JSLH Schistocyte Morphological Standardization Guidelines

Ver.1.1e

The Japanese Society for Laboratory Hematology

Contents

schistocyte（Japanese name：破砕赤血球, hasai sekkekkyū）

Schistocytes are abnormally shaped red blood cells that have sustained exogenous physical damage while circulating in the bloodstream. Their detection is crucial for the diagnosis of thrombotic microangiopathy (TMA). Although several criteria have been proposed, variability in judgment persists due to the diversity of morphologies and the subjective nature of the examiner's assessment. The International Council for Standardization in Haematology (ICSH) has developed and published specific recommendations to standardize the identification, enumeration, and reporting of schistocytes. In line with these recommendations, we have developed morphological standardization criteria for schistocytes with the aim of enhancing the clinical value of schistocyte reporting in the diagnosis of TMA.

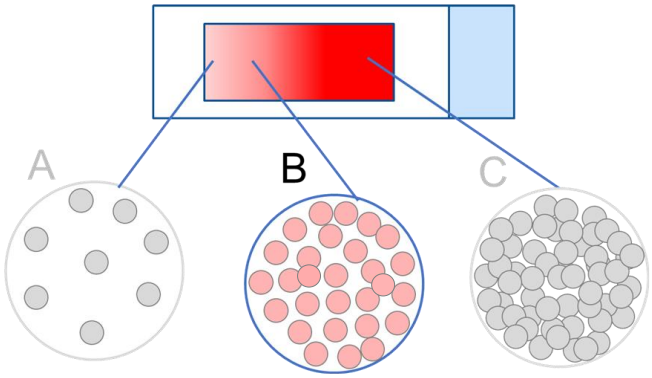
1. Handling of Specimens and Microscopic Examination Methods

1.1 Specimen Handling

To prevent morphological changes, it is recommended to prepare smear specimens within 3 hours after blood collection when stored at room temperature (18–25 °C), or within 8 hours if stored at 4 °C [1)]. Morphological changes in red blood cells can begin as early as 1 hour after collection at room temperature, and even when stored at 4 °C, alterations such as an increase in mean corpuscular volume (MCV) may occur after more than 6 hours [2)]. Therefore, when preparing smears from blood samples stored for extended periods, caution must be exercised and potential morphological changes taken into consideration.

1.2 Microscopic Examination Methods

First, examine the condition of the blood smear. Ensure that there is no generalized shrinkage or destruction of red blood cells; if such changes are present, prepare a new smear. After spreading the blood, perform thorough air-drying using cool air to prevent cellular shrinkage. Red blood cell counting should be performed in an area approximately one-third from the feathered edge of the smear, where the red cells are evenly distributed, closely spaced, and overlapping by less than 50% (Figure B). The schistocyte ratio should be calculated based on the number of schistocytes found in at least 1,000 counted red blood cells. Examination should be carried out under medium magnification (×400) or high magnification (×600–1,000). When using high magnification, note that the field of view is narrower and be mindful of potential uneven distribution of schistocytes.



Area of the smear for red blood cell counting.

Confidence limits for the schistocyte ratio when counting between 100 and 10,000 cells[3,4].

schistocyte(%)	/100 RBC	/1,000 RBC	/10,000 RBC
0	0.0 - 3.6	0.0 – 0.4	0.0 – 0.1
1	0.0 – 5.4	0.5 – 1.8	0.8 – 1.3
2	0.2 – 7.0	1.2 – 3.1	1.7 – 2.3
3	0.6 – 8.5	2.2 – 4.3	2.6 – 3.4
4	1.1 – 9.9	2.9 – 5.4	3.6 – 4.5
5	1.6 – 11.3	3.7 – 6.5	4.5 – 5.5
6	2.2 – 12.6	4.6 – 7.7	5.5 – 6.5
7	2.9 – 13.9	5.5 – 8.8	6.5 – 7.6
8	3.5 – 15.2	6.4 – 9.9	7.4 – 8.6
9	4.2 – 16.4	7.3 – 10.9	8.4 – 9.6
10	4.9 – 17.6	8.2 – 12.0	9.4 – 10.7
15	8.6 – 23.5	12.8 – 17.4	14.3 – 15.8

RBC : red blood cells

2. Morphological Features and Classification of Schistocytes

2.1 Morphological Features

The following morphological features are used to identify schistocytes:

- Size
- Contour (angles/spikes, straight lines, arcs, circles)
- Color tone
- Central pallor (CP)

Note: These features should always be evaluated in comparison with normal, non-deformed red blood cells present on the same smear.

