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Pre-operative skin preparation: History and current best practices

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Abstract

APre-operative skin preparation is a cornerstone of surgical infection prevention and has evolved substantially from early antiseptic practices to modern evidence-based protocols. Historical milestones, beginning with Semmelweis' hand hygiene interventions and Lister's antiseptic surgery techniques, established the foundation for contemporary surgical asepsis. Over time, antiseptic agents such as alcohols, povidone-iodine (PVP-I), and chlorhexidine gluconate (CHG) were developed and refined to improve antimicrobial efficacy and patient safety. Current evidence strongly supports the use of alcohol-based antiseptic preparations, particularly CHG-alcohol combinations, for reducing surgical-site infections (SSIs). Landmark trials and international guidelines from the World Health Organization, Centers for Disease Control and Prevention, and National Institute for Health and Care Excellence recommend alcohol-based CHG as the preferred pre-operative antiseptic in most surgical settings. However, recent studies suggest that optimally applied PVP-I-alcohol preparations may offer comparable outcomes, maintaining ongoing debate regarding the ideal agent. Modern best practices emphasize pre-operative bathing, avoidance of razor shaving, appropriate hair clipping, adequate antiseptic contact time, and complete drying before incision. Special considerations are necessary in pediatric, neonatal, implant-related, emergency, and mucosal surgeries because of variations in skin tolerance and infection risk. Despite significant advances, important gaps remain regarding pediatric-specific evidence, standardized application protocols, antiseptic resistance, and the long-term impact of antisepsis on the skin microbiome. This review summarizes the historical evolution, mechanisms of action, comparative evidence, guideline recommendations, practical applications, controversies, and future research priorities related to pre-operative skin preparation, highlighting its continuing role in improving surgical safety and reducing SSIs. .

Keywords: Alcohol-based antiseptics, Chlorhexidine gluconate, Clinical guidelines, Patient safety, Povidone-iodine, Pre-operative skin preparation, Surgical antisepsis history, Surgical site infection

1. Introduction

Pre-operative skin antisepsis has evolved dramatically from 19th-century discoveries to modern evidence-based protocols. Early pioneers such as Semmelweis (1847) and Lister (1867) demonstrated that handwashing and carbolic-acid dressings could dramatically reduce surgical infections.[1,2] Over time, new agents were introduced: Alcohols, iodine compounds (e.g., povidone-iodine [PVP-I]), and chlorhexidine gluconate (CHG, discovered 1946[3]). Techniques evolved from basic scrubbing to standardized "paint-and-dry" methods with specific contact times. Landmark trials (e.g., Darouiche *et al.*, 2010) and meta-analyses generally favor alcohol-based CHG over PVP-I for lowering surgical-site infections (SSIs),[4] a conclusion mirrored in global guidelines (World Health Organization [WHO] 2016, Centers for Disease Control and Prevention [CDC] 2017, National Institute for Health and Care Excellence [NICE] 2019).[5-7] Yet, recent high-quality data (Albanese *et al.*, 2020) show that povidone-alcohol can be non-inferior to CHG-alcohol,[8] keeping debate alive. Modern best practices include antiseptic showers, clipped hair (no razors), alcohol-based scrubs, and allowing antiseptics to dry before incision. Special contexts (pediatric, emergency, implant surgeries, etc.) have tailored recommendations due to differences in skin, infection risk, and agent tolerability. Unresolved issues include standardizing application protocols and filling pediatric evidence gaps.[9] This review traces historical milestones, details agent mechanisms, compares evidence from trials and guidelines, and provides practical recommendations, with comprehensive tables and a timeline summarizing key developments.

2. Historical Milestones and Timeline

Medical antisepsis began in the mid-1800s with the recognition of infection spread. In 1847, Semmelweis dramatically reduced puerperal fever by requiring physicians to disinfect their hands with chlorinated lime before examining patients.[1]

This intervention reduced mortality rates from approximately 18% to 1.3%, demonstrating the critical role of hand hygiene in preventing infectious deaths. A decade later, the germ theory of disease provided a scientific basis. In 1867, British surgeon Joseph Lister applied this theory to surgery: He began using carbolic acid (phenol) as an antiseptic on wounds, instruments, dressings, and even the surgeon's hands.[2] Lister's methods ("antiseptic surgery") sharply reduced post-operative infections.[10] These innovations laid the foundation for sterile techniques.

