Anaemia

Mean cell volume and red cell distribution width helped diagnose anaemia cause.

Red cell distribution width went up with deficiencies (whether iron, folate or B-12), and the anaemic haemoglobinopathies.
Red cell distribution width did not go up in chronic diseases, unless they were accompanied by deficiencies.

Mean cell volume (MCV)- reference range 79-101 fL
Red cell distribution width (RDW)- reference range <15.1

The evidence
Low MCV and normal RDW- possible cause:
Chronic disease
Heterogeneous thalassemia

Low MCV and high RDW- possible cause:
iron deficiency
red blood cell fragmentation (artificial valve)
haemoglobin H
S beta-thalessemia

Normal MCV and normal RDW- possible cause:
any chronic disease (including chronic liver disease)
haemorrhage
haemolysis
transfusion
haemoglobin AS,
haemoglobin AC

CLL with <150 x 10 3 white blood cells/l
hereditary spherocytosis

Normal MCV and high RDW- possible cause:

early iron or folate (or both) deficiency
haemoglobin SS,
haemoglobin SC
myelofibrosis
sideroblastic anaemia

High MCV and normal RDW- possible cause:
aplastic anaemia
preleukaemia
high MCV and high RDW- possible cause:
folate or B-12 deficiency
immune haemolytic anaemia
white blood cell/l
cold agglutination with >150 x 10 3

Comments

Red cell distribution width is the Coulter Counter's equivalent to anisocytosis on the blood smear (ie. a measure of how much cell size varies).
This classification method needs to be prospectively validated.

Clinical Question
Patient healthy,
anaemic or haematology patients
Intervention or Exposure Mean cell volume and red cell distribution width
Comparison final diagnosis
Outcome diagnosis of cause of anaemia

The diagnostic usefulness of red cell distribution width (RDW) in association with usual biochemical and haematological parameters in detection of iron deficiency has been studied in a representative sample population of 384 children aged six months to six years in Reunion. Traditional parameters measured included serum ferritin (Fri), total iron binding capacity (TIBC), serum iron (SI), transferrin saturation (TSat), free erythrocyte protoporphyrin (FEP), mean corpuscular haemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH), mean corpuscular volume (MCV) and haemoglobin concentration (Hb). RDW is an index of the variation in red cell size (anisocytosis). This recently derived parameter is measured by some models of electronic cell counter. It is not usually used in epidemiological investigations. Of the children studied, 13.6% had Hb<11 g/dl. The Pearson correlation coefficients between circulating iron parameters (SI, TSat, TIBC) or iron storage parameters (Fri) and RDW, MCV, MCH and FEP were greater than with Hb. The best correlations were observed for RDW, MCV and MCH with all other parameters. In this study, the upper limit value of RDW was defined as 18% using a Technicon model H-6000 counter. Other iron deficiency criteria were also defined and found to be in agreement with the international reference values for children aged six months to six years: MCV <70 fl, MCH <22 pg, MCHC <32%, FEP >35 µg/dl whole blood, SI <6 µmol/l, TIBC >85 µmol/l, TSat <10% and Fri > 12 µg/l. The combination of sensitivity and specificity was best for RDW and worst for MCHC. Use of RDW in association with habitual iron status parameters in screening surveys of iron deficiency would therefore be worthwhile.

Hematology Tests

Changes in time of day and fasting state may alter some values.
Blood consists of red cells (erythrocytes), white cells (leukocytes), and platelets (thrombocytes), suspended in a liquid called plasma. A CBC usually includes white blood cell count (WBC), red blood cell count (RBC), hemoglobin, hematocrit, red cell indices (MCV, MCH, MCHC), and platelet count. Some others tests listed under the CBC include red cell distribution width (RDW), mean platelet volume (MPV) and a differential examination of the quality and quantity of various white cells reported either in percent or absolute terms.
Reference values for the different parts of the CBC are difficult to list as some vary by age, sex, and altitude. Also different instruments will

have different principles of measurement that can impact on the final values.

Hemoglobin (Hb)

Hemoglobin is a large complex protein made up of globin chains and heme found inside the red cells. Heme contains iron which is the portion of the protein that actually binds to oxygen in the lungs and releases it into the tissues. This is one of those test that will vary in reference ranges although it is fair to say that values around or under 10 are usually seen in patients with some signs or symptoms of anemia such as shortness of breath or fatigue or pallor.