2.2 Schistocyte Shapes and Descriptions

Schistocytes can be broadly divided into two categories:

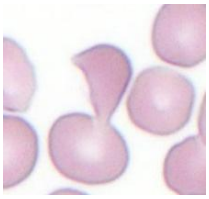
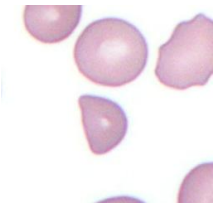
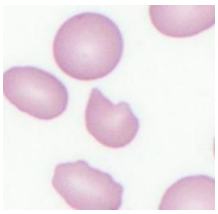
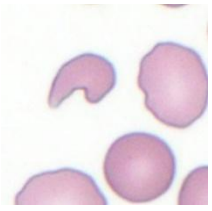
- Category A: Typical shapes observed in TMA
- Category B: Atypical shapes that may occur in conditions other than TMA and are not necessarily typical of TMA

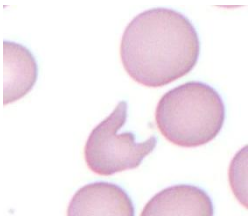
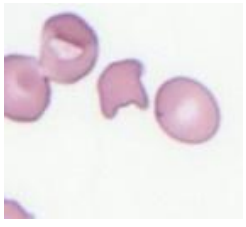
For Category B, caution should be exercised when considering them as schistocytes. They should only be included in the schistocyte count when the prevalence of Category A shapes is sufficiently high. The morphological categories are described below.

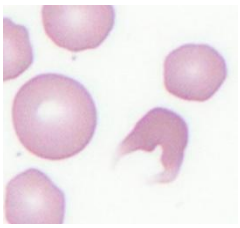
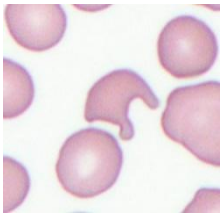
2.2.1 Category A (Typical Shapes)

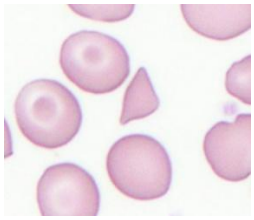
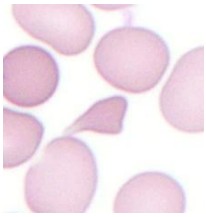
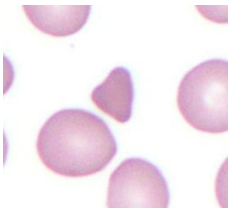
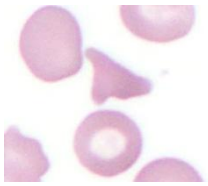
- Smaller than normal, non-deformed red blood cells, with shapes characterized by straight edges, sharp angles, or two to three pointed projections. Common forms include crescent-shaped, triangular, helmet-shaped, and keratocyte types. Identification should focus on size, straight edges, sharp angles, and color tone.
- Central pallor (CP) is often absent, but its presence does not rule out a schistocyte.
- The color tone is generally equal to or darker than that of the surrounding normal red blood cells; cells with a paler tone should be excluded to avoid confusion with conditions such as iron deficiency anemia.

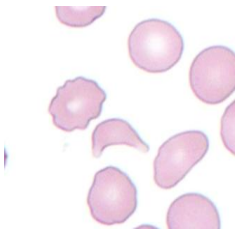
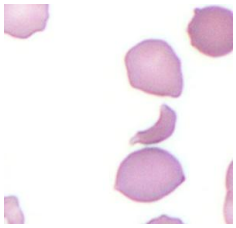
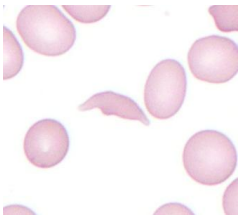
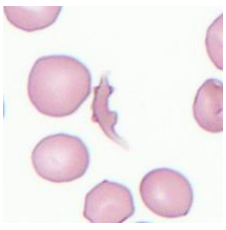
【Category A (Typical Shapes)】

	Small and dark-colored, helmet-shaped with straight edges and sharp angles.		Small and dark-colored, helmet-shaped with straight edges; slight central pallor present.
	Small, with equal or darker color tone; helmet-shaped with two straight edges; slight central pallor observed.		Small and dark-colored, helmet-shaped or C-shaped with two straight edges and sharp angles.

	Small, with equal or darker tone; keratocyte with three points opposite the arc.		Small and dark-colored, keratocyte with a single point opposite the arc.

