



## Editorial

### The sting in the tail: antiseptics and the neuraxis revisited

In 2001, Angelique Sutcliffe developed a progressive and debilitating adhesive arachnoiditis after apparently uneventful spinal anaesthesia for elective caesarean section, for which only hyperbaric bupivacaine 0.5% was administered. The path of her deterioration was steep and inexorable. Within a few days she had severe back pain, with urinary retention following shortly afterwards. Two weeks after delivery, she had signs of raised intracranial pressure, necessitating the insertion of a ventriculoperitoneal shunt to treat obstructive hydrocephalus. She developed worsening and ascending sensory and motor neuropathy in her legs over the following weeks and, having undergone further surgery to treat recurrent raised intracranial pressure, became progressively paraplegic with limited use of her arms. Her magnetic resonance imaging scans show a spinal cord severely damaged as a result of multiple dense adhesions.

Infection was ruled out early on as a cause for Ms Sutcliffe's neuropathology, and there was no evidence to support the view that a syringe swap error had led to administration of the wrong drug. After the lengthy delay that often accompanies civil claims, a High Court judge in 2007 had to decide whether she had been negligently treated and, if so, to award

monetary compensation. On expert advice, he concluded that, on the balance of probabilities, the injectate had become contaminated with 'a measurable quantity' – defined as 0.1 ml or more – of the chlorhexidine 0.5% in alcohol 70% used for skin preparation [1]. I robustly argued against this conclusion in an article in *Anaesthesia News*, on the grounds that the anaesthetist and operating department practitioner had been quite meticulous in minimising the risk of such chlorhexidine spillage on to the sterile field and that there was absolutely no evidence that such contamination had taken place [2].

Events since 2007 have, however, led me to conclude that the Honourable Mr Justice Irwin got it right, and I got it wrong. Specifically, in June 2010 in Sydney, Australia, Grace Wang, in labour in her first pregnancy, requested epidural pain relief. Chlorhexidine 0.5% in alcohol had been poured into one pot on the sterile field and saline into the other, and the anaesthetist chose the wrong container from which to draw up 8 ml of fluid to flush down the Tuohy needle into the epidural space (personal communication leads me to understand that – contrary to a widely stated view – the chlorhexidine was not colourless, but that the first epidural attempt had led to a bloody tap, the

fluid from which had turned the contents of the saline pot pink, thus masking the usual colour difference) [3].

The contrast between these two stories is of course that, in the latter case, we know for certain that chlorhexidine had been administered into the neuraxis, but otherwise they are strikingly similar. Grace Wang's clinical deterioration was, to all intents and purposes, identical to Angelique Sutcliffe's, including the time course, the progressive and relentless neurological deterioration, the need for emergency ventricular drainage and the development of an ascending motor and sensory neuropathy leading to paraplegia and upper limb involvement. This has inevitably led me to re-examine my response to the Sutcliffe case and to conclude that chlorhexidine in alcohol was the probable causative factor.

These cases are not isolated examples. Through my own medical practice, I am aware of two further obstetric cases. In the first, an epidural was sited in labour, the patient complaining of severe headache during the procedure. There is no record of how the skin was prepared. The epidural was later topped up for caesarean section, the only drugs used for labour and delivery being bupivacaine, levobupivacaine and fentanyl. In the

three weeks following delivery, the patient developed progressive leg weakness, back pain and neck stiffness, culminating in raised intracranial pressure, a diagnosis of severe hydrocephalus and insertion of a shunt. Her neuropathy deteriorated to the point where she was largely wheelchair-bound. In the second case, hydrocephalus and mid-thoracic paraplegia developed over a period of around six weeks following a difficult spinal anaesthetic administered for elective caesarean section. Chlorhexidine 0.5% had been used for skin preparation and bupivacaine and fentanyl for the spinal injection. In a third, non-obstetric, case, adhesive arachnoiditis with communicating hydrocephalus requiring emergency shunt surgery followed spinal anaesthesia with bupivacaine and diamorphine for orthopaedic surgery; the skin antiseptic is as yet unknown (Levy D, personal communication). I am also aware of seven other medicolegal cases in the last 15 years where severe arachnoiditic symptoms and signs have followed spinal anaesthesia for general surgical, orthopaedic and obstetric procedures and epidural injections for chronic pain, although none of these seven have, to the best of my knowledge, progressed to obstruction of cerebrospinal fluid flow warranting shunt surgery. In the majority of cases, the antiseptic used for skin preparation is unknown: where it is known, it was chlorhexidine.

This issue of *Anaesthesia* sees another case added to this series. Killeen et al. describe what appears to have been a straightforward spinal injection of bupivacaine and

fentanyl for elective caesarean section, following which the patient immediately complained of leg pain and headache [4]. Once again, hydrocephalus developed over the following 11 days, necessitating shunt surgery, followed by foramen magnum decompression and C1 laminectomy when the problem recurred. This was followed by a dramatic and progressive onset of leg weakness. Further laminectomies failed to halt the course of her deterioration and she was left with a paraplegia extending as high as T6 on the left with arm weakness and an indwelling suprapubic catheter.