Hematocrit (Hct)

If you think of the hemoglobin test as measuring just the weight of the protein in the red cells, the hematocrit is the percent of volume that is taken up by red cells. It is also called the packed RBC volume.

RBC indices (Mean Cell Volume/MCV; Mean Cell Hemoglobin/ MCH, Mean Cell Hemoglobin Concentration/MCHC)

Counting cells does not tell you much about their quality. These values try to describe the red cell population. Think of the 4th grade math question: "If 12 apples cost $1.20, how much does 1 apple cost?" If you know the red cell count and you know how much volume these cells take up (Hct), then by dividing the hematocrit by the red cell count will give you the average (or mean) cell volume. Similarly, if you know the total weight of hemoglobin and the red count, then you can find out the average or mean weight of hemoglobin in each cell; and, if you know the weight of hemoglobin and the volume of blood that is red cells, you can determine what percentage of an average red cell is taken up by hemoglobin. The benefit of these indices is that you can quickly narrow down the potential causes of anemia; the disadvantage is that these numbers assume a similar population of cells. For example, if the MCV is 90, does that mean all your cells are 90 femtoliters in volume or could some be 85 and 95 (within reference limits), or 75 and 105 (decidedly out of reference limits)?

Relative or Red cell Distributive Width (RDW)

This is a new test that can be performed only with modern instrumentation. The instrument measures every red cell it counts, finds the average, and compares each red cell size to that average. This indicates the variability in the size of the RBCs. Using this test with the indices allows you to answer questions about cell size and quality quickly.

While every laboratory will have developed their own specific reference ranges, you could assume that an MCV of 80 - 100 femtoliters, an MCH of 29 - 31 picograms, an MCHC of 30 - 35% would generally reflect a population of cells described as normochromic normocytic. An MCV less than 80 describes microcytes or small cells. An MCV greater than 100 reflects macrocytes. An MCHC less than 30 usually is taken to mean that the cells are not adequately filled with hemoglobin. When looking at red cells, it is the hemoglobin that gives the cell its red color so less than adequate hemoglobin is known as hypochromia.

White Blood Cell Count (WBC)

White cells are easily separated from red cells in that a mature red cell does not contain a nucleus. Cells are broken and only nuclei are counted. This works quite well unless immature red cells that still contain nuclei are present. These red cell nuclei are counted and the result is a falsely elevated number. Corrected white cell counts have had the red cell eliminated from the report.

Differential

White blood cells are evaluated by a differential count, which reports percentages of the types of WBCs present. These are neutrophils which fight infection (also known as polys and bands, polymorph nuclear leukocytes, PMN's, grans, segs and nonsegs), lymphocytes which produce antibodies and other immune system activities (lymphs), monocytes which also fight infection (mono's), eosinophils (eos) and basophils (basos) which are involved with allergies. The red cells are also evaluated for size, shape, color and the presence of any abnormalities

Manual differentials are performed by taking a drop of blood, spreading it on a slide, staining it, and evaluating 100 cells individually for quality and changes in morphology. For patients with elevated white cell counts, differentials of 200 cells or greater might be done.

Automated differentials are performed by either testing for specific compounds within the cells or comparing their size, shape, and content. Most instruments will count thousands of cells. For both types of differentials, the numbers are reported in percentages.

In some patients percentages might be misleading so absolute values of the types of WBC i.e., the number of white blood cells multiplied by the percentage seen are valuable in diagnosing illness or following therapy. Persons receiving chemotherapy often have decreased WBC. If a patient's absolute granulocyte count (ANC or AGC) goes below 2,000 cells, then physicians become concerned about the possibility of infection. A number below 1,000 is cause for greater concern and less than 500 usually lands the patient in the hospital.

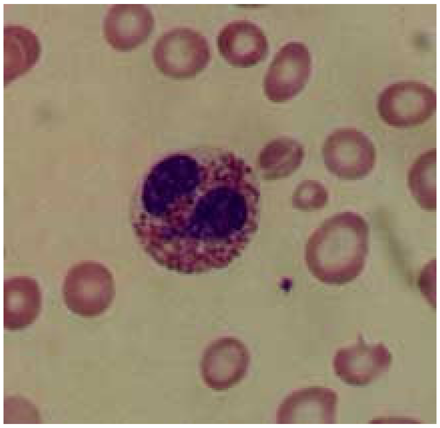
Platelets (PLT)