Subsequent decades saw refinement and new agents. Late 19th- and early 20th-century advances included aseptic techniques (sterile gloves, gowns, and heat sterilizers) and new antiseptics. By the 1900s, iodine-based antiseptics entered practice (e.g., tinctures). After World War I, iodine compounds (iodophors) were formulated to improve efficacy and safety. In the mid-20th century, two key antiseptics were introduced: Hexachlorophene (a bisphenol, used extensively in scrubs around 1930s–1950s but later limited by toxicity) and CHG. CHG was discovered in 1946[3] and introduced clinically by 1954,[3] offering a broad-spectrum, long-lasting antiseptic. Around the same time, PVP-I was developed as a safer, polymer-bound iodine.[11] By the 1960s, PVP-I formulations were widely used for skin preparation.[11] Alcohol (60–90% ethanol or isopropanol) has long been used in tinctures and rubs due to its rapid action; today, it is a major component of combo solutions.

In recent decades, practice shifted from discovery to evidence. Major guidelines have distilled clinical trials into recommendations: by 2010, Darouiche *et al.* (NEJM) found CHG-alcohol superior to PVP-I[4] and by 2016–2019, WHO, CDC, and NICE all favored alcohol-based CHG for pre-incision skin preparation.[5-7] In 2020, Albanese *et al.* (JAMA) demonstrated that 2% CHG-alcohol and 10% PVP-I-alcohol yielded statistically similar SSI rates.[8] The 2020s continue to refine these practices amid concerns of CHG allergy and resistance.

2.1. Timeline

Title: Evolution of Surgical Skin Antisepsis:

- 1847: Semmelweis mandates chlorinated-lime handwashing, plunging puerperal fever rates[1]
- 1867: Lister applies carbolic-acid spray to wounds (based on Pasteur's germ theory), pioneering antiseptic surgery[2]
- 1890: Halsted introduced rubber surgical gloves (first use in live surgery)
- 1920s: Hexachlorophene used widely for skin antisepsis (especially infants)
- 1946: Chlorhexidine discovered[3]
- 1954: Chlorhexidine introduced into clinical use[3]
- 1950s: Development of iodophor solutions; PVP-I becomes common[11]
- 1960s: PVP-I (Betadine) widely adopted in skin preparation
- 1970s: Alcohol-based surgical scrubs and rubs introduced
- 1999: First CDC SSI prevention guideline published (addressing skin preparation)
- 2010: Darouiche NEJM: CHG-alcohol significantly reduces SSI versus aqueous PVP-I[4]
- 2016: WHO SSI guidelines endorse alcohol-based CHG preparation[5]
- 2017: CDC SSI guideline (Cat IA) recommends alcohol-based antiseptic[6]
- 2019: NICE guideline NG125: Recommends alcohol+CHG as first-line[7]
- 2020: Albanese JAMA: Povidone-alcohol shown non-inferior to CHG-alcohol[8]
- 2025+: Ongoing research on optimal protocols and resistance concerns

3. Evolution of Antiseptic Agents and Mechanisms

Over time, antiseptics have been refined for broader efficacy and safety:

