Informed consent is now enshrined as a central component of the doctor–patient relationship. There is both an ethical and a legal obligation on doctors to provide patients with the fullest possible information on proposed treatments and interventions, including risks of adverse outcome, even when these risks are extremely rare. The primary achievement of the Third National UK Audit Project of the Royal College of Anaesthetists on major complications of central neuraxial block (CNB), published in this issue of the British Journal of Anaesthesia, is that it enables anaesthetists, other specialist doctors, and patients to more accurately define the risk of the specific rare but devastating complications of these procedures.

The impetus for this comprehensive audit encompassing both an estimate of the total number of CNBs conducted annually in the UK (the denominator) and the total number of cases of serious permanent sequelae, including death and irreversible neurological damage (the numerator), emanated from the lack of reliable evidence on the incidence of these rare but catastrophic complications, despite the widespread practice of CNB. Although CNB may have many potential benefits, these must be balanced against such risks in each individual risk–benefit assessment.

For the purposes of this audit, CNB was defined as encompassing epidural, spinal, combined spinal–epidural (CSE), and caudal techniques in adult and paediatric perioperative, obstetric, and chronic pain practice. Numerator data were obtained from a comprehensive audit of major reported complications of CNB over the 12 month period from September 2006 to August 2007. A network of local reporters in every hospital, supplemented by direct reports from clinicians in all relevant specialties, including not only anaesthetists, but also neurosurgeons, spinal surgeons, and radiologists, were able to electronically upload case details to a secure, password protected website. Although anonymous reporting was possible, a majority of reports came from identified individuals, mostly anaesthetists. In an effort to validate the completeness of the numerator, data from national databases including the NHS Litigation Authority and the Medical Indemnity bodies were accessed, but this did not yield significant additional data.

Denominator data were obtained from a census of all CNBs performed in all 309 NHS hospitals where surgery is undertaken, over a 2 week period at the end of September 2006. Again, the local reporter co-ordinated the collection of these data and estimated whether their data were ‘accurate’, a ‘close estimate’, or an approximation. Perhaps uniquely among large-scale clinical audits, there was a 100% return rate from all NHS hospitals in the UK, giving a high degree of confidence in the reliability of the denominator data. Data on activity over the 2 week period were multiplied by 25 to estimate total annual activity. Fifty-two cases of apparently permanent injury linked to CNB were examined by a Review Body and followed up for 6 months. The severity of outcome was graded according to the National Patient Safety Agency (NPSA) scale and deemed temporary or permanent.

Because of clinical ambiguity and subjectivity in linking CNB to adverse outcome in some complex individual cases and undetermined clinical outcome in others, the incidence of major complications is reported in terms of the best-case ‘optimistic’ and worst-case ‘pessimistic’ scenarios.

The headline results are largely reassuring. From an impressive annual denominator of more than 700,000 cases, even taking the ‘pessimistic’ scenario, the incidence of permanent injury from CNB is 4.2 (95% CI 2.9–6.1) per 100,000 and that of paraplegia or death was 1.8 (95% CI 1.0–3.1) per 100,000 cases. Of the 52 cases which were the focus of follow-up for permanent injury from CNB, 22 made a complete recovery from their serious complication within the follow-up period. In addition, of the 30 cases where damage was ‘permanent’ from the ‘pessimistic’ viewpoint, 16 were deemed likely to recover fully or the causal link to CNB was tenuous at best.

Detailed analysis of these data reveals a number of other telling findings. There was considerable variation between the incidence of severe complications between
the techniques constituting CNB, with perioperative epidurals being associated with higher incidence of adverse sequelae (8–17 per 100 000 CNB, based on the ‘optimistic’ or ‘pessimistic’ estimation, respectively) than other clinical settings. The authors wisely urge caution in interpreting subgroup comparisons because risk–benefit analysis differs between patient subgroups. For example, perioperative patients receiving epidurals tend to be older and in a higher risk category than the women receiving epidurals in obstetric practice. Nonetheless, this finding should prompt us to reflect seriously on our use of epidural analgesia perioperatively, and to satisfy ourselves that our judgement of the risk–benefit ratio justifies using the epidural in each individual case. Moreover, concerns about the safety of CSE techniques is supported somewhat by the observation that although CSE amounted to 6% of all CNB performed, they accounted for 13% of permanent injuries and two deaths. Again, information is not readily available on whether the patients with CSE, who developed permanent neurological damage or who died, were in a higher risk category than patients who had major complications after receiving other methods of CNB, but the finding behoves us to consider risk and benefit carefully in each case and to maintain vigilance during it.

‘Wrong route’ injection errors, that is, where local anaesthetics intended for CNB were inadvertently administered i.v., were prospectively identified by the authors as a problem requiring particular focus, even if there were no major adverse sequelae. Nine cases, six of which were in obstetric practice, were documented and this serves to emphasize the importance of devising a reliable risk management solution for this problem which unfortunately remains elusive. Further clinical learning points are published online by the Royal College of Anaesthetists.

