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EDITORIAL I

Defining persistent post-surgical pain: is an update required?

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Severe persistent post-surgical pain (PPP) affects 2–10% of adults undergoing surgery,[1] corresponding to at least 140 000 patients per year presenting with disabling pain in the UK.[2] Surgery is indeed pivotal in the treatment of a number of serious diseases, and, while the overall benefits to patients are unquestionable, the quest of identifying improved techniques of preventing or mitigating severe pain and functional impairment in patients post-surgery continues.

An important editorial in the *BJA* recently highlighted the need for a research agenda in the prevention and treatment of PPP.[3] However, the definition of PPP is an important tool for anchoring and tailoring future research strategies. The first definition containing operational criteria, proposed by Macrae and Davies[4] in 1999 and expanded by Macrae[5] in 2001 in the *BJA* (Table 1), has made an excellent working platform. Additional minor suggestions were presented in 2010[6] and 2012,[7] mainly in respect of the duration of PPP post-surgery and of PPP induced by surgical implants. Nevertheless, in the authors' opinion, the operational criteria regarding PPP would benefit from specific updates based upon current developments in the field. In what follows, we present arguments for the proposed updated criteria, comparing them chronologically with the existing criteria.

The first criterion (Table 1), 'The pain develops after a surgical procedure or increases in intensity after the surgical procedure', indicates a temporal relationship with surgery. In the majority of patients, the pain occurs post-surgery and is easily related to the surgical procedure *per se*. However, in a number of elective surgical procedures, pain and discomfort are prevalent findings pre-surgery (e.g. inguinal herniorrhaphy,[8] hysterectomy,[9] and cholecystectomy).[10] This obviously also holds true for acute surgical procedures where preoperative pain and discomfort are much more prevalent. In order to qualify as PPP, an increase in the perceived pain intensity is a minimum requirement, preferably accompanied by a change in location, in spatial distribution, or in the characteristics of the pain. If the characteristics of the pain are unchanged vis-à-vis pre-surgery, or decreased in severity by the surgery, the condition should not be termed PPP.

The second criterion, 'The pain should be of at least three to six months' duration and significantly affect the health-related quality of life (HR-QOL)', is in line with the criteria for chronic pain of the International Association for the Study of Pain: '. . .pain which persists past the normal time of healing. . .. . .-With non-malignant pain, three months is the most convenient point of division between acute and chronic pain, but for research purposes six months will often be preferred'.[11] The suggestion of increasing the duration of pain, from 2 months in the existing criteria to between 3 and 6 months, would leave sufficient time to examine the functional results of the surgical procedure. If examination reveals signs of complications, then the need for surgical re-exploration or other interventional measures will be evaluated. However, categorizing pain solely in terms of duration, and not considering the functional impairment or even the multidimensionality of persistent pain, may infer erroneous conclusions regarding the pathophysiological mechanisms, ultimately leading to an inadequate treatment approach. Interestingly, in a number of chronic pain states, the use of simple risk scores, constructed using a limited number of prognosis-related variables, has improved the prognostic capability;[12 13] however, so far, the approach has not been consistently evaluated in PPP. Furthermore, in the last part of the second criterion, it is proposed that the PPP must

Table 1 Present criteria[2 4 5] and proposed criteria regarding PPP

- Present criteria
  (1) The pain should have developed after a surgical procedure.
  (2) The pain should be of at least 2 months' duration.
  (3) Other causes for the pain should be excluded, e.g. continuing malignancy (after surgery for cancer) or chronic infection.
  (4) In particular, the possibility that the pain is continuing from a pre-existing problem should be explored and exclusion attempted. (There is an obvious grey area here in that surgery may simply exacerbate a pre-existing condition but attributing escalating pain to the surgery is clearly not possible as natural deterioration cannot be ruled out.)
- Proposed updated criteria
  (1) The pain develops after a surgical procedure or increases in intensity after the surgical procedure.
  (2) The pain should be of at least 3–6 months' duration and significantly affect the HR-QOL.
  (3) The pain is either a continuation of acute post-surgery pain or develops after an asymptomatic period.
  (4) The pain is either localized to the surgical field, projected to the innervation territory of a nerve situated in the surgical field, or referred to a dermatome (after surgery in deep somatic or visceral tissues).
  (5) Other causes of the pain should be excluded, e.g. infection or continuing malignancy in cancer surgery.

have a significant impact on the patient's physical, psychological, or socio-economic well-being.

