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Role of antimicrobial applications to the umbilical cord in neonates to prevent bacterial colonization and infection: a review of the evidence

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Abstract

In developing countries umbilical cord infections constitute a major cause of neonatal morbidity and pose significant risk for mortality, whereas outbreaks of cord infections continue to occur in developed country nurseries. Cord infections in developing countries can be prevented through increasing access to tetanus toxoid immunization during pregnancy, promoting clean cord care and reducing harmful cord applications and behaviors. Interventions introduced in both developed and developing countries to reduce exposure of the cord to infectious pathogens include clean cord cutting, hand-washing before and after handling the baby, bathing of the infant with antimicrobial agents and application of antimicrobials to the cord. Despite the importance of umbilical cord care, both traditionally and medically, there have been few randomized trials investigating the impact of different cord care regimens on rates of local or systemic infections, particularly in developing countries.

This review examines available data on umbilical cord care, with a particular focus on those comparing rates of bacterial colonization and/or rates of cord infection among neonates receiving different umbilical cord care regimens. Although most investigators agree that topical antimicrobials reduce bacterial colonization of the cord, a firm relationship between colonization and infection has not been established. Further research in developed countries, including follow-up beyond hospital discharge, is required before advising on “best cord care practices.” The paucity of published reports from developing countries indicates the need to investigate the impact of antimicrobial applications on cord and systemic infections in a community-based, prospective manner.

Keywords

Omphalitis; neonatal mortality; umbilical cord care; bacterial infections; tetanus; neonatal sepsis; antimicrobials; colonization

INTRODUCTION

The World Health Organization (WHO) estimates that ~4 million children die during the neonatal period each year, with most deaths occurring in developing countries.^{1, 2} Infections are the single most important cause of neonatal mortality. It is estimated that 300 000 infants die annually from tetanus, and a further 460 000 die because of severe bacterial infections, of which umbilical cord infections are an important precursor.^{1, 3, 4} Although increasing access to tetanus toxoid immunization during pregnancy must remain a priority, high rates of umbilical

cord infection and sepsis can occur in areas free of tetanus, attributable to unhygienic delivery or immediate postpartum care practices that lead to contamination of the umbilical stump.⁵

Despite the importance of umbilical cord care, there have been few randomized trials investigating the impact of different cord care regimens on cord infection rates. Many investigators have reported the role of antimicrobials in halting hospital nursery outbreaks or have compared rates of bacterial colonization of the cord, time to cord separation and/or maternal satisfaction with protocols between groups of infants receiving various cord care regimens. Data regarding the role of umbilical cord applications in preventing local or systemic infection in neonates, however, are lacking.

A Cochrane review limited to randomized trials identified just 10 studies, all from developed countries.⁶ None of the studies reported any systemic infections or deaths among subjects, and only two of the studies routinely followed infants beyond hospital discharge.^{7, 8} Thus local or systemic bacterial infections arising subsequent to discharge could not be assessed in most studies. The authors presented data from two studies in a combined analysis of risk of cord infection comparing antiseptic application to no application.^{7, 9} The homogeneity of these studies, however, and thus the validity of the conclusions reached on the basis of this analysis are questionable. Although concluding that bacterial colonization could be reduced with antimicrobial applications, the review did not find any evidence that antimicrobials are superior to dry care only in reducing infection.

The conclusions and recommendations of the Cochrane review provide little direction for decision-makers in developing country populations where the prevalence of cord infection is markedly higher than among developed country populations. This review extends discussion beyond developed country hospital-based randomized trials to a broader range of investigations on cord colonization and infection conducted in both developed and developing countries. In doing so we highlight the need for evidence to guide policy making in developing country settings, rather than extrapolating from results from developed countries.

The electronic database Medline was searched on terms including “omphalitis,” “umbilical cord care,” “umbilical infections,” “bacterial infections,” “tetanus,” “neonatal sepsis,” “triple-dye,” “chlorhexidine,” “antimicrobials” and “bacterial colonization.” English language studies from both developing and developed country settings were included in the initial review if umbilical cord care regimens were compared, and/or bacterial colonization of the cord or umbilical cord infections were assessed.

