Editorial

Guidelines on skin antisepsis before central neuraxial blockade

This issue of *Anaesthesia* sees the publication of the latest guidelines from the Association of Anaesthetists of Great Britain and Ireland (AAGBI), in partnership with the Obstetric Anaesthetists' Association (OAA), the Association of Paediatric Anaesthetists of Great Britain and Ireland (APAGBI) and Regional Anaesthesia-UK (RA-UK), on skin antisepsis before central neuraxial blockade [1]. Tellingly, the document is titled: 'Safety Guideline', raising the questions: just what is safe (or unsafe), and what is the evidence? However, before thinking about the impact of this new guideline, I want to comment on the current status of guidelines in general.

Guidelines – too much of a good thing?

The explosion in guidelines highlighted by Kearns and colleagues in this journal in 2013 [2] is a problem for the National Health Service (NHS) itself and for all NHS staff. They found more than 400 pages of guidance that applied to a fictitious patient with a hip fracture and three pre-existing co-morbidities. The total number of guidelines that apply to all patients receiving care in the UK is surely too many to count. How should we manage the current situation, and how should we plan for the future? If guidelines are to be of any use and if they are to retain their credibility, should their use be rationalised? On the other hand, does the fact that so many are produced and that, when published, they are often highly cited, imply that clinicians, readers, carers and perhaps even patients want them?

To be useful, guidelines need to be accessible, applicable and practical. (These criteria are my own. Others have developed more formal assessment tools for rating guidelines, for example the AGREE II initiative (see www.agreetrust.org) funded by the Canadian Institutes of Health Research). Accessing documents produced on such a grand scale is a real issue. Accessibility requires archiving and collating, providing a search mechanism, and making the results of such a search available at the point of care. Just the first part of this process – archiving – is problematic in itself, as there is no single resource or library where all guidelines applicable to UK patients are kept. The likelihood of such a library's creation is low – major IT projects in the NHS have a very poor track record [3]. Just collecting all guidelines in one place would be difficult enough, but they would need to be ordered using a suitable taxonomy, kept up-to-date and be written and presented in a uniform fashion.

Modern search engines can provide a solution to both archiving and collating. They continually index source documents – searching both the title and author data and the text of the document itself for key words. Users of the most up-to-date desktop operating systems such as Apple OS X Mavericks (Apple Inc., Cupertino, CA, USA) and Windows 8 (Microsoft Corp., Redmond, WA, USA) will be used to system searches (Apple Spotlight or Windows Search, retrospectively) where results are displayed almost instantaneously, ordered according to the type of result (documents, figures, PDFs, spreadsheets etc), and can be refined. An internet-based search, such as Google (www.google.co.uk), enables the user both to make a thorough search (by including all possible resources, sites, virtual libraries, etc.) and to refine the results by use of inclusion and exclusion criteria to yield only those documents of interest. For example, most readers will recognise that a simple Google search is too broad. (Entering the term 'clinical guidelines' into Google brings up ~145 000 000 results). Refining search criteria risks excluding important results and experience is necessary to ensure that all applicable source documents are found. (The current generation of young researchers and clinicians will not have struggled

with the early searches of Medline using slow, dial-up or university network connections, when practicality and cost limited each user to one attempt at getting their search right).

Where would a clinician undertake such a search – on a desktop computer, a computer terminal (in the operating theatre or other clinical area), a tablet computer or a smartphone? All of these solutions must be catered for and a good website (and search engine) should be optimised for all platforms. Rather than searching as needed, perhaps frequently used guidelines could be pre-loaded onto a portable device? Three years ago, United Airlines announced that all of its pilots would carry their flight manuals (the paper versions can weigh up to 17 kg) on an iPad (Apple Inc), saving 16 million sheets of paper per year and 1.2 million litres of fuel [4]!

The applicability of guidelines is a perennial problem. Simply the huge number of guidelines and their overlap, as demonstrated by Kearns et al. [2], ensures that not only is finding the right guideline difficult, but gauging the primacy of similar or overlapping (or even worse, contradictory) guidelines is even more problematic. Could national bodies take responsibility for rationalising guidelines in their area? If so, who would judge guidelines? Who would take responsibility to withdraw a guideline felt to be too old, too poorly researched or trumped by better advice? Perhaps the greatest problem is the risk of guidelines' simply expiring. Too many resources are filled with old documents that remain accessible and risk offering outdated advice. Nothing inspires less confidence in a web-based document than finding old material or links that do not work – though from a medicolegal perspective, an important aspect of guidelines is the ability to access older or superseded versions if it becomes necessary to consider the contemporaneous standard of care in cases that occurred some years ago.

