Chapter 4 Qualitative Abnormalities in Myeloid Cells-

Cytoplasmic Abnormalities

Mindray Morphology Corner | Series Course-IV WBC

Identify myeloid cytoplasmic abnormalities, standardize morphology-based hematological diagnosis.

If we compare bone marrow hematopoiesis to a white blood cell production workshop, myeloid cells are the front-line troops responsible for immune defense, anti-inflammation and pathogen clearance. This cell group includes neutrophils, eosinophils, basophils and monocytes.

When myeloid cells mature normally, their cytoplasm shows regular shapes. Once gene mutations, severe infection, toxins or nutritional deficiency interfere with cell development, cytoplasm will produce various pathological deformities, which we call **myeloid cytoplasmic abnormalities.**

These cytoplasmic changes are critical morphological clues for lab technicians. Mastering their features helps us quickly screen myelodysplastic syndrome, severe bacterial infection, inherited lysosomal disorders and other blood diseases.

I. What is myeloid cytoplasmic abnormality?

Cytoplasmic abnormalities of qualitative abnormalities in myeloid cells refer to pathological distortions in morphology, structure, granule characteristics of myeloid cells during differentiation and maturation caused by gene mutation, external toxins, severe infection, nutritional deficiency and other factors, which are different from normal physiological morphological differences, and is widely seen in benign stress lesions and malignant hematopoietic system diseases.

II. What are the types of cytoplasmic abnormalities in the myeloid cells?

1. Auer rod

Auer rods are bright red, needle-like structures inside cell cytoplasm. They form when primary granules develop abnormally. One cell can carry one or multiple Auer rods. When lots of rods bundle together, we name these faggot cells.

- Location: Mostly seen in leukemic myeloblasts and abnormal promyelocytes
- Chemical feature: Positive myeloperoxidase staining
- Diagnostic value: Special marker proving this abnormal cell belongs to myeloid leukemia

