Transfusion of blood (allogeneic concentrates of red blood cells) is an effective intervention and can be life saving in the contexts of bleeding or severe anaemia. In common with most medical interventions, it is associated with risks for the individual patient and wider costs to society. It is therefore desirable to take measures to limit transfusion and to clearly define the indications for transfusion.

In the past the approach has been the aim to maintain a haemoglobin concentration above 100g/l, with higher levels often aimed for in populations perceived to be at increased risk of adverse effects of anaemia: such as adults with cardiac disease and premature neonates. Trials comparing restrictive and more permissive blood transfusion policies in children and adults have not demonstrated an advantage to either approach, beyond a reduction in the amount of blood transfused to the 'restrictive' group (1-4). This has led to wider adoption of more 'restrictive' strategies.

How restrictive or how permissive a particular strategy is, will depend upon the haemoglobin level chosen as an indication for transfusion. Such consensus as exists suggests that in fit adults, transfusion should be considered if the haemoglobin is below 80g/l and will generally be required if below 70g/l(5). These levels approximately agree with WHO definitions of severe anaemia(6). There is no valid reason why this cannot be applied to the majority of children. Higher values (usually 100g/l) are often aimed for in adults with critical illness or ischaemic heart disease. In children with cyanotic heart disease, critical illness and in neonates higher targets may also be chosen.

If different thresholds are chosen for different groups of patients, it is important to be clear on how patients are allocated to these groups and for each group what threshold should be aimed for. 'Neonates' could apply to all new-borns or only preterm babies, or also apply to ex-preterm babies with a history of apnoea. Heart disease could apply to all children with heart disease, only to those with severe cyanosis or only to children recovering from heart surgery. Similarly 'critical illness' could apply to all children being ventilated for an acute illness or only to those with evidence of reduced tissue oxygenation. These are questions which generally only affect anaesthetists with highly specialist practice; however it is likely that the majority of peri-operative transfusions of children will occur in such children. More restrictive approaches have been used in selected children with cyanotic heart disease (7), children with critical illness (3) and in preterm infants (8). The thresholds used in these trials were higher in preterm infants and cyanotic children than those described above. Higher transfusion targets are probably appropriate for the highest risk cardiac patients (infants having just undergone Norwood procedures or BT shunt) or in children with severe critical illness and evidence of poor tissue oxygenation.

A more satisfactory answer to these questions is that haemoglobin concentration should not be considered the only, or the primary, indication for transfusion. Rather, transfusion should be given in an attempt to improve the patient's general condition and a doctor choosing to transfuse a patient should think explicitly how they expect the transfusion to benefit the patient. If a patient is recovering well from surgery it is unlikely that they will benefit from a transfusion despite a low haemoglobin concentration. If a child is sick and deteriorating despite other interventions, then increasing the haemoglobin concentration by transfusion will be a sensible step to take. There are limits to this approach. A patient with a haemoglobin concentration less than 60g/l should generally be transfused. A patient with a haemoglobin concentration greater than 120g/l is unlikely to benefit from transfusion. How the haemoglobin concentration is likely to change, in particular if there is potential for ongoing blood loss, should also be considered.

The survey also addressed the question of how much blood should be given. This was phrased in terms of 'therapeutic target' for haemoglobin following transfusion. This is the approach advocated by the British Blood Transfusion Service(9) who states that '*The dose of blood components for infants and children should always be carefully calculated and prescribed in mL, rather than as 'units' to prevent errors and avoid potentially dangerous circulatory overload*'. Formulae exist for calculating the volume required based on actual and target haemoglobin levels and the patient's weight. However, many of the adverse effects of transfusion will be related to the number of donors whose blood the child is exposed to, rather than the volume of blood transfused. This approach is inefficient (in terms of donor exposure) and probably unsuitable for perioperative use. For small infants, segmented (or 'paediatric') units of red cells are widely available and can reduce donor exposure if multiple transfusions are required. Generally the dose given should be rounded to a whole unit (or paediatric pack), unless this would result in an excessively large transfusion.

In summary:

- In otherwise well children and infants, transfusion of red blood cells should be considered when the haemoglobin is below 80g/l and is generally required when it falls below 70g/l.
- In deciding whether to transfuse, the child's clinical condition and the context should be considered, not just the haemoglobin level.
- In the majority of critically ill children, similar transfusion thresholds can be used.
- Transfusion at a higher haemoglobin level should be considered in neonates, in children with cyanotic heart disease and in children with critical illness and evidence of reduced tissue oxygenation.
- Other measures should be taken to reduce the need for transfusion of allogeneic blood: treatment of pre-operative anaemia, use of cell salvage, use of antifibrinolytic drugs and modification of surgical technique.
- It is reasonable to consider postponing elective surgery to allow treatment of iron deficient anaemia.

1. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, Rhoads GG, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med. 2011;365(26):2453-62.

2. Willems A, Harrington K, Lacroix J, Biarent D, Joffe AR, Wensley D, et al. Comparison of two red-cell transfusion strategies after pediatric cardiac surgery: a subgroup analysis. Critical care medicine. 2010;38(2):649-56.

3. Lacroix J, Hebert PC, Hutchison JS, Hume HA, Tucci M, Ducruet T, et al. Transfusion strategies for patients in pediatric intensive care units. The New England journal of medicine. 2007;356(16):1609-19.

4. Rouette J, Trottier H, Ducruet T, Beaunoyer M, Lacroix J, Tucci M. Red blood cell transfusion threshold in postsurgical pediatric intensive care patients: a randomized clinical trial. Annals of surgery. 2010;251(3):421-7.

5. JPAC - Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. 7.1: Transfusion in surgery. Available from: <u>http://www.transfusionguidelines.org.uk/transfusionhandbook/7-effective-transfusion-in-surgery-and-critical-care/7-1-transfusionin-surgery</u>.

6. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. . 2015. Available from: http://www.who.int/vmnis/indicators/haemoglobin/en/

7. Cholette JM, Rubenstein JS, Alfieris GM, Powers KS, Eaton M, Lerner NB. Children with single-ventricle physiology do not benefit from higher hemoglobin levels post cavopulmonary connection: results of a prospective, randomized, controlled trial of a restrictive versus liberal red-cell transfusion strategy. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2011;12(1):39-45.

8. Kirpalani H, Whyte RK, Andersen C, Asztalos EV, Heddle N, Blajchman MA, et al. The Premature Infants in Need of Transfusion (PINT) study: a randomized, controlled trial of a restrictive (low) versus liberal (high) transfusion threshold for extremely low birth weight infants. J Pediatr. 2006;149(3):301-7.

9. JPAC - Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. 10.3: Transfusion of infants and children. Available from:

http://www.transfusionguidelines.org.uk/transfusion-handbook/10-effectivetransfusion-in-paediatric-practice/10-3-transfusion-of-infants-and-children.