Platelets are essential for the clotting of blood. One could think of them as tying together the clotting mechanism and the damaged area. When platelets are low, it may take longer for the blood to clot. When platelet counts are too high, unnecessary blood clots may occur. Strangely enough, bleeding can also happen if the platelets interfere with each other! Platelet function is affected by many drugs; one of the most well known is aspirin. Easy bruising may be a sign of a decreased platelet count. Bruising like Goldilocks' companions comes in three "sizes". The largest is called hematoma; it's multicolored, raised, has very well defined edges, and painful. The middle one is flat, usually red/blue and not well defined edges. Many normal women get these on their thighs from bumping into furniture, etc. The smallest is called petechiae. These looks something like freckles. They occur in multiples, may be itchy, and are caused by very small blood vessel damage. Petechiae can be seen in nosebleeds and gum bleeding.

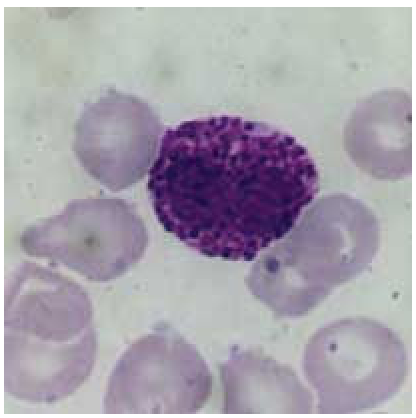
Mean Platelet Volume (MPV)
This is a test similar to the MCV and we don't know a whole lot about what it tells us.

White Blood Cells found in the normal differential.

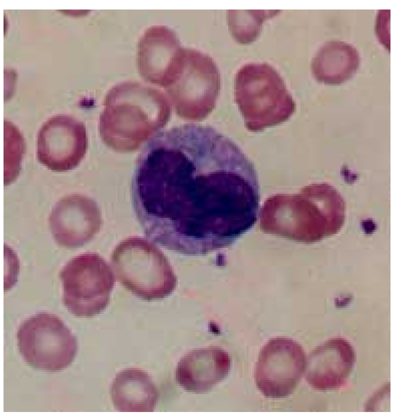
Granulocytes
Cells that contain large visible granules are sometimes called granulocytes. They can be separated into 3 distinct cell lines, based on the reaction of the granules to the most commonly used stain in Hematology, the Wright stain. The stain is a pH based stain. Structures that favor the basic stain stain dark blue or basophilic; while those that favor the acid stain, eosin, stain bright red-orange. Some structures seem indifferent to the stain and are called neutral.
The most numerous cell line of the granulocytes contain both light blue and light pink granules. As a result they are called neutrophils. This cell line is considered the first line of defense against most bacteria. It takes 6 steps for this cell to mature from a myeloblast to a fully mature cell. There have been several different ways to identify these cells so the following names are more or less synonymous: The most mature cells is called polymorphonuclear leukocytes (polys or PMN's) or segmented neutrophils (segs). One step from fully mature is the band or nonsegmented cell. Both these cells types are functional; the older one seems just a little bit faster. These cells are usually between 50 - 70% of all of the cells seen in a normal differential performed on an adult. These numbers do not work for infants and young children.



Cells whose granules stain bright red orange are called eosinophils and are part of the allergic response. Those granules contain histamine among other proteins. They should constitute between 0 - 4% of a normal differential for an adult.



Cells whose granules stain dark blue are called basophils and are also involved in allergic reactions.



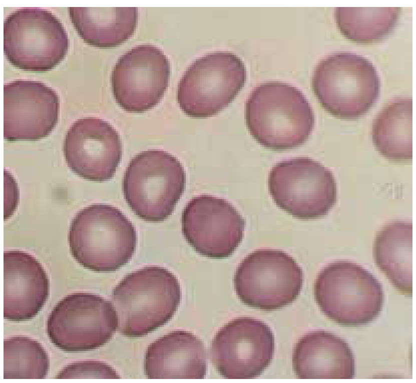
Monocytes are a type of cross over cell. Many people call them granulocytes because they do contain granules but the granules are not large or easily seen. At any rate, monocytes are your basic "junk food" eaters. They are primarily responsible for removing dead or damaged cells and constitute less than 10% of the adult differential.

Lymphocytes are cells that do not contain large numbers of any granules. They are responsible for producing antibodies against foreign material such as antigens found in viruses and some bacteria. They also are active against malignancy. In the adult, they range between

20 and 45% of the cells seen in the differential.

