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Problems in the Diagnosis of Anemia

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Anemia is a common condition that affects individuals in all populations, which may be caused by any condition in which there is increased blood loss, impaired cell production, or increased cell destruction. However, some anemic conditions are the result of more than one of these mechanisms. Anemia is defined ideally as a reduction of more than 10% of red blood cells (RBCs), amount of circulated hemoglobin (Hb) and red cell mass. A more conventional definition is a decrease in RBCs, Hb and hematocrit (Hct) below the previously established normal values for healthy persons of the same age, gender and race and under similar conditions. Problems with this conventional definition may occur for several reasons. The blood values of nonanemic persons may fall just below the normal level. Those of mildly anemic persons may fall within the low normal range. This latter group usually is not recognized unless the blood smear is evaluated or the RBC indices include mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) and RBC distribution width (RDW). In general, the clinical diagnosis of anemia is made from the history, physical examination, signs, symptoms, hematologic values, and other procedures and findings.

Presently, to detect the presence of anemia, laboratory personnel mostly perform a complete blood count on a hematologic analyzer. Modern automated blood cell analyzers generate a RBC histogram (RBC size frequency distribution curve). Abnormalities include a shift in the curve to the left (microcytosis) or to the right (macrocytosis), a widening caused by a greater variation about the mean, and two populations of cells. The histogram complements the blood smear in identifying variant RBC populations. In addition, the RDW is a quantitative measure of the size variation of circulating RBCs and the reticulocyte count classifies anemia as hypoproliferative or hyperproliferative, thus indicating whether the bone marrow is producing adequate RBCs for the degree of anemia. However, 4-15% of false negative results and 10-25% of false positive results can occur using automated blood cell analyzers. Moreover, other problems in RBC morphological identification are still unresolved, such as degree of hypochromia, dimorphic RBCs, polychromasia, target cell, spherocyte, elliptocyte, ovalocyte, schistocyte, burr cell, acanthocyte, stomatocyte, basophilic stippling, rouleaux formation, autoagglutination, Howell-Jolly body and cabot ring. Any flagging by the automated blood cell analyzers or suspect RBC examination should lead to careful specimen inspection. The most important evaluation in the work-up of anemia is to examine the peripheral blood smear, giving particular attention to the RBCs as to variation in size, shape, color content, and inclusions. The peripheral blood smear serves as a quality control to verify the results from automated blood cell analyzers.

The majority of anemia cases in Caucasian populations are iron deficiency anemia and anemia of chronic diseases, whereas the prevalence of iron deficiency anemia and thalassemia is relatively high in Southeast Asian countries. The thalassemia trait, characterized by mild to moderate microcytic anemia, is presumptively diagnosed as iron deficiency anemia when based only on RBC data and morphologic features. Thus, an unknown number of misdiagnosed thalassemia cases may be unnecessarily treated with iron

but the real danger of misdiagnosis in carriers of the thalassemic trait, however, is the potential for homozygous offspring. Additional confirmatory tests are needed such as iron studies, osmotic fragility test, dichloropheno l-indolphenol precipitation test, hemoglobin typing, determination of Hb A_2, Hb F and Hb E and DNA analysis.

In summary, automated blood cell analyzers provide valuable information for medical care that can be promptly reported. However, due to the prevalence of thalassemia, genetic defects and other traits in Southeast Asian populations, RBC analysis requires additional useful data such as MCV, MCH, MCHC, RDW including interesting histograms and examination of peripheral blood smear. All are useful parameters for anemia classification. Both the quality and skill of laboratory personnel and the knowledge and interpretative skill of the clinicians are important for the effective diagnosis of anemia.