

# Brazilian Society of Anesthesiology Recommendations for Safety in Regional Anesthesia

Cláudia Regina Fernandes, TSA<sup>1</sup>, Neuber Martins Fonseca, TSA<sup>2</sup>; Deise Martins Rosa, TSA<sup>3</sup>,  
Cláudia Marquez Simões, TSA<sup>4</sup>, Nádia Maria da Conceição Duarte, TSA<sup>5</sup>

**Summary:** Fernandes CR, Fonseca NM, Rosa DM, Simões CM, Duarte NMC – Brazilian Society of Anesthesiology Recommendations for Safety in Regional Anesthesia.

©2011 Elsevier Editora Ltda. All rights reserved.

## METHOD DESCRIPTION FOR EVIDENCE COLLECTION

Research was conducted in multiple database (MEDLINE from 1965 to 2011, Cochrane Library, and LILACS), and in crossed references with the surveyed material aiming the identification of articles with the best methodological design. Following the findings, critical evaluation of the contents and classification according to the strenght of evidence were performed. The research was conducted between December 2010 and April 2011. For PubMed, were used the following strategies:

1. “regional anaesthesia” OR “anesthesia, conduction” [MeSH Terms] AND “infection”[MeSH Terms] AND “prevention and control”[Subheading] OR “prevention” AND “control” OR “prevention and control”
2. “regional anaesthesia” OR “anesthesia, conduction” [MeSH Terms] AND “infection”[MeSH Terms]
3. “regional anaesthesia” OR “anesthesia, conduction” [MeSH Terms] AND “infection”[MeSH Terms] AND “etiology”[Subheading] OR “etiology” OR “causality” [MeSH Terms]
4. “regional anaesthesia” OR “anesthesia, conduction” [MeSH Terms] AND “immunocompromised host”[MeSH Terms] OR “immunocompromised patient”
5. “regional anaesthesia” OR “anesthesia, conduction” AND “meningitis”[MeSH Terms]
6. “regional anaesthesia” OR “anesthesia, conduction” AND “epidural abscess”[MeSH Terms]
7. Epidural AND [MeSH Terms] OR “catheters” AND “colonization” AND “infection”[MeSH Terms] OR “infection
8. single-use AND “equipment and supplies”[MeSH Terms] AND “devices” OR “medical devices” AND “reprocessing”
9. “single-use” AND “equipment and supplies”[MeSH Terms] AND “devices” OR “medical devices” AND “reprocessing” AND “anaesthesia”
10. “medication errors” [MeSH Terms] AND (“regional anaesthesia”[All Fields] OR “anesthesia, conduction”
11. “cost-effective” AND “pharmaceutical solutions” [MeSH Terms] AND “regional anaesthesia” OR “anesthesia, conduction”
12. “drug contamination” [MeSH Terms] AND (opening [All Fields] AND ampules [All Fields])

Received from the Brazilian Society of Anesthesiology (SBA), Brazil.

1. MD, PhD, Anesthesiologist; Professor at the Medical School of Universidade de Fortaleza (UNIFOR); Responsible for the Centro de Ensino e Treinamento (CET/MEC/SBA) at Hospital Universitário Walter Cantídio, Universidade Federal do Ceará (UFC); President of the Perioperative Medicine Committee of SBA

2. MD, PhD, Anesthesiologist; Professor at the Anesthesiology Department of Faculdade de Medicina da Universidade Federal de Uberlândia (FMUFU); Responsible for the CET/SBA at FMUFU

3. MD, Anesthesiologist at Instituto Nacional do Câncer (INCA); Co-responsible for the CET/SBA at Hospital Universitário Pedro Ernesto (HUPE), Universidade do Estado do Rio de Janeiro (UERJ); Instructor at the Curso Suporte Avançado de Vida em Anestesia – SAVA/SBA

4. MD, Anesthesiologist; Coordinator of the Anesthesiology Service at Instituto do Câncer de São Paulo (ICESP); Member of the SBA Malignant Hyperthermia Committee

5. MD, Anesthesiologist at Hospital Universitário Oswaldo Cruz, Universidade Estadual de Pernambuco (UPE); Co-responsible for the CET/SBA of Hospital da Restauração, Hospital Getúlio Vargas and Hospital Oswaldo Cruz, UPE; President of the Brazilian Society of Anesthesiology, 2011

Correspondence to:  
Dra. Nádia Maria da Conceição Duarte  
Rua Professor Alfredo Gomes, 36  
Botafogo  
22251080 – Rio de Janeiro, RJ, Brazil  
E-mail: nadiaduarte2011@gmail.com

In the field of regional anesthesia, studies on infectious complications focusing on risk factors, etiology, prevention, diagnosis and treatment were selected. We also included studies that assessed the risks of infectious complications in infected or immunocompromised patients undergoing regional anesthesia; studies addressing the use of reprocessed materials, the safe handling of drugs and vials; and studies on the cost-effectiveness in preparing solutions for continuous infusion.

## DEGREES OF RECOMMENDATION AND STRENGTH OF THE EVIDENCE

- A:** Experimental or observational studies of better consistency.
- B:** Experimental or observational studies of lower consistency.
- C:** Case reports or case series (uncontrolled studies).
- D:** Opinion devoid of critical assessment, based on consensus, experts, physiological studies or animal models.

## OBJECTIVE

This paper aims to evaluate safety aspects in anesthesia and regional analgesia, such as potential infectious complications resulting from the technique, associated risk factors, prevention strategies, diagnosis, and treatment. It also seeks to clarify the use of reprocessed materials in the practice of regional anesthesia; to clarify the factors that can lead to errors in drug administration; establish the implications of the aseptic management of vials and ampoules; and clarify the cost-effectiveness in preparing solutions to be administered continuously in regional blocks.

## INTRODUCTION

Infectious complications associated with regional anesthesia and pain therapy can result in devastating morbidity and mortality, including abscess, meningitis or spinal cord compression secondary to abscess formation. Possible risk factors include underlying sepsis, diabetes, immunosuppression, corticosteroids use, localized bacterial colonization or infection, and prolonged catheters use. Meningitis or epidural abscess may result from colonization of distant or localized infection, with subsequent hematogenous dissemination and commitment of the central nervous system (CNS). The anesthesiologist may also carry microorganisms into the CNS by contaminating into the material to be used for regional anesthesia, or when not following the aseptic technique.

A catheter used for neuraxial blockade, even if inserted under aseptic technique, can be colonized with the skin flora, which favors the infection of the epidural or subarachnoid spaces. There is no clear evidence in the literature about the frequency of such complications <sup>1</sup>(D).

Historically, severe CNS infections such as arachnoiditis, meningitis or abscess after neuraxial blockade are rare events, although some case reports or case series exist. Also rare is the drug administration errors in regional block.

However, recent epidemiological series suggest that the frequency of infectious complications and accidents related to safety of neuraxial techniques are increasing <sup>2,3</sup>(B)<sup>4,5</sup>(D). For this reason, it is mandatory to understand the natural history of these diseases and their causal factors, to allow for the development of preventive and safety strategies, ranging from the execution of the technique to the proper handling and administration of prepared drugs.

## THE IMPORTANCE OF THE ASEPTIC TECHNIQUE

### Does hand washing by the anesthesiologist reduces the incidence of infectious complications in conductive anesthesia?