When a lymphocyte is actively defending against an antigen, there will be changes seen in the cell and the cell is called a "reactive" lymphocyte.

Red blood cells in the differential



Normal red cells should be monotonous. They should all be about the same size, biconcave in shape, well filled with hemoglobin, and be about the same color. Changes in these descriptions are clues to many disease processes. Changes are usually graded as slight/moderate/ marked or 1+, 2+, 3+, and 4+ with 4+ being the most unusual. Terms that are used to describe these changes include: anisocytosis (changes in size), poikilocytosis (changes in shape), hypochromia (less than adequate hemoglobin) and polychromasia/polychromatophilia (changes in color).

Platelets in the differential

Platelets cannot be counted with any accuracy when viewing the blood smear. They are only be estimated and no comments about they ability to act in clotting can be made. So you are left with comments such as adequate or appears decreased/increased. Comments can be made about their size but since platelets swell when they come into contact with the anticoagulants used in the collection of blood for a CBC, this may sometimes not be very important,

Reticulocyte count (Retic count)
Red cells are formed in the bone marrow. As the cells matures, it goes through several stages. The last one prior to leaving the marrow as a mature red cells is called the reticulocyte. Counting reticulocytes can correlate with the ability of the marrow to produce red cells. Elevated retic's may mean that he marrow is capable of producing increased amounts of red cells. Decreased retic counts may mean that there is some damage to the marrow's red cell making apparatus. This test aids in the diagnosis of anemia and is an indicator of response to therapy for anemia. Either blood from a lavender topped tube or fingerstick can be used. Reticulocyte counts may be done manually at the microscope or by automated methods. The normal range is approximately 0.5 - 2.0 %, but varies with age and population.

Sedimentation Rate (ESR, Sed rate)
The erythrocyte sedimentation rate is a non-specific indicator of inflammation. It is measured by the degree of settling of red blood cells in a specific time period, usually one hour. There are several methods for determination of the ESR; the most common are the Wintrobe and the Westergren, named for the developers of the procedure. Blood for these procedures is drawn into either a lavender or blue top tube, depending on the procedure. There is also an automated method for determining the sedimentation rate. There is no special patient preparation.
ESR is best used when comparing changes over time. A single test does not give much usable information. Some things that can cause an elevated ESR include exercise, arthritis, rheumatic fever, myocardial infarct (MI), infections, some malignancies, menstruation, and normal pregnancy after the third month. The normal range varies by the method used.

Laboratory IndexAnemia FerritinAnemia Folate RBCAnemia Iron SerumAnemia ProtoporphyrinAnemia Reticulocyte CountAnemia Sucrose Hemolysis TestAnemia TIBCAnemia TransferrinAnemia

Transferrin SaturationCancer MarkerCancer Marker Acid Phosphatase serumCancer Marker CA125CBCCBC PancytopeniaCBC HematocritCBC HemoglobinCBC MCHCCBC MCVCBC RBCCBC RBC MorphologyCBC RDWCBC WBCCBC WBC LeukocytosisCBC WBC MorphologyCBC WBC BasophilCBC WBC EosinophilCBC WBC LymphocyteCBC WBC MonocyteCBC WBC NeutrophilCBC WBC Neutrophil LowCBC WBC Neutrophil Low CauseCoags Antithrombin IIICoags Bleeding TimeCoags D-DimerCoags Fibrin Degradation ProductCoags PFCTCoags PTCoags PTTCoags Thrombin timeHemolysis CoombsHemolysis Coombs DirectHemolysis Coombs IndirectHemolysis G6PDHemolysis Ham TestMarrowPeripheralPlateletPlatelet MorphologyPlatelet MPVReactant ComplementReactant CRPReactant CRP CADReactant Cryoglobulins serumReactant ESRReactant FibrinogenReactant HaptoglobinReactant ProcalcitoninSPEPSPEP Abnormal

Calculation
Hct = Mean Corpuscular Volume x Red Blood Cell Count

Normal Values per age (-2 SD to +2 SD)
Birth: 42 to 64% (mean 51%)
Age <1 month: 31 to 67% (mean 44%)
Age 1-2 months: 28 to 55% (mean 35%)
Age 2-6 months: 28 to 42% (mean 36%)
Age 0.5 - 2 years: 33 to 40% (mean 36%)
Age 2 to 6 years: 34 to 40% (mean 37%)
Age 6-12 years: 35 to 45% (mean 40%)
Female
Age 12-18 years: 36 to 46% (mean 41%)
Age >18 years: 36 to 44% (mean 41%)
Male
Age 12-18 years: 37 to 49% (mean 43%)
Age >18 years: 41 to 50% (mean 47%)