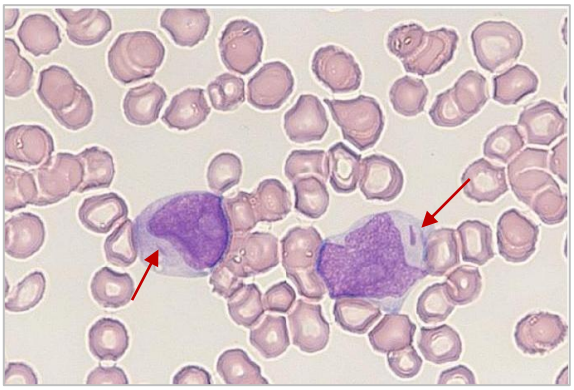


Figure 1.1

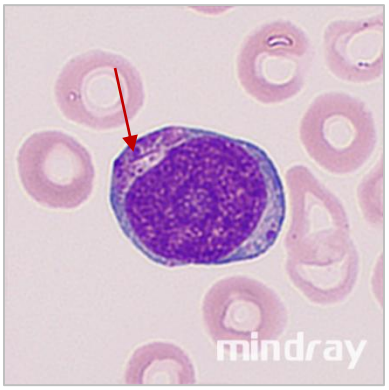


Figure 1.2

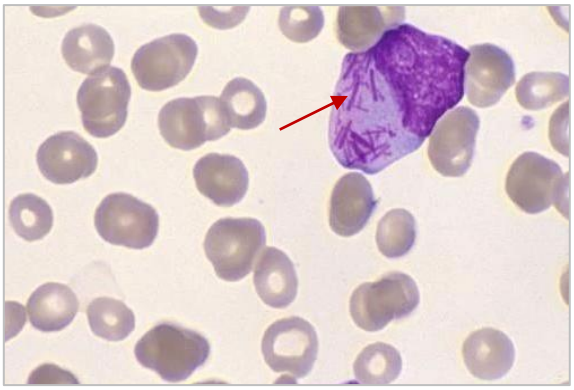


Figure 1.3

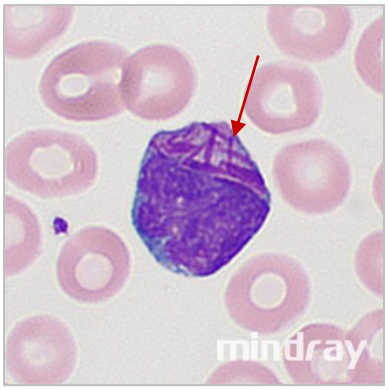


Figure 1.4

Figure 1.1&1.2: **Auer Rod**
Figure 1.3&1.4: **Faggot Cell**

- **Differences between Auer rods and Faggot cells**

Dimension	**Auer Rods**	**Faggot Cells**
Essential Nature	Intracellular granular crystalline structure	Complete abnormal leukemic cell (containing characteristic bundled Auer rods)
Quantity & Morphology	Single or a few scattered rods, slender or stubby in shape	**≥3** or dozens of thick, dense rods arranged in bundled/faggot-like cross pattern
Distribution Range	Observed in all **AML** subtypes (M1-M6) and high-risk MDS	Specifically present only in **M3 (APL)**
Diagnostic Value	Indicates myeloid lesions; **excludes lymphocytic leukemia**	Serves as a direct diagnostic basis for acute promyelocytic leukemia
Subordinate Relationship	Basic microscopic structure	Specific aggregated morphological manifestation of Auer rods

2. Döhle body

Döhle bodies are pale blue, cloud-shaped blobs at the edge of neutrophil cytoplasm. They form when immature ribosomes pile up inside cells. Acute stress reactions, including severe bacterial infection, burns, trauma and sepsis may case this situation.

- Matching signs: Usually come with toxic granules and cytoplasmic vacuoles
- Recovery feature: Reversible. Cell morphology turns normal once the primary disease gets controlled
- Special reminder: If Döhle bodies appear together with low platelets and giant platelets, we need to suspect **May-Haggin Anomaly (MHA)**, an inherited disorder.

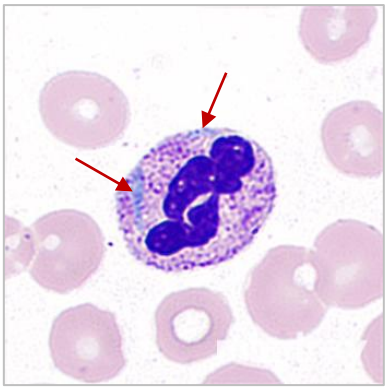


Figure 2.1

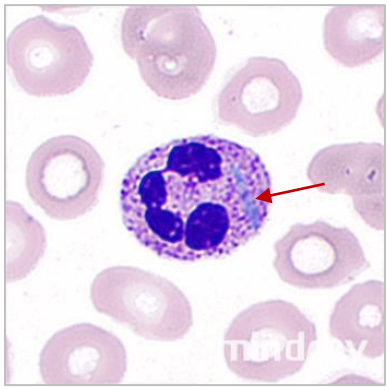


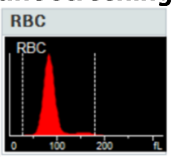
Figure 2.2

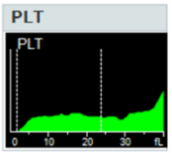
Figure 2.1&2.2: **Döhle Body**

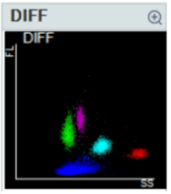
- **Clinical Case for May-Hagglin anomaly**

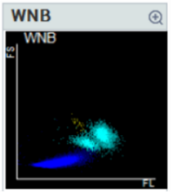
➢ **Background and blood routine screening**