The production of practical advice is the ultimate aim. Yet guidelines may be written that fail to match the real-world situation – on 'the shop floor'. Clinicians who wish to be seen to adhere to guidelines then struggle to match expectation with reality. By being so accessible, guidelines are found by lawyers (and, of course, why not – we should not be hiding these documents) and their lack of practical applicability may mean little to litigants. A further, unintended consequence of a guideline is 'guideline paralysis' whereby a real-world decision is delayed or avoided for fear of doing the wrong thing, compounded by guidance that fails to work in an acute situation. Phrases such as 'could', 'might be best served', 'in ideal circumstances', 'discuss with others/seniors/experts/national centres. . .' rarely help. Perhaps one reason for the failure of a guideline to offer practical advice is that it was not piloted first. (The Association of Anaesthetists has previously trialled guidelines before their publication to ensure their practicality [5]). Furthermore, it is difficult to predict all the circumstances in which a guideline may be consulted. All authors and sponsors of guidelines need to be aware of this risk and ensure that they do not make matters worse by publishing a document that cannot be used.

The skin antisepsis guideline

The new AAGBI guideline on skin antisepsis before central neuraxial blockade was written jointly with the OAA, APAGBI and RA-UK, although some might question why other interested parties, such as the British Society of Orthopaedic Anaesthetists, were not involved. A clear stimulus to their production were the recent cases of arachnoiditis that have reached the Courts and been the subject of previous commentaries and case reports [6, 7]. It is worth reviewing the evidence for harm, and how the Courts have interpreted this. (Detailed advice on the medicolegal aspects of guidelines is available elsewhere, for example the Scottish Intercollegiate Guidelines Network (SIGN) website: see http://www.sign.ac.uk/guidelines/fulltext/50/section1.html). Chronic adhesive arachnoiditis is a rare condition, and may occur as a complication after spinal [6, 7] and epidural analgesia [8]. It leads to a debilitating, progressive and sometimes devastating damage of the lower cord roots, often associated with hydrocephalus. There are many potential causes; in some cases it is obvious, in others much less so. The leading case associating this condition with skin antisepsis preparations has been described in this journal [6] and in *Anaesthesia News* [9] by Bogod. In short,

Angelique Sutcliffe developed chronic adhesive arachnoiditis after an apparently straightforward spinal anaesthetic and the Court found that on the balance of probabilities, there must have been a negligent contamination of the spinal injectate with antiseptic agent, as no other cause was offered [10]. This might have been a case where the legal maxim 'res ipsa loquitur' ('the thing speaks for itself') could have been used. It can be paraphrased thus: because an injury occurred, there must have been a cause, and in the absence of any other non-negligent cause, a negligent act must be to blame. This editorial is not the right place to debate the use of this argument, and the trial judge rejected its use (although it was one of the issues considered when the Sutcliffe case went to appeal [11]); the crucial point is that while there was clinical evidence of an injury, the exact mechanism of injury was unclear, and the act that led to the injury was inferred rather than proven. There is evidence that both chlorhexidine and alcohol are neurotoxic, and contamination of either the injectate or the apparatus used to perform the block may have led to the arachnoiditis in some or all of the cases reported after spinal or epidural anaesthesia. Thus, the issues are: is there a link between chronic adhesive arachnoiditis and skin antisepsis preparations; what component of the available antiseptics might be the cause of the injury (or pathological process); if the cause is chlorhexidine, can a different risk be attributed to the two available concentrations; and, is the use of different concentrations of antiseptic agents associated with a different risk of central neuraxial infection? All of these points are debatable and some may be controversial. (These particular guidelines attracted more comments when put out to consultation than any previous ones, though the Working Party was unable to find evidence to support most of them (F. Plaat, personal communication)). Importantly, the scientific evidence is limited and some of the guideline group's recommendations are extrapolations from small studies or based on case series. For example, despite its recommendation to support the use of 0.5% chlorhexidine in alcohol, the guideline states: "*. . .the Working Party acknowledges that there is a lack of data to support the use of one concentration of chlorhexidine over another for* [central neuraxial block]" [1]. Furthermore, there are commercial concerns to bear in mind. One of the currently available products uses 2% chlorhexidine in alcohol and is popular with clinicians for central venous cannulation. Importantly, there is no convincing evidence to suggest that this concentration (and therefore this product) should be withdrawn.

