Spotlight on hematology

Damaged Cells

MQZH 2016-3

Introduction

Various cell artifacts in the peripheral blood smear can complicate the microscopic evaluation. It is in part no longer possible to assign damaged and other artificially changed leukocytes to a specific leukocyte subpopulation. Because these artifacts are created only during the preparation of the blood smear, the leukocyte differentiation values of the hematology instruments are generally correct.
Damaged cells and other cell artifacts can nonetheless be important for the hematological finding. They can provide an indication for a specific disease such as, for example, chronic lymphocytic leukemia (CLL). On the other hand, artificial changes caused by EDTA, severe general diseases, or in intensive care patients can strongly complicate the assignment of the cells to the correct cell lineage.
Our current proficiency testing survey sample 2016-3 H3b is from a patient with chronic lymphocytic leukemia (CLL). Our annual proficiency testing survey 2016-01 H3B specimen, a T-cell prolymphocytic leukemia (t-pll), and the 2016-02 H3A specimen, from an intensive care patient with sepsis, also contain increased numbers of damaged cells.

Damaged cells

The destruction of cells in the peripheral blood can be the result of physiological as well as artificial factors. Mechanical damage caused during the preparation of leukocyte smears results in the breakup of the cell cytoplasm. A clear delimitation of the cell can no longer be seen. The remaining nuclear chromatin is spread out and appears as «smudge cells» or «basket cells».

Occurrence

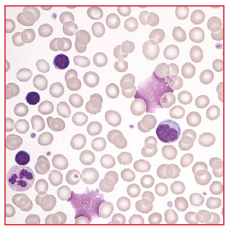
Damaged cells appear only rarely and in very small numbers in a normal, technically well-prepared blood picture.

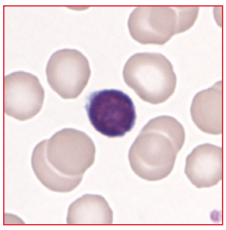
Causes for an increased appearance are:
- Chronic lymphocytic leukemia (CLL)—sometimes in very high numbers
- Acute leukemias
- Other non-Hodgkin lymphomas
- Reactive situations such as infectious mononucleosis

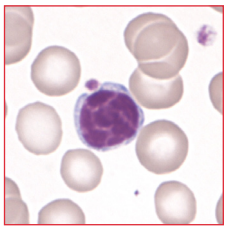
Various factors are likely responsible for the increased cell damage in CLL:
- Abnormal structure of the cytoskeleton
- Accumulation of older cells in the blood due to dysregulated apoptosis

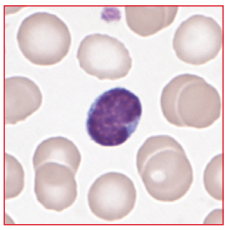
Notable high numbers of up to > 50 damaged cells/100 leukocytes can therefore be found in CLL patients.

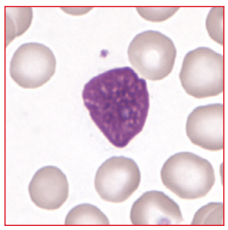
Pictures of MQ 2016-3-H3B CLL

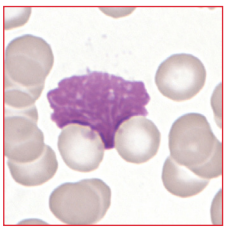

MQ 2016-3 H3B overview


Lymphocyte


Lymphocyte


Lymphocyte with cleaving


Damaged Cell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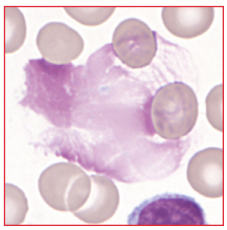
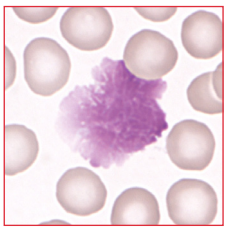

Damaged Cell


Damaged Cell

Recommendations for counting damaged cells

If the origin of the damaged cell can still be clearly determined based on the residues of the granuloma or the nucleus, the cell should be counted as part of the appropriate class.

If less than 5% damaged cells appear, they are not counted and not reported

If more than 5% damaged cells appear, they are counted as a separate class and reported as percentage of the leukocytes.

In CLL, the damaged cells are lymphocytes. In this case, the damaged cells are added to the lymphocyte count. The percentage of lymphocytes damage that had occurred is given in the commentary.

This approach has the advantage that the values from the hematology instruments correspond to those of the microscopic blood picture.

With proficiency testing survey specimens, we do not require a diagnosis. Therefore, please report the damaged cells separately even in obvious cases, such as with the current specimen.

Damaged cells as a prognostic factor with CLL?

Several studies from 2009/2010 investigated whether the amount of damaged cells can be used as a prognostic factor with CLL. There were indications that a large number of damaged cells is associated with slower disease progression.