DEVELOPED COUNTRY STUDIES

Umbilical cord colonization studies

Many studies have compared various umbilical cord care regimens for their impact on colonization and subsequent infection (Table 1). In a controlled trial comparing triple dye, hexachlorophene and no specific cord care, triple dye was superior to hexachlorophene in reducing colonization of the cord with group B *Streptococcus* (GBS).¹⁰ Although a single application of triple dye effectively reduced rates of staphylococcal colonization of the cord, growth of GBS and Gram-negative organisms was promoted.¹¹ This GBS promotion was halted, however, with daily applications of triple dye to the cord.¹² A comparison of daily applications of 0.33% hexachlorophene powder or 1% chlorhexidine to the cord during the first week of life revealed equal effectiveness in preventing *Staphylococcus aureus* colonization, but coagulase-negative staphylococci proliferated.¹³ A randomized clinical trial of three daily umbilical cord regimens (benzene, 0.05% chlorhexidine or 4.0% chlorhexidine) demonstrated significant reductions in colonization with *S. aureus* (35%), *Escherichia coli* (41%) and GBS (50%) in the 4.0% chlorhexidine group.⁷ The superiority of 4.0%

chlorhexidine in detergent vs. 0.5% chlorhexidine in ethanol, demonstrated in a pre-post comparison of cord colonization rates, was possibly the result of the increased binding efficiency of the detergent form to the umbilical tissues, resulting in an increased residual effect.¹⁴ In a retrospective nursery audit of bacterial colonization and infections before and after switching from triple dye to alcohol and back to triple dye, both colonization and infections of the umbilical cord were significantly decreased by triple dye applications.¹⁵ A comparison of daily applications of 4.0% chlorhexidine or 10% povidone-iodine demonstrated the superiority of chlorhexidine in controlling cord colonization with group A *Streptococcus* and *S. aureus*.¹⁶

A randomized trial of six umbilical cord antiseptic regimens, including combinations of triple dye, alcohol, bacitracin, povidone-iodine and silver sulfadiazine applied daily or once at birth showed no difference in colonization rates with a variety of Gram-negative and Gram-positive bacteria.¹⁷ A chlorhexidine care group was not included in the study. This study is widely cited as evidence for lack of superiority between different regimens, yet the sample size used was insufficient (group size ranged from 14 to 53 infants) to detect significant differences. Statistical power was inadequate to detect even 60% differences in colonization rates of *Staphylococcus epidermidis* with colonization prevalence rates of up to 50% of infants. Additionally there was no group that received clean cord care alone, without application of antiseptics, and overall colonization rates of important potential pathogens such as *S. aureus*, *E. coli* and *Klebsiella* spp. were at such low levels as to prevent detection of even 90% differences in colonization prevalence among regimens.

In another study 100 neonates were randomized to either no cord care or hexachlorophene applied daily to the umbilical stump; staphylococcal colonization was considerably higher [odds ratio (OR), 1.75; 95% confidence interval (CI), 1.08, 2.85] among those not treated.¹⁸

In a recent study infants were allocated to either triple dye application on the day of birth plus twice daily alcohol applications to the cord stump until cord separation or dry care only, consisting of soap and water cleansing of soiled periumbilical skin.²⁰ Cord stumps of all infants were cultured, and community health nurses conducted postdischarge home visits to record signs of infection. Among infants receiving dry care only, bacterial colonization was significantly higher (*E. coli*, 34.2% vs. 22.1%; coagulase-negative staphylococci, 69.5% vs. 50.5%; GBS, 11.7% vs. 6.0%), particularly with *S. aureus*, (31.3% vs. 2.8%). Whereas nurses recorded significantly more exudate and foul odor among infants in the dry cord group, the overall cord infection rates were very low; only one infant, who was in the dry care group, was diagnosed with omphalitis.

