# Antiseptic Agents

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**Myth: For an epidural injection, Betadine® (povidone-iodine) is just as good a skin antiseptic as any of those modern expensive skin preps.**

**Fact: Properly applied chlorhexidine in alcohol (ChloraPrep™) is a superior skin antiseptic.**

Application of an antiseptic to the skin prior to spinal interventions is an important component of the broader topic of surgical site infection risk management [1]. Indeed, an effective skin antiseptic is only one of the required elements of a good aseptic technique. Although rare, three types of infections have been reported following routine epidural steroid injection: superficial skin injection-site infection, discitis, epidural abscess [2-5]. There are two topical solutions commonly utilized to disinfect clean intact skin: povidone-iodine (PVI) and chlorhexidine gluconate (CHG). Both are commercially available, as either an aqueous or alcohol-based solution.

PVI, CHG, and alcohol all have broad-spectrum antimicrobial coverage against gram- positive and gram-negative bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), fungi, virus, and mycobacterium tuberculosis. Effectiveness of these agents has not degraded over time. PVI works primarily through the release of free elemental iodine, which denatures microbial proteins and damages microbial DNA. CHG's mechanism of action is primarily through disruption of microbial cell membranes. Alcohol works through a combination of disruption of microbial cell membranes and denaturation of proteins. The addition of alcohol improves the antiseptic profile of both PVI and CHG. Compared to aqueous-based antiseptics, alcohol-based antiseptics have a broader antimicrobial coverage, a briefer application process, a more rapid onset of action, and a longer duration of action.

CHG 2% in alcohol 70% kills over 99.999% of the 23 most common bacterial skin flora in less than 3 minutes. No skin antiseptic can eliminate all microbes because some reside deep off the surface in glands. The most important safeguard is to ensure that any skin antiseptic used must be allowed to completely dry prior to initiating an intervention.

**Table 1**. Comparison of four common pre-procedural antiseptics used for clean intact skin:

| PREP<br>PVI=povidone-iodine<br>CHG=chlorhexidine | ANTIMICROBIAL SPECTRUM | SPEED OF ONSET | APPLICATION/ DRYING TIME | DURATION OF ACTION |
|---|---|---|---|---|
| **Betadine®**<br>**(PVI + aqueous)** | Broad | Minutes | 4 min/4-8 minutes | 2 hours |
| **Hibiclens®**<br>**(CHG + aqueous)** | Broad | Minutes | 4 min/4-8 minutes | 6 hours |
| **DuraPrep™**<br>**(PVI+ Alcohol)** | Broader<br>More gram - | 30 Seconds | 40 sec/180 seconds | 48 hours |
| **ChloraPrep™**<br>**(CHG + Alcohol)** | Broader<br>More gram - | 20 Seconds | 30 sec/30 seconds | 48 hours |

Optimal antimicrobial activity of all preps requires careful adherence to application instructions provided by the manufacturer. Alcohol-based surgical preps are flammable until fully dried and require vigilance [6].

Many laboratory and clinical studies have been conducted comparing the relative safety and effectiveness of the various antiseptic agents in reducing both laboratory determined bacterial colony counts as well as surgical site infections (SSI). Alcohol-based skin preps are superior to aqueous-based preps in all measures. There is abundant evidence validating the superiority of CHG in alcohol over all other preparations [7-31]. Several systematic reviews and meta-analysis yield consistent results that the lowest risk of SSI follows the use of Chloraprep (CHG 2% in alcohol 70%), and the reduction of infectious complications is in the order of 30% [32-41]. Use of 70% alcohol, by itself, has not been adequately studied as a pre-procedural skin antiseptic, but compared to Betadine Paint: it possesses broader antimicrobial spectrum, is quick to apply, has a rapid onset, is not messy, and is the least expensive [42]. Adverse events such as skin irritation, erythema, and pruritus attributed to CHG and PVI are uncommon and are comparable [11,15,18,29].