In 1846, the Hungarian physician Ignaz Philip Semmelweis (1818-1865) confirmed the close relationship between puerperal fever and the hygiene of physicians. Since the study of Semmelweis, the hands of health care professionals (HCP) have been involved in the transmission of microorganisms in the hospital <sup>6</sup>(D).

Hand contamination of HCPs can occur during direct contact with the patient, or by indirect contact with surrounding products and equipment. Multidrug-resistant bacteria and fungi may be part of the transient skin flora of hands. Using this vehicle, microorganisms can spread among patients.

There is evidence regarding the transmission of pathogens by hands since the Crimean War times. Nurse Florence Nightingale introduced handwashing care and thus reduced the morbidity and mortality of war wounded. The hands contamination of HCPs can occur during patient handling and through indirect contact with other objects (beds, stethoscopes, anesthesia equipment and other materials from the operating room). Studies show the association of contaminated hands with infections outbreaks in health services <sup>7-9</sup>(B)<sup>10-12</sup>(C).

A recent study showed that the hands of anesthesiologists serve as an important source of contamination in procedures performed in the operating room. Proper hygiene is essential in the prevention of infectious complications <sup>13</sup>(B). Basic care is essential for safety during anesthesia procedures, including handwashing before assisting each patient <sup>14,15</sup>(D). Additional studies show that handwashing is considered one of the most important components of the aseptic technique to be employed before performing anesthetic procedures <sup>16</sup>(B). Proper aseptic practices should be employed in the preparation of regional anesthesia, both when using techniques with single puncture or catheters.

Watches and rings are risk factors for infectious complications. Recent studies have shown higher contamination when these are not removed <sup>17</sup>(B). Although there is controversy about the matter, the removal of ornaments is recommended as a prophylactic measure against infection <sup>18</sup>(B). Another recommendation to minimize the risk of infection is to avoid the use of artificial fingernails <sup>19,20</sup>(B).

There are measures that can be implemented to disseminate the importance of handwashing among health professionals, such as education on the subject, availability of sinks and alcohol gel devices in easily accessible locations. Alcoholic products used for hand's hygiene in health services are available as solution (liquid), gel and foam. The gel-based formulations present antimicrobial efficacy superior to other formulations <sup>21</sup>(B). However, there is insufficient evidence on what would be the best aseptic technique for the anesthesiologist hands before performing regional anesthesia.

**Recommendation:** It is recommended to wash hands prior to performing any procedure <sup>13</sup>(B) as an important item of the

aseptic technique in regional anesthesia (single puncture or catheter) <sup>16</sup>(B). Adornments such as watches, rings, artificial fingernails should be removed as a prophylactic measure to improve the technique <sup>17,18</sup>(B).

### **Does the use of surgical garment by anesthesiologists reduce the risk of infectious complications when performing continuous epidural block?**

The use of meticulous aseptic technique for regional anesthesia has been repeatedly described in previous studies. However, only recently defined standards for aseptic procedures during regional anesthesia have been established.

Handwashing remains the crucial component of the asepsis. Sterile gloves should be considered as a supplement and not as a replacement of handwashing <sup>1,22</sup>(D)<sup>23</sup>(B). Before washing hands, all jewelry (rings, watches, bracelets, etc.) should be removed <sup>3</sup>(B). Sterile gloves protect not only patients from contamination, but also HCPs themselves <sup>1</sup>(D).

As for glove perforation, it is well established that incidents occur more often with vinyl gloves than with latex gloves, leading to contamination of HCPs' hands <sup>1</sup>(D). To date no research has assessed the risk of microbial contamination or perforation of sterile latex or neoprene gloves. Sterile disposable or single-use gloves should never be washed, re-sterilized or disinfected. A new pair of gloves should be used in every new procedure <sup>22</sup>(D).

Surgical gowns are commonly used as a strategy to prevent cross-contamination between patients, preventing the contact of infectious material with HCPs' clothes. Currently there are not enough data to make definitive recommendations regarding the routine use of surgical gowns in the operating room during regional anesthesia, both for single punctures and for the temporary placement of neuraxial or peripheral catheters. It is recommended that aseptic techniques should always be applied during equipment preparation, such as the use of ultrasound in regional blockades <sup>5</sup>(C).

Reports draw an analogy between the installation of central venous access and neuraxial anesthesia, suggesting the use of surgical garment. However, some aspects are questioned, as the increased time to perform the procedure and the high associated costs <sup>25</sup>(A). It is argued that if full surgical garment is suitable for insertion of central venous access, comparatively, it would also be indicated for neuraxial anesthesia <sup>26</sup>(D). In central venous punctures, full barrier precautions (sterile gloves, full and long surgical garment, mask, cap and large sterile areas) reduce the incidence of infection associated with central venous catheters, when compared to standard precautions (sterile gloves and small sterile areas). In this context, the infection incidence is about 2.3% when using full barrier precautions, and 7.2% when using standard precautions. The extrapolated infection rate was 227:10.000 with the use of full barrier devices and 718:10.000 with the use of standard barrier devices <sup>27</sup>(D).

It is argued that, if the incidence of infection associated with neuraxial anesthesia were the same as for the insertion of central venous access, there would be no questioning about

the use of full body garment. However, infection associated with neuraxial blockade is 718 times lower than the infection rate with central access (considering 1:10.000 with standard precautions). Therefore, there is no robust evidence so far recommending the use of surgical gowns in simple blockade procedures or neuraxial catheter insertion procedures.

The surgical mask was initially considered to be a protective barrier mechanism for the HCP against patient's secretions and blood <sup>24</sup>(D).

However, an increasing number of cases of meningitis after spinal tap has been described <sup>2</sup>(B),<sup>27,28</sup>(D),<sup>29,30</sup>(C). Many of these cases result from epidural or subarachnoid space contamination with pathogens from the oropharyngeal mucosa of the anesthesiologist. Schneeberger et al. <sup>29</sup> described four cases of iatrogenic meningitis after spinal anesthesia in a period of four years, all involving the same anesthesiologist. The professional had a history of recurrent pharyngitis, did not wear masks, and spoke frequently during the procedure <sup>29</sup>(C). Another case was that of an epidural abscess caused by a unusual type of *Staphylococcus* from the nose of the anesthesiologist who placed an epidural catheter <sup>31</sup>(C). However, despite the reported cases, there is no definitive evidence that the use of mask causes reduction of infection rates <sup>24</sup>(D).

Face mask is critically important in protecting patients from doctors with sore throat, pharyngitis or suffering from recurrent tonsillitis, or who are chronic carriers of nasal *Staphylococcus aureus* <sup>2</sup>(B)<sup>24,28</sup>(D)<sup>29-31</sup>(C).

Aseptic technique should include handwashing and jewelry removal; however, there is doubt about the use of surgical gown and also if the aseptic technique must include changing the mask before each new case. However, the correct use of the face mask is recommended, which should cover nose and mouth <sup>26</sup>(D).

**Recommendation:** Sterile gloves should be used. However, they should be considered as a supplement to handwashing, not a replacement <sup>1,22</sup>(D)<sup>23</sup>(B). So far, there is no robust evidence recommending the use of surgical gowns in simple blockade or catheter insertion procedures <sup>1,24</sup>(D). The use of face mask is strongly recommended for those anesthesiologists who have signs and symptoms of upper respiratory tract infection <sup>2</sup>(B)<sup>24,28</sup>(D)<sup>29-31</sup>(C), and they should always cover mouth and nose <sup>26</sup>(D). It is still not determined if the aseptic technique should include the change of mask prior to each new procedure <sup>26</sup>(D).

