA – deoxyribonucleic acid, MDS – myelodysplastic syndrome, AML – acute myeloid leukaemia

Authors: Reinhild Herwartz, Prof. Dr. med. Roland Fuchs, Medizinische Klinik IV, Uniklinik RWTH Aachen

Sysmex Europe GmbH
Bornbarch 1, 22848 Norderstedt, Germany · Phone +49 40 52726-0 · Fax +49 40 52726-100 · info@sysmex-europe.com · **www.sysmex-europe.com**

In cooperation with:
Universitätsklinikum Aachen Klinik für Hämatologie, Onkologie, Hämostaseologie und Stammzelltransplantation
Pauwelsstraße 30, 52074 Aachen, Germany · Phone +49 241 80-0 · info@ukaachen.de · **www.ukaachen.de**

You will find your local Sysmex representative's address under www.sysmex-europe.com/contacts

ZE000793.EN.N.10/15