RED CELL DISTRIBUTION WIDTH (RDW)

TERM DEFINITION

The RDW is an objective measure of variation in the size (volume) of circulating red cells derived from automated counters. A normal RDW indicates that the cells are all about the same size, while a higher than normal RDW means they vary more widely in size (termed *anisocytosis*).

CLINICAL PEARLS

RDW is a statistical calculation of the dispersion in RBC sizes (the variation in cell size around the mean), **not a directly measured physiological parameter.** It is automatically generated by all routine automated counters.

An elevated RDW should prompt **examination of the peripheral smear,** specifically looking for abnormal red blood cells (e.g., polychromatophilic cells, microspherocytes) contributing to the increase.

The observation of a RDW value **below the conventional reference range** is infrequent and clinically meaningless.

The term "**width**" is misleading, as the value is not derived from the width of the red blood cell, but rather from the width of the distribution curve of the red cell volume.

Elevated RDW correlates with anisocytosis as seen on the **peripheral blood smear.**

Since mean cell volume (MCV) is an average value, it does not reflect the heterogeneity of the red cell populations; thus the **MCV should always be qualified by the RDW**.

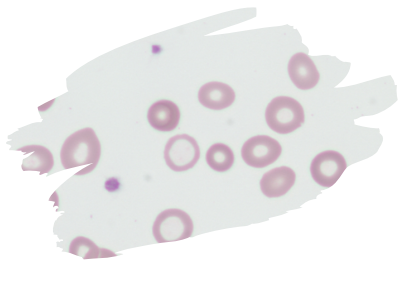
RDW has historically been used to help classify anemia; more recently it has been investigated as an **inexpensive prognostic biomarker** in many diseases.

METHODS

Modern automated hematological analyzers generate a histogram (volume distribution curve) by plotting the signals obtained from each individual cell passing through specific channels. The histogram, which follows a normal (Gaussian) distribution provides both the MCV and the RDW.

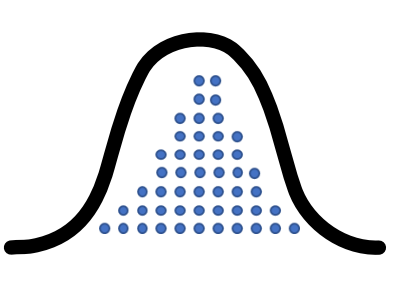
Detecting variation in red blood cell size

1 Examination of peripheral blood



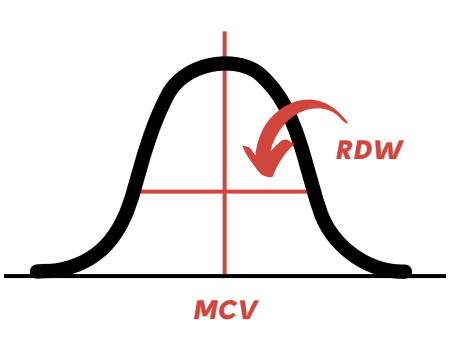
This peripheral smear shows significant variation in red cell diameter (anisocytosis).

2 Examination of RBC volume histogram



Each dot represents one cell, and there are millions in an RBC histogram. Typically, the data points (dots) are removed when showing the RBC histogram, leaving just the outline (as shown to the right).

3 RDW-CV or RDW-SD

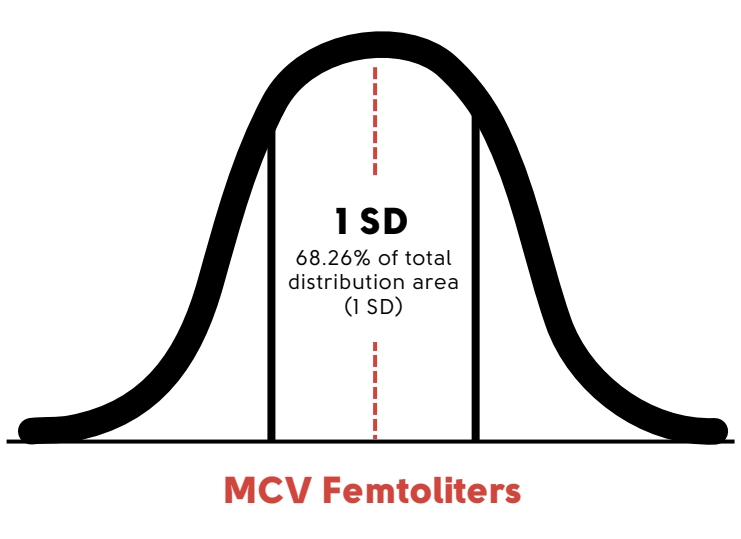


The methods used for RBC analysis and RDW calculation differ widely among the most commonly used hematological analyzers. There are two ways to express RDW: RDW-CV and RDW-SD.