It is right that the evidence is reviewed, a consensus reached and guidance published. Existing practice is ingrained in our psyche and experienced practitioners may have performed many thousands of central neuraxial blocks with few complications, and certainly nothing as devastating as arachnoiditis. However, even performing several thousand procedures without a complication does not exclude the existence of a risk. So, as the guideline states, practising clinicians are faced with balancing the risk of arachnoiditis – which is very rare, but circumstantial evidence suggests it may be linked with the use of skin antisepsis preparations – with the risk of central neuraxial infection, which can be equally devastating and for which we do have an estimate of the likely incidence. (For example, the 3rd National Audit Project study determined the 95% confidence intervals for the incidence of bacterial meningitis after peri-operative spinal anaesthesia as 0–2.7 per 100 000 [12]).

How does this new guideline score when judged for accessibility, applicability and practicality? To maximise accessibility, the document has been published as a free, full-text article under the Creative Commons Attribution license, allowing widespread distribution (as for other AAGBI guidelines published in *Anaesthesia*). The guideline is free to read, download and copy for local use, even by non-members and non-subscribers; all that the licence requires is that the provenance of the guideline is included in all reproductions. The applicability of the guideline seems clear. Many thousands of central neuraxial blocks are performed each week [12] and, as the authors describe, the need was to produce clear, up-to-date advice in the light of the recent developments about skin sepsis in terms of both case reports (and case law) and the scientific evidence. Thus, the guideline was written to offer practical advice to clinicians, and achieves that with one exception – 0.5% chlorhexidine in alcohol (the recommended anti-

septic) is currently not available as a 'swabstick' (a popular method of application). The other recommendations are relatively straightforward and common-sense.

The guideline will, in my opinion, help clinicians. It provides advice based on some evidence, some extrapolation of data and the consensus views of an informed group. Although the underlying cause and effect remains unclear, we do now have practical advice to guide us in our daily clinical practice.

Acknowledgment

I thank Dr David Bogod for his time while we discussed some of the legal issues.

Competing interests

I am a member of the AAGBI Board where these guidelines have been discussed; however, these views are my own and do not represent those of the AAGBI nor of my employer. I have provided expert witness (medicolegal) reports for the Court in cases of suspected arachnoiditis.

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Guidelines

Safety guideline: skin antisepsis for central neuraxial blockade

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Obstetric Anaesthetists' Association
Regional Anaesthesia UK
Association of Paediatric Anaesthetists of Great Britain and Ireland

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Summary

Concise guidelines are presented that recommend the method of choice for skin antisepsis before central neuraxial blockade. The Working Party specifically considered the concentration of antiseptic agent to use and its method of application. The advice presented is based on previously published guidelines, laboratory and clinical studies, case reports, and on the known properties of antiseptic agents.

All AAGBI guidelines are reviewed to ensure relevance/accuracy and are updated or archived when necessary. Date of review: 2019.
This is a consensus document produced by expert members of a Working Party established by the Association of Anaesthetists of Great Britain and Ireland, with representatives from the Obstetric Anaesthetists' Association, Regional Anaesthesia UK and the Association of Paediatric Anaesthetists of Great Britain and Ireland. It has been seen and approved by the elected Boards/Councils/Committees of all four organisations.
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- *What other guideline statements are available on this topic?*
  The Royal College of Anaesthetists [1], the American Society of Anesthesiologists [2] and the American Society of Regional Anesthesia [3] have all published guidance on prevention of infectious complications associated with neuraxial techniques.
- *Why was this guideline developed?*
  Although the current published guidelines comprehensively cover aseptic technique when performing central neuraxial blockade (CNB), they are lengthy and discursive documents that are impractical for use in the acute care setting. The remit of this Working Party was to produce a concise document that specifically considered which agent (including the concentration) to use for skin antisepsis before CNB, and the method of application.
- *How does this statement differ from existing guidelines?*
  This statement specifically considers which agent to use for skin antisepsis before CNB, and is more

concise than currently available guidelines. Unlike existing guidance, this statement includes a recommendation on which concentration of antiseptic agent to use.