- Carbolic acid (Phenol): Lister's original antiseptic. It denatures proteins and disrupts cell membranes, killing bacteria. Effective against many Gram+ organisms but also caustic. Its use waned as safer agents arose.[2]
- Alcohols (Ethanol/Isopropanol): Rapidly bactericidal through protein denaturation.[13] Effective at 60–90% concentration, alcohols kill vegetative bacteria, fungi, and enveloped viruses, but not spores. Alcohol provides no persistent effect, as it evaporates.[14] Today, it is used both alone (for hand antisepsis) and combined with other agents to speed action.
- Iodine and iodophors: Iodine kills microbes by iodinating lipids and oxidizing proteins.[15] Free iodine is limited in its native state (irritating), so it's bound in carriers. PVP-I releases iodine slowly. It has broad-spectrum activity (Gram+, Gram–, fungi, viruses, and protozoa).[15] Importantly, bacteria do not develop resistance to iodine. Downsides: PVP-I stains skin, can cause irritation, and is contraindicated in thyroid disease or pregnancy.[16] It also generally kills more slowly than alcohol or CHG.
- CHG: A cationic bisbiguanide discovered in 1946.[3] CHG binds to negatively charged bacterial cell walls, altering osmotic balance.[17] It is bacteriostatic at low concentrations and bactericidal at higher (≥0.5%).[17] CHG effectively kills Gram-positive cocci (including MRSA), many Gram-negatives, and enveloped viruses; spores are resistant. A key advantage is

its residual effect: CHG binds to skin and mucosa, providing prolonged antibacterial activity.[14] Standard skin preparations use ~2–4% CHG in 70% isopropanol. CHG's pros are rapid kill and persistence,[3] but its cons include rare anaphylactic allergies, and reports of bacteria acquiring tolerance. It can also cause chemical burns in infants, so guidelines advise caution (e.g., using aqueous CHG rather than alcohol-based near neonates or mucosa).

- Others: Mid-20th-century agents such as hexachlorophene and triclosan have largely fallen out of routine use. Hexachlorophene (Gram-positive spectrum) was effective but caused neonatal neurotoxicity. Quaternary ammonium compounds (e.g., benzalkonium) and octenidine see limited use (octenidine has broad activity, mainly in Europe). These "others" are typically not first-line for pre-op preparation today.

4. Techniques of Skin Preparation

The method of applying antiseptics is as important as the agent itself. Modern pre-operative skin preparation follows these steps:

- Patient bathing: Patients are usually instructed to shower or bathe with soap (often chlorhexidine-based if available) the evening before or morning of surgery. Evidence: While formal randomized controlled trials (RCTs) on pre-operative CHG showers show mixed results, guidelines (e.g., NICE) advise at least soap bathing to lower skin flora. Hospitals often use CHG washes for high-risk patients.
- Hair removal: Use clippers, not razors. Guidelines unanimously discourage shaving with razors, which can cause micro-abrasions and increase SSI. Hair should only be removed if it interferes with the incision or device placement. If needed, do it immediately before surgery using electric clippers with a single-use head. This minimizes skin trauma and avoids "bare" hairless skin changes that promote infection.
- Skin cleansing ("painting"): In the OR, the prepared solution (alcohol+CHG, PVP-I, etc.) is applied with sterile sponges or applicators. A standard approach is to paint the entire operative field, starting at the incision site and moving outward in widening circles or strokes. The solution should be applied liberally to cover all hair, skin folds, and relevant areas.
- Contact time and drying: After application, the skin must remain wet for the recommended contact time (typically at least 2–3 min) to ensure microbial kill. Crucially, do not wipe off the antiseptic; instead, let it air-dry fully (if using electrocautery afterward, drying is essential to prevent alcohol fires). NICE explicitly warns against leaving alcohol preparation pooled and instructs to allow evaporation. Some protocols (like in the Albanese trial) even apply multiple coats to reach a 3+ min wet contact.
- Draping: Once the antiseptic has dried, sterile drapes are placed. Historically, "incise drapes" (adhesive plastic films) were popular, but modern evidence questions their value. NICE (2008) advised against plain incise drapes (they may even increase infection) and permits iodine-impregnated drapes only if needed.[12] The WHO SSI guidelines also found no conclusive benefit of antimicrobial drapes. Thus, standard sterile draping (towels or incise drapes, optional) is used without relying on antiseptic coating of drapes.
- Staff preparation: Surgeons and staff perform a surgical hand scrub or alcohol rub before gloving, but that is beyond pre-operative skin preparation. However, patient decolonization (e.g., nasal mupirocin for *Staphylococcus aureus* carriers) is sometimes integrated into bundles based on SSI risk.