With what we now know from the Wang case, contamination of the spinal injection with chlorhexidine must be the most likely cause of these catastrophic outcomes. In all of the above cases where the antiseptic agent is known, it was chlorhexidine – usually 0.5%, the lowest concentration commercially available. Killeen and colleagues reach the same conclusion with respect to their patient, where a chlorhexidine 2% ‘swabstick’ was used to prepare the skin, the fluid being allowed to dry before skin puncture. Why this complication does not occur more frequently, if only a very small volume of contaminant is required to do such harm, is a reasonable question. It may be that the cases described above represent an idiosyncratic reaction to what might only be a minor inflammatory stimulant in others. Be that as it may – and it is certainly no more than conjecture – the place of chlorhexidine in spinal and epidural procedures must be carefully considered.

The advantages and disadvantages of chlorhexidine for central neuraxial block have been reviewed in detail in an excellent recent editorial in this journal by Checketts, who concluded that, while it may well be the best agent for providing skin asepsis, its known neurotoxicity [5, 6] should lead us to take great care in preventing its contaminating the equipment being used for the spinal or epidural procedure [7]. He advised applying the antiseptic separately – perhaps by spray – then removing it from the vicinity of the equipment to be used for the block itself, and also rightly pointed out that the other components for reducing the risk of infective complications – such as handwashing, the use of gloves, mask and gown and good aseptic technique – should not be forgotten. Specifically, Checketts compared chlorhexidine to povidone-iodine, and concluded that the former should still be used for neuraxial block, since its known neurotoxicity was outweighed by its superiority in reducing surgical site infection [8, 9]. Other bodies have drawn the same conclusion, with the Royal College of Anaesthetists, the American Society of Anesthesiologists and the American Society of Regional Anesthesia all recommending its use for central neural blockade [10–12].

It must be accepted that, while chlorhexidine has to be the most likely culprit in these cases, its guilt is far from proven. The Australian case shows us only what happens when 8 ml of chlorhexidine 0.5% is injected into the epidural space and, whilst parallels can clearly be drawn, this is not the same as the

putative 0.1 ml injected into the subarachnoid space that was postulated by the judge in the Sutcliffe case. The possible role of the alcohol, which constitutes the main component in both the 0.5% and 2% solutions of chlorhexidine, and which contributes both to the speed of drying and the antiseptic potency of the solution, remains unclear.

Even if chlorhexidine is the cause, other questions still arise. The widely-recommended precaution of allowing the solution to dry before starting the procedure cannot be allowed to pass without comment; if the alcohol dissolves, does this mean that a greater concentration of chlorhexidine remains on the skin? And if it is felt that the use of chlorhexidine should be abandoned, what of its obvious replacement, povidone-iodine? As Checketts concludes, it is not as effective a bactericide as chlorhexidine when used for skin preparation, raising the spectre of an increase in the incidence of infective complications. Furthermore, the possible neurotoxicity of povidone-iodine has itself been a largely evidence-free zone, although a recent study suggests that it damages a neuronal cell model *in vitro*, and that it is equally as toxic as chlorhexidine at concentrations used clinically [13].

If we do act on the best information available to date and regard chlorhexidine as the link between the cases described above, two questions still remain. First, what concentration should we use? Checketts referenced a study by Malhotra *et al.*, in which it was shown that a single spray of chlorhexidine 0.5% in alco-

hol rendered the skin sterile [14]. In the face of this, the use of a 2% solution, containing four times the effective concentration of chlorhexidine, seems like unnecessary 'overkill'. Partially in defence of the higher concentration, Checketts cites a large retrospective study of 12 000 neuraxial blocks carried out after skin preparation with chlorhexidine 2%, with no apparent cases of chemically-induced arachnoiditis [15]. However, this result would be compatible at the 95% confidence level with an incidence of chlorhexidine-related arachnoiditis as high as 1 in 4000 [16]. This would still be many times higher than would be acceptable, so no useful conclusion can be drawn on the safety of a 2% solution from such a study. With no good evidence to support the use of the stronger solution, the obvious conclusion is that chlorhexidine 0.5% in alcohol should be used in preference.

The second question relates to how the solution should be applied. If, as seems likely, some of these cases are arising from accidental contamination of needles or syringes with 'splashes' of antiseptic, then there ought to be an advantage in any system that minimises the possibility of such splashes. 'Swabsticks' are now commonly used by anaesthetists for skin preparation before central venepuncture and other procedures. They are certainly convenient and, with the chemical agent contained within the hollow handle of the stick, fluid spillage is normally minimised. However, the devices available in the UK all appear, like the one used in the case described in this issue, to contain a 2% solution of chlorhexidine in

alcohol. Despite suggestions that they would be revised, the Summary of Product Characteristics (SPC) and manufacturer's labelled warnings for these products continue to state that they should not be used 'for lumbar puncture' [17, 18]. In contrast, the SPC for the 0.5% solution does not mention lumbar puncture, and only says that it should not be used 'in contact with ...meninges...' [19]. Furthermore, it has been pointed out (O'Sullivan G, personal communication) that there is a small hole in the handle of the swabstick commonly used in the UK, presumably to allow ingress of air as the fluid flows on to the sponge. When the stick is held upside down, the natural grip when cleaning the back of a sitting patient, the chlorhexidine solution may leak from this hole and can spill on to the operator's gloves, with obvious potential for contamination of the equipment tray. Thus, until swabsticks are manufactured with chlorhexidine 0.5% instead of 2%, they should not be used for neuraxial block. If they do become available in the lower concentration then they should be handled in such a way that does not allow any drain hole to fall below the reservoir level in the handle.