Given the wide variation in treatment protocols, small sample sizes and inconsistent comparisons among different regimens, firm recommendations regarding best cord care practices cannot be made at present. Nevertheless, based on evidence of increased time to cord separation and the lack of an established relationship between colonization and infection, some neonatal skin care reviews have argued for the discontinuation of topical antiseptics.^{13, 21, 22} However, when antiseptics have been removed from routine cord care for neonates, increased colonization and infection rates have been reported.^{15, 23} The Cochrane review concluded that cord antisepsis reduced the odds of *S. aureus* colonization relative to no treatment (OR = 0.28; 95% CI 0.22, 0.36).⁶ Although unable to state that the use of antimicrobials also reduced the risk of infection relative to no treatment, the authors concluded, “there appears to be no good reason to stop the use of antiseptics in situations where the risk of bacterial infections remains high.” In light of available data, the impact of current trends in nurseries in the US to rely on dry cord care, without use of antiseptics, must be carefully evaluated.

Umbilical cord infection studies

A number of studies have included infection as an outcome, rather than colonization alone, and are summarized in Table 2. Considering the two studies of cord infections that were included in the Cochrane infection metaanalysis, Dore et al.⁹ gave newborns an initial bath only and compared three times daily applications of 70% isopropyl alcohol with natural drying, whereas Meberg and Schoyen⁷ gave daily soap-and-water baths and compared daily applications of 4.0% chlorhexidine with natural drying. The Dore study excluded babies who spent any time in the neonatal nursery, whereas in the Meberg study the same nursery attendants cared for all babies of both groups. Thus these studies differed significantly in design, and the validity of pooling data from them to draw general conclusions about impact of cord antisepsis may be questioned. Meberg and Schoyen⁷ found that 6 of 111 (5.4%) babies receiving natural drying had cord infection before discharge, whereas 2 of 105 (2.0%) were similarly diagnosed in the 4.0% chlorhexidine group (relative risk, 2.83; 95% CI 0.59, 13.75). The study was too small to provide an accurate estimate of the comparison. Infants in the Dore study were discharged from the hospital at a mean of 48 h after delivery, and postdischarge infection status was ascertained through self-reporting of events in a follow-up telephone interview conducted 2 to 3 weeks after discharge. With >1800 infants in the study, zero cases of infection were reported in either group.⁹ The combination of these studies helps little in understanding the relationship between topical applications and infection and leaves the question open to further investigation.

Other studies not included in the Cochrane review provide further information about the role of antimicrobials in reducing the risk of cord infection. After institution of daily application of 4.0% chlorhexidine in two Swedish hospitals, the 6-week rate of *S. aureus* pyoderma was reduced from 15.2% to 2.0% (relative risk, 0.13; 95% CI 0.09, 0.19), and a significant decrease (9.6% vs. 0.6%) was noted in the proportion of infants colonized with GBS at discharge.⁸ Another Swedish study demonstrated reductions in neonatal prevalence of pyoderma (58% reduction), paronychia (46% reduction) and omphalitis (100% reduction) in infants receiving 4.0% chlorhexidine compared with 70% ethanol.¹⁴ Similarly rates of superficial infections (sites included skin, conjunctivae and umbilical cord) were significantly lower among neonates receiving 4.0% chlorhexidine (21%) than among those receiving 10% Iodosan (38%).¹⁶ In a cross-sectional study of 370 live born infants receiving no specific cord care, higher levels of *S. aureus* umbilical cord colonization were associated with increased occurrence of skin pustules, omphalitis, "septic spots," and eye infections,²⁴ and significantly lower *S. aureus* colonization rates were found among babies randomized to receive 4.0% chlorhexidine than in babies receiving hexachlorophene or no specific cord care.¹⁹ These two studies from the same ward provide some evidence of a dose-response relationship between colonization and infection and indicate that chlorhexidine is effective in removing this risk factor. Moreover the dose of chlorhexidine may be important in producing an effect, because each of these studies utilized a relatively high concentration (4.0%).

