In Reply:

We thank Dr. Dunn for his interest in our case report. In response, Dr. Dunn erroneously states that we noticed "a higher than expected incidence of stridor after using the Microcuff® endotracheal tube in neonates." We made no such claim or statement.[1] We found it enigmatic that Dr. Dunn referred to a 20-cm H_2O air leak around a tracheal tube as a "standard of care." First, the presence of an air leak depends on the head position and degree of paralysis as much as it does on the tube fit.[2] Second, the leak pressure is not reproducible as a 38% difference between experienced anesthesiologists has been reported.[3] Third, the study cited by Dr. Dunn stated that in selecting the appropriate size tube in infants with age less than 1 yr, either "resistance to passage of the initial tube into the trachea, or … an audible leak when the lungs were inflated to a pressure of 20–30 cm water" was used with apparent equipoise.[4] We presume then he agrees with our practice that a tube that passes the subglottis without resistance is the correct size, as described in our report.[1] Returning the 0.5 ml of air, which was evacuated from the packaged cuff to the cuff as described in two of the cases in our report, did not substantively change the shape or pressure within the cuff of these tubes as we determined *in vitro*. Fourth, the incidence of stridor after leak pressures of 40 cm H_2O or more in children (twice that recommended by Dr. Dunn) was zero in one study on 200 children or more and 0.1% in the second of 5,000 children or more.[3,5] In fact, several studies have reported postextubation stridor after leak pressures between 10 and 40 cm H_2O without consistent results. Fifth, the "leak test" emerged from the pediatric intensive care unit to attenuate the incidence of stridor postextubation, although recent evidence suggests that stridor occurs with a similar incidence in children at a leak pressure of 20 and 30 cm H_2O and that a leak test at 40 cm H_2O in critically ill children does not predict extubation failure.[6] Surprisingly, the leak test is not used at all to size uncuffed tracheal tube for infants in several neonatal intensive care units that we canvassed. We believe this evidence repudiates the "leak test" as a "standard of care" for tracheal tube size in infants. In sum, we urge practitioners to follow the published guidelines and manufacturer's recommendations for sizing these tubes according to the patient's age and weight, and to limit the use of these tubes in neonates and infants to circumstances that warrant a cuffed tube, until further studies establish their safe use.

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Standard Kaolin-active Thromboelastography Cannot Detect Platelet Inhibition by Clopidogrel

To the Editor:

In the March 2013 issue of Anesthesiology, Dr. Ahn *et al.*[1] present a thorough and informative review of pain-associated respiratory failure. The review is based on a case report describing a 79-yr-old man with bilateral chest trauma, in whom the treating team decided to use epidural analgesia. This is not an uncommon scenario; however in this case, the patient was taking clopidogrel as prophylaxis after the placement of bare-metal coronary artery stents.

As stated in the article, there is little in the way of evidence to guide epidural placement in patients taking antiplatelet agents; furthermore, the response to these agents demonstrates intrapatient variability. The treating physicians used standard coagulation parameters and thromboelastography to assess coagulation before insertion of the epidural catheter.

It is my contention, supported by published data, that none of the tests performed on this occasion could have adequately assessed the contribution of clopidogrel to coagulopathy in this patient. Standard kaolin-activated thromboelastography in particular will not reflect any platelet inhibition that is caused by clopidogrel, as the thrombin generated in the sample is enough to fully activate platelets even when pathways reliant on adenosine diphosphate or arachidonic acid are blocked. This topic is more fully covered in an excellent review by Gibbs.[2]

The effect of clopidogrel on a blood sample can be assessed with the thromboelastography equipment using Thromboelastography Platelet Mapping™ assay[3] or with other proprietary tests.

I have no qualms with the use of epidural analgesia in this patient; the possible risk of hematoma was balanced by the

predictable benefits of analgesia on respiratory function. I am concerned that treatment decisions may have been made using an incorrect interpretation of the results of thromboelastography and that as a result of this article physicians might repeat this mistake.

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Standard Thromboelastography Should Not Be Used to Assess Candidacy for Neuraxial Procedures in Patients Taking $P2Y_{12}$ Inhibitors

To the Editor:

We read with interest and concern the case scenario by Ahn *et al.*[1] describing the use of the thromboelastograph to guide thoracic epidural placement in an elderly patient with chest trauma taking clopidogrel and aspirin. Despite presumed platelet inhibition, this patient's thromboelastograph demonstrated a slightly hypercoagulable state with an increased maximum amplitude of 76.1 mm. We agree that trauma-induced inflammation and acute-phase reaction are possible causes of the reported thromboelastograph findings in this patient. However, we are concerned about the authors' use of standard, kaolin-activated thromboelastography as a method to assess platelet function in the setting of a $P2Y_{12}$ antagonist as well as aspirin.

Thrombin is, by far and away, the most potent activator of platelets.[2] This activation is accomplished through thrombin-mediated cleavage of the protease-activated receptors. Adenosine diphosphate, in contrast, is a relatively weak activator of platelets.[3] Adenosine diphosphate agonism of the $P2Y_{12}$ receptor serves to amplify the platelet in response to thrombin and to stabilize platelet aggregates. This results in a critical issue that practitioners using the thromboelastograph to guide interventions need to understand; kaolin-activated coagulation generates thrombin in quantities that are sufficient to overcome the effects of $P2Y_{12}$ antagonists on platelet function as assessed by thromboelastography.[4] In a similar manner, platelet inhibition by aspirin is also masked in kaolin-activated thromboelastography.

Platelet inhibition can be assessed by a modified thromboelastograph assay known as TEG Platelet Mapping® (Haemonetics, Niles, IL). The details related to this assay can be found elsewhere. Despite the fact that authors' discussion correctly identifies the need for this modified thromboelastograph assay to assess platelet inhibition from clopidogrel and aspirin, the assay was not used in the presented case. Instead, a supranormal maximum amplitude result from a standard thromboelastograph assay was incorrectly interpreted as representing a safe environment for neuraxial intervention.

Fortunately, the patient described in this scenario did not appear to suffer any consequence. As the authors themselves note, several studies have found the risk of epidural hematoma to be extraordinarily low even in patients taking clopidogrel on the day of placement. Despite this, we strongly discourage the use of results from standard, kaolin-activated thromboelastography as evidence of a safe hemostatic milieu for neuraxial anesthesia or analgesia in a patient receiving any $P2Y_{12}$ antagonist. Instead, we recommend using TEG Platelet Mapping® or another assay capable of assessing platelet inhibition from these medications.

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