3. School Board of Nassau County v Arline, 480 US 273 (1987).
4. Centers for Disease Control and Prevention (CDC). Recommendations for preventing transmission of human immunodeficiency virus and hepatitis B virus to patients during exposure-prone invasive procedures. *MMWR Morb Mortal Wkly Rep* 1991;40(RR-8):1–9.
5. Turkel S, Henderson DK. Strategies for managing providers infected with bloodborne pathogens. In: *Programs and abstracts of the Fifth Decennial International Conference on Healthcare-Associated Infections.* Arlington, VA: Society for Healthcare Epidemiology of America, 2010. Abstract 684.
6. UK Department of Health, UK Expert Advisory Group on AIDS. *AIDS/HIV-infected health care workers: guidance on the management of infected health care workers.* Heywood Lancashire, England: UK Department of Health, 1994.
7. Reitsma AM, Closen ML, Cunningham M, et al. Infected physicians and invasive procedures: safe practice management. *Clin Infect Dis* 2005;40(11):1665–1672.
8. Tuboku-Metzger J, Chiarello L, Sinkowitz-Cochran RL, Casano-Dickerson A, Cardo D. Public attitudes and opinions toward physicians and dentists infected with bloodborne viruses: results of a national survey. *Am J Infect Control* 2005;33(5):299–303.
9. Sadoh AE, Sadoh WE, Fawole AO, Oladimeji A, Sotiloye O. Attitude of health care workers to patients and colleagues infected with human immunodeficiency virus. *SAHARA J* 2009;6(1):17–23.

Chlorhexidine Is Not the Main Active Ingredient in Skin Antiseptics That Reduce Blood Culture Contamination Rates

To the Editor—We read with great interest the article by Marlowe et al[1] describing a significant reduction in rates of pediatric blood culture contamination after implementation of skin antisepsis with 70% isopropanol plus 3.15% chlorhexidine, compared with 10% aqueous povidone-iodine. We would like to congratulate the authors on the achievement of this landmark study with a very large number of participants and blood cultures investigated.

However, we would like to raise the point that interpretation of the results by the authors contains a likely error in the attribution of the positive effects observed. In the title and abstract and throughout the text, the authors describe this as a study of chlorhexidine versus povidone-iodine and—by implication—attribute the positive effects to the chlorhexidine component. However, the solutions used were 70% isopropanol with 3.15% chlorhexidine and 10% aqueous povidone-iodine. The first solution has 2 active ingredients, and the second has only 1. The differential antimicrobial activity of these compounds has been a topic of intense research and evaluation since the 1970s and is well described in standard textbooks on antisepsis and infection control.[2-4] If chlorhexidine or povidone-iodine in aqueous solutions is compared with various alcohols, it turns out that the immediate antimicrobial activity (ie, the capacity to act as a disinfectant) of standard alcohol compounds is significantly greater than that of the other agents if they are used in an aqueous solution. The difference between alcoholic and aqueous hand and skin antiseptics is typically approximately 1 log, or a 10-fold difference in favor of the alcohols. Furthermore, overview tables on the differential activity of skin antiseptics have been published in the Centers for Disease Control guidelines on the prevention of surgical site infections[5] and in the World Health Organization guidelines on hand hygiene in health care.[6] According to this information, alcohols are the most rapid acting skin antiseptics, whereas both chlorhexidine and povidone-iodine only have intermediate speed of action. However, alcohols lack any residual activity, whereas chlorhexidine appears to exert such an effect. This is also well illustrated by a comparative experiment on surgical hand antisepsis as published in a textbook chapter.4 The results and associated figure indicate that 70% isopropanol generates an immediate reduction of resident hand flora of approximately 2.5 log, aqueous 10% povidone-iodine generates a reduction of approximately 1.8 log, and 4% aqueous chlorhexidine generates a reduction of approximately 0.8 log. The immediate microbial reduction achieved by both aqueous agents is significantly less than that of 70% isopropanol, and that caused by a 70% isopropanol plus 0.5% chlorhexidine mix is almost the same as of pure isopropanol. However, when a second time point of 180 minutes under surgical gloves is examined, it becomes apparent that there is bacterial regrowth after use of pure isopropanol, whereas continued microbial suppression occurs with use of the mix. These results indicate that there is almost no contribution from chlorhexidine to the immediate kill caused by isopropanol, and the benefit from such a mix is that of immediate plus sustained action. Similar results concerning immediate and sustained action of alcohols alone versus alcohol plus chlorhexidine were also obtained in a more recent study of antisepsis at various other skin sites.[7]

Mixtures of alcohol and chlorhexidine have benefits if both immediate and sustained action are required; examples include use for surgical skin antisepsis, with sustained action under surgical drapes; for surgical hand antisepsis under the gloves; and at the sites of vascular catheter insertion.[4,8,9] The biological principles underlying blood culture collection are different. Culture samples are obtained immediately after antisepsis and after observing the appropriate contact time of the antiseptic on skin. As opposed to the other applications mentioned above, there is no requirement for sustained action at the site of blood culture collection. Arguably, the positive effect observed in this landmark study by Marlowe et all is more likely to be derived from the action of the isopropanol component than from the chlorhexidine component. In conclusion, alcohol is likely the key component in the immediate disinfection process, and the impact of chlorhexidine would require further investigation.