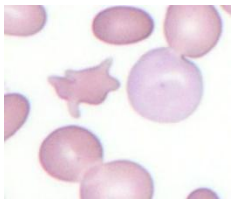
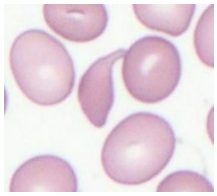
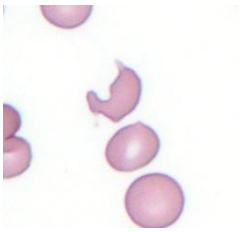
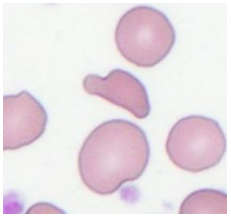
	Small and dark-colored, keratocyte with two points opposite the arc.		Small and dark-colored, keratocyte with two points opposite the arc.

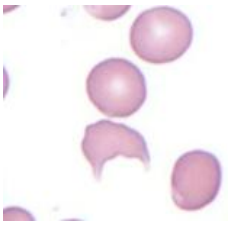
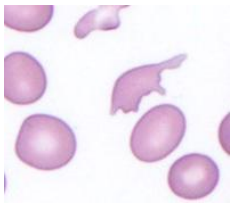
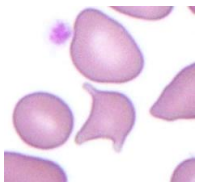
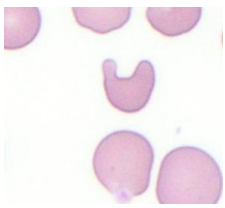
	Small and dark-colored, triangular-shaped with three slightly curved straight edges and two sharp angles.		Small and dark-colored, triangular-shaped with three slightly curved straight edges and two sharp angles, one of which is blunt.
	Small and dark-colored, triangular-shaped with three slightly curved straight edges, each corner having a blunt angle.		Small and dark-colored, triangular-shaped with three slightly curved straight edges and three sharp angles.

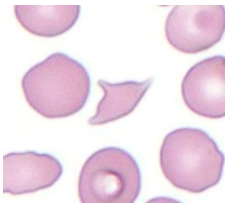
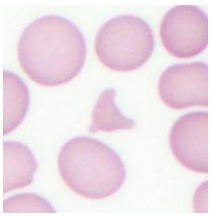
	Small and dark-colored, crescent-shaped with two curved edges and sharp angles at both ends.		Small and dark-colored, crescent-shaped with two curved edges and sharp angles at both ends.
	Small and dark-colored, crescent- or helmet-like in shape, with one curved edge, one straight edge, and sharp angles at both ends; narrower than the helmet type.		Small and dark-colored, crescent-shaped with a slightly irregular curved edge and sharp angles at both ends.

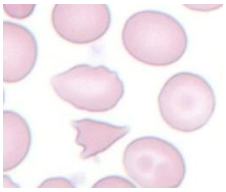
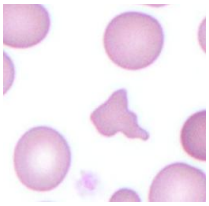
【Variations of Category A (Typical Shapes)】

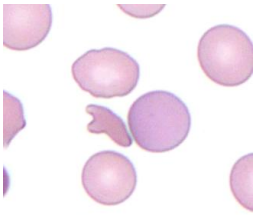
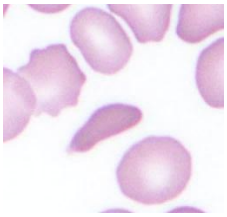
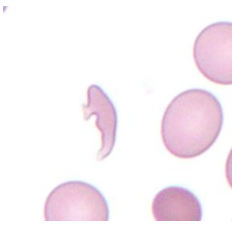
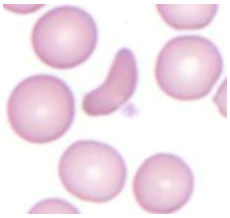
Shapes consistent with Category A that exhibit variations in their features.

	Small and dark-colored, helmet-shaped or horned helmet-like, with a horn on the side opposite a slightly curved straight edge.		Small and dark-colored, helmet-shaped with a slightly curved straight edge and a horn on one side.
	Small and dark-colored, helmet cell or keratocyte with a straight edge and two projections on one side, one broad with a blunt tip.		Small and dark-colored, helmet-shaped cell with a straight edge and a broad, rounded projection on one side.