The third criterion, 'The pain is either a continuation of acute post-surgery pain or develops after an asymptomatic period', questions the development of PPP in terms of automatic trajectories from acute to chronic pain. Needless to say, one of the most consistent predictive factors of PPP is high-intensity, acute post-surgical pain,[7] indicating a close correlation between acute and persistent pain. However, in a recent long-term follow-up study (n=736) examining the sequential prevalence of PPP after inguinal hernia repair, including patients (n=377) without preoperative pain, 52 patients were experiencing PPP at the 5-yr follow-up,[14] with only 12 of these also having experienced PPP at the 6-month follow-up. Reciprocally, 33 patients experienced persistent pain after 6 months, but did not report any pain after 5 yr. This means that, in 36 patients (69%) experiencing PPP at the 5-yr follow-up, pain was not being experienced at the 6-month follow-up, indicating that more than two-thirds of the PPP patients undergoing inguinal hernia repair had developed persistent pain with a delayed onset. A similar tendency in time-related change in pain phenotype was observed in two long-term follow-up studies of patients (n=2 411) after breast cancer surgery.[15 16]

Tentative causes of the delayed development of persistent pain: *first*, nerve damage is known be associated with the delayed onset of neuropathic pain symptoms[17 18] and since neuropathic pain components are considered a major contributor to PPP, this seems a plausible explanation.[1 18] *Secondly*, in implant surgery, as an example, the partial dehiscence of the inguinal mesh or the dislocation of orthopaedic prosthetic material may lead to PPP after a pain-free post-surgical period. Some authors do not consider this to be PPP, but a mechanical complication after surgery.[7] However, if the post-surgical examination, usually performed within 3 months of surgery, does not indicate any need for surgical re-exploration, and if the pain persists, the most reasonable alternative would be to term the condition PPP, bearing in mind that this does not negate the future possibility of corrective surgery. *Thirdly*, in surgical procedures, non-specific and beneficial effects may be prominent[19] and the immediate period post-surgery has been called, in this respect, the 'honeymoon period' by some authors.[20] Thus, post-surgical pain ratings and post-surgical functional performance may improve in the short term, but may eventually deteriorate, leading to delayed onset PPP. *Fourthly*, the reinstatement of nociception has been documented in animal experiments after severe tissue injury. Several weeks after complete normalization of pain-related behaviour, the administration of naltrexone, a μ-opioid receptor (MOR) antagonist, is associated with the re-instatement of tactile hypersensitivity and the guarding-behaviour related to the previously injured area.[21] During resolution of the injury, endogenous opioids are activated, leading to the reinforcement of inhibitory pathways. This up-regulated tonic activation of endogenous opioid receptors, blocked by naltrexone, seems responsible for the attenuation of latent sensitization, persisting beyond the resolution of the injury. Administration of the MOR-antagonist leads to a block of the endogenous opioid system and an uncovering of latent sensitization. The physiological role of latent sensitization in humans is speculative, but is currently being investigated.[22]

The fourth criterion is, 'The pain is either localized to the surgical field, projected to the innervation territory of a nerve situated in the surgical field, or referred to a dermatome (following surgery in deep somatic or visceral tissues)'. A large number of descriptive studies have shown that PPP is commonly situated at or near the surgical field. In these areas, concomitant thermal and mechanical sensory dysfunctions have been demonstrated. The sensory profiles of PPP, across a number of surgical procedures,[23–25] demonstrate an increase in cutaneous thermal thresholds that is accentuated in relation to pain-free surgical controls. Patients with PPP after breast cancer surgery and inguinal hernia repair additionally demonstrate decreased pressure thresholds and augmented temporal summation ('wind-up like pain') in the surgical field.[23 26] The hypersensitivity to noxious mechanical stimuli, generated from deeper somatic tissues, may indicate an inflammatory pain component, while the hyposensitivity to thermal stimuli in the skin may represent a neuropathic pain component. The increased temporal summation response probably indicates the development of central hypersensitivity.[27]

Nerves traversing or situated in the vicinity of the surgical field may either directly (attributable to incision, sutures, or staples) or indirectly (because of post-surgical inflammation or dislocation of the implant) sustain injury, leading to projected pain in the innervation territory of the nerve (e.g. the genital branch of the genitofemoral nerve in inguinal hernia repair, the intercostal nerve in lung cancer surgery, or the intercostobrachial nerve in breast cancer surgery). The distribution of this 'classical' neuropathic pain, related to nerve discontinuity, partial

deafferentation or entrapment, may reach beyond the surgical field,[28] leading to diagnostic ambiguities.