### **What is the best antiseptic technique for preparation of the patient's skin before performing the regional block?**

Disinfection is the process of destroying vegetative forms of microorganisms, pathogenic or not present in inanimate objects. Antisepsis is the set of measures employed to kill or inhibit the growth of microorganisms existing on the superficial (transient skin flora) and deep (resident skin flora) layers of skin and mucosa. Such measures involve the use of germicidal agents: the antiseptics <sup>32</sup>(D).

Controversies still exist about the safest and most appropriate antiseptic for skin preparation prior to regional anesthesia.

The skin should be treated with antiseptic agents in order to reduce the amount of germs present, the skin flora. The antiseptics should have immediate antimicrobial action, persistent residual effect and should not be toxic, allergenic or irritating. It is recommended that they be smooth and cost-beneficial<sup>33,34</sup>(C).

The antiseptic activity of alcohol occurs by protein denaturation and lipid removal, including the envelope of some viruses. In order to provide maximum germicidal activity, alcohol should be diluted in water, allowing for the protein denaturation. A concentration of 70% is recommended to achieve faster microbicidal activity. However, some characteristics of alcohol limit its use: it is volatile and evaporates rapidly at room temperature; it is highly flammable; and has little or none residual activity on surfaces. Moreover, the presence of high concentrations of organic matter may decrease the microbicidal activity of alcohol. Alcoholic preparations are not appropriate when the skin is visibly dirty or contaminated with proteic material<sup>35</sup>(D).

Most studies of alcohols have evaluated their individual effect in different concentrations or have focused on the combination with solutions containing limited amounts of hexachlorophene, quaternary ammonium compounds, polyvinylpyrrolidone iodine (PVP-I), triclosan or chlorhexidine gluconate<sup>35</sup>(D).

The antiseptic that best meets the requirements for application in living tissue is alcohol diluted in water in combination with chlorhexidine gluconate solution. The chlorhexidine is a potent germicide and, when added to alcohol, it had the effect potentialized<sup>36,37</sup>(A).

Chlorhexidine gluconate adheres to the stratum corneum of the skin, which results in prolonged action. To date there are no reports of adverse effects of chlorhexidine on the nervous system<sup>35</sup>(D).

The comparison of the antiseptic effect of chlorhexidine with iodophores – PVP-I (polyvinylpyrrolidone iodine) showed that chlorhexidine has a higher bactericidal effect, faster action and longer residual effect<sup>32</sup>(D)<sup>37-39</sup>(A).

**Recommendation:** It is recommended that the safe and effective antiseptics of the skin before regional anesthesia should be accompanied by the following precautions: if the skin surface is dirty, clean it by removing any organic or inorganic matter using soap and water with subsequent rinsing<sup>32</sup>(D); use alcoholic chlorhexidine<sup>36,37</sup>(A); employ appropriate amount of antiseptic, avoiding to remove the excess of liquid, waiting for it to evaporate. This way, the actual effectiveness of the solution is guaranteed<sup>32</sup>(D)<sup>37-39</sup>(A).

## FACTORS ASSOCIATED WITH INFECTIOUS COMPLICATIONS IN REGIONAL ANESTHESIA

### What are the risk factors related to infection in regional anesthesia with or without catheter insertion?

Severe CNS infections, such as arachnoiditis, meningitis and abscesses are rare complications of neuraxial anesthesia.

However, an increasingly greater incidence has been reported<sup>2</sup>(B)<sup>4</sup>(C).

In the last decades, infectious complications resulting from regional anesthesia were more frequently reported. This may be due to a greater initiative for publishing complications, but it may also be related to changes in clinical practice, such as the more frequent use of tunneled catheters.

Large epidemiological studies have shown surprising results related to demographics, frequency, etiology, and prognosis of infectious complications of neuraxial anesthesia. The epidural abscess occurs more often in immunocompromised patients with prolonged epidural catheterization. The most common causative organism is *S. aureus*, suggesting colonization and subsequent infection by this pathogen normally present in the skin flora.

Reports show that patients who developed meningitis after neuraxial blockade were healthy and underwent spinal anesthesia. In such cases, the most common source of the pathogen was the upper airway of the anesthesiologist who performed the blockade<sup>29,30,40,41</sup>(C)<sup>42</sup>(D).

Data suggest that epidural or subarachnoid anesthesia during an episode of bacteremia is a risk factor for infection in the neuraxis<sup>2</sup>(B)<sup>4,43</sup>(C)<sup>44</sup>(D). On the other hand, a study on the inclusion and permanence of the epidural catheter in patients with infection at a site distant from the nervous system cleared the blockade to be performed in such situations. A meticulous daily inspection of the catheter insertion site is recommended. If inflammation signs are present, it should be immediately removed<sup>45</sup>(B).

It is pertinent to mention the factors that affect bacterial colonization during epidural catheterization. Although the catheter tip is often colonized, the infection progression to the epidural space rarely occurs<sup>24</sup>(D)<sup>45</sup>(B)<sup>46</sup>(C).

Several factors may contribute to increased infection risk: colonization of the catheter insertion site, the infusate itself, the management of the catheter once disconnected, and other situations continuity loss in the system.

Making an analogy with the central venous catheter, the site of epidural catheter insertion interferes with the colonization occurrence and potential infection of the puncture site. Venous catheters are colonized more often when inserted into the femoral vein than into the subclavian. In continuous epidural technique, caudal catheters are colonized more often than those inserted in the lumbar region<sup>47,48</sup>(B).

It has been demonstrated that bupivacaine and lidocaine inhibit the growth of a number of microorganisms in culture media. However, the bactericidal effect decreases significantly at low concentrations of local anesthetics that are typically used to promote analgesia. Opioid solutions do not exhibit any ability to inhibit bacterial growth<sup>49</sup>(B).

The most commonly identified pathogens in the epidural infections are *S. aureus* and coagulase negative *Staphylococcus*. These pathogens are inhibited only at high concentrations of local anesthetics, such as a solution of lidocaine 2% or bupivacaine 0.5%<sup>24,49</sup>(C). However, further studies are necessary to investigate the bactericidal effect of local anesthetic solutions at low concentrations *in vivo*.

The catheter tip, the insertion site and the hematogenic dissemination are the three major ports of entry for microorganisms into the epidural space, being the catheter tip the main source of contamination<sup>46,49,50(B)</sup>. An antibacterial filter placed on the catheter tip acts as a physical barrier to block the entry of bacteria, and probably reduces epidural colonization. However, catheter's external tip culture presented mixed results, with reported cases of epidural infection despite the use of antibacterial filters. There is significant correlation between the incidence of colonization of tunneled catheter and the frequency of replacement (manipulation) of the bacterial filter when the catheter-filter connection is close to the contaminated skin<sup>51(B)</sup>. There are some brands of filters that maintain their unmodified antimicrobial function for up to 60 days when perfused with low volume and low pressure<sup>51(B)</sup>. Based on these data, it seems feasible to reduce the frequency of filter changes during tunneled catheterization, possibly reducing epidural catheter colonization<sup>51(B)</sup>. Bacterial colonization of short-term use catheters (73-120 hours; used to treat acute postoperative pain) has direct correlation with bacterial colonization of the skin around the insertion site and bacterial growth from the subcutaneous segment through the catheter tip<sup>52(B)</sup>. The occurrence of adverse events in the general ward, such as: catheter occlusion, damage or replacement of the transparent dressing (*tegaderm*), partial catheter displacement, disconnection between the tip and the connecting device, blood transfusion and positive culture of skin near the insertion site are risk factors for bacterial colonization of epidural catheters. It is suggested that bacterial migration along the catheter orifice is the most common colonization route. Some consider that maintaining a sterile skin around the insertion site can reduce catheter tip colonization<sup>52(B)</sup>. These data suggest that continued attention to the technique is required throughout the duration of epidural catheterization. The sole use of filters is probably ineffective in preventing colonization and infection<sup>46(C)</sup>.