5. Evidence from Trials and Guidelines

The literature contains numerous studies comparing antiseptic agents and techniques [Table 1]:

- CHG versus PVP-I: Multiple RCTs and meta-analyses have compared alcohol-based CHG to iodine-based preparation. The pivotal study by Darouiche *et al.* (2010, NEJM) randomized 849 adult patients (mostly cardiac/vascular surgeries) to either 2% CHG in alcohol or 10% aqueous PVP-I. SSI occurred in 9.5% of the CHG group versus 16.1% of the PVP-I group (relative risk ~0.58, $P < 0.002$).[4] Two meta-analyses (Pittet/SHEA and Kasatpibal, cited in reviews) found CHG-alcohol significantly reduced SSI rates compared to PVP-I.[4] These findings underpin the current preference for CHG.

Conversely, a large Swiss RCT (Albanese *et al.*, 2020, JAMA) with 3,360 patients in abdominal/cardiac surgery tested CHG-alcohol versus PVP-I-alcohol (both 3 scrubs, ≥3 min total) and found no significant difference in SSI: 5.5% versus 5.1%, respectively.[8] The pre-specified analysis showed PVP-I was non-inferior within a 2.5% margin.[8] The authors noted that multiple, high-quality applications may have equalized the effect, suggesting that when applied optimally, either agent can be effective. Thus, while CHG-alcohol generally performs well, well-implemented PVP-I can also work.

- Systematic reviews: Cochrane reviews and pooled analyses (Lee *et al*. 2006; Mead *et al*. 2016) consistently reported lower SSI rates with CHG in alcohol compared to iodophors. However, many reviews caution about heterogeneity in study design (different concentrations, contact times, surgical types). Current guidelines rely on both RCT data and expert consensus.
- WHO (2016): Recommends alcohol-based chlorhexidine for skin preparation, citing evidence of lower SSI rates.[5]

Table 1: Key historical milestones in surgical antisepsis. Chronology of discoveries and innovations from Semmelweis and Pasteur to modern guidelines (top) and trial evidence (bottom)

Year/Event	Milestone
1847	Semmelweis identifies cadaveric contamination as the cause of puerperal fever and mandates chlorinated lime handwashing.[1]
1867	Lister applies germ theory to surgery; he uses carbolic acid (phenol) to sterilize instruments, wounds, and dressings.[2]
1890s	William Halsted introduced rubber gloves in surgery, advancing aseptic technique.
1920s–1930s	Hexachlorophene (a bisphenol) was used for surgical scrub (later limited by neurotoxicity).
1946	CHG discovered.[3]
1954	CHG was introduced for medical use.[3]
1950s	Iodine iodophors developed; PVP-I introduced, reducing iodine volatility.[11]
1960s	Widespread adoption of PVP-I (e.g., Betadine) for skin preparation.
1970s	Alcohol-based surgical scrubs (e.g., Chlorhexidine-alcohol scrubs) have become common.
1999	CDC releases comprehensive SSI prevention guidelines (1st ed.ition).
2010	Darouiche *et al.* (NEJM): Chlorhexidine-alcohol cut SSI rates (9.5% vs. 16.1%) compared to PVP-I.[4]
2016	WHO Global SSI guidelines recommend alcohol-based CHG skin preparation.[5]
2017	CDC 2017 SSI guideline (Category IA) mandates alcohol-based antiseptic preparation.[6]
2019	NICE Guideline NG125: Endorses alcohol+CHG as first choice; restricts non-iodophor incise drapes.[7,12]
2020	Albanese *et al.* (JAMA): Povidone-alcohol found statistically non-inferior to CHG-alcohol (5.1% vs. 5.5% SSI).[8]
2023+	Emerging focus on CHG allergy, resistance, and optimal protocols; research ongoing.

