Red Cell Nomenclature

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The morphological abnormalities seen in the red cell offer a key to the interpretation of a particular pathological condition. This educational document on red cell nomenclature is designed to define observed red cell changes as seen on the Romanowsky stained blood film and on the scanning electron microscope.

The various red cell morphological changes as mentioned in the following text are illustrated by selected examples of causative disorders. For a comprehensive list of disorders, the reader is referred to standard haematology textbooks.

### NORMAL RED CELLS *(discós = disc / discocyte)*

Normal red cells are biconcave discs or discocytes. They have a mean diameter of 7µm or approximately the size of a small lymphocyte nucleus. The red cell membrane is very elastic and deformable, readily able to reassume its discoidal shape after cessation of a deforming force.

### MICROCYTES *(micrós = small)*

Microcytes are red cells with a diminished diameter, less than 6µm, and diminished thickness. The haemoglobin concentration of microcytes is reduced and often concentrated in a peripheral ring while the cell centre is pale. This pale centre may be so increased in size that the cell resembles a leptocyte or a thin, flattened red cell. Microcytes are a characteristic feature of iron deficiency anaemia and thalassaemia.

### ROUND MACROCYTES *(macrós = large)*

Round macrocytes are red cells with an increased diameter, more than 8µm. They maintain a normal discoid shape and have a well-defined central depression. Round macrocytes are a characteristic feature of alcoholism and liver disease.
Oval macrocytes are giant sized red cells with a diameter of more than 9µm. Oval macrocytes are a characteristic feature of megaloblastic anaemia (mégas = giant).

Target cells are bell-shaped, thin-walled cells, that have an increased surface area compared to volume. This is the result of red cell membrane expansion by the accumulation of lecithin and cholesterol from free exchange with plasma lipids.

The term target describes the appearance of these cells when dried on a glass slide. They have a characteristic distribution of haemoglobin in the centre of the cell as well as around the periphery with the two regions separated by a pale ring.

Target cells are associated with liver disease, thalassaemia, hyposplenism and some abnormal haemoglobins.
Elliptocytes are oval-shaped biconcave discs that vary in shape from slightly oval to cylindrical shaped. They have both a quantitative and qualitative abnormality in two major proteins comprising the membrane skeleton, namely spectrin and protein 4.1.

Whilst approximately 5% of elliptocytes are seen on normal blood films, between 30% and 100% are seen in hereditary elliptocytosis. Elliptocytes are also a feature of iron deficiency anaemia, but in this case, without spectrin or protein 4.1 abnormality.

Stomatocytes are bowl-shaped red cells which exhibit a slit-like area of central pallor. Stomatocytes are associated with alcoholism and are also a feature of two specific conditions, namely hereditary stomatocytosis and Southeast Asian ovalocytosis. In each of these conditions, the membrane defect is different.

In hereditary stomatocytosis, there is a deficiency of protein 7.2b or stomatin in the red cell membrane. This leads to an influx of Na⁺ into the red cell and a loss of K⁺ exiting the red cell. Hence the red cells swell and are transformed from discocytes to bowl forms. They have a high mean cell volume (MCV), usually about 130 fl.

In Southeast Asian ovalocytosis, there is increased ankyrin binding and decreased protein 3 mobility, leading to the production of rigid red cells. These red cells are oval in shape, often with double transverse slits. They have a normal MCV.

Stomatocytes may occur as an artefact in the presence of improper physico-chemical conditions occurring in vitro.
Sickle cells are biconcave discs that, upon deoxygenation, change shape to become crescent or sickle-shaped. They have an abnormal haemoglobin, HbS, which is due to the replacement of glutamic acid with valine at the sixth position on the β chain. Sickle cells are deformed by the precipitation of polymerised HbS. They appear as sickle or crescent-shaped red cells on the blood film.

As well as being a characteristic feature of sickle cell disease, sickle cells are also seen as a feature of double-heterozygote disorders that include HbS.

Spherocytes are red cells that are almost spherical in shape. They are no longer a biconcave disc. They appear as slightly smaller, hyperchromic red cells with little or no area of central pallor. The MCV of spherocytes is within the normal range.

Spherocytes are a characteristic feature of hereditary spherocytosis and autoimmune haemolytic anaemia. The spherocytes of hereditary spherocytosis are attributable to an intracorpuscular red cell membrane defect. Deficiency of spectrin, ankyrin or band 3 protein leads to the uncoupling of the skeletal lipid bilayer resulting in membrane loss in the form of microvesicles. The spherocytes of autoimmune haemolytic anaemia are the end result of the coating of red cells with immunoglobulin, namely IgG and/or complement proteins.
Teardrop-shaped red cells are characterised by a single elongated or pointed extremity. They are a characteristic feature of leucoerythroblastic disorders such as myelofibrosis and metastatic carcinoma. Teardrops are also present in thalassaemia and megaloblastic anaemia.

Acanthocytes are round, hyperchromic red cells, with several fine, spine-like projections spaced unevenly over their entire surface.

Acanthocytes are a characteristic feature of hyposplenism / splenectomy, abetalipoproteinaemia and the Mcleod phenotype.
Bite cells are formed when Heinz bodies (the product of oxidant stress on the haemoglobin molecule) together with some red cell content, are removed from red cells as they pass through the spleen. When the red cell membrane around the bite repairs, a blister-like structure forms, hence the term blister cell.

Bite and blister cells are a characteristic feature of the oxidant haemolysis seen in subjects with normal and reduced levels of glucose 6 phosphate dehydrogenase (G6PD) after the administration of dapsone, salazopyrin and some of the anti-malarial drugs.

Schistocytes are sharp, pointed fragmented red cells produced by a microangiopathic process. Red cells are fractured or ripped as they pass across strands of fibrin in damaged vessels, for example, in haemolytic uraemic syndrome, or as they pass across a damaged or prosthetic heart valve.
Burr cells are red cells with varying numbers of spines occurring at irregular intervals on the cell membrane. Burr cells are produced as a result of damaged glomeruli in severe glomerulonephritis and in acute renal failure.

Crenated cells are red cells with regularly placed projections on their surface. They are invariably present as an artefact that develops if blood is allowed to stand for a prolonged period of time at 20°C prior to the blood film being made.

Crenated cells, present in freshly made blood films, are a feature of renal disease. They are also present in dehydration resulting from severe gastroenteritis.
Spur cells are spiculated red cells with equally spaced, short spines, over the entire surface of the red cell. They appear as three dimensional on the blood film. Spur cells are produced in two stages. Firstly, excess cholesterol produced by a diseased liver, increases the surface area of the red cell membrane, resulting in a red cell with a scalloped or undulating periphery. In the second stage, these scalloped cells are converted to spur cells by a process of splenic conditioning. Over a period of a few days, the membrane lipids as well as the increased surface area are lost and the cell becomes rigid, assuming the appearance of a spur cell.

Spur cells are characteristic of fulminant hepatocellular disease. This haematological condition is commonly referred to as spur cell anaemia.