Anemia Cutoffs
Men
Age 12-14 years: <37.3%
Age 15-17 years: <39.7%
Age >17 years: <38% (WHO) or <39.9% (CDC)
Women (Non-pregnant, non-lactating)
Age 12-14 years: <35.7%
Age 15-17 years: <35.9%
Age >17 years <35% (WHO) or <35.7% (CDC)
Women in Pregnancy (CDC Guidelines <5th percentile)
First Trimester: <33.0%
Second Trimester: <32.0%
Third Trimester: <33.0%
Children (CDC Guidelines <5th percentile)
Age 1-2 years: <32.9%
Age 2-5 years: <33.0%
Age 5-8 years: <34.5%
Age 8-11 years: <35.4%

Increased Hematocrit
Erythrocytes, Dehydration, Profound dieresis, Hemo-concentration, Burn Injury, Trauma, Shock, Polycythemia Vera, High Altitude.

Decreased Hematocrit

- See Anemia
- Plasma Volume expansion with constant RBC mass
- Pregnancy
- Recovery stage after Acute Hemorrhage
- Hematocrit lags blood loss (not reliable indicator)

Anaemia of rheumatoid arthritis: serum erythropoietin concentrations and red cell distribution width in relation to iron status.

Immuno-reactive serum erythropoietin concentrations were measured in 35 patients with anaemia associated with active rheumatoid arthritis. Based on an evaluation of stainable iron in the bone marrow (marrow iron grade 0-4) and serum ferritin concentrations (concentrations less than or equal to 60 micrograms/l compatible with iron deficiency) the anaemia was found to be complicated by iron deficiency in 19/35 (54%) of the patients. The mean serum erythropoietin level (57.6 (SD) 27.3) U/l) was sufficiently raised for the degree of anaemia irrespective of the size of the marrow iron stores. Thus the data do not support the contention that suppressed secretion of erythropoietin is involved in the pathogenesis of anaemia of chronic disorders. There was a significant inverse correlation between the haemoglobin concentration and log serum erythropoietin in the patients with rheumatoid arthritis. In the patients with adequate iron stores, but not in the iron depleted patients, there was a tendency for serum erythropoietin concentrations to correlate positively both with C reactive protein and erythrocyte sedimentation rate. Red cell distribution width (mean (SD) 16.3 (1.8)%) was above normal (11.5-14.5%) both in the iron replete and the iron depleted patients, and the mean red cell distribution width values did not differ significantly among the two subpopulations. The plasma lactoferrin concentration (mean (SD) 137.6 (109.9) micrograms/l) was normal and did not differ significantly between the iron deficient patients and those with adequate iron.

Evaluation of Erythrocyte Disorders With Mean Corpuscular Volume (MCV) and Red Cell Distribution Width (RDW)

The red cell distribution width (RDW), which provides a quantitative measure of heterogeneity of red cells in the peripheral blood, and the mean corpuscular volume (MCV) are part of the routine red cell indices reported by automated blood analyses. This study evaluated 193 pediatric patients with a wide range of erythrocyte disorders and determined the diagnostic utility of the RDW in relation to the MCV. Six different groups of erythrocyte disorders by MCV and RDW values are described: low MCV/normal RDW, low MCV/high RDW, normal MCV/normal RDW, normal MCV/high RDW, high MCV/normal RDW, high MCV/high RDW. This combination established a useful differential diagnosis of erythrocyte disorders. The data provided a baseline against which future studies of infants and children can be compared, though each laboratory has to verify its own normals. It should be cautioned that different electronic counters yield different RDW values, so there have to be qualifications when reporting reference values. The RDW may find its best use as a guide in the differential diagnosis of anemia, rather than as a definitive test per se.