Other studies have not demonstrated a decrease in infection attributable to cord antisepsis, but the lack of impact appears to be caused, at least in part, by faulty study design and inadequate concentrations of antimicrobial, because none used chlorhexidine at concentrations above 0.5%. In one study there was no evidence that umbilical infection rates differed among babies randomized to receive daily applications of 0.5% chlorhexidine in ethanol compared with those receiving dry cord care only (hydrophobic gauze).²⁵ Another trial of no cord care vs. daily 0.05% chlorhexidine application reported no difference in infection rates; babies in both groups received a daily full body wash with soap and were cared for together by the same nursery attendants.⁷ After increasing the concentration of chlorhexidine to 4.0% however, the 6-week infection rate was 13% lower in the intervention group, although the result did not reach statistical significance. Elsewhere, comparing *S. aureus*-colonized and noncolonized neonates,

there was a 75% increased risk of infection among colonized compared with noncolonized infants, but this result was also not statistically significant (OR 1.75; 95% CI 0.51, 5.22).²⁶ In other studies in which omphalitis or other skin infections in neonates have been secondary outcomes, statistical power to detect differences in infection rates has been inadequate.^{9, 17, 22}

Evidence for reduced infection rates in infants treated with cord antiseptics may also be lacking because few studies have followed infants after discharge, yet the majority of infections occur in infants after leaving the nursery.^{7, 8, 15, 28} Low overall prevalence of infections in the majority of developed country institutions and the relatively clean home environment into which a large proportion of infants are discharged have precluded statistical comparison to detect important differences in rates among cord care regimens.

DEVELOPING COUNTRIES

The translation of findings from studies conducted in developed countries to developing country situations is problematic. In developing country nurseries and in homes where many infants are born, strict aseptic techniques may not be followed; or lack of resources, training and/or supervision may be associated with protocol breaches. The bacteriologic profile of agents colonizing and infecting neonates in developing countries is less well-documented and can change rapidly over time. In general, however, neonates in developing country nurseries are challenged with much higher loads of potential pathogens.²⁹ The principal pathologic agents, and perhaps their virulence of infection, may also differ from developed countries.^{3, 30, 31} Changing patterns of antibiotic use, varying antiseptic technique in hospital settings, the appearance of multidrug-resistant bacteria and variation in profiles between full term vs. preterm and healthy vs. unhealthy babies indicate the need for region-specific bacteriologic studies.^{3, 12, 30, 32–34}

The incidence of cord infections among neonates in developing countries is unknown, but may be underappreciated. Some studies have reported infection rates among hospitalized babies before discharge, but surveillance for postdischarge infection is rare. Moreover, no population-based studies of rates of cord infection in the community have been reported. There is wide variation in rates of umbilical infections among neonates in nurseries in developing countries, with rates ranging from 2 per 1000 to 54 per 1000 live births and case fatality rates ranging from 0 to 15%.³ A 2-year hospital-based study of neonatal omphalitis in eastern Turkey reported an even higher omphalitis incidence rate of 7.7 per 100 inpatient newborns per year.³⁵ Gram-positive bacteria (mainly *S. aureus*) were more commonly isolated from the cord than Gram-negative bacteria (mainly *E. coli*). A hospital in Nigeria reported a culture-proved neonatal omphalitis incidence rate of 2 per 1000 live births, with *S. aureus* and *E. coli* the predominant isolates. Anaerobic bacteria, including *Bacteroides* spp., were also isolated from ~30% of cultures.³⁶ Among infants hospitalized for sepsis in Uttar Pradesh, India, cord infection was the source of the illness in 47% of cases, and 21% of neonates admitted for other reasons had omphalitis.³⁷ Contrary to previous work, Gram-negative bacteria (*Klebsiella pneumoniae*, 39%) were most commonly isolated, especially among those delivered at home.