- *Why does this statement differ from existing guidelines?*
  This statement was written to provide useful and concise guidance for anaesthetists in the clinical setting.

Recommendations

1 Optimum aseptic technique for CNB requires thorough handwashing with surgical scrub solution and the use of barrier precautions including the wearing of a cap, mask, sterile gown and gloves, and the use of a large sterile drape.
2 Chlorhexidine in alcohol should be used for skin antisepsis before performing CNB.
3 The anaesthetist must be meticulous in taking measures to prevent chlorhexidine from reaching the cerebrospinal fluid (CSF):
   a Chlorhexidine should be kept well away from the drugs and equipment to be used for CNB and should not be poured into containers on or near the same surface as the equipment for CNB. Equipment should be covered or protected while the antiseptic is applied by swab, applicator or spray.
   b The solution must be allowed to dry before the skin is palpated or punctured.
   c The operator should check his/her gloves for contamination with chlorhexidine. If there is any doubt, they should be changed before continuing the procedure.
4 Given the lack of convincing evidence of the antimicrobial superiority of a 2% solution of chlorhexidine in alcohol over a 0.5% solution, but the presence of clear evidence of the neurotoxicity of chlorhexidine, the Working Party has concluded that the use of a 0.5% solution should be preferred over a 2% solution for skin antisepsis before CNB.
5 In children under two months of age, the volume of chlorhexidine used should be the minimum necessary while still ensuring antisepsis.

Introduction

The most appropriate and safe antiseptic solution to use on the skin before CNB remains controversial. A survey of consultant obstetric anaesthetists in 2009 revealed a wide range of practice across the UK in terms of both the antiseptic used and its method of application [4].

The ideal antiseptic agent should be effective against a wide range of micro-organisms, have immediate onset of action, exert a long-term effect, not be inactivated by organic material (e.g. blood), and have minimal toxic effects on the skin [3]. Commonly used antiseptic agents for CNB include chlorhexidine gluconate and povidone iodine. Both of these antiseptics are available as aqueous and alcoholic solutions.

Chlorhexidine vs povidone iodine

Chlorhexidine gluconate is a potent, broad-spectrum antiseptic that is effective against nearly all bacteria and yeasts. It has a faster onset and longer duration of action than povidone iodine, and it retains its efficacy in the presence of blood. It also has a lower incidence of skin reactions than povidone iodine [3].

Several investigators have compared the antiseptic efficacy of chlorhexidine and povidone iodine under a variety of experimental conditions [5–12]. In all but one investigation [7], chlorhexidine resulted in a more rapid and superior bactericidal effect that lasted several hours beyond its initial application. In one of these studies, Kinirons et al. [5] compared colonisation of epidural catheters following skin preparation using 0.5% chlorhexidine in alcohol with skin preparation using an aqueous solution of 10% povidone iodine. Catheters inserted following the use of chlorhexidine were six times less likely to be colonised than when povidone iodine had been used.

Chlorhexidine: aqueous vs alcoholic

Sakuragi et al. [10] investigated the effect of chlorhexidine and povidone iodine on the growth of *Staphylococcus aureus* (the pathogen most commonly associated with epidural space infections) in vitro. They found that both methicillin-resistant and -sensitive strains of the pathogen grew colonies after exposure for 60 s to aqueous 10% povidone iodine or

aqueous 0.5% chlorhexidine. In contrast, no bacteria grew after 15 s of exposure to 0.5% chlorhexidine in 80% alcohol.

Chlorhexidine: 0.5% vs 2%

The choice of concentration in the UK and Ireland is between 0.5% chlorhexidine in 70% alcohol (e.g. Hydrex® solution, Ecolab Ltd, Leeds, UK) and 2% chlorhexidine in 70% alcohol (e.g. ChloraPrep®, CareFusion UK Ltd, Reigate, UK).

Adams et al. [13] compared the efficacy of 2% chlorhexidine in alcohol with several other antiseptics including 0.5% chlorhexidine in alcohol against growth of a single strain of *Staphylococcus epidermidis* in vitro. In three out of four tests, no difference in efficacy could be demonstrated. In the fourth test (involving a biofilm with added human serum), all the antiseptics failed the test of efficacy ($\log_{10}$ reduction factor in colony-forming units per ml of > 5), although the failure of 2% chlorhexidine in alcohol was less than for 0.5% chlorhexidine in alcohol. The authors recommended in-vivo studies to assess the clinical efficacy of 2% chlorhexidine in alcohol. Crowley et al. found no difference in bacterial colony counts from skin and epidural catheter tips after preparation with 0.5% and 2% chlorhexidine in alcohol [14].