The literature is insufficient to assess whether the number of disconnections and reconnections of the infusion system is associated with the frequency of infectious complications. The disconnection and reconnection of the neuraxial infusion system should be limited<sup>26(D)</sup>. As for the duration of the inserted catheter, infection and epidural abscess occur more often in the presence of long-term indwelling catheters<sup>53-55(B)</sup><sup>56(C)</sup>. However, there is no specific period associated with increased risk of infectious complications. Thus, permanence of the epidural catheter should be restricted to the period in which it is medically necessary<sup>26(D)</sup>.

As for peripheral regional anesthesia techniques, the frequency, diagnosis and prognosis of infectious complications remain unclear. Several series involving continuous peripheral block technique have reported erythema at the insertion site and/or high incidence of colonization (20%-60%)<sup>57(B)</sup><sup>58(C)</sup>, but few significant infections. Special attention to the risk of the infection with continuous peripheral nerve blockade should be paid. Bacterial colonization is present in 29% of the catheters, the most common agent being *Staphylococcus epidermidis*. The incidence of local inflammation is present in 3% of patients. In those, 44% of the catheters are colonized while

only 19% of the catheters are colonized in patients with no inflammatory signs. There is no correlation between inflammation and fever. Local inflammation/infection risk factors are: admission to the intensive care unit, male gender, presence of the catheter for more than 48 hours, and no antibiotic prophylaxis<sup>57(B)</sup>. Infectious complications in continuous femoral catheters occurs 48 hours later, being *S. epidermidis* (71%) the main agent<sup>58(C)</sup>. Bacteremia cases are attributed to the femoral catheter presence.

While the need for antibiotic prophylaxis during placement of indwelling epidural catheters or implantable devices to treat chronic pain is well defined, its importance during catheter placement and maintenance of peripheral nerve is less clear. In axillary catheters the infectious complication may be rare<sup>59(C)</sup>. Reported cases of infectious complications after peripheral nerve blocks have *Streptococcus* or *S. aureus* as etiological agents<sup>60,61(C)</sup>.

**Recommendation:** Attention should be paid to predisposing factors for the development of septic complications in neuraxial or peripheral nerve blocks. However, this occurrence is rare. Immunocompromised patients with prolonged epidural catheterization are at higher risk of epidural abscess<sup>2(B)</sup><sup>4(C)</sup>. The main causative agent is *S. aureus*<sup>2(B)</sup><sup>4(C)</sup>. Bacterial meningitis can occur in healthy individuals, being pathogens from anesthesiologist's upper airway flora the commonest causal agents<sup>28,29,40,41(C)</sup><sup>42(D)</sup>. Colonization of epidural catheter tip occurs much more frequently than infections of the neuroaxis<sup>51(B)</sup>. Factors that contribute to infection risk: prolonged use of the catheter, colonization of the insertion site, contamination of the infusion solution, excessive management of system connections, including frequent replacement of antibacterial filters and loss of system continuity. Bacterial colonization of peripheral nerve catheters is more frequently associated with inflammatory signs at the insertion site<sup>57(B)</sup>, being *S. epidermidis* the most commonly agent found<sup>58(C)</sup>.

#### **What is the risk of infectious complications in regional anesthesia in the febrile or infected patient?**

There are specific recommendations regarding regional anesthesia in the febrile or infected patient<sup>62(D)</sup>.

Severe infections of the neuraxis are rare, such as arachnoiditis, meningitis, and abscess after epidural and spinal anesthesia. The decision to perform a regional anesthetic technique should be individualized, considering the anesthetic alternatives, the benefits of regional anesthesia and the risk of CNS infection, which can theoretically occur in any bacteremic patient. Despite conflicting results, many experts suggest that, except in the most extraordinary circumstances, neuraxial blockade should not be performed in patients with untreated systemic infection. Available data suggest that patients with evidence of systemic infection can safely be submitted to spinal anesthesia, provided that the appropriate antibiotic therapy is started before the puncture and the patient has shown response to treatment, such as reduction of fever. The placement

of epidural or subarachnoid catheter in these patients remains controversial. Available data suggest that spinal anesthesia can be safely performed in patients with low risk of transient bacteremia after dural puncture. Epidural catheter should be removed in the presence of erythema and/or local secretion; and there is no convincing data suggesting that concurrent infections in remote locations or the absence of antibiotic therapy are risk factors for infection. The delay in diagnosis and treatment of major CNS infections, even for a few hours, may significantly worsen the neurological outcome.

**Recommendation:** eremia increases the risk of CNS infectious complications following neuraxial blockade. <sup>62(D)</sup>. It is recommended that neuraxial blockade should not be performed in patients with untreated systemic infection, except in the most extraordinary circumstances <sup>62(D)</sup>. Patients with evidence of systemic infection can be submitted to subarachnoid anesthesia, provided that the antibiotic therapy is initiated prior to puncture and signs of response to treatment, such as decreases of body temperature, are observed. <sup>62(D)</sup>.

#### What is the risk of infectious complications in regional anesthesia in immunocompromised patient?

The regional anesthesia advantages are numerous: improved analgesia, reduced pulmonary complications, decreased incidence of graft occlusion, improved mobility after major orthopedic surgery, and decreased risk of infection by attenuating stress response and preserving immune function <sup>63,64(D)</sup><sup>65,66(A)</sup>.

Patients with impaired immune function, such as: diabetics, malignancy, recipients of solid organ transplantation, patients chronically infected by human immunodeficiency virus (HIV) or herpes simplex virus (HSV), are often candidates for regional anesthesia. These patients are susceptible to infection by opportunistic microorganisms. Antimicrobial therapy is less effective in those cases. This fact results in higher morbidity and mortality compared to patients with preserved immune function. Therefore, immune system impairment increases both the frequency and severity of infection.

There are some recommendations before performing regional anesthesia in immunocompromised patients, as described below <sup>67(D)</sup>:

Regarding the administration of epidural and subarachnoid anesthesia in the febrile patient <sup>62(D)</sup>, as in any other clinical judgment, the decision to perform a regional anesthetic technique should be individualized. The anesthetic alternatives, the regional anesthesia benefits and the risk of CNS infection must be taken into consideration, since this is theoretically a more common complication in immunocompromised patients. The attenuation of the inflammatory response in patients with compromised immune systems could reduce the signs and symptoms that are often associated with infection.

The amount of pathogenic microorganisms (atypical and/or opportunistic pathogens) is much higher in the immunocompromised host than in the general population. Consultation of an infectologist is recommended to facilitate early and effective

antibiotic therapy for suspected infection of the neuraxis. Delay in diagnosis and treatment of CNS infection worsens the neurological outcome and increases mortality. The risk of epidural abscess increases proportionally to period of catheterization in these patients.