Few reports have been published from developing countries describing the role of antimicrobial applications to the cord or behaviors in preventing neonatal omphalitis or sepsis. After noting high body temperature and/or signs of umbilical cord infection in 29.6% of a cohort of neonates in rural Papua New Guinea, investigators implemented daily application of 10% acriflavine in ethanol to the umbilical cord and followed infants for signs of umbilical cord infection and sepsis. Cases of probable neonatal sepsis were 9.4 times ($P < 0.02$) as likely and fever ($>37.4^{\circ}\text{C}$) was 6.7 times as likely among the historic control group that did not receive the intervention.⁵ In a large community-based case-control study of tetanus deaths in Pakistan, investigators

found that infants who received application of antimicrobials (type unspecified), both at birth and subsequently, were at substantially lower risk of death than those who received dry cord care alone, even after adjusting for confounding factors including application of cow dung, ash or ghee (OR 0.4; 95% CI 0.21, 0.77).²⁷

SUMMARY

Current clinical procedures for aseptic cord care are based on research from developed country hospital nurseries. This research does not provide a clear understanding of optimal cord care practices. Although there is sufficient evidence to establish that the application of antiseptic to the cord reduces bacterial colonization, specific antiseptics vary in effectiveness depending on their antibacterial properties, the mode or frequency of application, the concentration of the antiseptic used and the degree of contamination in the environment. Chlorhexidine appears to be a favorable choice of antiseptic because of its wide-ranging activity against Gram-positive and Gram-negative bacteria, its residual effect on the skin and its low toxicity. Furthermore a number of nonrandomized trials have provided consistent evidence that 4.0% chlorhexidine can reduce the risk of both umbilical cord and periumbilical infections. Firm conclusions regarding the effect of topical antiseptic applications in reducing infection await large, well designed and sufficiently powered investigations. Given the paucity of data, the current trend in many developed country nurseries to rely on dry cord care in lieu of antimicrobial applications to the cord requires ongoing evaluation.

In developing country settings where significant differences exist in resource availability, social customs, environmental cleanliness and bacteriologic profile, results from developed countries are difficult to apply. The scarce data suggest that umbilical cord infection contributes a high burden of neonatal morbidity in developing countries, and local or systemic bacterial infection originating from umbilical cord colonization can lead to neonatal sepsis and death. The WHO currently recommends dry cord care in developing countries and the use of soap and water solution to clean the cord if visibly soiled. However, the possible benefit of using topical antiseptics, particularly as a substitute in situations where harmful practices are common, is also acknowledged.^{4, 27}

Available data from developing country community-based studies suggest that cord infection rates are high and, moreover, that cord antisepsis may decrease neonatal sepsis and death. Further prospective, community-based research is needed, however, to define the relationship between antimicrobial use and cord infection and to guide the development of improved cord care protocols. Likewise the efficacy of using a simple soap and water solution, possibly already present in the home or easily accessible in many rural settings, has not been investigated.

Community-based trials investigating the role of topical antimicrobials and/or other cord care regimens on local and systemic infections in the neonatal period are needed. Cord care interventions, if proved effective in reducing neonatal infections and deaths, would be well-placed within the framework of neonatal health programs promoting clean, safe delivery practices, early and exclusive breast-feeding and overall hygiene. Investigations must be of sufficient size to detect differences in infection rates between regimens, should include a dry cord care only regimen for comparison and must follow subjects through the entire neonatal period. Until data from such trials are available, caution must be exercised in extending conclusions drawn from scarce, inadequately designed trials in developed countries. Specifically dry cord alone, the current trend in neonatal care in developed and developing countries alike, must be properly evaluated before being further promoted as best practice.