ACKNOWLEDGMENTS

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

Matthias Maiwald, MD, PhD; Andreas F. Widmer, MD, MS; Manfred L. Rotter, MD, DipBact

From the Department of Pathology and Laboratory Medicine, KK Women's and Children's Hospital, Singapore (M.M.); the Division of Infectious Diseases and Hospital Epidemiology, University of Basel Hospitals, Basel, Switzerland (A.F.W.); and the Institute of Hygiene and Applied Immunology, Medical University of Vienna, Vienna, Austria (M.L.R.).

Address reprint requests to Matthias Maiwald, MD, PhD, Department of Pathology and Laboratory Medicine, KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore 229899, Singapore (matthias.maiwald@kkh.com.sg).

Infect Control Hosp Epidemiol 2010; 31(10):1095-1096

 0899-823X/2010/3110-0023$15.00. DOI: 10.1086/656561

REFERENCES

1. Marlowe L, Mistry RD, Coffin S, et al. Blood culture contamination rates after skin antisepsis with chlorhexidine gluconate versus povidone-iodine in a pediatric emergency department. *Infect Control Hosp Epidemiol* 2010; 31:171–176.
2. Gröschel DHM, Pruett TL. Surgical antisepsis. In: Block SS, ed. *Disinfection, Sterilization and Preservation.* 4th ed. Philadelphia: Lea and Febiger; 1991:642–654.
3. Rotter ML. Hand washing, hand disinfection, and skin disinfection. In: Wenzel RP, ed. *Prevention and Control of Nosocomial Infections.* 3rd ed. Baltimore: Williams and Wilkins; 1997:691–709.
4. Rotter ML. Hand washing and hand disinfection. In: Mayhall CG, ed. *Hospital Epidemiology and Infection Control.* 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 2004:1727–1746.
5. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR; Hospital Infection Control Practices Advisory Committee. Guideline for prevention of surgical site infection, 1999. *Infect Control Hosp Epidemiol* 1999;20:250–278.
6. World Health Organization. *WHO Guidelines on Hand Hygiene in Health Care.* Geneva: World Health Organization; 2009.
7. Reichel M, Heisig P, Kohlmann T, Kampf G. Alcohols for skin antisepsis at clinically relevant skin sites. *Antimicrob Agents Chemother* 2009;53:4778–4782.
8. Darouiche RO, Wall MJ Jr, Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med* 2010;362:18–26.
9. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med* 2002;136:792–801.

Reply to Maiwald et al

To the Editor—We thank Maiwald et al[1] for their interest in the findings of our study,[2] which found improved skin antisepsis associated with chlorhexidine-isopropanol, compared with aqueous povidine-iodine solution. Maiwald and colleagues raise an important fact in their letter with respect to the active antiseptic ingredient in the 3.15% chlorhexidine–70% isopropanol preparation. We certainly do not mean to attribute the effectiveness of the chlorhexidine-isopropanol preparation to the incorrect component. Although their assertion that the isopropanol component is the "main" active ingredient is plausible, the established literature surrounding this claim is far from conclusive.

Several studies, including one randomized clinical trial,[3] comparing alcohol-based and aqueous iodine skin antiseptics prior to blood culture have shown equivalent rates of blood culture contamination,[4-6] refuting the claim that alcohol is a more active agent than aqueous iodine for skin antisepsis. Unfortunately, we were unable to locate studies that have directly compared the effectiveness of chlorhexidine alone with the effectiveness of isopropanol or alcohol-based solution alone. In addition, the possible additive or potentiating effect on skin antisepsis from both components, chlorhexidine and isopropanol, must be considered. Moreover, although the procedures of antisepsis and venipuncture for blood culture often occur within a very short period of time, there are many occasions when a procedure—from needle insertion to the collection of an adequate blood sample—can be delayed, thus potentially favoring the utility and sustained action of the chlorhexidine component. This is particularly true for young children, who comprised the study population in our investigation.

We respect the opinions of Maiwald et al[1]; however, our primary finding that use of chlorhexidine-isopropanol is associated with reduced blood culture contamination rates for pediatric patients still holds true, irrespective of the debate regarding the active component in this antiseptic preparation.

ACKNOWLEDGMENTS

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

Rakesh D. Mistry, MD, MS; Lauren Marlowe, MD; Theoklis E. Zaoutis, MD, MSCE

From the Divisions of Emergency Medicine (R.D.M.), General Pediatrics (L.M.), and Infectious Diseases (T.E.Z.), Department of Pediatrics, Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

Address reprint requests to Rakesh D. Mistry, MD, MS, Division of Emergency Medicine, Department of Pediatrics, Children's Hospital of Philadelphia, 34th and Civic Center Boulevard, Philadelphia, PA 19104.

Infect Control Hosp Epidemiol 2010; 31(10):1096-1097

 0899-823X/2010/3110-0024$15.00. DOI: 10.1086/656562

REFERENCES

1. Maiwald M, Widmer AF, Rotter ML. Chlorhexidine is not the main active ingredient in skin antiseptics that reduce blood culture contamination rates [letter]. *Infect Control Hosp Epidemiol* 2010;31(10):1095–1096 (in this issue).
2. Marlowe L, Mistry RD, Coffin S, et al. Blood culture contamination rates after skin antisepsis with chlorhexidine gluconate versus povidone-iodine in a pediatric emergency department. *Infect Control Hosp Epidemiol* 2010;31(2):171–176.