STAT	Para.	Flag	Result	Delta(#)	His. 1	His. 2	Unit
	WBC		6.44				10^9/L
	Neu#		2.98				10^9/L
	Lym#		2.13				10^9/L
	Mon#		0.50				10^9/L
	Eos#	H	0.79				10^9/L
	Bas#		0.04				10^9/L
	IMG#		0.01				10^9/L
	Neu%	L	46.3				%
	Lym%		33.0				%
	Mon%		7.8				%
	Eos%	H	12.3				%
	Bas%		0.6				%
	IMG%		0.1				%
	RBC		4.39				10^12/L
	HGB		123				g/L
	HCT	L	36.3				%
	MCV		82.8				fL
	MCH		28.0				pg
	MCHC		339				g/L
	RDW-CV		13.3				%
	RDW-SD		40.9				fL
⚠	PLT	R L	32				10^9/L
	MPV	R H	14.0				fL
	PDW	R	15.8				
	PCT	R L	0.044				%
	P-LCC	R L	20				10^9/L
	P-LCR	R H	62.6				%
	NRBC#		0.000				10^9/L
	NRBC%		0.00				/100WBC







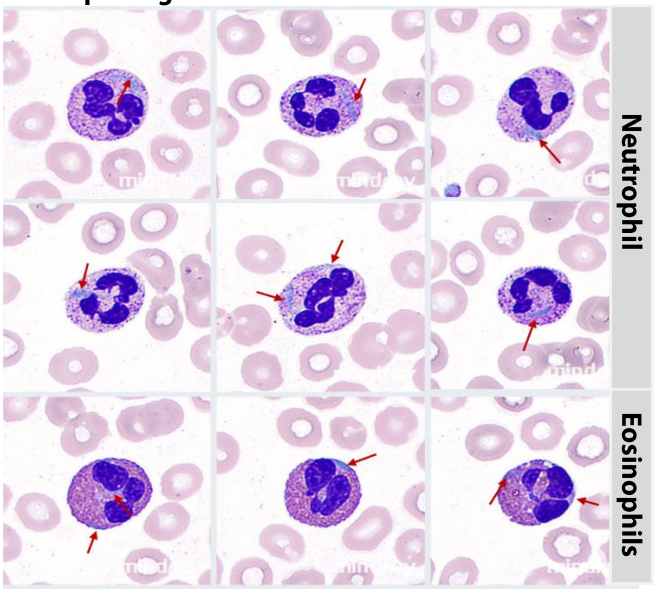


Case background: 30-year-old female patient, visited hospital for persistent tiredness and frequent nosebleeds.

Blood analyzer triggered abnormal flags, and the report showed three classic MHA markers:

1. Thrombocytopenia (platelet count decreased)
2. Massive giant platelets in peripheral blood

➢ **Morphological examination confirmation**



3. Blue cloud-like inclusions inside neutrophils and eosinophils

Confirmation steps:

- Blood smear microscopy to observe cytoplasmic inclusions
- Genetic test to detect MYH9 gene mutation (gold standard for final diagnosis)

➢ For case details, please go to: [Automation Meets Morphology: Critical Steps for May-Hegglin Diagnosis in Routine Blood Work].

- **Differences between Döhle bodies and MHA inclusions**

Morphological identification of Dohle bodies and MHA inclusions:			
Type	**Morphology**	**Accompanied Symptoms**	**Prognosis**
MHA inclusion	In neutrophils, eosinophils, and monocytes, located around or in the center of the cytoplasm, with diverse and irregular shapes, sizes ranging from 2-5 μm, and clear boundaries	Accompanied by the presence of giant platelets	The blue spots in MHA patients persist throughout their lives.
Dohle body	Only appearing in neutrophils, located around the cytoplasm, with a small volume of 1-3 μm, often in a cloud like shape with unclear circular or elliptical boundaries	Accompanied by granulocyte toxicity granules, vacuolar degeneration, nuclear condensation and other manifestations of granulocyte toxicity	When the infection is under control, the dohle bodies will disappear

3. Hypergranulation–neutrophil, (toxic granulation)

Toxic granules are manifested as coarse, purple staining primary (azurophilic) neutrophil cytoplasmic granules distributed in the cytoplasm of neutrophils, which are landmark morphological changes of severe bacterial infection, sepsis and severe inflammatory stress. The more severe the infection, the more significant the granule abnormality. A non-specific reactive change, it is a result of abnormal primary granule maturation with retention of their azurophilic staining properties.