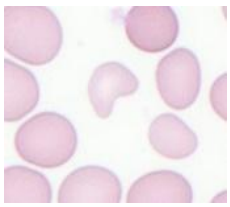
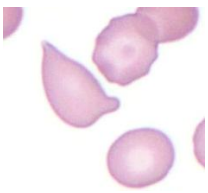
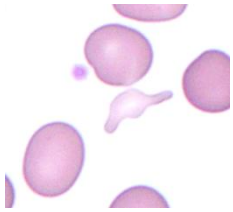
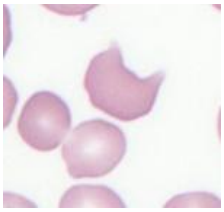
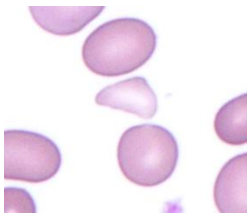
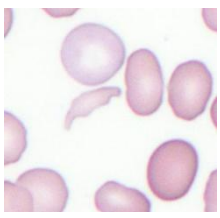
	Small and dark-colored, keratocyte with two projections opposite the arc, with a slightly irregular outline.		Small and dark-colored, keratocyte with a serrated projection opposite the arc.
	Small and dark-colored, keratocyte-like cell with one projection opposite the arc and two at both ends.		Small and dark-colored, keratocyte-like cell with two broad, blunt projections opposite the arc.

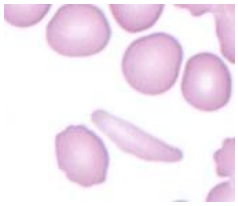
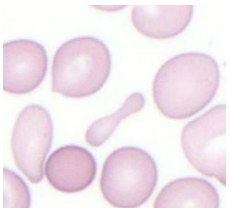
	Small and dark-colored, triangular-like or keratocyte-like cell with a slightly curved straight edge, an arc, and three sharp projections.		Small and dark-colored, slightly curved triangular-like cell with three sharp projections.

	Small and dark-colored, triangular-like cell with two slightly curved straight edges, one serrated edge, and sharp projections.		Small and dark-colored, distorted triangular-like cell with a curved straight edge and two sharp projections.

	Small and dark-colored, crescent-like cell with two arcs whose ends are blunt, and with an additional blunt projection on one arc.		Small and dark-colored, crescent-like or helmet-like cell with blunt ends at both the arc and the straight edge, narrower than a typical helmet cell.
	Small and dark-colored, crescent-like cell with one serrated arc.		Small and dark-colored, crescent-like cell with blunt ends on both arcs.

【Shapes Resembling but Not Classified as Schistocytes】

	Small and helmet-shaped, but not a schistocyte due to its pale color.		Equal or darker in color and helmet-shaped, but not a schistocyte because it is larger than the surrounding RBCs.
	Small and helmet-shaped or keratocyte-like, but not a schistocyte due to its pale color.		Dark-colored and keratocyte-like, but not a schistocyte because it is larger than the surrounding RBCs.
	Small and helmet- or triangular-shaped, but not a schistocyte due to its pale color.		Small, crescent-like with one serrated edge and sharp angles at both ends, but not a schistocyte due to its pale color.

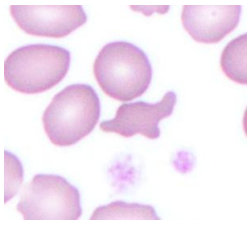
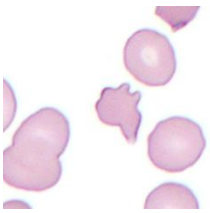
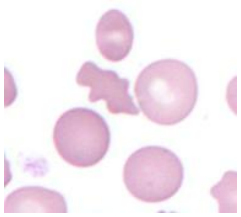
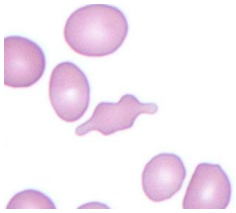
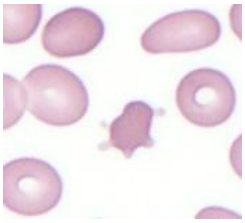
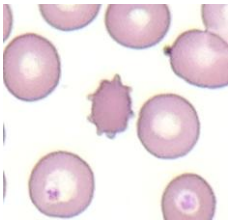
	Crescent-like in shape, but not a schistocyte because its color is equal to or paler than surrounding RBCs and it is larger than them.		Small and club-shaped, but not a schistocyte due to its pale color.

