

# SCHISTOCYTES

## TERM DEFINITION

Schistocytes are fragments of red blood cells (RBCs) or amputated erythrocytes, from which those fragments have arisen, produced by extrinsic mechanical damage within the circulation.

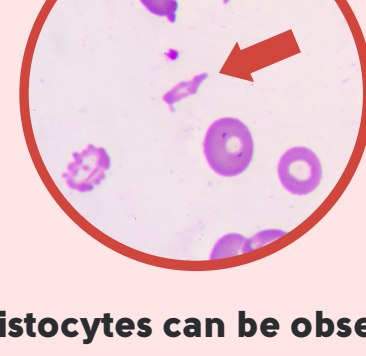
## CLINICAL PEARLS



Schistocytes, or schizocytes derive from the Greek word schisto, broken or cleft, or the correspondent verb schizo.



All schistocytes are red blood cell (RBC) fragments; not all red cell fragments are schistocytes.



Schistocytes can be observed on blood smears from healthy individuals at a frequency of 0.2–0.5% of RBCs.



An elevated schistocyte count is clinically meaningful only if schistocytes represent the main morphologic abnormality of the RBCs on the blood smear.



Schistocytes are always smaller than intact red blood cells; their presence may lower the mean cell volume (MCV) and/or be counted as platelets by the automated cell counter, leading to a falsely elevated platelet count.

## TYPES

Schistocytes are morphologically polymorphic, which complicates their detection and identification.

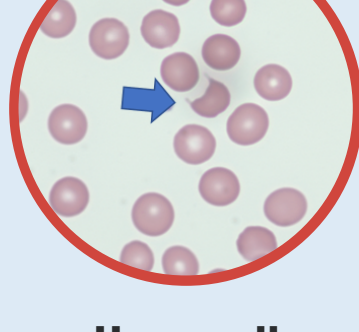
According to the ICSH Schistocyte Working Group, schistocytes should be identified by specific positive morphological criteria. Schistocytes are always smaller than intact red cells and can have the shape of fragments with sharp angles and straight borders, small crescents, helmet cells, keratocytes, or microspherocytes (only in the presence of triangular/crescent, helmet schistocytes and keratocytes).

TYPE	DESCRIPTION	CENTRAL PALLOR	SPECIFIC TO MAHA
Helmet cell	One single, rarely a double, amputated zone highlighted by a straight border, with sharp angulated edges.	No	Yes
Keratocyte (horn cell)	Pair of spicules separated by a semicircular concave segment of membrane, sometimes even two or three pairs.	Yes	No. They are morphologically identical to bite cells seen in oxidative hemolysis, consisting of a curved bite-shaped peripheral defect in their surface.
Triangle cell	Small fragments with sharp angles or spines.	No	Yes
Crescent cell	Small fragments with a round outline on one side.	No	Yes
Microspherocyte	Small-sized hyperdense RBCs with a round shape and increased staining.	No	No. They may also be seen in infection (e.g., Clostridial sepsis), autoimmune hemolytic anemia and other conditions. Included within the schistocyte count only when other shapes are present.

MAHA, microangiopathic hemolytic anemia



Helmet cell



Horn cell



Triangle cell



Microspherocyte

## CAUSES

Schistocytes > 1% suggest microangiopathic hemolytic anemia caused by either of the following:

- Thrombotic microangiopathy
- Valve dysfunction

**Note:** > 1% corresponds to about > two schistocytes per high power field on light microscopy.

## DDX

Red cell fragments similar to schistocytes can be found in non-TMA-related genetic or acquired red blood cell (RBC) disorders often associated with intrinsically defective RBCs including:

- RBC membrane defects
- Thalassemia
- Megaloblastic anemia
- Primary myelofibrosis
- Thermal injuries

In these cases, they are not the predominant erythrocyte abnormality. They show highly variable shapes and are associated with a more global marked anisopoikilocytosis and a wide range of additional RBC size and morphological changes, not typically seen in TMA.

When a blood film shows concurrent major morphological abnormalities consistent with these alternative diagnoses, quantitation of schistocytes is not recommended.