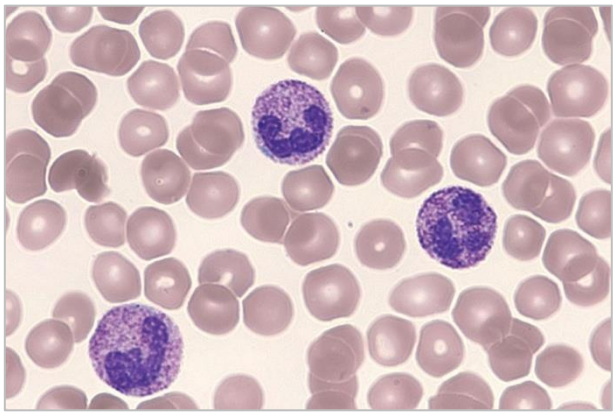


Figure 3.1

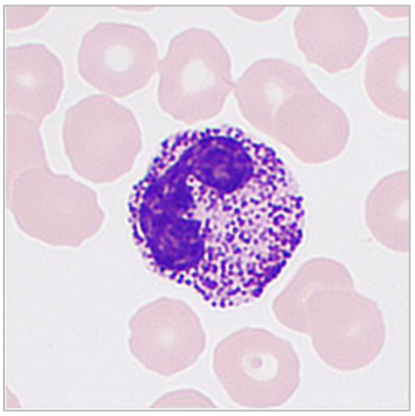


Figure 3.2

Figure: 3.1&3.2: **Hypergranulation–neutrophil, (toxic granulation)**

- **Characteristic:**

DESCRIPTION: Prominent dark purple-black granules in the cytoplasm of neutrophils, unevenly distributed.
COMPOSITION: Primary granules
NUMBER: Few to many
ASSOCIATED WITH: Wide range of conditions including bacterial infection, sepsis and following administration of granulocyte colony-stimulating factor

- **The impact of increased neutrophil toxicity particles on the WBC classification results of a hematology analyzer:**

The DIFF channel of the Mindray blood cell analyzer is mainly used to detect the number of WBC, classify neutrophils, lymphocytes, monocytes, and eosinophils, and alert abnormal cells. The normal DIFF channel scatter plot shows the main distribution of cells as shown in the following figure (Figure 3.3).

After being processed with reagents, the hematology analyzer can distinguish the complexity of different WBC cell contents through SS signal detection, thereby achieving classification differentiation.

When severe bacterial infection hits the body, neutrophil immature granules accumulate extra sticky acidic substances and turn into toxic granules.

Toxic granules make neutrophils more structurally complex:

1. **Side scatter (SS) signal rises and shifts right on DIFF scattergram**
2. **The machine misjudges these abnormal neutrophils as eosinophils, causing falsely elevated eosinophil percentage**

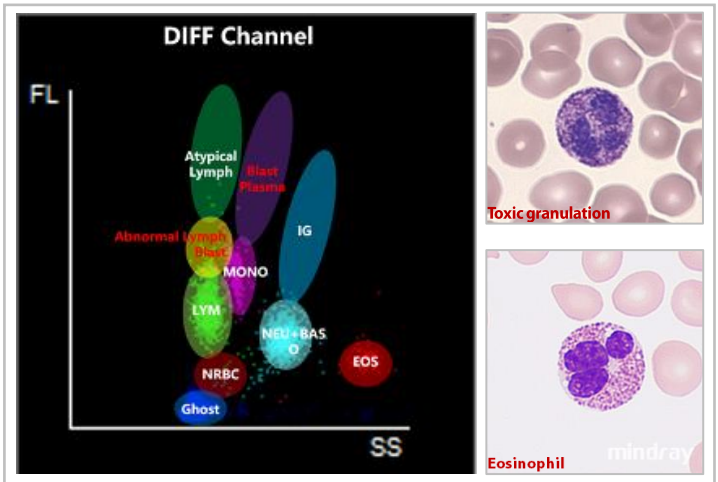


Figure 3.3

Therefore, when facing complex cell morphology, the accuracy of instrument classification may be limited, and manual microscopy or other detection methods are still necessary supplements. When EOS%>15% and abnormal WBC scattergram alarm is triggered, manual microscopy is required to ensure the accuracy of WBC classification and counting results.