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References

1. World Health Organization. WHO 2001 estimates. In: State of the world's newborns. Washington, DC: Save the Children Federation, 2001:1–49.
2. World Health Organization. Perinatal mortality: a listing of available information. FRH/MSM. 96.7. Geneva: WHO, 1996.
3. Stoll BJ. The global impact of neonatal infection. Clin Perinatol 1997;24:1–21. [PubMed: 9099499]
4. World Health Organization. Care of the umbilical cord. WHO/FHE/MSM-cord care. Geneva: WHO, 1998.
5. Garner P, Lai D, Baea M, Edwards K, Heywood P. Avoiding neonatal death: an intervention study of umbilical cord care. J Trop Pediatr 1994;40:24–8. [PubMed: 8182776]
6. Zupan J, Garner P. Topical umbilical cord care at birth (Cochrane Review). In: The Cochrane library, Issue 4. Oxford, UK: Update Software, 2001.
7. Meberg A, Schoyen R. Bacterial colonization and neonatal infections. Acta Paediatr Scand 1985;74:366–71. [PubMed: 3890463]
8. Seeberg S, Brinkhoff B, John E, Kjellmer I. Prevention and control of neonatal pyoderma with chlorhexidine. Acta Paediatr Scand 1984;73:498–504. [PubMed: 6464737]
9. Dore S, Buchan D, Coulas S, et al. Alcohol *versus* natural drying for newborn cord care. J Obstet Gynecol Neonatal Nurs 1998;27:621–7.
10. Wald ER, Snyder MJ, Gutberlet R. Group B beta-hemolytic streptococcal colonization: acquisition, persistence, and effect of umbilical cord treatment with triple dye. Am J Dis Child 1977;131:178–80. [PubMed: 319653]
11. Speck WT, Driscoll JM, Polin RA, O'Neill J, Rosenkranz S. Staphylococcal and streptococcal colonization of the newborn infant. Am J Dis Child 1977;131:1005–8. [PubMed: 331941]
12. Speck WT, Driscoll JM, O'Neil J, Rosenkranz HS. Effect of antiseptic cord care on bacterial colonization in the newborn infant. Chemotherapy 1980;26:372–6. [PubMed: 6993111]
13. Alder VG, Burman D, Simpson RA, Fysh J, Gillespie WA. Comparison of hexachlorophane and chlorhexidine powders in prevention of neonatal infection. Arch Dis Child 1980;55:277–80. [PubMed: 6998381]
14. Belfrage E, Enocksson E, Kalin M, Marland M. Comparative efficiency of chlorhexidine and ethanol in umbilical cord care. Scand J Infect Dis 1985;17:413–20. [PubMed: 4089546]
15. Paes B, Jones CC. An audit of the effect of two cord-care regimens on bacterial colonization in newborn infants. Qual Rev Bull 1987;13:109–13.
16. Smales O. A comparison of umbilical cord treatment in the control of superficial infection. N Z Med J 1988;101:453–5. [PubMed: 3399182]
17. Gladstone IM, Clapper L, Thorpe JW, Wright DI. Randomized study of six umbilical cord care regimens. Clin Pediatr 1988;27:127–9.
18. Watkinson M, Dyas A. *Staphylococcus aureus* still colonizes the untreated neonatal umbilicus. J Hosp Infect 1992;21:131–6. [PubMed: 1353088]
19. Verber IG, Pagan FS. What cord care—if any? Arch Dis Child 1993;68:594–6. [PubMed: 8323363]
20. Janssen PA, Selwood BL, Dobson SR, Peacock D, Thiessen PN. To dye or not to dye: a randomized clinical trial of a triple dye/alcohol regime *versus* dry cord care. Pediatrics 2003;111:15–20. [PubMed: 12509548]
21. Medves JM, O'Brien BAC. Cleaning solutions and bacterial colonization in promoting healing and early separation of the umbilical cord in healthy newborns. Can J Public Health 1997;88:380–2. [PubMed: 9458563]
22. Mugford M, Somchiwong M, Waterhouse IL. Treatment of umbilical cords: a randomized trial to assess the effect of treatment methods on the work of midwives. Midwifery 1986;2:177–86. [PubMed: 3643399]

