Spotlight on hematology

RDW and erythrocyte anisocytosis

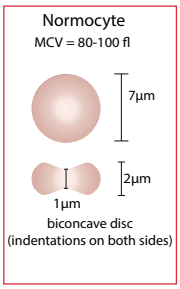
MQZH 2017-1

Introduction

Erythrocytes (English RBC – red blood cells) account for the largest part of cells circulating in the peripheral blood. In healthy people, the erythrocytes formed differ from each other with respect to their volume (size) only minimally. Diverse factors (intrinsic as well as extrinsic) can lead to the formation of populations within erythrocytes that deviate from the norm. The deviation of size is referred to as anisocytosis. It can be detected in a microscopic exam. The hematology instruments offer other possibilities of evaluation by means of their RBC histograms, the mean corpuscular volume (MCV) and the derivation/calculation of the red cell distribution width (RDW) by means of RBC histogram and MCV.

Our current proficiency testing survey specimen shows marked anisocytosis in microscopy, which is also confirmed by the highly elevated RDW value. It was obtained from a 37-year-old patient with known beta thalassemia (intermedia/major).

Erythrocyte anisocytosis and MCV

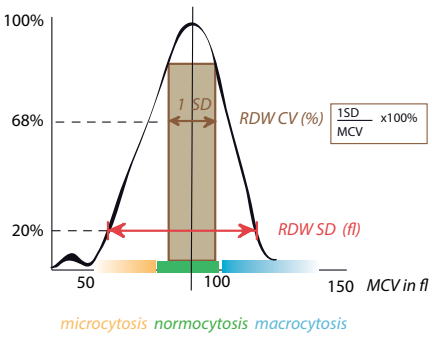


In humans and mammals, the circulating erythrocytes are cells with a biconcave shape without nuclei, which developed in the bone marrow from nucleated red precursors. Their biconcave shape results in the largest possible cell surface, which facilitates optimal gas exchange, and, in addition, the cell has the required flexibility to move even in the smallest capillary vessels without becoming damaged. The deformability of the erythrocyte membrane and the relatively low proportion of hemoglobin molecules gives the cells the remarkable ability of extreme contractibility and expandability.

RDW - red cell distribution width

RDW is derived from the erythrocyte histogram and can be reported both as standard deviation (SD) in femtoliters and as coefficient of variation (CV) as a percentage of the measurement of the erythrocyte volume.

Measurement: RDW-CV and RDW-SD



RDW-CV
Reference range 11.5-14.5 %
Is calculated by all hematology instruments
Formula: (1SD/MCV)X100%

RDW-SD
Reference range 35-45 fl
Is measured by us only with the Sysmex instruments (in addition to RDW-CV)

The two RDW measurement methods and their effect on the RDW result

As RDW-CV corresponds to a ratio of 1SD (standard deviation) and the MCV, a change in any one of these two parameters changes the results. A low MCV and a normal curve width (SD) lead to a high RDW-CV. On the other hand, a broad curve and a markedly elevated MCV can still produce a normal RDW value. In other words, microcytosis tends to increase the RDW-CV solely because of the reduction in the denominator in the ratio. Conversely, macrocytosis increases the denominator and can therefore compensate the value from a broad curve, thus leading to a normal RDW-CV.
In contrast, the RDW-SD is a direct measurement of the curve width at the level of 20% above baseline. As this value is independent of MCV and the effective width of the erythrocyte curve taken into consideration far above +/- 1SD, it is superior to RDW-CV, in particular with highly abnormal findings.

Causes for development of anisocytosis

It can be generally said that deficiency anemia is (e.g. iron, vitamin B12, folic acid deficiency) are more frequently associated with anisocytosis of erythrocytes than anemias caused by genetic defects or primary bone marrow diseases.

Physiological causes for a RDW elevation:
- Age
- Black skin color
- High physical exertion
- Possibly pregnancy

Possible new fields for RDW analytics

In the past decade, a large number of publications were concerned with the possible meaning of an elevated RDW in connection with many different diseases. Thus, it was determined that the RDW is a strong negative predictive value for the short and long-term course (morbidity, mortality) of patients with
- Cardiovascular diseases
- Thromboembolic events (e.g. pulmonary embolism)
- Colon carcinoma
- Diabetes .

The pathological relationships between these RDW elevations have not yet been sufficiently clarified. However, an elevated RDW appears to reflect abnormal erythropoesis or an abnormal erythrocyte survival time, which is caused by various metabolic abnormalities. These include shortened telomers, oxidative stress, inflammation, poor nutritional status, dyslipidemia, high blood pressure, erythrocyte fragmentation and changes in the erythropoietin function.

