5. Cote M, Menager MM, Burgess A, et al. Munc18-2 deficiency causes familial hemophagocytic lymphohistiocytosis type 5 and impairs cytotoxic granule exocytosis in patient NK cells. *J Clin Invest.* 2009;119(12):3765-3773.
6. Martin-Verdeaux S, Pombo I, Iannascoli B, et al. Evidence of a role for Munc18-2 and microtubules in mast cell granule exocytosis. *J Cell Sci.* 2003; 116(pt 2):325-334.
7. Houng A, Polgar J, Reed GL. Munc18-syntaxin complexes and exocytosis in human platelets. *J Biol Chem.* 2003;278(22):19627-19633.
8. Meeths M, Entesarian M, Al-Herz W, et al. Spectrum of clinical presentations in familial hemophagocytic lymphohistiocytosis (FHL) type 5 patients with mutations in STXBP2. *Blood.* 2010;116(15):2635-2643.
9. Rohr J, Beutel K, Maul-Pavicic A, et al. Atypical familial hemophagocytic lymphohistiocytosis due to mutations in UNC13D and STXBP2 overlaps with primary immunodeficiency diseases. *Haematologica.* 2010;95(12): 2080-2087.
10. Nurden P, Nurden AT. Congenital disorders associated with platelet dysfunctions. *Thromb Haemost.* 2008;99(2):253-263.

To the editor:

Platelet interior imaging technologies

Harry F. G. Heijnen and his colleagues recently reported studies of the platelet interior using electron tomography.[1] The methods used to freeze platelets and prepare them for cryo-electron tomography are of interest. However, most of the information presented is not new. A major finding was that the open canalicular system and dense tubular systems of channels were highly intertwined and formed close associations in specialized membrane regions. This observation is not new. Interaction of the 2 channel systems was first reported in 1972,[2] and the name "membrane complexes" assigned to them. Their similarity to the sarcoplasmic reticulum of embryonic muscle and ability of the dense tubular system to bind divalent cations suggested a role of membrane complexes in platelet muscle physiology.[3]

A review chapter, "Platelet Structure," at page 70 (Figures 3-74, 3-75, and 3-76) in the second edition of Michelson's textbook *Platelets*[4] provides a more comprehensive picture of membrane complexes. Identification of α granule subtypes included organelles containing the multimeric von Willebrand factor assemblies in tubules eccentrically located in the α granule matrix.[1] Heijnen and colleagues cite a paper by Cramer et al[5] for recognizing the tubular elements in α granules, demonstrating that they are von Willebrand factor multimers similar to Weibel-Palade bodies. However, an earlier study in 1968[6] described them in thin platelet sections by transmission electron microscopy (TEM). The authors of the current paper[1] frequently encountered α granules with an elongated, "tubular shape," and their Figures 4 and 5 provide images of the tubular subtypes. However, images in Figure 3-49 on page 62 of Michelson's text[4] provide an image of α granules with extensions taken by TEM that is clearer than provided by tomography. The extensions appear as dense as the granules from which they originate. Therefore, we referred to them as "rod-like," rather than "tubular." The presence of cross-striations in the rods also was noted in another study.[7]

Electron tomography or its interpretation may make errors in organelle identification. The tomographic slices of a "tubular" α granule in Figure 5C-F and its reconstruction in 5G-H are interesting, but the organelle is not an α granule. It is a δ granule (dense body). Several examples are shown in Michelsen[4] on page 62 in Figures 3-50 and 3-51, on page 63 in Figure 3-52, and in examples included here (Figure 1). The images in the enclosed illustrations were taken by TEM on whole-mount preparations of normal platelets.

In summary, Heijnen et al have used a useful new technology to review the platelet interior. However, based on the concerns raised in this letter, it does not appear that electron tomography has replaced thin-section and whole-mount TEM.

James G. White
Regents Professor of Laboratory Medicine, Pathology and Pediatrics, University of Minnesota, Minneapolis, MN

Conflict-of-interest disclosure: The author declares no competing financial interests. **Correspondence:** James G. White, MD, University of Minnesota

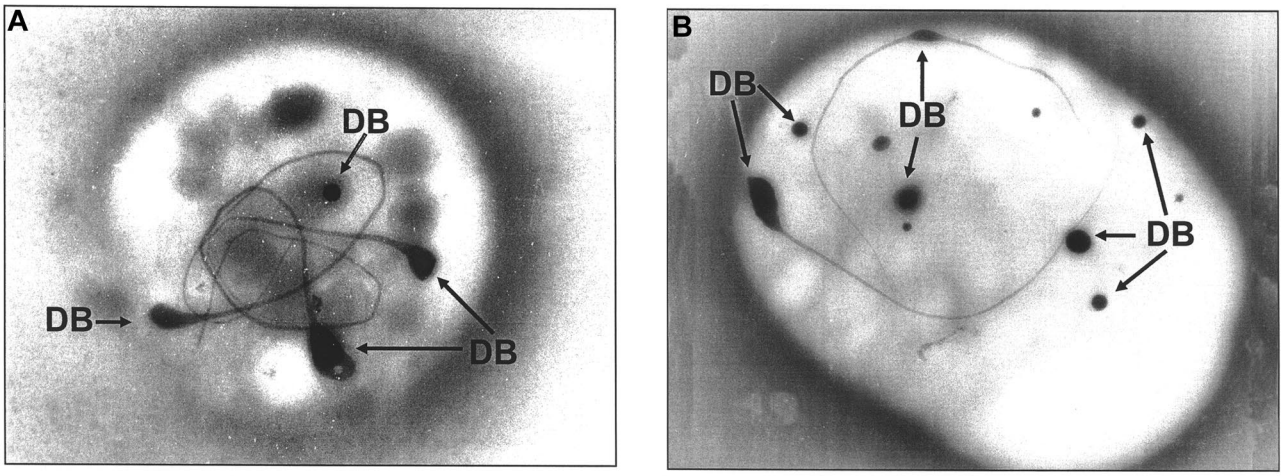

Figure 1. Whole-mounted platelets viewed by TEM. Two micrographs (A-B) of whole-mounted platelets viewed by TEM contain many spherical dense bodies (DBs) and DBs with 1 or 2 tails.

School of Medicine, Mayo Bldg, Box MMC 490, 420 Delaware St SE, Minneapolis, MN 55455; e-mail: white003@umn.edu.

References

1. Pannerden HVNT, de Haas F, Greets W, Posthuma G, van Dÿk S, Heijnen H. The platelet interior revisited. *Blood.* 2010;116(7):1147-1156.
2. White JG. Interaction of platelet membrane systems. *Am J Pathol.* 1972;66(2): 295-312.
3. White JG. Is the canalicular system the equivalent of the muscle sarcoplasmic reticulum? *Hemostasis.* 1975;4:184-191.
4. White JG. Platelet structure. In: Michelson A, ed. *Platelets.* IInd edition. Burlington, MA: Academic Press; 2006:1343.
5. Cramer EM, Meyer D, le Menn R, Breton-Gorius J. Eccentric localization of von Willebrand factor in an internal structure of platelet alpha-granule resembling that of Weibel-Palade bodies. *Blood.* 1985;66(3):710-713.
6. White JG. Tubular elements in platelet granules. *Blood.* 1968;32(1):148-156.
7. White JG. Structural defects in inherited and giant platelet disorders. In: Harris H, Hirschorn KH, eds. *Advances in Human Genetics.* New York, NY: Plenum Pub Corp; 1990:168.