23. Allen KD, Ridgway EJ, Parsons LA. Hexachlorophene powder and neonatal staphylococcal infection. *J Hosp Infect* 1994;27:29–33. [PubMed: 7916360]
24. Stark V, Harrison SP. *Staphylococcus aureus* colonization of the newborn in a Darlington hospital. *J Hosp Inf* 1992;21:205–11.
25. Meberg A, Schøyen R. Hydrophobic material in routine umbilical cord care and prevention of infections in newborn infants. *Scand J Infect Dis* 1990;22:729–33. [PubMed: 2284579]
26. Wang E, Elder D, Mishkel N. *Staphylococcus aureus* colonization and infection after discharge from a newborn nursery. *Infect Control* 1987;8:30–3. [PubMed: 3643890]
27. Bennett J, Macia J, Traverso H, Banoagha S, Malooly C, Boring J. Protective effects of topical antimicrobials against neonatal tetanus. *Int J Epidemiol* 1997;26:897–903. [PubMed: 9279625]
28. Gooch JJ, Britt EM. *Staphylococcus aureus* colonization and infection in newborn nursery patients. *Am J Dis Child* 1978;132:893–6. [PubMed: 685907]
29. Bhutta ZA. Neonatal bacterial infections in developing countries: strategies for prevention. *Semin Neonatal* 1999;4:159–71.
30. Darmstadt GL, Black RE, Santosham M. Research priorities and postpartum-care strategies for the prevention and treatment of neonatal infections in less developed countries. *Pediatr Infect Dis J* 2000;19:739–50. [PubMed: 10959744]
31. Darmstadt GL, Mao-Qiang M, Saha SK, et al. Impact of topical oils on the skin barrier: possible implications for neonatal health in developing countries. *Acta Paediatr* 2002;91:546–54. [PubMed: 12113324]
32. Jellard J. Umbilical cord as reservoir of infection in maternity hospital. *Br Med J* 1957;1:925–8. [PubMed: 13413254]
33. Eshali H, Ringertz S, Nystrom S, Faxelius G. Septicemia with coagulase negative staphylococci in a neonatal intensive care unit. *Acta Paediatr Scand Suppl* 1989;360:127–34. [PubMed: 2642248]
34. Yu VYH. Neonatal sepsis and infection control policies in Australia. *J Pediatr Child Health* 1990;26:252–6.
35. Güvenç H, Güvenç M, Yenioglu H, et al. Neonatal omphalitis is still common in eastern Turkey. *Scand J Infect Dis* 1991;23:613–6. [PubMed: 1767258]
36. Airede A. Pathogens in neonatal omphalitis. *J Trop Pediatr* 1992;38:129–31. [PubMed: 1507308]
37. Faridi MMA, Rattan A, Ahmad SH. Omphalitis neonatorum. *J Ind Med Assoc* 1993;91:283–5.

TABLE 1

Summary of colonization outcomes in the neonatal/postneonatal period

Author, Yr	Location	Design, Size	Study Group(s)	Outcome/Organism(s) Studied
Wald et al., 1977 ¹⁰	Maryland, US	Randomized trial, N = 805	TD or HEX daily application while in ward, dry care only	TD superior to HEX and dry care groups in reducing GBS colonization and GBS acquisition
Speck et al., 1977 ¹¹	New York, US	Randomized trial, N = 284	TD single application, dry care only	TD reduced staphylococcal colonization but promoted GBS
Speck et al., 1980 ¹²	New York, US	Randomized trial, N = 240	TD daily, dry care only	TD reduced staphylococcal colonization; no promotion of GBS
Alder et al., 1980 ¹³	UK	Randomized trial, N = 174	0.33% HEX powder daily, 1.0% CHX powder daily	CHX superior in preventing staphylococcal colonization but promoted growth of coagulase-negative staphylococci
Meberg and Schoyen 1985 ⁷	Norway	Randomized trial, N = 333	Benzene daily, 0.05% CHX daily, 4.0% CHX daily, dry care only	4.0% CHX vs. control group <i>Staphylococcus aureus</i> , 35% reduction <i>Escherichia coli</i> , 41% reduction
Belfrage et al., 1985 ¹⁴	Sweden	Pre-post comparison, N = 2016	4.0% CHX daily, 0.5% CHX in 70% ethanol daily	4.0% CHX protocol reduced colonization of umbilical cord by <i>S. aureus</i> from 92% to 27%
Paes et al., 1987 ¹⁵	Canada	Retrospective audit, N = 1545	TD daily, alcohol daily	Significantly decreased colonization of umbilical cord during TD application time period
Smales, 1988 ¹⁶	New Zealand	Prospective cross-over, N = 468	4.0% CHX daily, 10% Iodosan daily	CHX superior in reducing colonization rates of <i>S. aureus</i> ; no overgrowth of coagulase-negative staphylococci or GBS
Gladstone et al., 1988 ¹⁷	Maryland, US	Randomized trial, N = 271	TD initial and daily, TD initial + alcohol daily, TD initial only, POV daily, SIL daily, BAC daily	No difference in colonization rates between any of the groups
Watkinson and Dyas 1992 ¹⁸	UK	Randomized trial, N = 100	HEX daily, dry care only	Staphylococcal colonization rate significantly higher in group receiving dry care only
Verber and Pagan 1993 ¹⁹	UK	Randomized trial, N = 619	4.0% CHX daily, HEX daily, dry care only	<i>S. aureus</i> colonization rates significantly lower in the CHX care group
Janssen et al., 2003 ²⁰	Canada	Randomized trial, N = 766	TD initial and alcohol daily, dry care only	<i>S. aureus</i> , <i>E. coli</i> , GBS and coagulase-negative staphylococci significantly reduced among group receiving TD/alcohol

