These young platelets can be identified by different technologies—such as flow cytometry—using antibodies to RNA. Automated hematological analyzers can recognize them based on non-specific staining of their cytoplasmic material or, alternatively, simply because younger platelets have comparatively larger cell volumes if compared to mature platelets.

**Proposed Clinical Utilizations**
As indicators of the rate of thrombopoiesis, the main clinical utilization of reticulated platelets is the discrimination between thrombocytopenias caused by peripheral destruction of platelets and those caused by bone marrow pathology with decreased platelet production. This discrimination will guide other confirmatory testing. For example, patients with destructive thrombocytopenias will likely be tested for immune conditions such as idiopathic thrombocytopenic purpura (ITP) or for mechanical destruction of platelets seen in microangiopathic anemias or splenomegaly. Patients with suspected decreased platelet production will be evaluated for bone marrow diseases such as myelodysplasia (MDS) or acute leukemias.

More recently, some authors have proposed the utilization of reticulated platelets as an indicator of upcoming recovery of the platelet counts in patients with severe thrombocytopenia with the objective of reducing the costs and risks associated with platelet transfusion.

**Pitfalls, Concerns**
In general, the proposed clinical utilizations of reticulated platelets are valid;
however, some dangerous pitfalls must be considered. Increased platelet reticulation, while typically a marker of immaturity, can be present due to various platelet pathologies. In these scenarios, increases in reticulated platelets do not mean higher rates of thrombopoiesis. For example, Saigo et al\textsuperscript{1} performed a study to evaluate the value of the immature platelet fraction (IPF), a hematological parameter derived from reticulated platelets, in determining prognosis for MDS patients. They observed a significant proportion of MDS patients with elevated reticulated platelets — the exact opposite of what is expected in a bone marrow disease where thrombopoiesis is significantly suppressed. In their study, 12 out of 31 MDS patients had IPF values above 10 percent. The most difficult challenge for clinicians in MDS care is the initial diagnosis of this disease, which usually presents itself with thrombocytopenia. Therefore, if clinicians relied on the reticulated platelet findings, they would be misled into searching for a destructive cause of thrombocytopenia and the correct diagnosis would be delayed.

The fact that increased platelet reticulation is not only a marker of immaturity, but also of platelet disease poses serious concerns with their utilization for predicting an upcoming recovery of platelet counts. This is particularly dangerous if clinicians use this information to withhold platelet transfusion because in a significant proportion of cases the platelet count may not rebound as predicted, exposing the patient to increased risk of life-threatening bleeding. Hennel et al\textsuperscript{2} followed 17 pediatric patients after stem cell transplantation, and the time between the peak in reticulated platelet values and platelet count recovery varied between 1 and 16 days. During this time, four patients did not show platelet recovery at all after elevation of the reticulated platelet values.

Moving to more common diseases, Cannavo et al\textsuperscript{3} studied the value of reticulated platelets in the differential diagnosis of thrombocytopenia. Acute leukemia patients had elevated reticulated platelets to levels undistinguishable from ITP patients. As discussed above for MDS, acute leukemia is a bone marrow disease with suppressed thrombopoiesis, and if clinicians assume that the presence of reticulated platelets is solely due to immaturity, they may be led into a diagnostic mistake.

The use of reticulated platelets also poses practical workflow challenges. Traditionally, destructive and low production thrombocytopenias have been discriminated against based on the mean platelet volume (MPV) due to the larger volume of immature platelets. Unlike the MPV, reticulated platelets are not reported routinely as part of the CBC diff. Therefore, if a laboratory is facing challenges reporting the MPV, an attempt to bypass this challenge by reporting the reticulated platelet parameters will lead to increased reagent costs and increased turnaround time due to repeat and reflex testing.

There are also technical challenges due to variation in reticulated platelets during sample storage. This is concerning because this measurement is not readily available as part of the routine CBC-diff, so typically testing will occur at a later stage after the thrombocytopenia is recognized. Osei-Bimpong et al\textsuperscript{4} recognized this challenge and proposed a correction factor. Laboratories wishing to report reticulated platelets should develop algorithms to apply this correction factor and must carefully track sample storage time for it to be effective.

Since the initial description of reticulated platelets and their proposed clinical utilizations, important pitfalls and practical limitations have been recognized. Laboratorians must be aware of these before implementing this new parameter in their test menu.

\textbf{References}


