Indications for bone marrow examination and decision criteria for bone marrow cytology or bone marrow histology

In adults all cells of the peripheral blood are generated in the bone marrow (haematopoiesis). They all derive from stem cells that are dividing and either remain stem cells (autoreplication) or become precursors of the different cell lineages. The generation of three main cell lineages are distinguished as erythropoiesis, granulopoiesis and thrombopoiesis. For lymphocytes the bone marrow is also an important compartment. In adults haematopoiesis takes place far from the blood vessels (sinus). With increasing maturity the cells get closer to the sinus. The sinus wall represents a barrier. Normally, only mature cells can enter the peripheral blood (blood-bone marrow barrier).

A bone marrow examination is performed in certain clinical conditions (e.g. lymphoma) or when findings in the peripheral blood (such as anaemia, leukocytosis) are otherwise inexplicable.

In general there are two different types of bone marrow examination: Bone marrow cytology, which requires a bone marrow aspiration, and bone marrow histology, which requires a biopsy. Puncture site for both types of examination is usually the iliac crest (Posterior superior iliac spine). If both, a bone marrow cytology and a histology need to be performed it is recommended to do the biopsy before the aspiration.

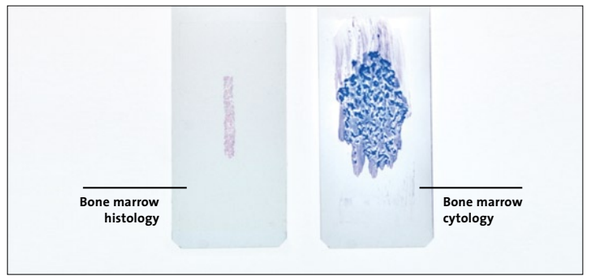
By using a hollow needle in a biopsy, a cylinder is obtained (at least 15 mm long and 1 mm wide), fixed, dehydrated, decalcified and in most cases embedded in paraffin. Subsequently thin sections are prepared (see figure below, left slide). Apart from number and type of the haematopoietic cells also their spatial distribution, their relative position to the bone trabeculae and these themselves can be evaluated. The bone marrow histology provides a one-to-one picture of the bone marrow structure.

For aspiration the bone marrow will also be punctured with a needle, but after this it is aspirated with a syringe. During the following preparation the so called spicules are squeezed flat (right slide) to generate a mono- or multilayer of cells that is suitable for light microscopy. The topography of the cells is mostly lost in this process. However, the cells can be better examined individually. Since the cells in the cytological preparations usually remain completely preserved and are not truncated, the analysis of the morphology of a single cell is easier done by cytology compared to histology.

However, if there is an increase in fibre content of the bone marrow, like for example in some myeloproliferative syndromes or lymphomas, the cells are fixed to the bone trabeculae and cannot be aspirated and analysed by cytology. If no small spicules can be obtained in a puncture, it is called a dry tap or *punctio sicca*.

Nowadays molecular biological analyses can often be conducted from paraffin sections of the biopsy, although it is better to use the aspirate. However, cytogenetic analyses (e.g. mandatory in acute leukaemias and chronic myelogenous leukaemia) can only be performed with aspirated cells, using heparin for anticoagulation because these living cells need to be stimulated to divide *in vitro*.

Bone marrow aspiration and biopsy often complement each other and are frequently performed in one operation.