CHG: Chlorhexidine gluconate, PVP-I: Povidone-iodine, WHO: World Health Organization, CDC: Centers for Disease Control and Prevention, NICE: National Institute for Health and Care Excellence, SSI: Surgical-site infection

- CDC (2017): Gives a Category IA recommendation for alcohol-based agent (implicitly endorsing CHG-alcohol as the exemplar).[6]
- NICE NG125 (2019): Lists *"alcohol-based chlorhexidine"* as first choice; alcohol-based PVP-I as an alternative if CHG is unsuitable.[7]
- Surgical Infection Society and others: Also advise using an alcohol-based formulation; if CHG is used near mucosa (eyes/genitals), use aqueous CHG or PVP-I.
- Other techniques: RCTs have tested variations in technique. Notably, Ellenhorn *et al.* (2005)[17] compared a full scrub (PVP-I brush scrub plus paint) to a single paint-only method in general surgery and found *identical* infection rates (~10%). This suggests the extra scrubbing step added no benefit in that trial. Cochrane reviews on skin preparation versus hygiene (soap) generally show no clear advantage to chlorhexidine showering; a plain soap wash may be equivalent to CHG bath for reducing SSI. Thus, many surgeons focus resources on operative antisepsis rather than routine pre-operative scrubs.
- Incise drapes and dressings: The evidence is weak for adhesive drapes. A WHO review (Appendix) found no reduction in SSI from antimicrobial or plain incise drapes. NICE advises against non-iodophor drapes and only permits iodine-impregnated ones (like Ioban) if needed.[12] Dressings over closed incisions (occlusive vs. absorbent) also lack strong evidence for SSI impact, so the choice is based on comfort and exudate control.
- Microbial concerns: CHG's residual effect (binding to skin) means that it continues to suppress regrowth.[14] Alcohol alone has no residue.[14] Neither CHG nor iodine sterilizes deep within follicles, so some bacteria remain in ducts (hence risk of later infection). Resistance is a controversy: some *Staphylococcus* and *Enterococcus* isolates carry CHG efflux genes, raising MICs. However, "clinical resistance" (infection despite antiseptic preparation) remains rare. No clinically important resistance to iodine has been documented. Allergies are real: dozens of perioperative anaphylaxis cases to CHG have been reported, prompting warnings (e.g., Food and Drug Administration label changes). Iodine reactions are mostly irritant or thyroid-related rather than a true allergy.

6. Current Best Practices and Controversies

Contemporary experts and guidelines converge on several points, with some ongoing debate:

- Agent of choice [Table 2]: Alcohol-based CHG solutions are generally recommended first-line.[7] This is due to their broad activity and residual effect. CDC's Category IA evidence statement advises "alcohol-based antiseptic agent."[6]

Table 2: Comparison of common skin antiseptics. Agent, typical concentration/formulation, contact time, spectrum, advantages, disadvantages, and key evidence

Antiseptic	Conc./ Formulation	Contact time	Spectrum of activity	Advantages	Disadvantages	Key evidence/Use
Chlorhexidine gluconate (CHG)	2–4% CHG in 70% isopropanol (alcohol-based)	~2–3 min (dry completely)	Broad: Gram-positive, some Gram-negative, fungi, enveloped viruses[3]	Rapid kill; persistent residual effect[3]; well-tolerated on intact skin	Rare anaphylaxis; potential for decreased susceptibility; irritating if in eyes or neonates	Darouiche (2010, NEJM): CHG-alcohol reduced SSI significantly versus PVP-I;[4] WHO/ CDC/NICE recommend alcohol+CHG.[5-7] Albanese (2020, JAMA): CHG-alcohol≈PVP-I-alcohol (non-inferior).[8]
PVP-I	10% PVP (≈1% available iodine), often 50–70% alcohol	~2–3 min (dry)	Broad: Gram-positive, Gram-negative, fungi, viruses, protozoa[15]	Broad microbicidal action; no reported resistance; inexpensive; historically proven	Stains tissue; skin irritation; contraindicated in thyroid disease/ pregnancy;[16] less persistent (no strong residual); somewhat slower kill	Used as control/ alternative in trials. In Darouiche, PVP-I less effective than CHG.[4] Guidelines allow PVP-I if CHG contraindicated.[7] Albanese (2020): PVP-I-alcohol non-inferior to CHG-alcohol.[8]
Alcohol (ethanol or isopropanol)	60–90% (v/v) solution	30–60 s (evaporates)	Kills vegetative bacteria, fungi, enveloped viruses (not sporicidal)[13]	Very rapid kill; broad spectrum; inexpensive; synergizes with CHG/ PVP	No lasting effect;[14] flammable (fire risk if pooled); stings on open wounds	Main component in combo preparation s (e.g., "ChloraPrep"). CDC/WHO/ NICE recommend alcohol-based solutions.[5,6]
Other (e.g., quats, triclosan)	Varied (e.g., 0.2% benzalkonium, 0.3% triclosan)	1–5 min	Limited: Primarily Gram-positive; some antivirals (triclosan); octenidine broader	Some are used in hand/skin cleansers; octenidine has long residual	Generally less effective on Gram-negatives and spores; triclosan is banned in soaps; not standard in SSI guidelines	Octenidine (Europe): effective broad-spectrum antiseptic, but few large SSI studies; not commonly used in OR preparation.

