Pain psychology for the non-psychologist

Editor—We read with interest Eccleston and colleagues’ review of psychological approaches to chronic pain management and would like to share some observations on psychology for the non-psychologist. Chronic pain sufferers often have multiple unrewarding medical consultations before referral to a pain clinic. Eccleston and colleagues state that patients may appear obsessed with their pain, equally though patients focus on the expectation that they can be cured. These unrealistic expectations can be detrimental to the patient. Calman hypothesized that the larger the gap between a patient’s experiences and their hopes and expectations, the poorer their quality of life.

Improving a patient’s experience of life through reduced pain and disability is often the primary focus of pain medicine, but clearly patient expectations play a role in the success of treatment. A 50% reduction in pain levels may be seen as a treatment success by some patients but a failure by others. Furthermore, if ‘the most likely outcome of any treatment is failure’ then to improve quality of life, we must narrow this gap by realigning patient expectations. This does not mean creating a pretreatment expectancy that pharmacotherapy or cognitive behavioural therapy will fail. Nor should it remove hope; it would seem patients need some degree of gap to give them something to aspire to. Realigning expectations should create realistic and achievable targets for the patient. Even if we cannot successfully cure a patient’s pain, an appropriately managed pain consultation has the potential to improve a patient’s quality of life through challenging ideas and creating realistic expectations.

Declaration of interest

None declared.

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Inflammatory response, immunosuppression, and cancer recurrence after perioperative blood transfusion

Editor—We read with interest the paper of Cata and colleagues concerning perioperative blood transfusions, inflammatory response, and immunosuppression. In this interesting review, the authors discuss the understanding of the mechanisms by which transfusion affects immune function and could affect cancer progression. The authors conclude that transfusion of allogenic blood causes substantial alterations to the anti-/pro-inflammatory milieu in the recipient that seems to be proportional to the stored age of the blood products. It seems that biological factors included in these packed red blood cells that affect the innate immune function, rather than leucocytes or soluble fractions, may be responsible for tumour-promoting effects.

Arginase has gained importance due to the fact that NO synthases are dependent on the availability of L-arginine in the extracellular environment. L-arginine is metabolized by NO synthase (NOS) to produce nitric oxide (NO) or by arginase to produce urea and ornithine, which is a precursor of polyamines, which are important during cellular proliferation. Expression of NOSs and arginases could co-regulate each other. Depletion of L-arginine by macrophages has been postulated as one of the several mechanisms that causes a decrease in CD3-zeta chain expression in cancer. In a tumour microenvironment, macrophages deplete arginine via their high arginase activity and profoundly down-regulate the tumour-infiltrating T-cells. L-arginine deficiency caused by high arginase activity, both at the tumour site and in circulating blood, has been associated not only with sustained tumour growth via polyamine synthesis but also with tumour escape from immune response. Although arginase has a short half-life of only a few hours in human blood, it might act in early stages of immunosuppression. High levels of free arginase after blood transfusion could underlie many of the deleterious outcomes, including immunosuppression and infection-related processes associated with transfusion of blood stored for long periods.

The proposed detrimental effects of prolonged blood storage have been attributed in part to haemolysis of packed erythrocytes stored for a prolonged period, which leads to an increased oxyhaemoglobin concentration and NO scavenging. Indeed, the haemoglobin level in the storage bag supernatant was found to be higher after 40 days of storage than after...
3 days of storage, indicating increased haemolysis, and infusion of 40-day packed erythrocytes was recently suggested to lead to increased NO production from endothelial NOS, as a compensatory mechanism for reduced NO bioavailability caused by plasma oxyhaemoglobin scavenging of NO. However, although leucoreduced units of packed red blood cells contain fewer than $5 \times 10^{-6}$ white blood cells, it should be noted that neutrophils, which undergo spontaneous cell death, constitutively express large amounts of arginase and even small contamination of packed red cell bags by neutrophils might, therefore, produce significant levels of arginase activity, apart from that derived from the red cells themselves. Recently, we found raised levels of free arginase in blood stored for long periods, which could corroborate these arguments and have implications for patients in whom immunosuppression is a major challenge.

Thus, we suggest that increased haemolysis might be an important aspect in blood transfusion, leading to elevated levels of arginase and NOS, and, thereby, to L-arginine depletion that could eventually affect immune function and cancer progression.

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**Factors for perioperative delirium**

Editor—I read with interest the paper by Radtke and colleagues addressing the important issue of anaesthetic depth and its relationship with postoperative delirium. Any measure which may ameliorate delirium warrants attention, given the personal cost to the patient and patient’s family along with the financial strain that postoperative delirium carries with it for the healthcare system.

I do, however, kindly request clarification regarding two methodological issues with the paper that may affect interpretation of the results presented: (i) benzodiazepine administration and (ii) intraoperative hypotension.

First, perioperative benzodiazepine use is associated with emergence delirium based on earlier work by Radtke and colleagues; in a prospective observational study examining over 1800 patients, those receiving a benzodiazepine as premedication were 2.39 times (95% confidence interval 1.01–5.62) more likely to experience emergence delirium than patients who were not administered a benzodiazepine. According to the methods used in the current study, in case a sedative premedication is needed midazolam is prescribed in a dosage of 0.1 mg per kg. Given their conclusion that ‘intraoperative neuromonitoring is associated with a lower incidence of delirium’, and in an effort to contextualize their findings with the

**Reply from the author**

Editor—I have to thank Palomero-Rodrı´guez and colleagues for their important contribution to this topic as raised in our review. Certainly, L-arginine and arginase I and II are important modulators of the immune response after blood transfusion. No less important is the evidence provided by several investigators suggesting that a deficiency of L-arginine also occurs as part of the stress response to surgery and this deficiency has been implicated as one of the mechanisms behind the known shift from a Th1 to a Th2 response after surgery. This phenomenon may even have been worsened by the transfusion of mainly ‘old’ blood which would further deplete levels of L-arginine. Perhaps, a more relevant question to answer in the clinical setting is whether the administration of L-arginine in the context of perioperative immune-nutrition could ameliorate immunosuppression and perhaps improve long-term oncological outcomes in patients in whom blood transfusion cannot be avoided and undergo major surgery.

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