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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 al¹ describing a significant reduction in rates of pediatric blood culture contamination after implementation of skin antiseptics 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 antiseptics 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 infections⁵ 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 antiseptics 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 antiseptics, with sustained action under surgical drapes; for surgical hand antiseptics 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 antiseptics 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 al 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.

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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).

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Reply to Maiwald et al

To the Editor—We thank Maiwald et al¹ for their interest in the findings of our study,² which found improved skin antiseptics associated with chlorhexidine-isopropanol, compared with aqueous povidone-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 antiseptics. 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 antiseptics from both components, chlorhexidine and isopropanol, must be considered. Moreover, although the procedures of antiseptics 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 al¹; 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.

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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.

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