Several medical societies have endorsed the routine use of ChloraPrepTM specifically for spinal injections as the first choice for a skin antiseptic. The Spine Intervention Society's (SIS) *Practice Guidelines for Spinal Diagnostic and Treatment Procedures* (Second Edition) and The American Society of Regional Anesthesia and Pain Management (ASRA) endorse ChloraPrep™ as the preferred skin disinfectant [43, 44]. The CDC Guideline for the Prevention of Surgical Site Infection (2017), as well as, the WHO Global Guidelines for the Prevention of SSI recommends the use of chlorhexidine in alcohol for skin antisepsis because of its superior effectiveness and speed of application [1, 45]. Preoperative skin antisepsis with chlorhexidine in alcohol is not only more effective than preoperative skin antisepsis with iodine formulations for preventing SSI, it also results in cost savings [45].

Concerns over toxicity of chlorhexidine are based upon two reports on the effect of injection of large amounts of CHG directly into the cerebrospinal fluid in monkeys (1955) and into the anterior chamber of the eye in rats (1984), which resulted in neuronal damage [46, 47]. After 30 years of extensive clinical use, there are no reports of chlorhexidine causing nerve damage in humans and the incidence of neurologic complications following neuraxial blockade utilizing ChloraPrep™ is no different than that of Betadine® [48]. Anything which kills bacteria such as CHG, PVI, and alcohol is potentially harmful to neural structures.

## Recommendations

1. Chlorhexidine 2% in isopropyl alcohol 70% (ChloraPrep™) is the preferred choice for topical antisepsis of clean intact skin prior to spinal interventions.
2. Povidone-iodine in alcohol (DuraPrep™) is a reasonable alternative to ChloraPrepTM for patients sensitive to CHG.
3. Aqueous-based skin preps are proven to be less efficacious than alcohol-based preps.
4. Directions for using Chloraprep should be carefully followed, particularly: systematically paint the area for 30 seconds (not scrub), avoid solution pooling, allow time for complete drying.

## References

1. Berreios-Torres SI, Umscheid CA, et al. Center for Disease Control and Prevention guideline for the prevention of surgical site infection. JAMA Surg 2017;152(8):784-91.
2. Darouiche RO. Spinal epidural abscess. N Engl J Med 2006;355:2012-20.
3. Davis DP, Salazar A, Chan TC, Vilke GM. Prospective evaluation of a clinical decision guideline to diagnose spinal epidural abscess in patients who present to the emergency department with spine pain. J Neurosurg Spine 2011;14:765-70.
4. Hamda H, Russell P, Peterson S. Epidural abscesses following chronic pain injections. Ind J Pain 2015;29(1):46-51.
5. Hooten W, Michael L, et al. Discitis after lumbar epidural corticosteroid injection: A case report an analysis of the case report literature. Pain Medicine 2006;7(1):46-51.
6. Cowles CE, Chang JL, et al. Flammable surgical preps require vigilance. Anesthesia Patient Safety Foundation Newsletter 2014;29(2):25-40.
7. Hakkarainen TW, Dellinger EP, et al. Comparative effectiveness of skin antiseptic agents in reducing surgical site infections: A report from the Washington state surgical care and outcomes assessment program. J Am Coll Surg 2014;218(3):336-44.
8. Park HM, Han SS, et al. Randomized clinical trial of preoperative skin antisepsis with chlorhexidine gluconate or povidone-iodine. Br J Surg 2017;104(2):145-50.
9. Charehbili A, Swijnenburg RJ, et al. A retrospective analysis of surgical site infections after chlorhexidine-alcohol versus iodine-alcohol for pre-operative antisepsis. Surg Infect 2014;15(3):310-13.
10. Kaoutzanis C, Kavanagh CM, et al. Chlorhexidine with isopropyl alcohol versus iodine povacrylex with isopropyl alcohol and alcohol- versus nonalcohol-based skin preparations: The incidence of and readmissions for surgical site infections after colorectal operations. Dis Colon Rectum 2015;58(6):588-96.