4. Hypogranulation–neutrophil

Mature neutrophils lose most or all cytoplasmic granules, leaving pale blue-gray cytoplasm. This sign is highly specific for **myelodysplastic syndrome (MDS)**.

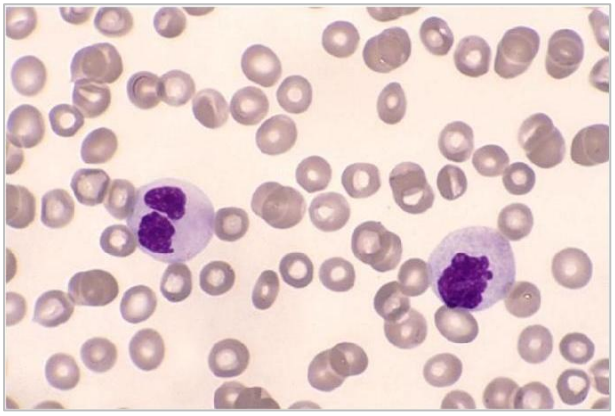


Figure 4.1

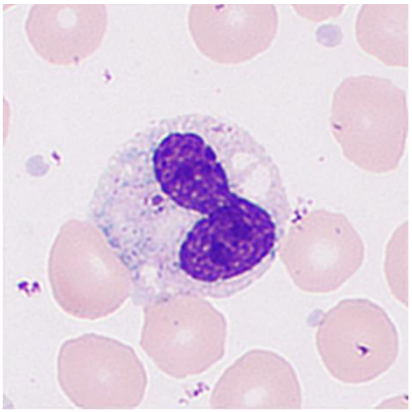


Figure 4.2

Figure: 4.1&4.2: **Hypogranulation–neutrophil**

- **Characteristic:**

  DESCRIPTION: Decreased number or absence of specific granules giving the cytoplasm a colorless appearance.
  ASSOCIATED WITH: Myelodysplastic syndrome, myeloproliferative neoplasms, infection.

MDS patients experience genetic mutations and chromosomal abnormalities in bone marrow hematopoietic stem cells, leading to disrupted granulocyte differentiation programs and interference with granule synthesis.

MDS-induced granule loss: Permanent. Cells cannot recover normal granule production automatically. If we see lots of agranular neutrophils plus nuclear deformities and multi-lineage cytopenia, MDS is highly suspected.

Benign reactive granule changes: Temporary. Cell morphology returns to normal after

infection or stress is relieved.

5. Vacuolation– neutrophil

Neutrophil cytoplasmic vacuolation in infection is due to granule fusion with a phagocytic vacuole and release of lysosomal contents to kill bacteria. This vacuolation may appear as 'pin-hole' vacuolation– small, discrete vacuoles, but the vacuoles may be larger. Other causes of neutrophil vacuolation include alcohol toxicity and prolonged exposure to EDTA anticoagulant (storage artefact).