The RDW-CV and RDW-SD are measures of the dispersion of data around the mean. The more spread apart the data, the higher the SD. Although both methods use SD to measure the degree of anisocytosis, they measure cell variations differently.

RDW-CV

- The RDW-CV (**coefficient of variation** of RBC volume) quantifies the heterogeneity of RBC volume as the ratio of the standard deviation of RBC volume to the mean corpuscular volume (MCV) . Normal range 11% - 16%.

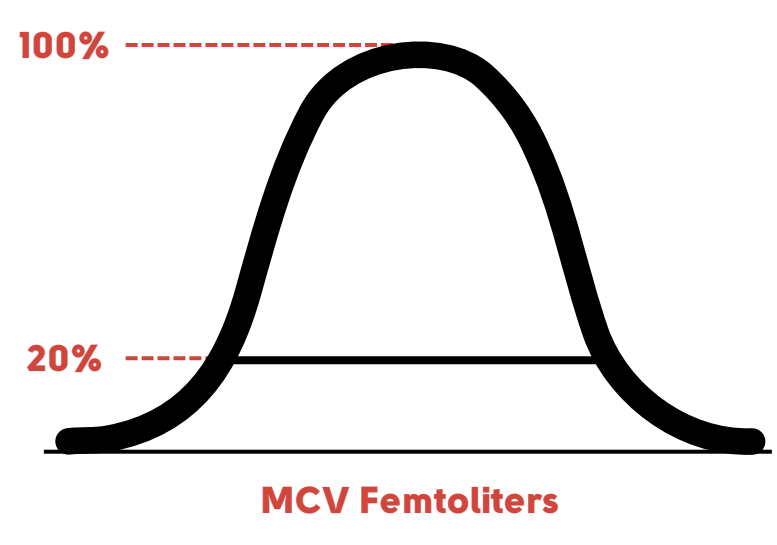


$$\text{RDW-CV} = \frac{1\ \text{SD}}{\text{MCV}} \times 100$$

- Earliest method provided by automated counters to measure red cell variations.
- Measures dispersion by means of a ratio formula of 1 SD to the MCV. The 1 SD value imposed by the formula weakens and restricts its capability to measure red cell dispersion as high as 1 SD only.
- Because the MCV serves as the denominator, it can greatly influence the results:
  - Microcytosis tends to elevate the RDW-CV simply by lowering the denominator of the ratio.
  - Macrocytosis, by increasing the MCV in the denominator, may offset the change or increase in the width of the curve, thereby producing a normal RDW-CV.

RDW-SD

- RDW-SD (**standard distribution** of RBC volume) is a direct measure of RDW taken at the 20% frequency level of the histogram and is expressed as standard deviation in fL. Normal range: 39-46 fL.



- A direct measure of RDW taken at the 20% frequency level of the histogram.
- Because this method is independent of the MCV and is considered to be the absolute measure of dispersion regarding measurement, far beyond ±1 SD or across the MCV, it is the better and more reliable measure of RBC variability, particularly in highly abnormal conditions.

Complete blood counts from 2 different patients:

A

WBC	RBC	Hgb	Hct	MCV	MCH	MCHC	RDW	RDWSD	PltCt
3.8*	6.47*	12.2*	40.5	63*	18.9*	30.1*	18.7*	36.7	122*

B

WBC	RBC	Hgb	Hct	MCV	MCH	MCHC	RDW	RDWSD	PltCt
6.4	3.16*	10.1*	34.2*	108*	32.0	29.5*	14.6	57.1*	674*

A. Note how the low MCV results in a falsely increased RDW-CV (labeled RDW), while the RDW-SD remains normal.

B. An elevated MCV leads to a normal RDW-CV and increased RDW-SD.

Abbreviations: *WBC, white blood cell count; RBC, red blood cell count; Hbg, hemoglobin concentration; MCV, mean cell volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width-CV; RDW-SD, red cell distribution width-SD, Plt Ct, platelet count.*

DDX

PHYSIOLOGICAL CAUSES OF INCREASED RDW

- Administration of erythropoietin
- Ageing (no significant gender differences)
- RDW values significantly higher in Blacks that in the other ethnical cohorts.
- Significant increase in RDW values after physical exercise
- Pregnancy