PVP-I: Povidone-iodine, CHG: Chlorhexidine gluconate, SSIs: Surgical-site infections, WHO: World Health Organization, CDC: Centers for Disease Control and Prevention, NICE: National Institute for Health and Care Excellence, OR: Operation room

(CHG-alcohol is the usual interpretation). Alternative preparations include alcohol-based PVP-I or aqueous CHG if alcohol or CHG is contraindicated (e.g., CHG allergy, some mucosal sites).[7]

- Technique: The "paint-and-dry" method is standard. Important practices include:
  - No razor shaving: Ever use clippers if hair removal is needed.
  - Adequate contact time: Allow at least 2–3 min of wet contact, and air-dry completely.
  - Avoid pooling: No alcohol puddles under drapes (fire risk).
  - Sterile draping: Use standard drapes; antimicrobial drapes are not routinely needed.[12]
  - Differences by context: While most guidelines do not differentiate by wound class, surgeons often consider the context:
  - Clean (e.g., ortho, neuro): Priority is maximal microbial kill with minimal tissue irritation. Alcohol+CHG is appropriate. Some institutions add iodine drapes for implants, though evidence for added benefit is scant.
  - Clean-contaminated (Gastrointestinal [GI], Obstetrics/Gynecology): Highest SSI risk among routine cases. Full use of antiseptics plus other measures (antibiotics, bowel preparation) is crucial.
  - Contaminated/dirty: In emergency or grossly contaminated cases, immediate debridement and irrigation may matter more. Still, skin preparation is done if time allows, using the fastest effective method (often alcohol-CHG).
  - Dermatologic/minor: On the face or genitals, avoid alcohol (stings/burns); use aqueous CHG or PVP-I. Coverage

differs (smaller fields).

- Pediatric/Neonatal: Preterm infants (<2 months) should NOT get alcohol-CHG (risk of burns and absorption). Aqueous PVP-I or dilute CHG is used. Older children follow adult protocols. A 2022 review concluded that "direct extrapolation from adults is not appropriate" due to a lack of data.[9]
- Orthopedic/Implant: Many orthopedic surgeons mandate CHG-alcohol since prosthetic infections are devastating. CHG's biofilm activity (some evidence) may help prevent bacterial adherence. Routine post-preparation iodine drapes are used by some, but evidence is weak.
- Emergency/Field: In limited-resource settings, any antiseptic is better than none. The WHO suggests using whatever alcohol/CHG is on hand; focus on quick drying to allow surgery.
- Controversies: The CHG versus PVP-I debate is ongoing. While CHG-alcohol is favored, Albanese *et al*. remind us that well-applied PVP-I (with alcohol) can perform equally. CHG allergy and resistance are also debated concerns. Some question whether vigorous antisepsis might alter normal flora (staph vs. strep, etc.) in ways we do not fully understand. Finally, cost and compliance issues (cost of CHG products vs. generic iodine, proper staff training) influence practices.