There are insufficient data on the safety of spinal and epidural anesthesia in patients with HSV-2 primary infection. However, there are reports of viremia, fever and meningitis. These findings may suggest a more conservative approach. Neuraxial anesthesia has shown to be safe in patients with recurrent infection by HSV, although there are reports of exacerbation of HSV-1 infection associated with use of epidural or intrathecal opioids. Scarce data suggests that it is possible to perform neuraxial and peripheral nerve blocks, including blood patch in patients infected with HIV. Pre-existing neurological disorders are common in these patients and should be taken into account when making the decision of performing a neuraxial blockade.

**Recommendation:** In theory, infectious complications associated with regional anesthesia are more common in immunocompromised patients <sup>62(D)</sup>. The attenuation of the inflammatory response can decrease the signs and symptoms, and mask the early infection diagnosis. When infection of the neuraxis is suspected, consultation with infectologist is recommended to facilitate early and effective antibiotic therapy <sup>67(D)</sup>.

#### DIAGNOSIS AND TREATMENT OF INFECTION ASSOCIATED WITH REGIONAL ANESTHESIA

##### How to make the diagnosis and treatment of meningitis and epidural abscess?

The delay in diagnosis and treatment of major CNS infections, even for a few hours, significantly worsens the neurological outcome. Bacterial meningitis is a medical emergency. The mortality rate is around 10%-30%. Sequelae such as nerve damage and hearing loss occur in 5%-40% of patients <sup>68(D)</sup> <sup>69,70(C)</sup>.

Meningitis is most often associated with fever, headache, altered level of consciousness and meningism. The diagnosis is confirmed by lumbar puncture. Usually, the clinical manifestations begin 48 hours after the puncture for spinal anesthesia. The antibiotic therapy can delay the onset of symptoms CSF exhibits increased polymorphonuclear cell count (pleocytosis), low glucose (< 30 mg.dL<sup>-1</sup>), increased proteins (> 150 mg.dL<sup>-1</sup>) and presence of bacteria on Gram-stain and positive cultures <sup>42(D)</sup>. Concentration lactate level in CSF differentiates between and aseptic lactate levels in CSF higher than 35 mg.dL<sup>-1</sup> distinguish bacterial meningitis from aseptic meningitis <sup>71,72(B)</sup> <sup>73(D)</sup>. The use of dexamethasone as an adjuvant to antibiotic therapy in improving outcomes is controversial. No significant reduction in mortality or neurological dysfunction has been demonstrated. Thus, the benefit of dexamethasone remains unclear <sup>74,75(A)</sup>.

Lumbar puncture should not be performed if epidural abscess is suspected. The abscess after epidural or spinal anesthesia may be superficial, requiring limited surgical drainage and intravenous antibiotic administration. Superficial infections with local tissue swelling, erythema and supuration are often associated with fever, but rarely cause neurological problems, unless untreated.

The epidural abscess is usually formed days to weeks following neuraxial blockade, usually after the patient has been discharged<sup>76-79(C)</sup>, with clinical signs of severe back pain, local hypersensitivity and fever associated with leukocytosis<sup>24(D)</sup>.

The clinical presentation of epidural abscess progresses from back pain and pain suggesting radicular compression to weakness (including symptoms related to bladder and bowel) and eventually paralysis. The initial back pain and radicular symptoms may remain stable from hours to weeks. However, after the onset of muscle weakness, progression to complete paralysis usually occurs within 24h<sup>80(C)</sup><sup>81(D)</sup>. The delay in diagnosis of epidural abscess is common and often leads to irreversible neurological deficit. Attention should be given to associated risk factors. Erythrocyte sedimentation rate (ESR) may be useful in screening prior to magnetic resonance imaging<sup>82(B)</sup><sup>83(C)</sup>. The radiological image of an epidural mass in the presence of variable neurological deficit clarifies the diagnosis. MRI is recommended for being the most sensitive test for evaluation of vertebral-spinal system when infection is suspected<sup>84(B)</sup>. However, more recent evidence shows that clinical guidelines are needed to improve the MRI efficiency in cases of suspected epidural abscess<sup>85(B)</sup>.

The combination of antibiotics and surgical approach (drainage and/or debridement) is the treatment of choice. The duration of the neurological deficit and of the amount of neurological damage present before initiation of treatment<sup>84(B)</sup><sup>86(D)</sup>.

**Recommendation:** Meningitis after spinal anesthesia usually starts 48 hours after the puncture and is manifested as fever, headache, altered level of consciousness and meningism. The diagnosis is confirmed by lumbar puncture<sup>42(D)</sup><sup>71,72(B)</sup><sup>73(D)</sup>. Antibiotic therapy can delay the onset of symptoms<sup>42(D)</sup>. Treatment is done with antibiotics<sup>74,75(A)</sup>. Mortality is approximately 10%-30%<sup>68(D)</sup><sup>69,70(C)</sup>. Epidural abscess usually produces signs and symptoms in days to weeks after neuraxial blockade, usually after the patient has been discharged<sup>76-79(C)</sup>. The clinical presentation includes severe back pain, local hypersensitivity and fever associated with leukocytosis<sup>24(D)</sup>. The delay in diagnosis leads to irreversible neurological deficit. MRI is the recommended diagnostic test<sup>84(B)</sup>. Treatment includes antibiotics and surgical approach<sup>84(B)</sup><sup>86(D)</sup>.

## ANTIBIOTIC PROPHYLAXIS AND REGIONAL ANESTHESIA

### Should the patient under continuous regional analgesia should receive antibiotic prophylaxis?

Systemic infection or local abscess due to the use of a catheter for regional analgesia are rare, although the colonization of the catheter is more frequent<sup>87(B)</sup>. Tunneling of short-term

use catheter (mean 48 hours) appears to decrease bacterial colonization of the catheter tip. The incidence of colonization is 6.2%, being higher in trauma victims. However, the use of prolonged antibiotic therapy when compared to the use of a single dose does not alter in the incidence of catheter colonization<sup>88(C)</sup>. The epidural catheter hold in place for an average of 2.3 days without tunneling, resulted in 28% of positive culture without correlation between the antibiotics prior to surgery. Except for surgical prophylaxis, the use of antibiotic therapy for short-term epidural catheter is not recommended<sup>89(B)</sup>.

The use of at least one prophylactic antibiotic dose before surgery reduces the bacterial colonization risk of catheters used for continuous plexus postoperative analgesia<sup>90(B)</sup>. The systemic antibiotics administration for at least 24 hours postoperatively reduces significantly the risk of catheter colonization. There are three potential risk factors for bacterial colonization of the catheter: location in the groin, multiple manipulations, dressing changes and omission of antibiotic use postoperatively. These associated factors not necessarily caused the bacterial colonization of the catheter in the postoperative period<sup>91(B)</sup>. The antibiotic prophylaxis effect over a prolonged period (several weeks) of epidural catheterization may<sup>92(C)</sup> or not<sup>93(C)</sup> reduces catheter infection.