I. **See Also**
   A. Erythrocyte Morphology
II. **Physiology: Erythropoiesis (mature red cell development)**
   A. See Bone Marrow (Erythroblast)
   B. Development in Marrow
      1. Proerythroblast is RBC stem cell in marrow (0.5 days)
      2. Basophilic erythroblast (0.8 days)
         a. Nucleus shrinks, cytoplasm darkens with ribosomes
      3. Polychromatophilic erythroblast (1.3 days)
         a. Cell produces Hemoglobin
         b. Stains with basic and eosin stains
      4. Orthochromatic erythroblast (2.0 days)
         a. Cell appears more Eosinophilic
   C. Reticulocyte: Transition to Circulation
      1. Orthochromatic erythroblast sheds nucleus
      2. Marrow Reticulocyte spends 1.7 days in marrow
      3. Blood Reticulocyte spends 1.3 days in circulation
   D. Red Blood Cells in Circulation
      1. Mature Red Blood Cell (120 day life-span)
III. **Normal Values (in 10^6/ul or 10^12/L) per age**
   A. Age <1 month: 3.6 to 6.6
   B. Age 1-6 months: 2.7 to 5.4
   C. Age 0.5 - 6 years: 3.7 to 5.3

D. Age 6-12 years: 4.0 to 5.2
E. Female
   1. Age 12-18 years: 4.1 to 5.1
   2. Age >18 years: 3.8 to 5.2
F. Male
   1. Age 12-18 years: 4.5 to 5.3
   2. Age >18 years: 4.4 to 5.9

IV. **Increased Red Blood Cell Count**
   A. Polycythemia Vera
   B. Tobacco Abuse
   C. High altitude
   D. Renal cell carcinoma
   E. Cardiovascular disease
   F. Stress
   G. Dehydration

V. **Decreased Red Blood Cell Count**
   A. Anemia
   B. Hemolytic Anemia
   C. Acute Hemorrhage
   D. Marrow failure
   E. Chronic Renal Failure

Overview

Known as the measure of diversity of red blood cell volume, RDW is also reported as part of a standard complete blood count. Red blood cells are normally of a certain size. When there is a drastic change then it is brought about by disorders.

When anemia is observed, red cell distribution width (RDW) is the test used together with mean corpuscular volume (MCV) in order to determine what the cause is. It is dominantly utilized to distinguish between iron deficiency anemia and other microcytic conditions that can also denote hereditary spherocytosis.

A percentage from 10.2 to 14.5 is the normal RDW level. Once again, keep in mind that the ranges differ because it will depend on what equipment is used in the examination to check the blood. Just constantly utilize the normal range printed on laboratory report to decipher what is the standard scale.

Calculating Red Cell Distribution Width

There are a lot of automated machines that are designed to analyze blood samples. It also detects the pulses that are brought about by red blood cells. The bigger the red blood cells are in size, the stronger the pulses will be. At the same time, when the pulses are weaker, it specifies red blood cells that are small in size.

Cause (High Red Cell Distribution Width)

Over 14.5% is considered a high level of RDW. It indicates that the red blood cells differ a lot in size. To determine the possible cause of an increased RDW, there should be an assessment made between mean corpuscular volume (MCV). If both have surged in number, then there are plenty of factors.

- Liver disease. The largest organ in the human body, the liver is responsible for removing hazardous chemical elements and produce essential substances.
- Hemolytic anemia. This is the condition where the red blood cells are wrecked much earlier than they should be.
- Too little folic acid of vitamin B12. It is one of the group of substances made up partly of carbon that significant in small quantities for normal functioning and chemical processes.
- Iron deficiency anemia (IDA). This is brought about by decrease in hemoglobin which is a matter present in the red blood cells that assist in carrying oxygen to the body.
- Thalessemia intermedia. A disorder where there is impaired production of not just a single element that consist the hemoglobin.

Cause (Low Red Cell Distribution Width)

Below 10.2% defines a decrease in RDW level. Only anemias in macrocytic and microcytic conditions are the possible reasons.

- Macrocytic anemia. It is a disorder where there is not enough red blood cells produces and the ones that are detected are huge.

- Microcytic anemia. It is an abnormality where the red blood cells are small

Red Cell Distribution Width (RDW)
The RDW is an index of the variation in cell volume within the red cell population. It is a parameter provided by both impedance and flow cytometric analyzers. Mathematically, it is the coefficient of variation, i.e.,
RDW = (Standard deviation of red cell volume ÷ mean cell volume) x 100
Red cell populations with higher than normal RDW are termed *heterogenous*; those with normal RDW are *homogeneous*. For example, increased numbers of reticulocytes will cause an increased RDW. In some instances, the RDW is the first test result to increase with changes in red cell population sizes. For example, in early iron deficiency, there are only low numbers of microcytic red blood cells. This will increase the standard deviation and the RDW, but the mean cell volume is unchanged because there are insufficient numbers of microcytic cells to change the **mean** volume