Although the authors suggest that the quoted incidence of key adverse sequelae from this audit is the ‘minimum’ that exists in reality, there are, however, grounds for believing that they may have in fact over-estimated the incidence of adverse outcomes. First, the denominator may itself have been underestimated, because based on a 2 week census sample, the multiplier should have been 26 (to reach the 52 week year), not 25 as used. Secondly, the numerator may have been overestimated because some 13% cases with incomplete data or uncertain aetiology of permanent damage were deemed attributable to CNB, and not all of these may be valid cases. Although there is always the possibility that cases of severe complications attributable to CNB were not reported, the evidence presented that 100% of all NHS hospitals participated, that 10% cases were reported by non-anaesthetists, and that no additional cases were identified in independent searches of medical indemnity, litigation and literature databases suggests that under reporting is unlikely to have occurred. In fact, this audit has surprisingly revealed that a majority of the serious complications reported to it were not reported simultaneously to the statutory bodies such as the National Reporting and Learning Service (NRLS), as would have been expected.

By some distance, this is the largest reported prospective audit of complications occurring from CNB. The findings are even more reassuring than two similarly large retrospective reviews from Scandinavia and comparable with a smaller retrospective review of 34 000 epidurals in Turkey. However, continuing and improved vigilance is a prerequisite for maintaining and improving this level of safety. A recent survey of UK hospital protocols for monitoring and investigating potentially serious neurological complications after perioperative epidural anaesthesia showed that although 91% had regular assessment of the sensory and motor block, only 55% had a protocol for investigation of an abnormally dense motor block, and up to 30% respondents admitted to knowing of the occurrence of an epidural haematoma related to an epidural anaesthesia in their hospital.

Furthermore, this is the first review audit to estimate prognosis in the event of a serious complication from CNB. Of 41 major neurological complications attributed to CNB, 25 (61%) achieved complete recovery within ~1 yr. Spinal cord ischaemia and vertebral canal haematoma were associated with the worst outcome, with infective complications faring better.

In conclusion, this national audit of complications of CNB is a triumph not only for its authors and the NHS anaesthetists who delivered it, but also for UK NHS risk management systems, audit databases and processes. It is the largest prospective audit in this field to date, with robust numerator and denominator data acquisition techniques. It provides a new, reliable resource which anaesthesia doctors and patients can use to inform clinical decision-making and consent where CNB is involved, in the context of individual risk–benefit analysis. Although reassuring, it emphasizes the importance of an accessible, confidential reporting system for the serious adverse outcomes which may, extremely rarely, be associated with CNB, and the ongoing need for vigilance in perioperative monitoring of these powerful techniques.

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References

Capsaicin receptor antagonists: a promising new addition to the pain clinic

Capsaicin is the pungent vanilloid found in chilli peppers. Sensitivity to this substance has been used for many years to identify nociceptive fibres. These are predominantly unmyelinated C fibres with slow conduction velocity but also a small number of myelinated Aδ fibres. The cell bodies of these fibres lie in the dorsal root and trigeminal ganglia. The latter is involved in the pathogenesis of migraine. It is now well established that capsaicin activates a specific member of the transient receptor potential ligand-gated ion channel family, TRPV1 (previously known as the vanilloid receptor, VR1). The endogenous activators for this receptor are noxious heat (>43°C), protons (acidosis, pH 5–6), the endocannabinoid anandamide, and a range of other putatives including NADA (N-arachidonoyl-dopamine). There is also evidence for a central role of TRPV1 receptors including an interaction with dopaminergic neurones. The roles and activators of TRPV1 receptors have been the subject of reviews.1–5

The polymodal activation profile in response to heat and acidosis, coupled with modulation by several other inflammatory mediators, especially prostaglandins and bradykinin, has led to TRPV1 receptors being described as integrators of inflammatory signalling.6 TRPV1 receptor activation leads to an influx of Ca2+ and prolonged application of an agonist, such as capsaicin, leads to release of central transmitters (glutamate and substance P) from nociceptive afferents and a desensitization of the channel. As a consequence of exhaustion of transmitters and desensitization, the afferent becomes ‘chemically denervated’ and functionally silent. This is the basis for the well-established use of capsaicin cream in clinical settings where efficacy has been reported in osteoarthritis, diabetic neuropathy, and psoriasis.7 There is also evidence of effectiveness in post-herpetic neuralgia and post-mastectomy pain.7,8 The problem with capsaicin, as is well known, is that application produces an intense burning sensation and thus compliance can be a problem (Table 1).

There is now a body of evidence in support of TRPV1 receptor up-regulation in disease. For example, in experimental animals, there is an up-regulation in inflammatory hyperalgesia,9 osteoarthritis,10 and cancer-induced bone pain (see below). Interestingly, in animals with genetic deletion of TRPV1 receptors, the symptoms of experimental arthritis are reduced.11 In this case, deletion of the receptor represents an extreme form of ‘antagonism’. In humans, there are data showing up-regulation of TRPV1 in a wide range of conditions including inflamed bowel, vulvodynia, mastalgia, neurogenic bladder,4,5 and dental pulp inflammation.12 This up-regulation of receptor numbers and function, coupled with initial irritation when using TRPV1 agonists (like capsaicin) and the limited agonist formulation options (e.g., topical cream), forms the basis on which the antagonist strategy has been developed.

In this issue of the British Journal of Anaesthesia, Niyama and colleagues13 describe the use of the selective TRPV1 antagonist SB-366791 [N-(3-methoxyphenyl)-4-chlorocinnamide] in an animal model of bone cancer pain. Mice were injected with NCTC 2472 osteolytic sarcoma cells directly into the femur and then assessed over a 2 h period for pain-related behaviours (limb use, spontaneous

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6 Available from http://www.rcoa.co.uk/

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Editorial II