

studies that the transmission of noxious afferent input from the periphery to the spinal cord induces a prolonged state of central neural sensitisation, which amplifies subsequent input.^{2,3} This finding suggests that the following three factors may contribute to the development of persistent post-amputation pain by inducing central sensitisation at different times relative to surgery:

- pre-amputation pain;
- noxious intraoperative inputs brought about by cutting skin, muscle, nerve and bone; and
- acute postoperative pain (including that due to pro-inflammatory processes).

It follows that regional anaesthetic blockade of one or more of these factors may prove effective in reducing the incidence of persistent phantom limb pain. Pinzur and colleagues tried to examine this possibility for postoperative pain, though they in fact examined blockade for intraoperative pain as well since most the patients underwent amputation under spinal anaesthesia.⁴ They randomly assigned 21 patients undergoing lower-limb amputation to receive a continuous perineural infusion of 0.5% bupivacaine (1 mL/h) or saline into the sciatic or posterior tibial nerve sheath starting immediately after surgery and continuing for 3 days. Postoperatively, patients self-administered morphine intravenously using a patient-controlled analgesia pump. The paper is short on pain data but Pinzur et al report that, although the bupivacaine groups used less morphine than did the saline group on postoperative days 1 and 2, phantom limb and stump pain did not differ significantly between the groups 3 or 6 months after surgery. There is good reason to hypothesise that the development of persistent phantom-limb pain and stump pain may be attenuated by post-operative perineural infusion of a local anaesthetic. However, in the light of the minute differences between the groups in morphine consumption (between 0.23 and 2.2 mg per day) and in the absence of pain data, the 3 and 6 month data may indicate that bupivacaine is no more effective than saline. Alternatively, administration of spinal anaesthesia during amputation may have pre-empted pain in both groups, leading to non-significant differences in long-term pain. Since we know neither the number of patients in each group who were contacted at follow-up nor the number in pain, these possibilities remain speculation.

Nevertheless, the Pinzur study raises the issue of the role of noxious peri-operative inputs in the pathogenesis of persistent pain after amputation and whether it is possible to prevent persistent phantom limb and stump pain by perioperative regional anaesthesia. Traditional approaches to the management of acute postoperative pain have focused primarily on treating the patient after surgery in an effort to reduce already established pain. It is becoming increasingly clear, however, that the very act of cutting tissue, nerve, and bone may induce long-lasting changes in central neural function that amplify postoperative pain intensity and increase the need for analgesics. Pre-emptive analgesia represents a novel approach to postoperative pain management in which analgesic agents are administered before surgical incision in an effort to prevent nerve impulses arising from noxious intraoperative events from reaching and

Prevention of phantom limb pain by regional anaesthesia

Most patients who undergo major surgery do not end up with long-term pain. However, after certain procedures pain persists in an alarming percentage of patients. For example, phantom limb pain develops in more than 70% of patients years after amputation.¹ We do not know why the incidence of phantom limb pain is so high, but we know from basic science and clinical

sensitising central neural structures involved in the perception of pain^{5,6} The possibility remains however, that even if a pre-emptive analgesic approach to amputation is effective in the short term, neural impulses generated at an abnormal site (eg, at transected nerves that develop in transected nerves have formed a neuroma) may induce a state of central sensitisation after the short-term effects of the regional anaesthesia have worn off.⁷

What is the evidence that pre-operative, intra-operative, and/or postoperative regional analgesia actually prevents long-term phantom limb pain? Recent studies of patients undergoing lower-limb amputation show that epidural anaesthesia started before and continuing for the duration of surgery⁸ or for several days after amputation^{9,10} seems to confer the most protection from long-term pain. By contrast, blockade of late intra-operative and postoperative noxious inputs does not seem to influence the development of persistent pain.^{4,11-13} probably because the blockade is administered after central sensitisation has been established. Well-controlled studies are required before we will have an answer to the above question. Discovering the relative contributions to long-term pain of factors such as preexisting pain, noxious perioperative events, and postoperative pain will enable us to design multi-agent, pre-emptive treatments aimed specifically at minimising the detrimental effects of these factors.

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