It is argued that the conduct in relation to the handling of short-term catheter should be as follows: to establish minimal catheter manipulation after insertion; if possible, like a system must be continuous and closed aseptic technique must be reinforced; one should use transparent dressings avoiding constant changes. It is recommended to increase monitoring of the epidural catheter. The puncture site should be inspected two to three times a day and on the day following removal. The occurrence of inflammation, swelling or pus at the site of catheter insertion requires it to be removed, sampling for culture and initiation of antibiotic therapy (ceftriaxone – 2 g 12/12h, associated to vancomycin – 1 g 12/12h). An MRI should be performed urgently to guide future decision making<sup>94(C)</sup>. Following standards and recommendations on the central nervous catheter use, it appears that it is inappropriate to use prophylactic antibiotics solely for insertion of a catheter for regional analgesia<sup>95(D)</sup>.

**Recommendation:** It is controversial whether the use of prophylactic antibiotics decreases the colonization of catheters used for regional analgesia<sup>88(C)</sup><sup>89(B)</sup><sup>90(B)</sup>. The tunneling of short-term catheter is associated with lower incidence of bacterial colonization of the catheter tip<sup>88(C)</sup>. The following procedures regarding the handling of short-term catheter are recommended: aseptic technique, minimal handling of the catheter after insertion; use of transparent dressings avoiding dressing changes; puncture site monitoring two to three times a day and on the day after removal. Inflammatory signs at the site require the removal of the catheter, sampling for culture, and use of antibiotic therapy (ceftriaxone – 2 g 12/12h associated with vancomycin – 1 g 12/12h). MRI should be requested to guide future decision making<sup>94(C)</sup>.

## REUSE OF MATERIALS IN REGIONAL ANESTHESIA

### Are there materials that can be reprocessed for the practice of regional anesthesia (glass syringe, needles)?

The recycling or reuse of hospital items is one of the most controversial issues discussed by health care systems worldwide. Many industries are against reprocessing, citing possible reuse dangers. Many health services are in favor of reprocessing, in view of the following aspects: high cost of some products, access difficulties and reduced availability of certain products, the possibility that the product is not intact after use, and concerns about the ecological impact of systematic disposal.

Several types of materials for health services are produced and labeled by manufacturers as single-use materials, ensuring safety both in function and in the sterilization of the product and avoiding any possibility of cross infection. The products used for regional anesthesia are considered critical by coming into direct contact with sterile tissue, according to the classification of Alvarado <sup>96</sup>(B).

The reprocessing of single-use materials coexists in different parts of the world, including developed countries. It is estimated that in Europe approximately 72.6 billion Euros are spent annually in disposable and single-use products <sup>97</sup>(B). Even though there are studies showing reduction of 50% in the cost of materials by reprocessing single-use medical materials. The literature does not provide sufficient evidence for adopting this practice <sup>98</sup>(B).

In Canada, the practice of reprocessing and reuse of materials still exists in 28% of hospitals. Authors consider it an alternative practice of relevant economic aspect. However, the infection risk and other complications do not justify the adoption of such measure <sup>96</sup>(B)<sup>99</sup>(C). Reprocessing can affect the products' mechanical, thermal or chemical features, affecting their effective performance. Reprocessed product must be equivalent in safety to that provided by the manufacturer, that is the patient can not be exposed to any risk <sup>100,101</sup>(D).

The recycled products represents a potential risk related use of improper cleaning, disinfection and/or sterilization, which can result in microbiological or chemical contamination. There is evidence that the recycled products use is related to the transmission of viral diseases and diseases caused by unconventional agents (Creutzfeldt-Jakob Disease) <sup>102</sup>(D).

The potential risk of virus transmission during catheter reuse, depending on cleaning disinfection, and sterilization of the catheter is variable when it should be zero <sup>103</sup>(D).

After studying different recycled products, 11% of the packages had some type of damage, which compromises the safety of using the product <sup>104</sup>(D).

Cleaning and autoclaving routines do not remove protein deposits of laryngeal masks <sup>105</sup>(D).

Regarding the reprocessed product safety after different sterilization cycles, bacteria has been detected, even after undergoing 10 cycles of reprocessing. Changes in surface integrity of the product were identified by electron microscopy

resulting from chemical interactions during reprocessing. These changes can lead to impaired performance of the original article <sup>106</sup>(D).

Following the reprocessing of rigid catheters without lumen, bacterial spores were identified suggesting that the sterilization protocol used was ineffective to ensure asepsis after 5 reuses. In this study, the reprocessing protocols were inadequate to ensure a safe decontamination <sup>107</sup>(D).

Sterilization of reprocessed materials is usually done with ethylene oxide, formaldehyde, oxidizing gas (hydrogen peroxide), ozone or peracetic acid. Residual gases resulting from the sterilization process may compromise products' safety and efficacy, especially those undergoing reprocessing several times, which became bio-incompatible <sup>108</sup>(D). The presence of chemical residues that may remain after cleaning or by absorption of the re-sterilized material is a latent risk that should not be underestimated. The physical properties highly resistant metals change by corrosion the metal surface resulting from re-sterilization processes <sup>109</sup>(D).

Angioplasty catheter reprocessing induces changes in their properties (shrinkage of the balloon) modifying specifications of the product as to compromise the safety of its use <sup>110</sup>(D). Successive reuse of polyvinyl chloride (PVC) catheters results in loss of plasticity and a decrease in molecular weight. Increase in roughness and cracks on the surface are also observed, which may cause severe impairment of product performance. Therefore, it is not recommended to reuse these catheters <sup>111</sup>(D).

In Brazil, the first regulatory action on this issue by the National Health Surveillance Agency (ANVISA); an agency of the Ministry was the Public Consultation No. 98, 2001, proposing standards for safe reprocessing of single-use articles. In 2005 the ANVISA Public Hearing presented a proposal to representatives of governmental agencies, councils, associations, civil society, regulators and industry specialists. In February 2006, through the resolutions of ANVISA in RDC No. 30 and SR No 515, criteria for reprocessing of materials were defined, with clear rules for the reuse of those who have the possibility of reuse. Subsequently, the matter was reviewed by ANVISA, together with observation of health legislation, with the edition of three new resolutions published in the Official Gazette (*Diário Oficial*) of 14<sup>th</sup> August. They are: DRC 156 and the 2605 and 2606 REs.

Some rationalizations were considered. Epidural needles large caliber. Even though, there is difficulty in cleaning, especially on the inner surface, even when using washers with ultrasound technology. Residues of organic matter such as fragments of skin, hair and other materials in the lumen and plug-ins can infect other patients. Chemicals used in cleaning can accumulate inside glass syringes or needles so that they can later be injected into the epidural space and cause chemical neuritis. Cleaning agents and/or sterilants may react with the materials and form new toxic residues, ethylene glycol, formed by the reaction of ethylene oxide and traces of water (left at rinsing) is a neurotoxic substance. Any deficiency in the control process of preparation and sterilization can lead to harmful consequences.



**Recommendation:** Once used, every material that comes to contact with patients may contain some type of contaminating material, such as pathogenic microorganisms, which can be difficult to eliminate by cleaning processes, disinfection and sterilization <sup>94(C)</sup><sup>100(D)</sup>. Due to the characteristics of the materials, many single-use products should not be processed at high temperature, being the sterilization allowed only by gas or radiation; this can also put the health of the individual at risk <sup>100,108,109(D)</sup>. There are no studies showing safety in the use of a reprocessed product in relation to the microbiological risk, toxic waste or changes in physical and chemical characteristics that justify its use. ANVISA does not recommend reprocessing of materials for use in regional anesthesia be those needles, glass syringes or catheters.