Because the number of damaged cells is also known to depend on the streaking method and the location of the investigated area on the microscopic slide, a standardization would first have to be performed in order to make a direct comparison.

Spotlight on hematology

Determining the cell lineage damaged cells belong to

As long as the nucleus is still surrounded by cytoplasm, even if it is no longer intact, a conclusion on the association to the lineage can be made for neutrophils, eosinophils, and basophil granulocytes. If the cell degeneration is so strong that this is no longer the case, the cell is referred to as a «damaged cell».

Development of cell artifacts and the effect of EDTA on blood cells

EDTA-mediated changes generally appear after one to two days of storage.

Cell artifacts can already appear within one to two hours after blood withdrawal in cases with extremely severe general disorders and in intensive care patients. Conceivable factors that are responsible for the increased number of fragile cells in these patients include e.g., medicinal drugs and also extracorporeal membrane oxygenation, such as ECMO, that is used in intensive medical care.

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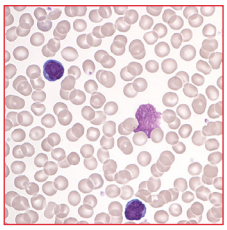
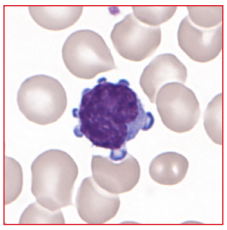
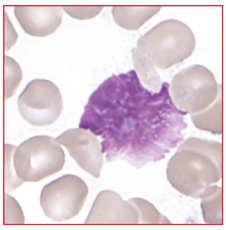
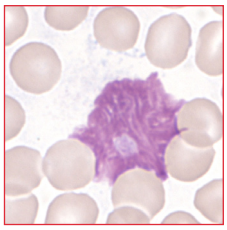
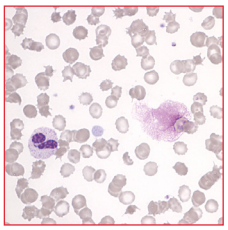
Pictures of damaged cells from different proficiency testing survey specimen

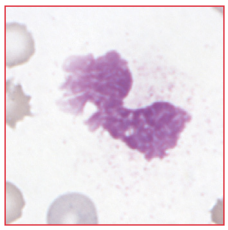

MQ 2016-1 H3B T-PLL

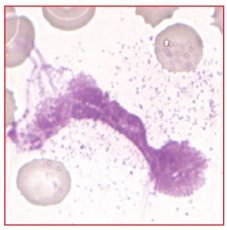

Lymphocyte

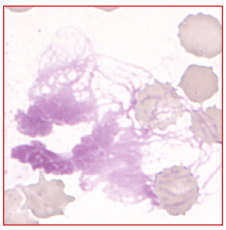

Damaged Cell


Damaged Cell


MQ 2016-2 H3A Sepis


Damaged Cell


Damaged Cell

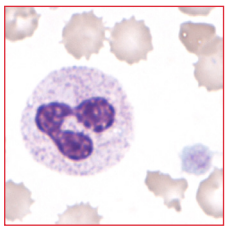

Damaged Cell

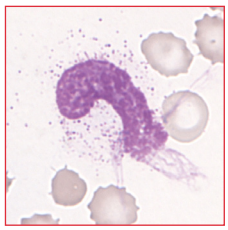
Mechanism of development of other cell artifacts

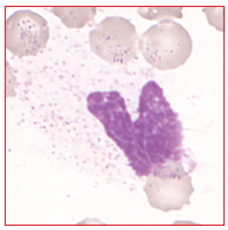
Additional cell artifacts include «edematous nuclei», «karyopyknosis», and «karyorrhexis forms». These effect are tightly associated with the amount of fluid in the nucleus. The nucleus, enclosed by the nuclear membrane, contains dense chromatin strands (DNA filaments) that are separated from each other by the nuclear plasma.

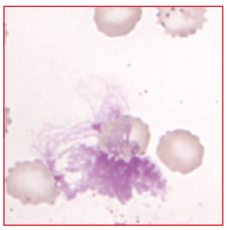
Edematous nuclei

If the amount of plasma in the nucleus increases, edematous spelling of the nucleus occurs. The structure of the nucleus becomes massively decondensed and cloud-like. In a more extreme form, the cytoplasm is no longer visible and the lineage the cell is part of can no longer be determined. With neutrophil granulocytes, this effect can at first lead to problems in distinguishing unsegmented cells from segmented cells (pseudo-left shift).


normal neutrophil


edemotous nucleus


cell autolysis


damaged cell (basket cell)

Karyopyknosis

If the amount of nuclear plasma decreases, the nucleus appears smaller than normal and the nuclear chromatin increasingly condenses and becomes clumpy. This is referred to as «karyopyknosis» or a «pyknotic nucleus». The cytoplasm can generally still be seen in these cells and an association to a certain cell lineage can be made. However, karyopyknosis can strongly compromise the evaluation of the fine morphology, e.g., of lymphocytes.