CAUSES OF INCREASED RDW IN DISEASE

- **Nutritional deficiencies of:**
  - Iron
  - Vitamin B12
  - Folate
- After recent hemorrhage or rapid hemolysis, as the acute drop in hemoglobin results in increased production of reticulocytes, which are larger than mature erythrocytes.
- **Other less common causes including patients with:**
  - Autoimmune disorders
  - Myelodysplastic syndrome
  - Hemolytic anemia
  - Liver impairment
  - Sickle cell disease
  - Blood transfusions

USE OF RDW IN ANEMIA CLASSIFICATION

Anemia

- MCV low → **Microcytic anemia**
  - **Normal RDW**: AI; Thalassemia
  - **Increased RDW**: IDA; MAHA
- **Normocytic anemia**
  - **Normal RDW**: AI; CKD
  - **Increased RDW**: Early IDA; Early B12; Transfusions; SCD; Liver
- MCV high → **Macrocytic anemia**
  - **Normal RDW**: AA; Liver
  - **Increased RDW**: Immune hemolytic anemia; B12 / folate deficiency

Abbreviations: *MCV, mean cell volume; RDW, red cell distribution width; AI, anemia of inflammation; IDA, iron deficiency anemia; MAHA, microangiopathic hemolytic anemia; CKD, chronic kidney disease; AA, aplastic anemia, SCD, sickle cell disease.*

Emerging data suggest that the RDW may also have prognostic value (increased risk for morbidity and mortality) in nonhematologic diseases, including:

- Cancer
- Infections
- Renal disease
- Cardiovascular disease
- Ischemic stroke
- Subarachnoid hemorrhage
- Pulmonary disease
- Acute pancreatitis
- Septic shock

Notes:

- In many of these individuals elevated RDW is the only abnormality in the CBC and thus is likely to be an important biomarker.
- The mechanisms by which all of these diseases lead to increased RDW are unknown.
- Currently, using the RDW to assess prognosis remains investigational, and how best to interpret it in daily practice requires further study.

PROXIMATE MECHANISMS

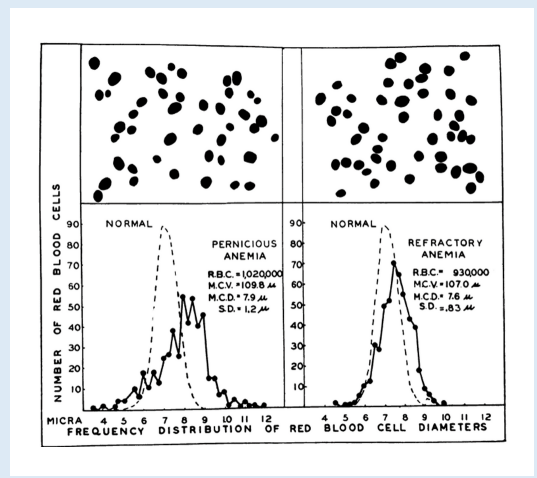
During the life-span of the red blood cell (RBC), the density of the cell increases and the surface area gradually decreases (**RBCs become smaller as they age**), which then could lead to a heterogeneous population of RBCs and RDW elevation. Hence, increased RDW could be a marker of increased age of the RBCs, possibly due to delayed RBC clearance (expanding the low volume tail of the RBC population's volume distribution, and thereby increasing RDW).

Inflammation and oxidative stress both may increase anisocytosis by disrupting erythropoiesis, altering blood cell membrane deformability and red blood cell circulation half-life, and ultimately leading to increased RDW.

DID YOU KNOW?

HISTORY OF MEDICINE

Before automated counters were invented, red blood cell (RBC) size was determined by microscopic assessment of RBC diameter. Early studies of RBC diameters were used to generate histograms based on manual measurement of 200-500 cells. This assay was pioneered by Price-Jones in 1910, and the histograms (curves) became widely known as **Price-Jones curves**. The degree of anisocytosis was recognized over 100 years ago as a useful characteristic for differentiating types of anemia.



Example of Price-Jones curves (right) generated by measurement of red cell diameters traced from microscopic images (top) in patients with pernicious anemia (left) and "refractory anemia" (right). The original figure legend stated: "From the drawings of the red blood cells, this difference in degree of anisocytosis can readily be seen". *Blood.* 1946;1: 67-75.

NOTES

ATTRIBUTIONS
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The Blood Project
ENCYCLOPEDIA OF BLOOD