Editorial

Blood transfusion in orthopaedic surgery

The article reviewing protocols for the use of homologous blood transfusion which appears later in this journal[1] serves to raise awareness not only of the inconsistency of our practice but also to raise issues around developments that have occurred in haematology and immunology and that are presented at meetings or published in journals not frequently, if ever, attended or read by orthopaedic surgeons. In truth, the tunnel vision that has developed around each area of expertise, not only in orthopaedic surgery but in the broader sense of medicine as a whole, has not been beneficial to the spread of information. Information not central to one's own area of interest will by osmotic permeation eventually trickle through to clinical consciousness allowing the relevance of such information to finally surface, often years later. This phenomenon is well recognised by clinical administrators who advocate the cross-pollination of academic ideas by the presentation of interesting and new information at combined forums or 'Grand Rounds'. But, of course, life is too full and busy to attend meetings or read journals that ostensibly offer little to advance an interest in one's own specific area of interest.

The example of policies around the administration of blood is a case in point. The traditional wisdoms regarding the hazards of transfusion prevail. The risk of incompatibility, transmissible diseases, such as HIV, CMV, Hep C and other bacterial contaminants, minor problems like pyrexia and urticaria or other reactions, and the dangers of identification errors and religious preferences are well known.[2]

What is less well known are the 'newer' developments associated with the administration of homologous blood primarily because they have been published in journals of immunology, haematology and anaesthesiology to name a few. Since the '80s homologous blood transfusion has been implicated as a modulator of the host immune system in a number of clinical settings resulting in either immune activation, associated with a variety of transfusion reactions, or immunosuppression. The bulk of experimental and clinical data supports the theory that homologous transfusion causes significant down-regulation of immunologic functions in a number of settings.[3] The effects may be **beneficial** as was first observed by improved renal allograft survival in patients receiving peri-transplant transfusions and reduced recurrence of active inflammatory bowel disease in transfused patients with Crohn's disease.· On the other hand **deleterious** immunomodulatory effects of transfusion may explain the association between transfusion and increased susceptibility to cancer recurrence and bacterial and viral infection.[4-7] Severe postoperative infections, not as a consequence of contamination, have been shown to have an association with allogeneic RBC transfusions.[8-10] Postoperative infections in orthopaedics have also been strongly associated with patients receiving transfusions. In studies on patients undergoing total hip replacement the data suggest that allogeneic blood transfusion is associated with an increased incidence of wound-healing disturbances and prolonged hospitalisation, and that avoidance of allogeneic blood transfusion may be relevant to limiting the duration of hospitalisation after elective orthopaedic surgery.[11-13] Similar findings were recorded in a neonatal cohort with coagulase negative Staphylococcus septicaemia which was difficult to clinically eradicate despite *in vitro* antibiotic susceptibility.[14]

Work in the 2000s has demonstrated changes in lymphocyte subsets, lymphocyte activation, natural killer cell activity, antigen-presenting function, and phagocytic cell function in patients and animals that receive allogeneic blood.[15] The involved lymphocytes are termed Regulatory T cells (Tregs), are suppressive $CD4^{+}CD25^{+}Foxp3^{+}$ cells with a central role in immunosuppression and are induced by allogeneic transfusion.[8] The induction is dependent on exposure to allogeneic plasma and not to transfused cells, implying a plasma fraction.

There has been argument made that for those patients who require a blood transfusion the disease process is likely to be more severe or advanced, hence the more likely it is for recurrence of tumours or infections to occur. However there is strong evidence to support a causal relationship as demonstrated by two studies conducted to control for the confounders. Bower *et al*[16] concluded that after controlling for the factors associated with an increased likelihood for receiving a blood transfusion, the actual transfusion was predictive of a slower and more eventful postoperative recovery (including wound site infection) with associated costs to both the patient and health services. According to the findings of a study by Benson *et al*[6] the use of syngeneic murine models allowed many confounding variables to be controlled, and they concluded that transfusion does indeed promote pancreas cancer progression. Whatever the cause of infections and wound healing problems in our post-transfusion patients will prove to be, it is clear that **it happens**, thus an increased awareness for the possibility must be borne in mind and appropriate precautions should be taken.

Based on all these findings it is abundantly clear that apart from the commonly accepted risk factors, the administration of blood products is far from safe. This is especially true when implantables are being used. Infection in orthopaedic surgery is arguably the worst non-fatal complication we encounter and suppression of the immune system at the time of wound contamination with either pathogenic organisms or commensals is highly undesirable. How many of us are aware of this risk with the administration of blood? Hence, to ensure our patients' safety, alternate strategies to transfusion management are warranted.

Firstly the most obvious solution is to avoid giving blood. Mostly this can be achieved but under certain circumstances there will be a continued need for blood replacement therapy The Cochrane database (Carless *et al*[17]) interrogating blood administration thresholds state that if blood is to be administered the existing evidence supports the use of restrictive transfusion triggers (Hb = 7g%.) in patients who are free of serious cardiac disease. While this view point is supported by Blajchman and Hébert[1] and others, there is a school of thought that believes this level is a bit aggressive.

Perhaps not exploited to its full potential is the identification of patients undergoing elective surgery with low or marginal haemoglobin levels prior to surgery. The majority of these patients can be treated with iron and the surgery deferred until acceptable haemoglobin concentrations have been achieved. Studies by Andrews *et al*[11] and Myers *et al*[12] have shown that asymptomatic anaemia (<12.5 g/dl in men and <11.5 g/dl in women), which may escape attention until admission, is associated with increased intra- and postoperative morbidity and mortality, despite being easily correctible pre-operatively. The use of other modalities such as human recombinant erythropoietin administration,[18] self pre-donation for transfusion, haemodilution, anaesthetic hypotension, intra-operative and postoperative blood recovery techniques[19] and transexamic acid[18] to minimise bleeding should all be re-visited as preferable alternatives to transfusion.

From the available information it would appear that the administration of allogeneic blood transfusion can potentially do more harm than most of us anticipate. This is particularly relevant in orthopaedic surgery when implants are employed and more specifically in arthroplasty where long-term failure by loosening is being increasingly linked with infection.

Every effort should be made to avoid transfusion.

Prof J Walters
Guest Editor

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