PLATELET DENSITY HETEROGENEITY

To the Editor:

In their recent article on the density heterogeneity of human whole blood platelet subpopulations,1 Dr Corash and colleagues conclude that the "basic intrinsic heterogeneity [is] due to events during thrombocytopenia." This statement is welcome. However, they qualify it by maintaining that decrease in density due to aging may be superimposed upon that primary determinant. In doing so, they fail to discuss those studies which actually suggest that there may be a small increase in density with platelet age.2-4

Two similar studies, both using a primate model and isotopically labeled platelets, have produced opposing conclusions about the origin of platelet density heterogeneity.4,5 The difference may well be related to the use of continuous density gradients by one4 and discontinuous by the other.7 In a study in which continuous and discontinuous gradients are compared side by side in the separation of platelets, each produced a different result.2 There are theoretical reasons why this may be so.5

The increases in platelet density that have been observed in myocardial infarction6 suggest the origin of platelet density heterogeneity may have clinical importance. Perhaps it would be helpful in future studies for workers to use continuous and discontinuous density gradients side by side. Corash et al.1 state that the use of discontinuous gradients allows red cells to be separated accurately into density subpopulations. However, because that method is effective for erythrocytes it cannot be assumed that it is valid for thrombocytes.

Corash et al.1 also postulate that aging effects may be extended to platelet volume heterogeneity. The aging hypothesis of platelet heterogeneity relies on a process that is independent of random destruction.9 There is now evidence that in normal function in man random platelet destruction is equally as important as constant platelet destruction.10 The linear appearance of the platelet survival curve in man can be explained by the small parametric values in the exponent of the exponential decay of isotopically labelled platelets.10 Thompson and his colleagues11,12 have demonstrated conclusively that platelet size does not correlate with age.

With this evidence, even the proposed superimposition of aging heterogeneity upon the principal thrombopoietic determinant seems unlikely in normal physiology.

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REFERENCES


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Although there is general agreement that platelets are heterogeneous, the origin of platelet heterogeneity continues to be a controversial scientific topic. Drs Martin and Trowbridge have raised multiple issues which bear directly on this controversy and are deserving of comment.

We did not refer to the papers which suggest that platelet density increases with aging1-3 because the primary objective of our report was to examine platelet density-dependent properties,4 not to test the hypothesis that platelet age and density are related. Moreover, the papers cited by Martin and Trowbridge contain conflicting observations that make interpretation difficult. Boneu et al.1 reported that post-aspirin recovery of prostaglandin synthesis (PS), an index of new platelet production, was more rapid in "light" platelets due to the delayed maturation of dense platelets. Mezzano et al.4 using a similar model, found more rapid recovery in low density platelets overall, but equal early recovery in both density fractions. He also described increased platelet density with aging and decreased survival of high density platelets. In contrast, Martin and Penington1 reported a minimal shift in platelet density with aging but shortened "light" platelet survival. The contradictory conclusions of Boneu et al.1 and Mezzano et al.4 may be explained partially by the recent finding of Di Minno et al.7 that when a potent stimulus is used, PS recovery can be detected as early as four hours after discontinuing aspirin. Thus, the presumed lag phase in dense platelet PS recovery1,3 may be due to experimental artefact.

More importantly, the inconsistencies of these papers emphasize a common problem in the measurement of density-dependent platelet properties: the necessity of a valid isopycnic centrifugation technique to obtain platelet density cohorts. Platelet activation can cause organelle secretion with decreased density but not necessarily
Platelet density heterogeneity [letter]

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