11. Tuuli MG, Liu J, et al. A randomized trial comparing skin antiseptic agents at cesarean delivery. N Engl J Med 2016;374(7):647-55.
12. Florenzano FH, Juliano Y, Ferreira LM. Povidone iodine versus chlorhexidine in skin antisepsis before elective plastic surgery procedures: A randomized controlled trial. Plast Reconstr Surg 2008;122(5):170-71.
13. Berry AR, Watt B, et al. A comparison of the use of povidone-iodine and chlorhexidine in the prophylaxis of post- operative wound infection. J Hosp Infect 1982;3(1):55-63.
14. Brown TR, Ehrlich CE, et al. A clinical evaluation of chlorhexidine gluconate spray as compared with iodophor scrub for preoperative skin preparation. Surg Gynecol Obstet 1984;158(4):363-66.
15. Paocharoen V, Mingmalairak C, Apisarnthanarak A. Comparison of surgical wound infection after preoperative skin preparation with 4% chlorhexidine and povidone iodine: A prospective randomized trial. J Med Assoc Thai 2009;92(7):898-92.
16. Sistla SC, Prabhu G, et al. Minimizing wound contamination in a 'clean' surgery: Comparison of chlorhexidine-ethanol and povidone- iodine. Chemotherapy 2010;56(4):261-67.
17. Rodrigues AL, Simoes ML. Incidence of surgical site infection with pre- operative skin preparation using 10% polyvidone-iodine and 0.5% chlorhexidine-alcohol. Rev Col Bras Cir 2013;40(6):443-48.
18. Abreu D, Campos E, et al. Surgical site infection in surgery for benign prostatic hyperplasia: comparison of two skin antiseptics and risk factors. Surg Infect 2015;15(6):763-67.
19. Bibi S, Shah SA, et al. Is chlorhexidine-gluconate superior than povidone-iodine in preventing surgical site infections? A multicenter study. J Pak Med Assoc 2015;65(11):1197-201.
20. Kunkle CM, Marchan J, et al. Chlorhexidine gluconate versus povidone iodine at cesarean delivery: A randomized controlled trial. J Matern Fetal Neonatal Med 2015;28(5):573-77.
21. Ngai IM, Van Arsdale A, et al. Skin preparation for prevention of surgical site infection after cesarean delivery: A randomized controlled trial. Obstet Gynecol 2015;126(6):1251-57.
22. Srinivas A, Kaman L, et al. Comparison of the efficacy of chlorhexidine gluconate versus povidone iodine as preoperative skin preparation for the prevention of surgical site infections in clean-contaminated upper abdominal surgeries. Surg Today 2015;45(11):1378-84.
23. Hannan MM, O'Sullivan KE, et al. The combined impact of surgical team education and chlorhexidine 2% alcohol on the reduction of surgical site infection following cardiac surgery. Surg Infect 2015;16(6):799-805.
24. Casey A, Itrakjy A, et al. A comparison of the efficacy of 70% v/v isopropyl alcohol with either 0.5% w/v or 2% w/v chlorhexidine gluconate for skin preparation before harvest of the long saphenous vein used in coronary artery bypass grafting. Am J Infect Control 2015;43(8):816-20.
25. Davies BM, Patel HC. Does chlorhexidine and povidone-iodine preoperative antisepsis reduce surgical site infection in cranial neurosurgery? Ann R Coll Surg Engl 2016;98(6):405-8 .
26. Yasuda H, Sanui M, et al. Comparison of the efficacy of three topical antiseptic solutions for the prevention of catheter colonization: a multicenter randomized controlled study. Crit Care 2017;1:320.
27. Savage JW, Weatherford BM, et al. Efficacy of surgical prep solution in lumbar spinal surgery. JBJS 2013;94(6):90-94.
28. Swenson BR, Hedrick TL, et al. Effects of preoperative skin preparation on postoperative wound infection rates: A prospective study of 3 skin prep products. Infect Control Hosp Epidemol 2009;30:964-971.
29. Crowley L, Preston R, Wong A, Book L, Kuzeljevic B. What is the best skin disinfectant solution for labor epidural analgesia? A randomized prospective trial comparing ChloraPrep™, DuraPrep™, and Chlorhexidine 0.5% in 70% alcohol. Anesthesia & Analgesia 2008;106:A-3.
30. Darouiche RO, Wall MJ, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. New Engl J Med 2010;362:18-26.
31. Birnbach DJ, Medows W et al. Comparison of povidone iodine and Duraprep an iodophore-in-isopropyl alcohol solution for skin disinfectant prior to epidural catheter insertion in parturients. Anesthesiology 2003;98:164-169.
32. Lee I, Agarwal RK, et al. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. Infect Control Hosp Epidemiol 2010;31(12):10.
33. Ayoub F, Quirke M, et al. Chlorhexidine-alcohol verses povidone-iodine for pre-operative skin preparation: A systematic review and meta-analysis. International Journal of Surgery Open 2015;1:41-46.
34. Lai NM, Lai NA, et al. Skin antisepsis for reducing central venous catheter-related infections. Cochrane Database Syst Rev. Jul 13;7:CD010140
35. Yasuda H, Sanui M, et al. Comparison of the efficacy of three topical antiseptic solutions for the prevention of catheter colonization: a multicenter randomized controlled study. Crit Care 2017;21(1):320.
36. Privitera GP, Costa AL, et al. Skin antisepsis with chlorhexidine verses iodine for the prevention of surgical site infection: A systematic review and meta-analysis. American Journal of Infection Control 2017;45(2):180-189.
37. Zhang D, Wang XC, et al. Preoperative chlorhexidine verses povidone-iodine antisepsis for preventing surgical site infection: A meta-analysis and trial sequential analysis of randomized controlled trials. Int J Surg 2017;44:176-184.
38. Hemani ML, Lepor IT. Skin preparation for the prevention of surgical site infection: which agent is best? Rev Urol 2009;11(4):190-198.
39. Sidhwa F, Itani KM. Skin preparation before surgery: options and evidence. Surg Infect 2015;16(1):14-23.