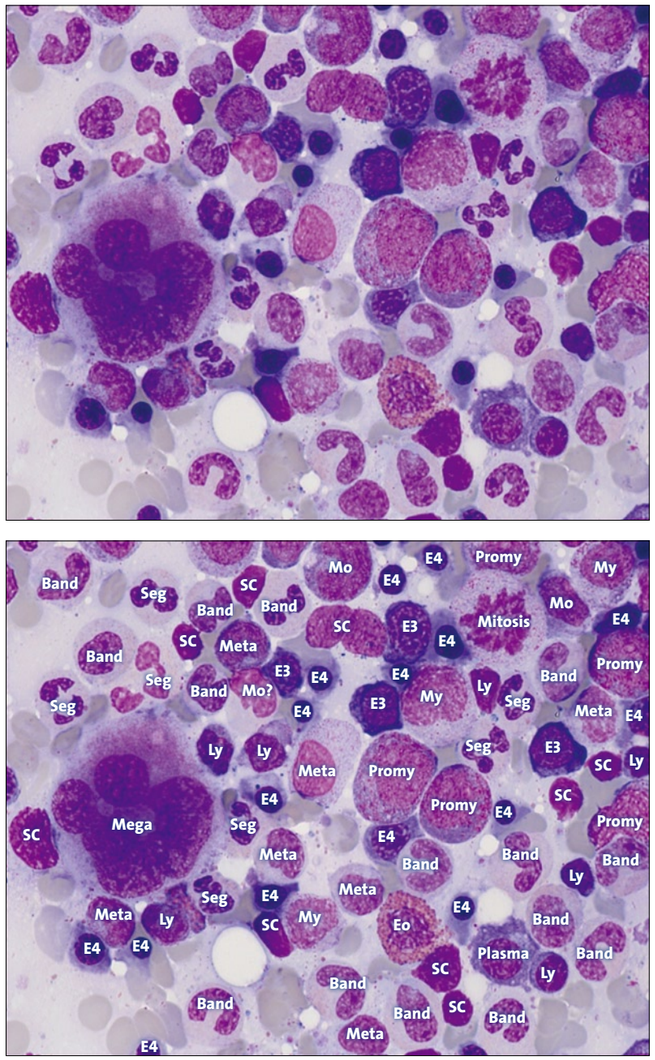


The following table contains the indications for bone marrow cytology and histology.

\+ examination is mandatory
(+) examination is helpful, but not mandatory
ø examination is usually not indicated

Changes in the peripheral blood or suspected diagnosis	Bone marrow cytology (Aspiration)	Bone marrow histology (Biopsy)
Otherwise inexplicable **isolated neutropenia**	+	(+)
Otherwise inexplicable **isolated anaemia**	+	(+)
Otherwise inexplicable **isolated thrombocytopenia**	+	(+)
Dry tap aspiration ***(punctio sicca)***		+
Otherwise inexplicable **bi-** or **tricytopenia (pancytopenia)**	+	+
Myelodysplastic syndrome (MDS)	+	+
Acute leukaemia	+	+ In case of dry tap or reduced cell count in the aspirate.
Chronic lymphocytic leukaemia (B-CLL) (No neutropenia, no anaemia, no thrombocytopenia, typical blood count and typical expression profile in immunophenotyping)	ø	ø
Malignant lymphomas except **chronic lymphocytic leukaemia (B-CLL)**	+	+
Chronic myelogenous leukaemia (CML)	+	+ If the *BCR-ABL* fusion gene or the Philadelphia chromosome cannot be detected in the peripheral blood or if enough material cannot be aspirated.
Polycythemia vera (PV)	+	+
Chronic idiopathic myelofibrosis (CIMF)	+	+
Essential thrombocythaemia (ET)	+	+
Multiple myeloma	+	+
Bone metastases	(+)	+
Granulomatous diseases	ø	+
Hodgkin's disease	ø	+
Osteoporosis, osteomalacia* and other **systemic diseases**	ø	+
Leishmaniasis	+	ø

*Special fixation necessary. Please make sure to contact the laboratory.



Normal bone marrow cytology. Some cells are always squeezed and damaged. These cells are called smudge cells. Smudge cells cannot be examined and must not be regarded as pathological (They have nothing to do with Gumprecht shadows in the peripheral blood smear). On the top right a mitosis is visible. The abbreviations mean:

Band	Band neutrophil
E3	Polychromatic erythroblast
E4	Orthochromatic erythroblast
Eo	Eosinophil granulocyte
Ly	Lymphocyte
Mega	Megakaryocyte
Meta	Metamyelocyte
Mo	Monocyte
My	Myelocyte
Plasma	Plasma cell
Promy	Promyelocyte
SC	Smudge cell
Seg	Segmented neutrophil
?	No clear assignment possible

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