## SAFETY IN THE ADMINISTRATION OF DRUGS

### How to improve safety in the administration of drugs in regional anesthesia?

To perform regional anesthesia, the anesthesiologist uses different types of drugs, both to perform the proposed technique and to maintain anesthesia or sedation. The risk of medication errors during the anesthetic is real and should not be disregarded.

Currently, wrong medication administration is considered a worldwide epidemic, resulting in thousands of deaths annually. A study analyzing this type of complications indicates that there was an increase in incidence over the years, causing substantial financial losses as well as human lives. In the United States there are about 7,000 annual deaths due to errors in medication administration <sup>112(C)</sup>.

Medication error is characterized, as defined by ANVISA, as any preventable event that can actually or potentially lead to inappropriate use of medication. It may be related to professional practice, products used in health care, procedures, communication problems including prescription labels, packaging, names, preparation, dispensing, distribution, administration, education, monitoring and drug use <sup>113(D)</sup>.

Anesthesiologists are health professionals who work constantly vigilant. For this reason, the incidence of medication errors is relatively low. The incidence of errors in drug administration in anesthesia is 0.33 to 0.76% representing estimated prevalence of one adverse event per 133 anesthetic procedures <sup>114(B)</sup>.

There are recommendations for reducing errors in medication administration, as described below.

The following are actions that have strong evidence to recommend: carefully label reading of any drug, ampoule or syringe before use <sup>115(B)</sup><sup>116-118(C)</sup>; only use vials and syringes that have clear identification on the label and follow the minimum standards set by the competent organ <sup>118-120(C)</sup><sup>121(B)</sup>; always identify the syringes <sup>117(C)</sup> and systematically organize the drugs used in the anesthetic routine <sup>115(B)</sup><sup>118,119(C)</sup>.

These are actions that show recommendation evidence: drug double-checking by a second person <sup>115(B)</sup><sup>118(C)</sup>; sys-

tematic events review with erroneous administration of medication during anesthesia in the institution <sup>122(C)</sup>; technical drug manipulation focused on minimizing the possibility of erroneous administration <sup>118,122(C)</sup>; and avoiding handling drugs that have similar presentation <sup>115(B)</sup>.

These are actions that constitute possible recommendation evidence: use of available drugs in syringes instead of ampoules <sup>123(C)</sup><sup>124(B)</sup>; the preparation and identification of drugs should be made by the anesthesiologist who will administer the drug <sup>115(B)</sup>; use a coding color to identify the drug according to drug class in line with national or international standard recommendations <sup>115(B)</sup><sup>118(C)</sup>.

There are proposals for practical routines in order to avoid errors in administration of medication <sup>122(C)</sup>: detailed label reading of any medication prior to administration; periodic review of the label readability on the drug packaging or vials; routine identification of the syringes filled with drugs; systematization of a formal organization of the drugs routinely used; prefer pre-conditioned medication in labeled syringes if available at the institution and, when possible, ask for someone else to read the label of the drug.

The introduction of the infusion systems for pre-labeled, pre-filled syringes reduces the complexity of the drugs preparation by the anesthesiologist. It represents an important system in reducing the incidence of in the medications administration, reducing the reported errors incidence of up to seven times compared to the traditional preparation <sup>124(B)</sup>. However, it is still not a reality in Brazil when it comes to performing regional anesthesia.

There are essential and necessary elements to improve safety and prevent errors in drug administration <sup>125(D)</sup>: the development of a safety culture among team members; the logistical support to the team with encouragement to the description of adverse events that have occurred; integration between sectors (anesthesiology, pharmacy, risk management of the institution); encouragement to the detailed description of the facts by the professional involved and sharing safety lessons from team members.

It is recommended to describe the adverse events occurring in the institution without reservations. There is strong evidence of a direct relationship between the amount of reports to the risk management department and the reduction of medication errors.

In Brazil, the regulations on this topic refer to the ANVISA Resolution establishing criteria for the labels and tags SPPV (Small Volume Parenteral Solution). They are constituted by the collegiate resolutions DRC No. 9, January 2, 2001, replaced by the DRC No. 333, November 19, 2003, which had its article 2 repealed and replaced by another in the DRC No. 297, November 30 2004, by the date change to allow manufacturers to adequate to this standard. In 2009 the new resolution was published, the RDC 71 on Drug Labeling. Among the innovations incorporated in the DRC, one in particular was very well received by companies that own the brands of reference products. In accordance with Article 17, section V, it has been forbidden "to use labels with layout (box) similar to a drug with the same active ingredient, dosage form and con-

centration, previously registered by another company.” One hopes that this results in improvement in the identification of drugs and consequent increase in safety <sup>113,126</sup>(D).

**Recommendation:** Regional anesthesia is a practice that requires human skills and is, consequently, subject to errors. Adopting a safety routine is essential to prevent accidents during an anesthetic block. Among them are: detailed label reading of any medication prior to administration; periodic review of the label readability on the packaging or vials of drugs; identification of syringes filled with drugs; formal organization of the drugs routinely used; have the drugs double-checked by a second person; and if possible, using drugs pre-conditioned in labeled syringes <sup>115</sup>(B)<sup>116-118</sup>(C)<sup>121</sup>(B)<sup>119,120</sup>(C)<sup>124</sup>(B). The development of an institutional safety culture is essential, as well as the stimulus to a description of adverse events such as errors in medication administration <sup>125</sup>(D).

#### **Does the use of solutions in vials or bottles in sterile packaging for regional anesthesia seem to be safer?**

As an possible contamination evidence of local anesthetic solution in vials, 16 ampoules of lidocaine 1% were streaked with a swab of *S. epidermidis*; half of these ampoule bottle-necks (08) were subsequently cleaned with pre-packaged alcohol swabs, and all vials were opened in the supine position with sterile gauze. As a result, it was observed that none of the blisters treated with alcohol showed bacterial growth, 3 of 8 ampoules of lidocaine not cleaned with alcohol showed strong bacterial growth. It was also observed in this study, the cleaning of vials of lidocaine did not significantly reduce the contamination risk. It is argued that the contamination risk of solutions stored in vials at the moment of manipulation and opening is small, but should not be overlooked. Possible solutions to the contamination problem of solutions in the moment the ampoule is opened should include: changing the drugs packaging to a different form such as single-use vials sealed with rubber septum; cleaning the ampoules neck with alcohol before opening; or sterilization of the glass ampoules outer surface with subsequent sterile packaging, as it is already done with a few vials for epidural spinal anesthesia <sup>127</sup>(D).

Another study observed the effect of cleaning the bulb upper third with alcohol to reduce contamination of ampoules used for neuraxial anesthesia. Also observed was the use of filter-type device coupled to the reduction in needle aspiration of particles. One hundred vials of fentanyl and morphine (often used in regional anesthesia) were opened by a health professional wearing no gloves. There was no bacterial growth from swabs of ampoules cleaned with alcohol, while there was colony growth in 18% of the vials that were not clean. The authors suggested that cleaning the ampoule with alcohol before opening should be a routine in neuraxial anesthesia. However, the effectiveness of using specific filters connected to the syringe and needle to prevent bacterial contamination is less certain, since they prevent the aspiration of large uncontaminated particles <sup>128</sup>(D).

