Topical Antiseptics and the Skin Microbiota

Jan Claesen

The impact of antiseptics on the skin microbiota is poorly understood. SanMiguel et al. (2018) use a sequencing-based approach to compare treatment effects and find that they are dependent on interpersonal and body site—specific community differences. While treatment results in an immediate depletion of the skin microbiota, not all bacterial families are affected equally.


Antiseptics prevent commensals from going systemic

Our skin microbiota are clinging to a continuously shedding, nutrient-poor, acidic environment. On top of that, we constantly challenge their habitat through actions in our daily lives, including (hand) washing, use of alcohol-based gels, cosmetics, clothes, as well as occasional abrasions and wounds. Despite this, several bacterial families have adapted well and establish robust colonization, resulting in communities that remain surprisingly stable over time (Oh et al., 2016). In a clinical context, our skin microbiota undergo additional challenges caused by (topical) antibiotics use, diluted bleach baths, photodynamic therapy, and preoperative antiseptics. Even though antiseptics like povidone-iodine, chlorhexidine, and ethanol are commonly used to reduce the risk of surgical site infection and bacteremia, it is remarkable how little we know about their relative effects on different members of the microbiota. The study by SanMiguel et al. (2018) sheds more light on the effects of antiseptic-induced perturbations on bacterial community composition and dynamics.

Antibiotic treatments are typically used to target specific pathogenic skin colonizers, such as methicillin-resistant Staphylococcus aureus or group A streptococci. Unfortunately, these treatments often lack specificity and cause collateral damage to our benign communities by reducing microbial loads and diversity. Antiseptics are different—their activity is deliberately broad-spectrum and the detrimental effect on the commensal microbiota is actually desired. Indeed, postoperative shoulder infections, biofilms on catheters and implanted medical devices, and even endocarditis are often caused by abundant skin commensals like coagulase-negative staphylococci and Cutibacterium acnes (formerly Propionibacterium) (Martin-Rabadan et al., 2008; Portillo et al., 2013; Sohail et al., 2009). These bacteria do not typically cause harm when they reside in their natural skin habitat, but surgical procedures can promote access to the systemic circulation, enabling their new role as manmade pathobionts. Once established, biofilms are difficult to treat, requiring systemic antibiotics and often surgical replacement of indwelling devices. Prevention is better than cure, and this is why a thorough preoperative antiseptic treatment is imperative.

Which antiseptic works best?

Antiseptics that are commonly used for preoperative skin disinfection have broad-spectrum activity, impacting bacteria, viruses, and eukaryotic skin residents. However, this broad activity raises some toxicity concerns. Povidone-iodine works by releasing iodine, killing both prokaryotic and eukaryotic cells through oxidation of cell membrane compounds and lipid iodination (Fleischer and Reimer, 1997). Bacterial resistance to povidone-iodine has not been described and toxicity to mammalian cells is minimized because of the slow iodine release rate from the complex. Chlorhexidine’s mechanism of action involves membrane disruption, causing leakage and eventually cell death. Bactericidal activity is dependent on high chlorhexidine concentration, while low amounts inhibit bacterial growth only. Chlorhexidine skin treatment is not compatible with downstream DNA-based microbiota analysis (SanMiguel et al., 2018). Ethanol exerts its bactericidal action by dissolving lipid membranes and denaturing proteins. There is an ongoing debate about antiseptic efficacy and it has been suggested that chlorhexidine and ethanol might be better preoperative skin cleansers than others. A comparative culture-based study isolated more coagulase-negative staphylococci from povidone-iodine–treated patients, while Propionibacteriaceae tended to be more resistant to chlorhexidine treatment (Yeung et al., 2013).

SanMiguel et al. (2018) are the first to compare antiseptic perturbation effects on the microbiota using a 16S ribosomal RNA community analysis approach. Their study design accounted for interpersonal variation by subjecting each participant to all analyzed types of treatment. Six time points were sampled up to 72 hours after treatment, allowing for a detailed longitudinal analysis. The authors found that a single-application antiseptic treatment causes an immediate depletion of the skin microbiota, but recovery occurs quickly (6–12 hours post treatment).

The skin microbiome is a complex collection of distinct micro-ecosystems that are specifically adapted to thrive in the conditions encountered across different body sites (Grice et al., 2009). The present study incorporates this layer of complexity by comparing treatment effects on the upper back and the volar forearm. The upper back environment is sebaceous in nature and tends to harbor...
mostly Propionibacteriaceae and Staphylococcaceae. Communities living in the dry volar forearm environment are typically more diverse and additionally include Streptococcaceae and Corynebacteriaceae. Alcohol treatment resulted in a decrease of the forearm microbial diversity but not diversity on the back (SanMiguel et al., 2018). This observation is in accordance with the hypothesis that our skin contains both resident and transient bacteria (Kong and Segre, 2012). Increased exposure to the outside environment might result in a larger proportion of transient organisms on the forearm, which are more susceptible to antiseptic perturbation. Upper back communities might contrarily contain more stably colonizing residents. Despite their differences, none of the tested antiseptic treatments rendered the skin completely aseptic and microbial communities recovered quickly.

Towards a better understanding of our skin ecosystems

Pulse perturbations with antiseptics provide a controlled experimental setting to test hypotheses regarding characteristics and dynamics of our skin ecosystems. Low-abundance microbiota members are more readily displaced after treatment by members of the taxa that dominated a specific site before treatment. Among highly abundant members, the resilience of Propionibacteriaceae stands out across treatments. Other major families, including Corynebacteriaceae, Incertae Sedis XI, Staphylococcaceae, and Streptococcaceae were all significantly depleted compared to their levels at adjacent control skin sites (SanMiguel et al., 2018). A possible explanation for this difference could reflect the relative localization of these different families. Propionibacteriaceae are anaerobes that successfully colonize hair follicles, where they degrade sebum fatty acids. Their secluded habitat could provide enhanced protection from antiseptics in comparison to the other bacterial families, which are thought to reside closer to the skin surface. To more precisely localize and quantify live bacteria in their natural habitats, sequencing-based approaches could be complemented by fluorescent in situ hybridization techniques (Mark Welch et al., 2017).

The dominant taxon in upper-back communities tends to persist after treatment (SanMiguel et al., 2018). Propionibacteriaceae were the dominant members in most upper-back communities and, given their resilience, it is not surprising to find them regaining dominance after treatment. However, subjects with upper backs dominated by Staphylococcaceae prior to antiseptic depletion did not experience takeover by their more resilient Propionibacteriaceae. Mechanisms that underlie interpersonal differences in colonization are poorly understood. The current study suggests that there may be intrinsic host and/or environmental factors that cause similar dominant species to regain control after substantial disturbance. The propensity of Propionibacteriaceae to abundantly and stably colonize different skin locations puts them in a key position to impact colonization by other families, likely by occupying specific niches and producing small molecule metabolites. The bugs that fought hard to carve out niches in your skin do not allow themselves to be removed easily.

Clinical Implications

- Commensal skin bacteria can cause surgical site infections and form biofilms on indwelling medical devices.
- Antiseptics are used as a deliberately broad-spectrum preventative measure, impacting pathogens and commensal microbiota.
- Propionibacteriaceae are the skin bacteria most resilient to topical antiseptics.

REFERENCES