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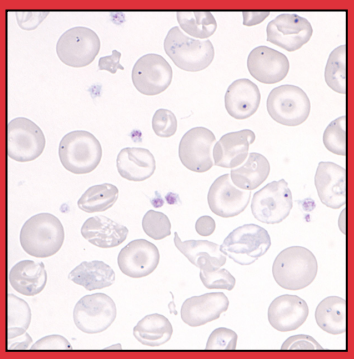
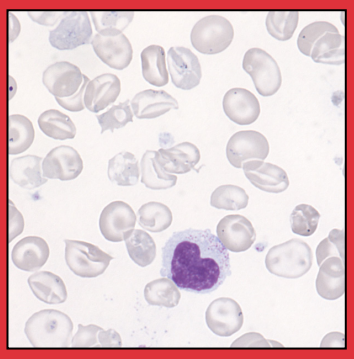
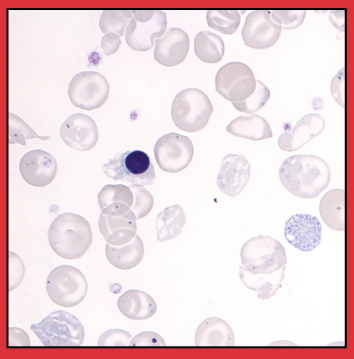
Pictures from the current proficiency testing survey specimen

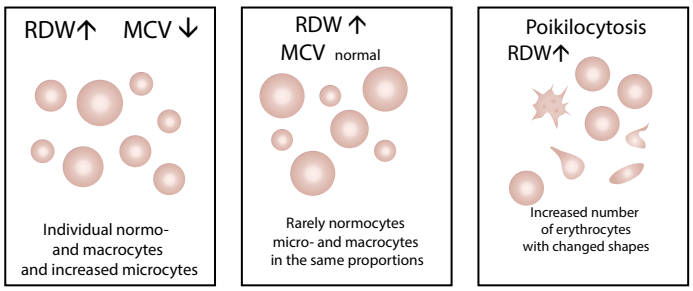






Changes in the MCV and RDW

Although extremely macrocytic erythrocytes lose their biconcave shape and become round, they can reach MCV of up to 150 fl without the membrane rupturing. Very small erythrocytes can also develop, for example, in cases with thalassemia or iron deficiency. The MCV can then drop to 60 fl or even lower without the membrane stability of the cell being strongly affected. As the MCV notes an average value for the volume of all analyzed erythrocytes, the number of macro- or microcytes must be predominant in order for the value to be elevated/reduced. Smaller subpopulations with changed sizes are therefore not included by the MCV.
In contrast, RDW measures the red cell distribution width directly in the RBC histogram and records even small deviations of the size distribution of the erythrocytes, sometimes even before the MCV is reduced.
In addition to anisocytosis, poikilocytosis – the increased presence of unround erythrocytes (such as, e.g. nonspecific poikilocytes, acanthocytes, stomatocytes, sickle cells, ovalocytes, teardrop forms, fragmentocytes - can lead to an elevation of the RDW value.



Anemia classification taking into account RDW and MCV

	MCV normal normocytic	MCV elevated macrocytic	MCV reduced microcytic
Normal RDW Not heterogeneous, no anisocytosis	- Chronic anemia diseases - acute/subacute blood loss - Concomitant anemias with malignant tumors and systemic hematological diseases - Renal anemia	- Aplastic anemia - Myelodysplastic syndrome - Chronic liver diseases - Status post chemotherapy and antiviral drugs - Alcohol	- Anemia in chronic diseases - Thalassemia minor (heterozygous)
High RDW Heterogeneous, anisocytosis	RDW elevation before MCV changes: - Early iron deficiency - Early folic acid deficiency Anemias due to hemoglobinopathies, such as e.g. sickle cell anemia. Dimorphic anemia (e.g. combined iron and folic acid deficiency) - hereditary spherocytosis	- Vitamin B12 deficiency - Folic acid deficiency - Autoimmune hemolytic anemia - Cold agglutinins - Myelodysplastic syndrome	- Iron deficiency anemia - Anemia with fragmentocytes - HbH - Thalassemia intermedia/major

This list is not final. In individual cases deviations from this scheme can occur. Reduced RDW values are not relevant.

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