Pratt et al. [15] recommend that before insertion of a central *venous* access device, the skin should be decontaminated using 2% chlorhexidine in 70% alcohol. However, no such guidance exists for CNB, possibly because of concerns about neurotoxicity associated with chlorhexidine.

Chlorhexidine, alcohol and neurotoxicity

Recently, the issue of which antiseptic to use before CNB, and in which concentration, has become contentious. This follows cases of permanent neurological injury in obstetric patients in which chlorhexidine was alleged to have been responsible. In one of these cases [16], a whole syringe of 0.5% chlorhexidine in alcohol was mistakenly injected into the epidural space; in another case it was suggested that a syringe of bupivacaine injected spinally had become contaminated with 'a measurable quantity' (defined as 0.1 ml or more) of 0.5% chlorhexidine in alcohol [17]. All patients developed a chronic adhesive arachnoiditis with a similar clinical course of progressive neurological deterioration leading to paraplegia [16–19].

Limited information is available on the risk of neurotoxicity with chlorhexidine. In 1955, Weston-Hurst reported that the neurotoxic concentration of aqueous chlorhexidine when injected into the CSF of monkeys appeared to be in the region of 0.05% [20]. In 1984, Henschen and Olsen showed that injection of just 5 µl of 0.05% aqueous chlorhexidine into the anterior chamber of the eye produced adrenergic nerve degeneration in rats, and the authors postulated that the thin unmyelinated nerves of the central nervous system might be equally affected [21]. More recently, Doan et al. found that chlorhexidine was neurotoxic at a concentration of 0.01% (the lowest concentration tested) when applied directly to neurons [22]. However, in a rat model using a radioactive tracer, the same authors estimated mathematically that provided the antiseptic is allowed to dry fully, the concentration of antiseptic that could be delivered to the neuaxis would be extremely low [22].

It has been suggested that alcohol, which constitutes the main component of chlorhexidine solutions, might be the causative neurotoxic agent [23]. Alcohol-induced neurolysis is well established and is used therapeutically in a number of procedures [24]. Accidental injection of a syringe of alcohol (with or without chlorhexidine) into the epidural space may therefore be expected to result in neurological injury, although the effect of the tiny quantities that may contaminate a spinal needle has been questioned [25].

In a recent editorial on skin antisepsis for CNB [26], the author concluded that chlorhexidine in alcohol should still be used as the potential for neurotoxicity was outweighed by the superiority in reducing surgical site infection. Other bodies have drawn the same conclusion: the Royal College of Anaesthetists (in its Third National Audit Project (NAP3)) [1], the American Society of Anesthesiologists [2] and the American Society of Regional Anesthesia [3] all recommend chlorhexidine in alcohol as the skin disinfectant of choice for CNB. None of these guidelines specifies the concentration of chlorhexidine to use,

although the authors of the NAP3 report have stated that in their opinion, based on the limited evidence available, 0.5% chlorhexidine in alcohol is the optimal skin preparation for CNB [27].

The Working Party is aware that some anaesthetists choose to use 2% chlorhexidine in alcohol because they consider it reduces the risk of infectious complications compared with the 0.5% solution. As neuraxial infectious complications are rare, and cases of chronic adhesive arachnoiditis even rarer, the Working Party acknowledges that there is a lack of data to support the use of one concentration of chlorhexidine over another for CNB. However, evidence for the greater efficacy of 2% chlorhexidine compared with 0.5% is lacking, while the neurotoxicity of chlorhexidine is well established in vitro and in animal models. It is consequently the opinion of the Working Party that skin antisepsis for CNB using 0.5% chlorhexidine in alcohol provides the safest compromise between the risk of infection and the risk of neurotoxicity. The Working Party acknowledges that meticulous attention to the method of application of the antiseptic, and to other infection control precautions, are likely to be more important factors in reducing the risks of neurotoxicity and infection than the choice of concentration of chlorhexidine.

Method of application

As it is possible that cases of arachnoiditis have been caused by accidental contamination with antiseptic of needles, syringes and catheters used for CNB, a method of skin application that minimises the risk of contamination of equipment should be used.