TD, triple dye; POV, povidone-iodine; HEX, hexachlorophene; CHX, chlorhexidine; BAC, bacitracin; SIL, silver sulfadiazine.

TABLE 2

Summary of infection outcomes in the neonatal/postneonatal period

Author, Yr	Location	Design, Size	Study Group(s)	Outcome
Seeberg et al., 1984 ⁸	Sweden	Pre-post comparison, N = 5220	4.0% CHX daily, dry care only	6-wk pyoderma rate reduced in CHX group (15.2% vs. 2.0%)
Belfrage et al., 1985 ¹⁴	Sweden	Pre-post comparison, N = 2016	4.0% CHX daily, 0.5% CHX in 70% ethanol daily	1-mo prevalence rates reduced for pyoderma (58% reduction), paronychia (46% reduction), and omphalitis (100% reduction) in 4.0% CHX group
Smales, 1988 ¹⁶	New Zealand	Prospective cross-over, N = 468	4.0% CHX daily, 10% Iodosan daily	"Superficial infections" reduced in CHX group (21% vs. 38%)
Stark and Harrison, 1992 ²⁴	UK	Prevalence study, N = 370	No specific cord care given, no comparison group	<i>S. aureus</i> umbilical cord colonization associated with increased occurrence of skin pustules, omphalitis
Meberg and Schoyen, 1990 ²⁵	Norway	Randomized trial, N = 2441	0.5% CHX daily, hydrophobic gauze	No differences in umbilical cord infection rates
Meberg and Schoyen, 1985 ⁷	Norway	Randomized trial, N = 333	Benzene daily, 0.05% CHX daily, 4.0% CHX daily, dry care only (all babies washed daily with soap and water)	No difference in umbilical cord infections between the no care and 0.05% CHX group, 13% reduction in 6-wk infection rate in the 4.0% CHX group vs. no care (not significant)
Wang et al., 1987 ²⁶	Canada	Prospective, observational study, N = 181	<i>S. aureus</i> colonized vs. noncolonized infants	No difference in infection risk (OR 1.75; 95% CI 0.51, 5.22); infant range 1–18 wk
Garner et al., 1994 ⁵	Papua New Guinea	Case control, N = 132	Exposure groups: 10% acriflavine in ethanol, no specific cord care	Odds of neonatal sepsis 9.4 times higher among controls than in the acriflavine group
Bennett et al., 1997 ²⁷	Pakistan	Case control, N = 23670	Exposure groups: any antimicrobial application, no antimicrobial application	Odds of tetanus death decreased in the group receiving antimicrobial applications, adjusted for risky practices (ash, dung, ghee) (OR 0.4; 95% CI 0.21, 0.77)
Janssen et al., 2003 ²⁰	Canada	Randomized trial, N = 766	TD initial and alcohol daily, dry care only	No difference in umbilical cord infections rates

CHX, chlorhexidine; TD, triple dye.