2.2.2 Category B (Atypical Shapes)

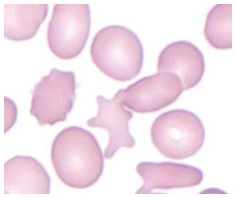
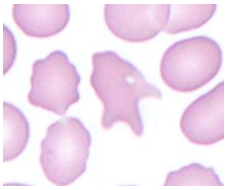
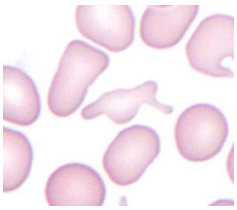
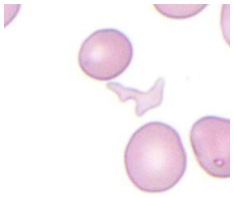
- Irregularly Shaped Cells

Smaller than surrounding normal, non-deformed red blood cells, hyperchromic, and with irregular shapes that do not meet the criteria for Category A. This group also includes burr-like forms resembling chestnut burrs, as well as small spherical shapes bearing spicules. Cells that possess central pallor (CP), are similar in size to surrounding red blood cells, or have a color tone that is pale or equivalent to that of surrounding cells are excluded. Care must be taken to differentiate these from morphologically similar cells such as acanthocytes.

【Category B (Atypical Shapes)】

	Small and dark-colored, irregularly shaped cell with projections.		Small and dark-colored, irregularly shaped cell with projections, slightly rounded.
	Small and dark-colored, irregularly shaped oval cell with projections around the entire perimeter.		Small and dark-colored, irregularly shaped cell with two projections at both ends.
	Small and dark-colored, microspherocyte-like cell with an irregular outline and spicules.		Small and dark-colored, microspherocyte-like cell with short spicules around the entire circumference.

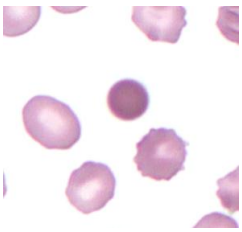
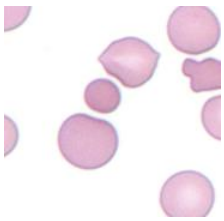
【Shapes Resembling but Not Classified as Schistocytes】

	Small and irregularly shaped with projections, but not a schistocyte because its color is equal to or paler than that of surrounding RBCs.		Dark-colored and irregularly shaped with projections, but not a schistocyte because it is larger than the surrounding RBCs.
	Small and irregularly shaped with projections, but not a schistocyte due to its pale color.		Small and fragment-like with projections, but not a schistocyte due to its pale color.

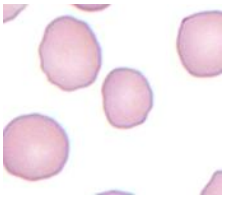
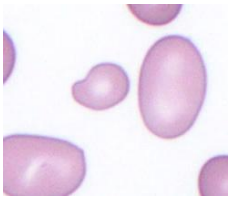
- Microspherocyte

Smaller than surrounding normal, non-deformed red blood cells, and spherical with a hyperchromic appearance. Cells that possess central pallor (CP), are similar in size to surrounding red blood cells, or have a color tone that is pale or equivalent to that of surrounding cells are excluded.

【Microspherocyte】

	Small in size and dark in color, spherical form.		Small in size and dark in color, spherical form.

【Shapes Resembling but Not Classified as Schistocytes】

	Small and resembling a microspherocyte with indistinct central pallor, but not a schistocyte because it is not dark in color.		Small and resembling a microspherocyte, but not a schistocyte because it is not dark in color and has a distinct central pallor.

3. Reporting Methods

To minimize inter-observer variability in the semi-quantitative assessment of schistocytes and to improve agreement rates in morphological diagnosis, this reporting method emphasizes the prevalence of Category A shapes, which are most typical of TMA.

When the prevalence of Category A shapes is ≥1%, Category B shapes should also be included in the count. Based on the prevalence, reporting is recommended according to the following criteria:

- <1%: “−”
- ≥1% to <3%: “1+”
- ≥3% to <10%: “2+”
- ≥10%: “3+”

Note: Points to Consider Regarding the Reporting of Schistocytes.

Schistocytes can be observed in various conditions other than TMA.

They may also occur in severe vitamin B12 deficiency; when accompanied by thrombocytopenia at onset, this is referred to as pseudo-thrombotic microangiopathy[5,6,7].

Other reported conditions include:

- Infections[8,9]
- Autoimmune atrophic gastritis[10]
- Myelodysplastic neoplasms[11]
- Disseminated intravascular coagulation (DIC)[12]
- Splenic angiosarcoma[13]
- Severe burns[14]

For differential diagnosis, it is essential to assess:

- Serum lactate dehydrogenase (LD)
- Bilirubin
- Haptoglobin
- Reticulocyte count

4. References

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