Traditionally, antiseptic solutions were poured into a gallipot on the anaesthetist's sterile field. However, if there is another open container for a fluid intended for neuraxial injection (e.g. saline), the potential for a crossover error is created (the aetiology in one of the reported cases of arachnoiditis [15]). Moreover, Evans et al. [28] have shown that pouring chlorhexidine into a gallipot generates splash that spreads at least 40 cm. The authors recommended that antiseptic solutions should not be poured into containers located on the same tray as equipment for CNB, and that the equipment should be covered until the back has been prepared with antiseptic.

Pre-soaked antiseptic sponge applicators ('swabsticks') are now commonly used for skin preparation before central venipuncture and other procedures. The applicators are manufactured with a reservoir containing 3 ml or 10.5 ml of antiseptic, and the solution may be dyed to allow identification of the area of prepared skin. Because the antiseptic solution is contained within the hollow of the handle, crossover errors are impossible and fluid spillage should be minimised. However, it has been observed that leakage of antiseptic solution over the operator's gloves may occur via a hole at the end of the handle when the device is held upside down (the hole below the level of the antiseptic reservoir) to clean a patient's back [19]. Currently, the 'swabstick' applicators available in the UK and Ireland contain a 2% solution of chlorhexidine in alcohol. The manufacturer has advised that a 0.5% version is unlikely to come onto the market in the near future (CareFusion, personal communication). The Working Party is aware that some anaesthetists prefer to use these devices for skin preparation for CNB, and would encourage the development of applicators containing 0.5% chlorhexidine in alcohol.

Skin antisepsis before CNB using 0.5% chlorhexidine in 70% alcohol (Hydrex) from a multi-use spray bottle is widely practised in the UK. Advocates of this technique argue that contamination is minimised: the fluid is kept in a closed container and it can be applied at a distance from the sterile field, before or during preparation of the equipment for CNB. However, others have suggested that spraying might result in aerosol contamination of equipment with chlorhexidine and may compromise sterility by missing an area of skin [29]. Malhotra et al. [30] showed that a single spray application of 0.5% chlorhexidine in alcohol sterilised the skin over the lumbar spine in healthy volunteers. The authors concluded that repeated application was unnecessary, and might increase the risk of contamination of the CSF if the antiseptic was not allowed to dry completely. Robins et al. [31] compared application of chlorhexidine using a spray with application from a sachet in parturients undergoing combined spinal-epidural anaesthesia. Both techniques were effective in reducing skin colonisation, but the time to achieve skin preparation was significantly shorter in the spray group.

Use of chlorhexidine in children

Chlorhexidine has been used for vaginal lavage, whole body cleansing and umbilical cord care in large, well-designed clinical trials on tens of thousands of neonates without significant adverse events [32, 33]. Despite chlorhexidine's proven efficacy, there are concerns about the risk of skin reactions and percutaneous absorption into the bloodstream, particularly in preterm and low birth weight infants. Transient contact dermatitis has been reported in preterm, very low birth weight infants after long-term placement of chlorhexidine-impregnated dressings for central venous catheters [34]. However, it has been suggested that the effect may have been caused by external pressure from the dressing rather than the chlorhexidine itself [35]. Alcohol-based chlorhexidine preparations have been reported to cause burns in infants of 24–26 weeks' gestational age [36, 37]. There are few data addressing the potential for chlorhexidine absorption following topical application. Cowan et al. [38] took blood samples from 24 infants after whole body bathing with 4% aqueous chlorhexidine and found that five had detectable chlorhexidine levels. All were < 36 weeks' gestational age and the authors suggested that their immature skin was likely to have increased the permeability of the epidermis. The clinical significance of traces of chlorhexidine in the blood is unknown. There are no established values for a safe concentration of chlorhexidine in the blood, and there are no reports of adverse consequences as a result of absorption of chlorhexidine in neonates [39]. Because of the limited safety data in neonates, the Society for Healthcare Epidemiology of America states that 'chlorhexidine products are not approved by the US Food and Drug Administration for children younger than 2 months of age' [40]. Despite this recommendation, chlorhexidine is commonly used in neonatal intensive care units in the USA, mostly for skin preparation and maintenance for central venous access [41].

