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**Title:** Anemia of prematurity: time for a change in transfusion management?  
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The association between allogeneic RBC transfusions and a negative clinical outcome in premature neonates has contributed to the introduction of blood transfusion guidelines with recommended transfusion triggers. Despite the use of a national blood transfusion guideline significant differences exist concerning the total amount of allogeneic RBC transfusions administered to premature infants. However, as shown by comparison of two Dutch tertiary neonatal centers, a more liberal transfusion strategy and a higher transfusion volume was not associated with obvious poor short-term outcome, nor delayed neuromotor development at 2 years of age. A methodological bias due to the use of different assessment tools for neuromotor development or a too small study population however cannot be ruled out and long-term follow-up evaluation is lacking.

Due to use of the current transfusion triggers, most transfusions are administered early in life. Therefore less suppression of endogenous EPO could be expected. Future studies focusing on transfusion triggers and transfused RBC volume can elucidate whether differences in transfusion practices result in variable degrees of EPO supression.

Umbilical cord blood may be an easy accessible alternative for allogeneic RBC transfusions but can also be used for autologous purposes. Premature infants born < 30 gestational weeks suffering from anemia of prematurity can be treated with autologous RBCs derived from UCB. Ex vivo expansion of UCB derived CD34 positive stem cells and progenitor cells provides a potential source of ex vivo expanded RBC for autologous use, and as such could supplement autologous UCB red cells in minimizing allogeneic RBC transfusions. In the future, the culturing methods should be optimized for clinical use.

Current neonatal transfusion practice and clinical studies have focused on more restrictive transfusion triggers and optimizing RBC product volume and hematocrit to minimize allogeneic RBC transfusions. Use of autologous UCB cells and expanded UCB red cells can assist in reducing allogeneic blood. However, much remains to be done before this can be achieved. Until then, the presumed disadvantages of allogeneic RBCs on neonatal outcome should be further clarified, because avoidance of allogeneic transfusions is unattainable in current clinical practice.

**Recommendations**

- Future studies on RBC transfusion triggers and/or effects should mention transfusion volume as well as product hematocrit. As such international data on actual transfused RBC effects can be compared in a more precise manner.
- Follow up studies on transfusion related outcome should use a uniform method for neuro-cognitive testing and also a longer follow up period (at least up to school age) is recommended.
- To widen the use of autologous cord blood transfusion; there exist ample possibilities for improvement of collection and fractionating techniques of umbilical RBC products and of erythrocyte expansion protocols from UCB leukocytes.