7. Practical Recommendations

Key practical points distilled from evidence and guidelines:

- Clean surgery (e.g., ortho, neurosurgery): Use an alcohol-based CHG preparation.[7] No razors. Clipper hair removal only if it obstructs (e.g., around a prosthesis site). Allow full drying. Sterile drapes cover beyond the incision field.
- Clean-contaminated surgery (e.g., GI, gynecology): Similar regimen (CHG-alcohol). Ensure broad coverage (e.g., abdomen, groin). Since endogenous gut flora are risk factors, systemic antibiotics and bowel preparation should also be emphasized.
- Contaminated/dirty surgery (e.g., trauma, perforated viscus): Apply antiseptic if possible (often still CHG-alcohol). Time is critical - preparation should be as quick as possible. Note that CHG-alcohol may sting if used on heavily traumatized tissue; in extreme emergencies, an alcohol wipe may be used to speed up.
- Pediatric surgery: For neonates (especially preemies), avoid alcohol; use aqueous CHG (0.5–1%) or dilute PVP-I. For older children, use adult regimens. Consult pediatric infection control protocols for specifics.
- Dermatologic/minor: If the face or mucous membranes are involved, use an antiseptic safe for mucosa (e.g., aqueous CHG or low-concentration PVP-I). Avoid alcohol. For fingers or toes, CHG or PVP-I is fine.
- Implant surgery (e.g., joint replacement, vascular grafts): Maximize antisepsis. Alcohol-based CHG with multiple coats is typical. Some centers also bathe patients with CHG cloths the night before. Ensure the antiseptic reaches even around incisions and implants. Intraoperative antibiotic irrigation (sometimes CHG solution) may be considered (aseptic but adjunct).
- Emergency and resource-limited settings: Use available antiseptic (e.g., PVP-I if CHG not on hand). Even a single alcohol swab is beneficial if no other agent is available. Focus on covering gross contamination and moving quickly.

8. Gaps in Evidence and Research Priorities

Despite much research, important gaps remain:

- Pediatric data: High-quality trials in children are scarce.[9] Research is needed on safe CHG concentrations, optimal preparation agents, and neonatal protocols. Many recommendations are extrapolated from adults.
- Standardized application: There is no consensus on the optimal contact time or number of applications. Studies often differ (60s vs. 120s, 1 vs. 3 coats). Research could establish minimal effective contact times or verify if multiple coats improve outcomes.
- Alternative antiseptics: New agents like octenidine or novel formulations (e.g., chlorhexidine + alcohol gels) warrant study. With CHG resistance emerging, other broad-spectrum agents may become important.
- Incise drapes and dressings: Large RCTs on iodine-impregnated drapes versus standard, or no drape at all, could clarify their role. Similarly, studies on post-operative dressings (transparent vs. traditional) and SSI rates would be useful.
- Environmental factors: The impact of operating-room environment (ultraviolet lights, ventilation) on skin flora and antiseptic efficacy is understudied. Also, the interplay between skin preparation and antibiotic prophylaxis timing needs more evidence.
- Microbiome considerations: How skin antisepsis affects the skin microbiome and potential recolonization patterns over time is not well understood. Metagenomic studies could explore this.
- Implementation science: Research on compliance (does real-world practice match guidelines?) and interventions to ensure proper application (e.g., reminders to allow drying) is needed to bridge the gap between evidence and practice.

9. Conclusion

Pre-operative skin preparation remains a fundamental component of surgical infection prevention and has evolved significantly through advances in antiseptic science and evidence-based practice. Current guidelines strongly support the use of alcohol-based antiseptic solutions, particularly chlorhexidine-alcohol combinations, to reduce surgical-site infections. Proper application techniques, including adequate contact time, hair clipping instead of shaving, and complete drying before incision, are equally important for optimal outcomes. Further research is needed to standardize protocols, address pediatric evidence gaps, and evaluate emerging concerns regarding antiseptic resistance and safety.

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