Allergic reactions to chlorhexidine

Several hypersensitivity reactions due to chlorhexidine have been described. These include allergic contact dermatitis (commonly after prolonged and repeated application) [42], contact urticaria [43], photosensitivity [44], occupational asthma [45] and anaphylaxis [46–48]. Most of the cases of anaphylaxis to chlorhexidine involved topical application to mucous membranes [46] and the use of chlorhexidine-impregnated medical devices (e.g. central venous catheters) [47], although anaphylactic reactions have also followed application of chlorhexidine to intact skin [48]. The severity of these cases prompted the Medicines and Healthcare products Regulatory Agency (MHRA) to issue a Medical Device Alert in 2012 about the potential for anaphylactic reactions due to the use of medicinal products and medical devices containing chlorhexidine [49].

Other infection control precautions for CNB

Application of antiseptic to the skin is only one component of aseptic technique before CNB. Both the Association of Anaesthetists of Great Britain and Ireland and the Obstetric Anaesthetists' Association have issued guidance on the other precautions that should be employed [50, 51]. These include thorough handwashing with surgical scrub solution, the wearing of a cap, mask, sterile gown and gloves, and the use of a large sterile drape [3]. The Working Party is aware that some anaesthetists do not employ this level of asepsis for spinals or 'one-shot' epidurals, but believes that full aseptic precautions are required whenever CNBs are performed. The NAP3 report stated that aseptic technique had been suboptimal in a number of the reported cases of epidural abscess [1].

Skin antisepsis for peripheral nerve blocks

These guidelines address only CNBs. However, as the nerves targeted by some peripheral nerve blocks lie a shorter distance beneath the skin than the neuraxis, and the evidence of the neurotoxicity of chlorhexidine is not restricted to the neuraxis, the Working Party considers it reasonable to recommend that 0.5% chlorhexidine in alcohol be used for peripheral nerve blocks as well.

Suggestions for further research

The duration of antiseptic action required for different types of CNB may vary. A single intrathecal injection may only require antisepsis for a few minutes, whereas

insertion of an epidural catheter requires antisepsis to be maintained throughout the time the catheter remains in situ. Isopropyl alcohol causes a rapid reduction in the number of skin micro-organisms, but does not have any residual activity. In comparison, chlorhexidine exerts an antiseptic effect for up to 24 h [52]. Hibbard et al. [53] compared the effect of 70% isopropyl alcohol with 2% chlorhexidine in alcohol on abdominal sites. The authors found that both maintained antimicrobial activity for at least 6 h, but the chlorhexidine solution was more effective at 24 h. It may be that isopropyl alcohol alone could provide adequate antisepsis for a single-injection CNB, obviating the need for chlorhexidine and therefore avoiding exposure of the neuraxis to a second neurotoxic substance. A CNB involving an indwelling catheter, on the other hand, probably requires the more prolonged action of a chlorhexidine solution. Research is needed comparing the duration of antimicrobial activity of 0.5–2% chlorhexidine in alcohol with 70% isopropyl alcohol when used for CNB.

Costerton has shown that *S. epidermidis* exists at depths of up to five cell layers in the skin [54]. Dead skin cells are constantly being shed, along with the colonising bacteria. These, together with sebum, sweat and environmental material, form an oily layer covering the skin. It is possible that a single application of antiseptic to the skin removes bacteria from this oily layer covering the surface, but is ineffective at removing bacteria at depth. It might be more effective first to apply an antiseptic that will dissolve this oily surface layer and remove its bacteria. This could then be wiped away before applying antiseptic again to remove bacteria living within the epithelium. This 'apply-wipe-apply' technique requires both in vitro and in vivo investigation.

Several cases of severe neurological damage have been attributed to contamination of equipment for CNB with chlorhexidine in alcohol, caused by splashes, aerosols, or insertion through solution that has not dried on the skin, or through chlorhexidine crystals that have dried on the skin [17–19]. Further studies are needed to address the risk of 0.5% over 2% chlorhexidine in 70% alcohol, and 70% alcohol alone, in causing neurological damage from such sources of contamination.

Competing interests

FP and DB have provided expert opinions in cases of neurological damage following neuraxial block, in which the possibility of antiseptic contamination of injectate was considered. DB has received hospitality from Care Fusion, manufacturers of Chloraprep, and consequently took no part in any discussions relating to the use of this product. No external funding or other competing interests declared.

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