We studied the bacterial contamination in solutions of 30 fentanyl ampoules stored in non-sterile packaging. The study was done in the operating room environment, with proper handwashing and proper garment of the anesthesiologist. The vials were removed from the carton and opened by a health professional with bare hands or using non-sterile gloves. The vials contents were aspirated in three ways: through a needle filter of 5 µm only; aspirated with a needle filter of 5 µm after cleaning the vial neck with alcohol; and in the third group, the contents were aspirated through an antibacterial filter plus a needle filter of 5 µm. There was no contamination of the fentanyl solution, regardless the three extraction methods used <sup>129</sup>(D). However, it is suggested that opioid drugs manufacturers must provide the product in sterile packages, because the vials surface contamination is demonstrated, and this should act as an incentive for pharmaceutical companies from providing a more appropriate presentation of products used extensively by anesthesiologists.

**Recommendation:** We recommend that cleaning the glass ampoule neck with alcohol before opening should be part of the anesthesiologist's routine <sup>127,128</sup>(D). There is no hard evidence that the use of drugs from sterile packaging is critical in reducing the bacterial contamination risk of solutions used in regional anesthesia, although it is suggested that the use of such packaging provided by the pharmaceutical industry is a way to increase safety of regional anesthesia <sup>127-129</sup>(D).

#### **Is there cost-effectiveness in handling and preparation of sterile solutions for patient-controlled analgesia?**

In the acute postoperative pain treatment, the usual duration of therapy by catheters use is 2 to 5 days. Analgesic solutions are usually administered in the ward or intensive care setting at room temperature. The extension of the solution administered expiration time at room temperature can reduce or eliminate the system manipulation, especially the epidural system during therapy. This reduces the potential for contamination through circuit manipulation. Solutions with more extended expiration dates may also reduce the number of epidural solutions units dispensed to the patient. Therefore, waste and costs related to the preparation of solutions containing opioid analgesics and anesthetics are reduced.

In a study evaluating the cost-effectiveness of solutions for administration through an epidural catheter, all solutions were prepared in the pharmacy department, using aseptic technique and horizontal laminar airflow. Solutions containing opioid and/or local anesthetic at a low concentration were included in the study. A total of 54 units were prepared in polyethylene bags containing 0.9% saline solution. Some bags were stored at room temperature in the nursing sector, and others were examined after having being used in patients. The average evaluation of all solutions was 70 days. From 115 cultures prepared, 5 samples presented bacterial growth. No growth was reported in subsequent cultures, so the initial positive cultures have been attributed to contamination by handling

during sample collection, considering that most of the microorganisms identified corroborate this hypothesis. Based on these findings, it is recommended that, in mixtures of solutions prepared with opioids, local anesthetic/opioid or local anesthetic only, the system replacement and manipulation of the solutions should not be more frequent than every 72 hours. This is a clear pharmacoeconomic measure, especially for institutions that adopt this as a routine in the acute postoperative pain treatment <sup>130(D)</sup>.

In order to evaluate the viability of sterile solutions of local anesthetics and opioids used as continuous infusion for chronic pain treatment at home, solutions were stored in an environment of common household refrigerator. There was no bacterial growth in these solutions after 7 months from preparation. It is recommended for selected patients, outpatients and those in domiciliary follow up with indwelling epidural catheter, the use of solutions that have been prepared with sterile techniques and stored in standard household refrigerator for a period of up to 14 days <sup>131(C)</sup>.

Regarding compatibility between different solutions, a group studied morphine associated with ropivacaine, sufentanil, fentanyl and clonidine in a plastic bag of commercially available solutions of ropivacaine 2 mg.mL<sup>-1</sup>, 214 mL, which were re-diluted using the aseptic preparation standards with 0.9% saline solution to result in a 1 mg.mL<sup>-1</sup> solution <sup>132(D)</sup>. The new dilution was later associated with different concentrations of opioids and clonidine. These solutions were stored for 30 days at a temperature of 30°C and relative humidity of 40%. It was observed that combinations of ropivacaine 1-2 mg.mL<sup>-1</sup> with morphine sulfate 20-100 µg.mL<sup>-1</sup>, sufentanil 0.4-4 µg.mL<sup>-1</sup>, fentanyl 1-10 µg.mL<sup>-1</sup>, or clonidine 5-50 µg.mL<sup>-1</sup> are physically and chemically compatible and stable for 30 days after preparation when stored in plastic bags at 30°C <sup>133(D)</sup>.

Although not widely reported, the contamination of infusion solution can lead to devastating infectious complications in regional anesthesia. The adoption of handling practices that minimize contamination should be a priority for the anesthesiologist, especially when such components are infused in patients treated outside the hospital environment. Since the continuous infusion of several days is considered a medium risk, these infusates must be purchased as sterile prefabricated products, or be handled in accordance with USP-797 guidelines <sup>134(D)</sup>.

The anesthesiologist should be aware of the handling conditions of the institutional pharmacy, ensuring that it actually follows the recommendations of USP-797 guidelines <sup>134(D)</sup>.

Several recommendations can also be made regarding the duration of regional anesthetic infusion. Evidence suggests that when the mixture of local anesthetic or local anesthetic with opioids is prepared using sterile procedures, the microbiological stability is maintained for longer than 72 hours. There is evidence to suggest that the breaking of the infusate's sterile circuit in regional anesthesia increases the infection risk. That includes handling of connections via infusion or solution replacement. Duration of infusion up to 72 hours with no handling has been indicated. Nevertheless, additional studies are needed to determine the safety of infusions beyond 72 hours <sup>135(D)</sup>.

Levobupivacaine and sufentanil in syringes may be used for labor analgesia. Levobupivacaine combined with sufentanil and sodium chloride solutions reaching the concentration of 1 µg.mL<sup>-1</sup> sufentanil and a 1 mg.mL<sup>-1</sup> levobupivacaine should be stored in polypropylene syringes and protected from light for 30 days. Through the results of microbiology and chemical stability one can observe that it can be stored at a temperature of 4°C or 21°C, and should not be stored at 36°C because of the potential for bacterial growth <sup>136(D)</sup>.

The stability of the mixture of sufentanil, bupivacaine, and sodium chloride 0.9%, stored in a PVC bag leads to the observation that sufentanil citrate (500 µg) with levobupivacaine hydrochloride (625 mg) in sodium chloride solution 0.9% - 500 mL in PVC infusion bags may be prepared in advance by a specialized service, in sterile conditions and stored for 58 days at 4°C without major changes in the concentration of the product <sup>137(B)</sup>.

The stability of commercially available solutions containing bupivacaine 0.1% combined with fentanyl 2 µg.mL<sup>-1</sup> in PVC infusion bags with the addition of epinephrine (1 mg) shows that this solution is stable when stored at 4°C and 22°C for 184 days, being refrigeration the preferred storage conditions <sup>138(D)</sup>.

**Recommendation:** There is cost-effectiveness in the preparation of sterile solutions used in neuraxial analgesia <sup>130(D)</sup><sup>131(C)</sup>. It is recommended that solutions are prepared in a sterile environment <sup>134(D)</sup>. They can be stored at low temperatures (21°C or 4°C) for several days, with maintenance of physical and chemical characteristics and absence of bacterial contamination <sup>136(D)</sup><sup>137(B)</sup><sup>138(D)</sup>. The recommended time interval for replacing the analgesic prepared under sterile condition is up to 72 hours <sup>130,135(D)</sup>.