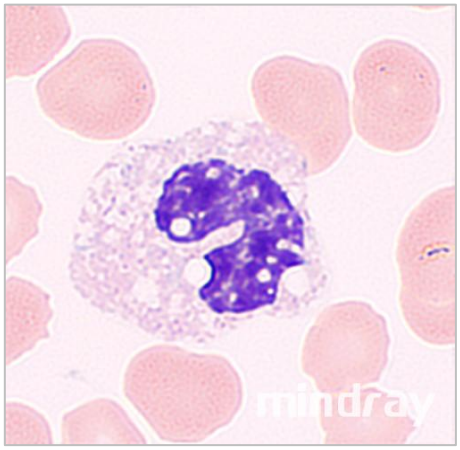


Figure 5.1

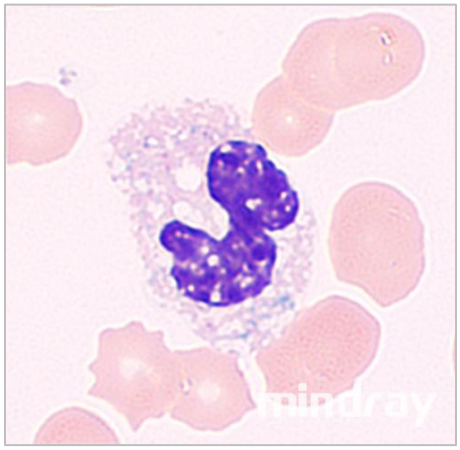


Figure 5.2

Figure: 5.1&5.2: **Vacuolation– neutrophil**

- **Characteristic:**

  DESCRIPTION: Unstained circular area within the cytoplasm.
  NUMBER: Few to many
  ASSOCIATED WITH: Bacterial or fungal infection, poisoning, burns, chemotherapy, artifact.

Neutrophil vacuolization generally belongs to reversible damage after cellular stress and poisoning, indicating the presence of acute inflammation, poisoning, or severe stress in the body. When accompanied by other typical abnormal forms such as granular reduction and nuclear malformation, MDS may be considered.

When **neutrophil vacuolization** is found in peripheral blood, due to the similarity with **monocytes with vacuoles**, it is necessary to pay attention to distinguishing them:

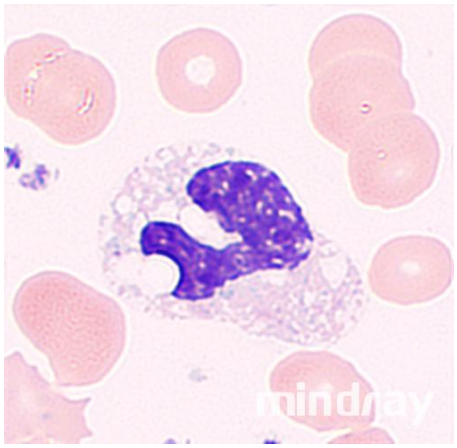


Figure 5.3

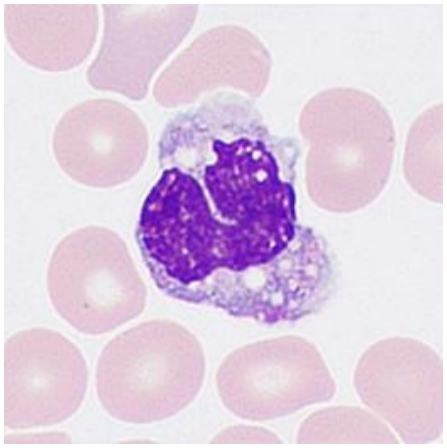


Figure 5.4

Figure: 5.3: **Vacuolation– neutrophil**; Figure: 5.4: **Monocytes**

Identification Item	Vacuolated Neutrophil	Monocyte
Nucleus	Segmented/band, When vacuolar degeneration is caused by **MDS**, it is often accompanied by abnormal nucleation	Irregular, twisted, folded & notched; no regular lobulation
Chromatin	Coarse, condensed and clumped, dark purplish-red	Fine, loose and reticular, pale staining
Cytoplasm Background	Pale pink; slightly blue in MDS cases; Vacuolation caused by **infection** may be accompanied by toxic particles and Döhle bodies	Grayish-blue, ground-glass and translucent
Cytoplasmic Granules	Pink granules or coarse toxic granules; may be decreased/absent	Fine dust-like azurophilic granules, uneven distribution
Vacuole Feature	Scattered or honeycomb-like, regular border; pathological change	Diffuse & irregular, foamy; inherent normal feature
Cell Contour	Round/oval, smooth edge, no pseudopodia	Irregular shape, often with pseudopodia

Also, when **the smear is air dried too slowly, the slide pushing technique is improper, the specimen is left for too long (aged sample), the staining solution deteriorates**, etc., it may lead to abnormal morphology caused by non-sample reasons. It is important to rule out artificial factors before re-making the slide.

