

THE AUTHORS REPLY: Considering the complexity of airway management and the time allotted for this video, we struggled in deciding what to include and what to omit.

With regard to the comments by Caruso and Sungur, upper-airway obstruction in unconscious patients is a multifactorial phenomenon that may involve several structures, including the tongue, soft palate, and epiglottis. The majority of texts describe the tongue as the most common cause of airway obstruction. However, data suggest that under certain circumstances, such as during anesthesia with propofol in infants, other mechanisms are involved.¹

Kheterpal and colleagues comment on the removal of dentures. To emphasize the role of the tongue, the video illustrates how the application of pressure to the submandibular soft tissues may push the tongue against the palate, leading to airway obstruction. This situation is worsened in edentulous patients and can be minimized, as described in the video, by leaving full dentures in place. The video also illustrates how an inappropriately small oral airway may push the tongue against the pharynx, causing or worsening air-

way obstruction. Further studies are needed to elucidate the extent of the tongue's contribution in airway obstruction in a variety of clinical situations.

With regard to the comments by Torri, the American Society of Anesthesiologists difficult-airway algorithm is a valuable strategy.² Our video is in concert with the algorithm's recommendations and stresses the importance of face-mask ventilation as a potentially lifesaving and temporizing maneuver. Finally, the video demonstrates how raising the head of a bed may facilitate the delivery of adequate tidal volumes.

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1. Crawford MW, Rohan D, Macgowan CK, Yoo SJ, Macpherson BA. Effect of propofol anesthesia and continuous positive airway pressure on upper airway size and configuration in infants. *Anesthesiology* 2006;105:45-50.

2. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology* 2003;98:1269-77. [Erratum, *Anesthesiology* 2004;101:565.]

Multiple Alloantibodies after Transfusion in an Infant Treated with Infliximab

TO THE EDITOR: Infliximab (Remicade) is a humanized mouse monoclonal antibody that blocks tumor necrosis factor α .¹ It down-regulates type 1 helper T-cell (Th1) immune responses and increases type 2 helper T-cell (Th2) responses, thereby favoring antibody production.² There are many reports of autoantibody formation after the administration of infliximab, including a case of autoimmune hemolytic anemia.¹ We report on a 10-month-old boy who received infliximab for systemic-onset juvenile rheumatoid arthritis and who had a severe hemolytic transfusion reaction.

At the time of his initial admission, the patient's hemoglobin level was 8.3 g per deciliter, and his hematocrit was 19.2%. He had a negative test for red-cell antibodies and no history of blood transfusion. The patient received a unit of blood; after the transfusion, his hemoglobin level was 13.6 g per deciliter and his hematocrit was 39%. The boy received infusions of infliximab at a dose of 10 mg per kilogram of body weight (for a total of 300 mg) for his juvenile rheumatoid arthritis

4, 7, and 9 days after transfusion. Symptoms of his disease improved, and he was released from the hospital.

Three weeks later, he was readmitted with severe anemia. Laboratory values included a hemoglobin level of 4.7 g per deciliter, a hematocrit of 14.1%, a reticulocyte count of 5.6%, and a lactate dehydrogenase level of 8695 U per liter. The result of testing for red-cell antibodies was now strongly positive, and anti-E, anti-Fy^a, and anti-Jk^a antibodies were identified. A pretransfusion specimen of the patient's blood was typed and found to be negative for the E, Fy^a, and Jk^a antigens, whereas residual blood from the transfused unit carried these antigens. However, when the circulating red cells were typed for E, Fy^a, and Jk^a, there was no reactivity, which indicated that there were no detectable transfused red cells in his circulation. The patient had elevated levels of IgE (440 IU per milliliter; mean level, 3.2 IU per milliliter in infants between the ages of 10 months and 12 months), IgG (3486 mg per deciliter; normal range, 286 to

1680), and IgM (246 mg per deciliter; normal range, 21 to 192). He received a transfusion of blood lacking the E, Fy^a, and Jk^a antigens and had no further complications.

The production of antibodies against blood groups in infants under the age of 1 year is extremely rare,^{3,4} and to our knowledge, the simultaneous development of multiple antibodies has not been described. These antibodies may result from altered regulation of the immune system,^{3,4} a concept supported by a recent report.⁵ In our patient, the infusion of infliximab may have favored a Th2 response, resulting in increased antibody production, including red-cell alloantibodies. Unlike typical primary immune responses to red-cell antigens, which are IgM-predominant, low-titer, and clinically insignificant, our patient's immune responses were IgG-predominant, high-titer, and hemolytic.

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1. Vermeire S, Noman M, Van Assche G, et al. Autoimmunity associated with anti-tumor necrosis factor alpha treatment in Crohn's disease: a prospective cohort study. *Gastroenterology* 2003;125:32-9.
2. Bobbio-Pallavicini F, Alpini C, Caporali R, Avasse S, Bugatti S, Montecucco C. Autoantibody profile in rheumatoid arthritis during long-term infliximab treatment. *Arthritis Res Ther* 2004; 6:R264-R272.
3. DePalma L, Criss VR, Roseff SD, Luban NLC. Presence of the red cell alloantibody anti-E in an 11-week-old infant. *Transfusion* 1992;32:177-9.
4. Albiero AL, Novaretti MCZ, Llacer PED, Chamone DAF. Early primary immune response against erythrocytes: a case report. *Transfus Med* 2003;13:93-7.
5. Hendrickson JE, Desmarests M, Deshpande SS, et al. Recipient inflammation affects the frequency and magnitude of immunization to transfused red blood cells. *Transfusion* 2006;46:1526-36.

The above letter was referred to Centocor, the manufacturer of infliximab, which offers the following reply:

TO THE EDITOR: Tyler and colleagues report on the use of infliximab in an infant with systemic-onset juvenile rheumatoid arthritis (an unapproved indication), which was administered in three doses totaling 30 mg per kilogram of body weight (300 mg) over a 6-day period (an unusually intense regimen and a higher dose than that which is approved for any indication). They postulate that infliximab favored a Th2 response, resulting in the formation of alloantibodies against transfused red cells. This single-patient observation contrasts with a controlled study showing that infliximab does not augment antibody responses to pneumococcal vaccine.¹ Although infliximab may induce the formation of antinuclear antibodies, the postulated mechanisms that are involved include cellular apoptosis and the release of nuclear antigens or a reduction in the clearance of nuclear debris, not a generalized increase in antibody responses.² Levels of other autoantibodies, such as rheumatoid factor, are not increased with infliximab therapy. The suggestion that infliximab may have contributed to alloantigen responses is speculative.

We reviewed available reports of adverse events associated with infliximab and did not identify any cases of hemolytic anemia mediated by alloantibodies. Hematologic events (e.g., hemolytic anemia) have been reported in patients receiving infliximab, but the cause remains unclear.

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1. Visvanathan S, Keenan GF, Baker DG, Levinson AI, Wagner CL. Response to pneumococcal vaccine in patients with early rheumatoid arthritis receiving infliximab plus methotrexate or methotrexate alone. *J Rheumatol* 2007;34:952-7.
2. De Rycke L, Baeten D, Kruithof E, Van den Bosch F, Veys EM, De Keyser F. Infliximab, but not etanercept, induces IgM anti-double-stranded autoantibodies as main antinuclear reactivity. *Arthritis Rheum* 2005;52:2192-201.

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