Surgery nearly always involves either deep somatic or visceral tissues, or both. Detailed and comprehensive knowledge of the acute and chronic pain trajectories, with regard to intensity, duration, and spatial distribution, is surprisingly scarce. Because of the viscera-somatic convergence of afferent input, the pain and the hypersensitivity are referred to corresponding dermatomes, something that has been demonstrated for various visceral pain states (e.g. appendicitis, cholecystitis, and nefrolithiasis).[29–31] So far, only one study containing a detailed pre-surgical assessment of quantitative sensory testing (QST) profiles and a 4-month follow-up has followed up the trajectory and distribution of pain in patients who have had a hysterectomy.[32]

The fifth criterion, 'Other causes of the pain should be excluded, e.g. infection or continuing malignancy in cancer surgery', is a reasonable and important exclusion criterion that should be explored and, if possible, causally managed.

The operational advantages of the proposed amendments to the definition of PPP are *first*, that the pain may have developed before surgery, conditionally upon the pain intensity having increased significantly after surgery. In such cases, changes in the spatial distribution of the pain, or its character, are descriptive characteristics that may support the diagnosis of PPP. *Secondly*, the duration of PPP, from 3 to 6 months, is more in agreement with criteria used in chronic pain research. *Thirdly*, perhaps the most important issue, an objection to the concept of an automatic trajectory from acute to PPP, is presented. The delay of onset from many months to years post-surgery has been demonstrated in PPP in some surgical procedures. *Fourthly*, different distributions of PPP depend on the pathophysiological mechanism of the pain. Pain localized to the surgical field indicates neuropathic (skin) or nociceptive (deep tissue) components, or both, while pain projected to the innervation territory of a nerve probably indicates 'classical' painful neuropathy. Pain distributed specifically to the relevant dermatomes may indicate referred pain from deep somatic or visceral tissues.

Anaesthetists and surgeons have a genuine interest in collaborative research in their attempts to solve the conundrum behind PPP. This work would seem to prosper by means of well-defined and accurate operational criteria delineating PPP from other pain states that are not related to the surgical procedure *per se*.

Authors' contributions

M.U.W.: contributed to conception and design, drafted the preliminary version, and approved the final version. U.E.K.: contributed to conception and design, critically revised the draft, and approved the final version.

Declaration of interest

None declared.

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EDITORIAL II

Needle phobia: a psychological perspective

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Needle phobia is probably seen as a simple issue in its purest form. Your patient does not like needles—who does? Use a good topical numbing agent and let's get on with it. Job done. . . Or is it?

When I first started out as a clinical psychologist in a district general hospital, I have to admit that the anaesthetists were not a group I saw myself having a lot to do with. Since then, I have learned that my colleagues in the anaesthetics department encounter some of the most difficult situations, the sharpest edges of human distress. Far from being people who only deal with sedated patients, anaesthetists end up dealing with some of the most extraordinary situations with complex psychological trauma involved. I now work regularly with the team in a variety of settings and have an enormous amount of respect for their psychological management skills.

I was heartened to see in the November 2013 Bulletin of the Royal College of Anaesthetists, an article on anaesthesia of the anxious and agitated child.[1] As I hope to discuss below, early experiences in the anaesthetic room can have an enormous impact on a person's future engagement with the healthcare system. Regardless of the problem that child is being sedated for here and now and the problems with pain, recovery, and behaviour postoperatively, described by Marshall and Courtman, the patient's experience could make the difference in whether they seek medical help in the future or not, even to the extent of refusing life-saving interventions further down the line. Good management of needle phobia can literally save lives.

The very nature of needle phobia makes it very hard to determine incidence. By definition, people who suffer from needle phobia will avoid healthcare settings and so any population estimate is likely to underrate the true number, but estimates range from 3.5 to 10%.[2 3]

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (*DSM-IV*)[2] classes needle phobia as part of a group of specific phobias of blood-injection-injury (B-I-I) type. This group is classified as a discrete subtype of phobia owing to the very high familial links, and the often extreme vasovagal response to the stimuli. Up to 80% of people with needle phobia report a first-degree relative with a strong phobic response. In most specific phobias, exposure to the feared object (e.g. dogs, heights) causes arterial pressure (AP) and heart rate to increase, as the body gets ready for action. The B-I-I subgroup differs in that 75% of sufferers will experience an initial increase in heart rate and AP, followed by an often almost immediate decrease, leading to fainting.[3] Sadly, in turn, the fear of fainting itself can then lead to the development of a more standard phobic response. Needles produce fainting; fainting is anxiety provoking; and anxiety produces feelings of being light-headed, sweaty, and blurred vision, which mimic the symptoms of fainting. The patient therefore gets into a vicious circle of avoiding the situation as the symptoms of anxiety convince them they are going to faint even before the procedure has begun. In an evolutionary sense, it would appear to make sense to decrease AP and heart