Myeloid cytoplasmic abnormalities are core observation markers in blood smear microscopy, covering granule defects, cytoplasmic inclusions and vacuolar degeneration. Their root causes sometime are due to:

1. Benign stress changes (severe infection, trauma, poisoning, reversible)
2. Malignant hematopoietic lesions (MDS, acute myeloid leukemia, permanent dysplasia)
3. Inherited hematological disorders (May-Hagglin anomaly, caused by gene mutation)
4. Others

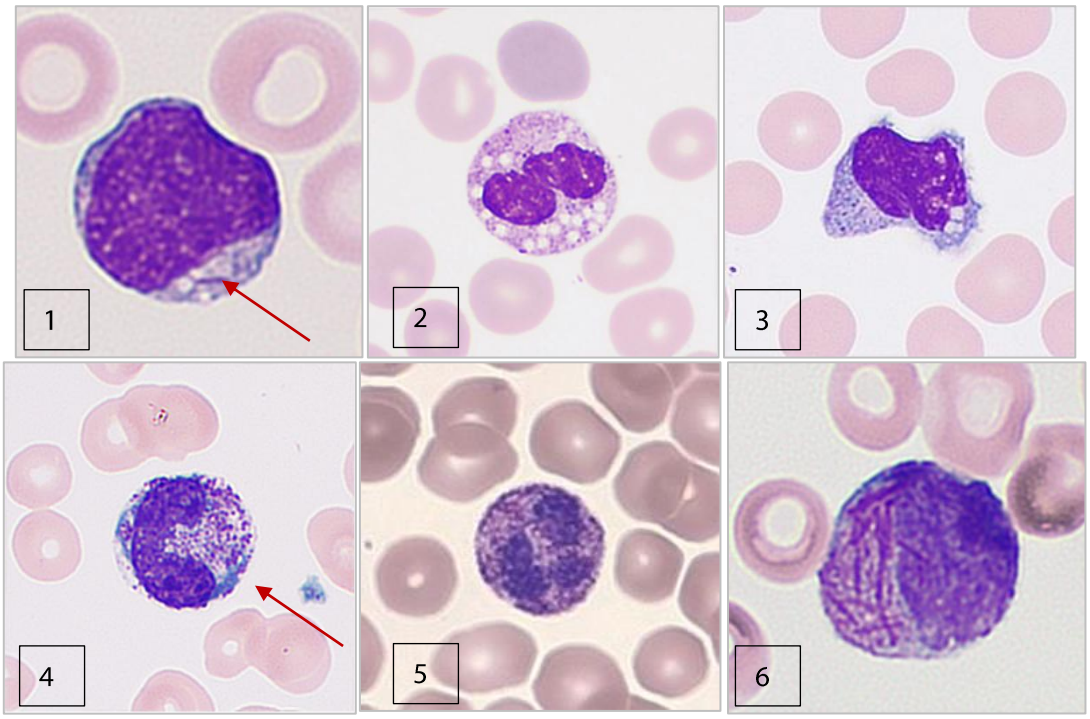
In daily lab work:
Combine cell morphology, abnormal cell counts and patient clinical history to separate normal physiological differences, benign reactive changes and malignant blood disease signs. These morphological findings provide solid evidence for evaluating infection severity, screening blood malignancies and tracking disease progression, and greatly improve lab diagnostic accuracy.

References & Image Sources

References:
1. Carr J H. Clinical Hematology Atlas. 6th ed. Elsevier; 2021.
2. Palmer L, Briggs C, etc., ICSH recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features. Int J Lab Hematol. 2015 Jun;37(3):287-303.

Images & Technical Support: Some morphology images in this course are derived from analysis by the **Mindray automated digital morphology analyzer MC-80.**

Practice



[The answers will be at the end of the next chapter]

The answer of last chapter: 1. Lymphoblast; 2. lymphocyte; 3. lymphocyte;

Author

Romin Zhang
— Clinical Application Specialist

— Coming Next: **Qualitative Abnormalities in Myeloid Cells- Nuclear Abnormalities**—