Spherocytes, irregularly contracted cells, dacrocytes, acanthocytes, and echinocytes, as well as bite cells that are a feature of oxidant damage, should not be included within the schistocyte count.

## DIAGNOSIS

Because of the association of schistocytes with TMA, their **detection** and **quantification** has significant diagnostic and therapeutic importance.

### PERIPHERAL SMEAR

- Schistocytes are identified and counted on a peripheral blood smear stained using standard procedures and observed by microscopy.
- Counts should be performed within a smear area of correct thickness, usually behind the tail, where RBCs are just beginning to separate from each other. This excludes the 'feather edge' at the tail of the smear.
- The results should be expressed as a percentage of RBCs, after counting at least 1000 RBCs in optimal areas of the film.
- A quantitative assessment is important for diagnosis and monitoring of patients.
- In the final report, it should be stated whether schistocytes are the main morphological RBC abnormality in the smear or are part of a severe generalized anisopoikilocytosis or occur in the context of other abnormalities, suggesting an alternative diagnosis.

### AUTOMATED COUNTER

- Fragmented red cells (FRCs) are a new parameter determined automatically by the latest generation of blood cell counters. The count must be correlated with the peripheral smear.
- The absence of FRC by automated analysis can be used to exclude with high likelihood the presence of schistocytes on the blood film.
- Automated methods are not recommended without manual morphological confirmation and are not in widespread routine clinical use.
- Presence of many schistocytes may increase the red cell distribution width (RDW) and lower the mean cell volume (MCV).

CONDITION	SCHISTOCYTE COUNT (% OF RBCS)	COMMENT
Healthy	< 0.2%	Varies from 0.2-0.5%; likely caused by manual fragmentation of red blood cells during venesection or manual spreading of the blood film smear.
DIC	0.2-1.0% (in one study, mean 0.33%, median value was 0.1%, and range was 0–1.4%)	Schistocytes are frequently observed in DIC patients, mostly at low percentage, within or close to reference values. Not part of clinical prediction scores.
TTP, HUS	> 1%	Often in TMA the degree of schistocytes is much greater than 1%.

DIC, disseminated intravascular coagulation; TTP, thrombotic thrombocytopenic purpura; HUS, hemolytic uremic syndrome

The ICSH Schistocyte Working Group agreed that a schistocyte percentage above 1% in a peripheral blood smear in adults is a robust cytomorphological indication in favor of a diagnosis of TMA, when additional features suggesting an alternative diagnosis are absent.

## PROXIMATE MECHANISMS

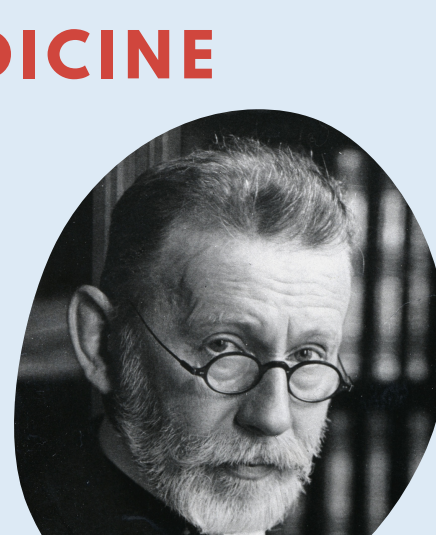
Schistocytes are formed by **mechanical damage** to the red blood cell (RBC) membrane caused by strands or filaments of fibrin on the endothelial surface of microvessels and/or increased turbulence and shear stress, as occurs, for example, across a paravascular leak.

They form because red blood cells are sheared as they try to pass through small vessels narrowed by microthrombi, or, in the case of valve hemolysis, by passing through turbulent paravascular streams.

## DID YOU KNOW?

## HISTORY OF MEDICINE

The term schistocyte was introduced in 1891 by **Paul Ehrlich** in his book *"Farbenanalytische Untersuchungen zur Histologie und Klinik des Blutes."* Ehrlich, a Nobel prize-winning German-Jewish physician and scientist labeled all poikilocytes as schistocytes. Schistocytes have a far more restricted meaning today.



## NOTES

**ATTRIBUTIONS**  
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