Separating Thalassemia Trait and Iron Deficiency by Even Simpler Inspection

To the Editor

I read with interest the correspondence relating to recent articles published in the Journal describing mathematical approaches to the differentiation of thalassemia trait (TT) and iron deficiency anemia (IDA).1-3 I found this and the accompanying authors’ responses to be thoughtful and informative.

There has been a clear revival of interest in the application of discriminant functions to these areas as demonstrated by the increasing number of publications in recent years. Doubtless this reflects the interest in population screening, and from a UK perspective, in the antenatal and newborn screening programs.

Ntaios2 admirably summarizes the key issue in that mathematical formulas and simple examination of indices work extremely well only in classical cases of TT and IDA. The biologic variability seen in both conditions, and especially when TT is complicated by coexisting IDA, as is common in some populations and highlighted by Rathod,3 or in the presence of another hemoglobinopathy such as hemoglobin (Hb) E/Tt makes this relationship considerably more complex, and a numeric approach alone will be insufficient to accurately resolve these cases.

An alternative approach used in preference by our laboratory is visual analysis of the cytograms produced by our hematology analyzers, specifically the Advia 120 (Siemens Medical Solutions Diagnostics, Tarrytown, NY). Classical TT and IDA exhibit characteristic RBC cytogram profiles as shown in Figure 1. Figure 1A shows the triangular shape of the RBC population tending toward more hypochromia than microcytosis commonly seen in IDA. Conversely, Figure 1B shows the comma-shaped RBC population resulting from an excess of microcytosis rather than hypochromia so characteristic of TT and often referred to as “Cooley’s comma” in recognition of the eponymous physician who first described the disorder in 1925.

Subtle perturbations in the appearance of these cytograms often hint at a compound erythropoietic disorder that numeric approaches are neither sufficiently sensitive nor specific enough to detect. Cytograms of combined TT/IDA and HbE/Tt and such conditions as HbH disease, HbE trait, and others differ from classical TT and IDA alone and often sufficiently from each other to alert to the requirement for further investigation.4

My own view is that cytogram analysis should form part of routine hematology practice because it can often significantly extend the “reach” of a traditional CBC in many areas of hematology. Although the examples offered here are only applicable to the Advia 120 and 2120 series analyzers, it would be of great interest to the hematopathology community to know if other analyzers offer similar information to clinical and laboratory staff.

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References
The Author’s Reply

Dr. Gibbs may be right, and I thank him for drawing my attention to the subject. Our hospital uses the Beckman Coulter LH750, which graphs WBCs but not RBCs, so I have little previous experience in reading RBC cytograms. However, I visit a commercial laboratory that analyzes more than 5,000 CBCs daily, on 12 Advia 2120 machines, which generate RBC cytograms. The Advia 120 cytogram reproduced by Gibbs is labeled RBC VHC, while on the Advia 2120, the same graph is labeled RBC V/HC, so I believe that the ordinate and abscissa are mean corpuscular volume and mean corpuscular hemoglobin. The spread of points parallel to the y-axis gives an indication of the red cell distribution width. The printed graphs are small, and it is difficult to read more than a few at a time. They are a little easier to read directly on the CRT screen. After reviewing a large number of cytograms, I came away feeling that they are analogous to abstract art. That is, the adept viewer reaches a deeper understanding of the subject, while the ingenuous are suspicious that they are being hoodwinked.

Gibbs notes that “subtle perturbations” in the cytogram can suggest the need for further studies. I am sure that is true. It is similar to the situation in which the numeric red cell indices are discordant to the proposed diagnosis, also suggesting further studies. The Advia 2120 generates large amounts of data. Including parameters presented in different formats, such as percentages and absolute values, I count 49 numeric metrics on each report. The cytograms help organize these large amounts of data under the rubrics of RBC, reticulocytes, WBC, and platelets.

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