40. Cook TM, Fischer B, et al. Antiseptic solutions for central neuraxial blockade: Which concentration of chlorhexidine in alcohol should we use? Correspondence Brit J Anesth;103(3):456-62.
41. Dumville JC, McFarlane E, et al. Preoperative skin antiseptics for preventing wound infections after clean surgery. Cochrane Database Syst Rev. 2015;21(4).
42. Maiwald M, Chan ES-Y. The forgotten role of alcohol: A systematic review and meta-analysis of the clinical efficacy and perceived role of chlorhexidine in skin antisepsis. PLoS ONE 2012;7(9).
43. Bogduk N (ed). Practice Guidelines for Spinal Diagnostic and Treatment Procedures. International Spine Intervention Society 2nd Edition San Francisco, 2013.
44. Hebl JR. The importance and implications of aseptic techniques during regional anesthesia. Reg Anesth Pain Med 2006;31:311-23.
45. WHO Surgical Site Infection Prevention Guidelines www.who.org Web Appendix 8 Summary of a systematic literature review on surgical site preparation.
46. Weston-Hurst E. Adhesive arachnoiditis and vascular blockage caused by detergents and other chemical irritants: An experimental study. J Pathol Bact 1955;38:167-78.
47. Henschen A, Olsen L. Chlorhexidine-induced degeneration of adrenergic nerves. Acta Neuropathol 1984;63:18-23.
48. Sviggum HP, Arendt KW, Jacob AK, Mauermann ML, Horlocker TT. The risk of neurologic complications following chlorhexidine antisepsis for spinal anesthesia. Regional Anesthesia and Pain Medicine. Conference: 36th Annual Regional Anesthesia Meeting and Workshops, ASRA 2011 Las Vegas, NV United States. Conference Publication: (var.pagings). 36 (5), 2011.