Obvious problems arise from pouring the antiseptic solution into a container on the sterile field, especially if another open container is to be used for a fluid to be deliberately injected, such as saline. While the majority of the cases described above probably do not result from 'crossover' errors, this was the aetiology in the Wang case, and commentators in the popular

press have expressed incredulity that a neurotoxic substance can come to lie in an identical container and directly adjacent to a fluid intended for administration into the neuraxis [20]. It is difficult for the dispassionate professional observer to disagree with this view, whether or not the fluids are initially coloured differently.

The use of spray bottles of chlorhexidine is popular, and this was the method employed by Malhotra et al. in their study [14]. Advocates argue that the fluid can then be kept in a closed container, that it is employed at a distance from the equipment tray, and that it can be applied by an assistant who will be taking no direct part in the rest of the procedure. However, applying a spray from a distance must increase the possibility of splashes going astray, and an assistant could equally prepare the skin using an open container and a sponge applicator. In short, whichever of these techniques is used, several precautions should be followed. First, equipment and sterile surfaces should be kept covered or otherwise protected while the antiseptic is applied. Second, antiseptic containers and sponges should be removed from the immediate vicinity before uncovering equipment. Third, at least until evidence to the contrary is presented, the fluid must be allowed to dry before the skin is palpated or punctured. Fourth, if the operator has applied the antiseptic, he/she should check his/her gloves for contamination and, if there is any doubt, change them before continuing the procedure.

For readers in the UK, currently struggling to safely implement government-driven changes to neuraxial equipment to make them incompatible with Luer connectors [21, 22], it will be starkly evident that these changes would not have prevented any of the injuries described above. Even in the case of Wang, the one proven true ‘crossover’ incident, the chlorhexidine could have just as easily been drawn up into a non-Luer syringe as into a Luer type [3]. Indeed, at least one of the new connectors, being significantly larger in internal cross-section than the Luer, would theoretically increase the chance of contamination if it came to lay in a pool of chlorhexidine, the postulated mechanism in the Sutcliffe case [1].

What should we tell our patients if, as seems to be the case, this is indeed an extremely rare but very serious complication of neuraxial block? The 3rd National Audit Project of the Royal College of Anaesthetists (NAP3) identified a risk of permanent harm from spinal or epidural injections of 1: 23 500 – 50 500 and of paraplegia or death of 1:54 500 – 141 500 [10]. The cases described above and in this issue of *Anaesthesia* do not, in my view, alter these incidences and, other than elucidating, if asked, that ‘permanent harm’ might include the consequences of blocked cerebrospinal fluid flow, I do not see a need to add further to this warning. As ever, consent is a fluid process that, when carried out ethically and meaningfully, involves as much listening to the patient's concerns as

spelling out a list of complications and percentages.

In short, spinal and epidural techniques, as with so many other procedures carried out by anaesthetists, are potentially hazardous, but are made safe by our meticulous attention to detail. Nowhere is such attention needed more than where highly toxic substances come to lie in close proximity to vulnerable nerve tissues.

## Competing interests

I am a practising medicolegal expert witness who has provided reports for the Court on the instructions of either Claimant or Defence in several of the cases described in this editorial. I served on the Review Panel for NAP3.

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# Editorial

## Innovations, inventions and Dr Archie Brain

*“He that will not apply new remedies must expect new evils; for time is the greatest innovator.”*

– Sir Francis Bacon (1561–1626)

The main theme of the opening ceremony of the 2012 London Olympics was a celebration of the British spirit of innovation and progress featuring the inventions of Watt, Stephenson and Brunel. In the same year, the innovations of Dr Archie Brain are celebrated in

recognition of the 30th anniversary of the first pilot study of the laryngeal mask airway (LMA) and its registration for a patent. His design revolutionised the practice of anaesthesia and along with the symbiotic advent of propofol, routine oximetry and capnography, made a unique contribution to simplifying airway management, thereby greatly enhancing patient safety. In this issue of *Anaesthesia*, van Zundert et al. [1] pay a well-deserved tribute

to Archie Brain and his development of the LMA.

The history of anaesthesia is, in essence, a continuum of innovations and inventions. Anaesthesia itself is hailed as one of the ten most significant inventions and milestones in the history of medicine [2]. Innovation (Latin: innovare – to change) relates to different, usually better, usage of an existing product or technology, while invention (invenire – to find) relates to a completely new