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What is left to justify the use of chlorhexidine in hand hygiene?

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Summary The CDC guideline for hand hygiene describes chlorhexidine gluconate as an agent with "substantial residual activity". But not all studies support this claim. In both suspension tests (e.g. EN 13727) and tests under practical conditions (e.g. EN 1500) it is crucial to neutralize any residual activity in the sampling fluid in order to make sure that the agent does not continue to damage surviving cells after exposure. The neutralization step must also be validated. If this is not done the efficacy may be significantly overestimated, and the healthcare professional may rely on data which do not represent the true efficacy of an agent. A review of eight studies which are cited to support "substantial residual activity" show that none of them were performed with validated neutralization. Seven of them do not demonstrate any residual activity for chlorhexidine gluconate. Only in one study some residual activity is described but the validity of the study design does not allow make this claim as no neutralizing agents were used at all. The benefits of using an active agent must outweigh any risks in order to justify its use. If no real benefits are left for chlorhexidine gluconate in hand hygiene, all the risks count even more such as skin irritation, allergic reactions including anaphylactic shock, and acquired bacterial resistance. Unless there is new and valid evidence to clearly support a benefit of using chlorhexidine gluconate in hand hygiene, healthcare workers should prefer formulations without this agent.

Introduction

A major factor for selecting a specific hand hygiene agent is its efficacy. This is measured first of all in suspension tests in order to determine the spectrum of antimicrobial activity (e.g. bactericidal, fungicidal, virucidal). It is, in addition, measured in tests under practical conditions in which the reduction of test organisms is measured on artificially contaminated hands. Healthcare workers rely on validated efficacy data. In both types of tests the number of test organisms

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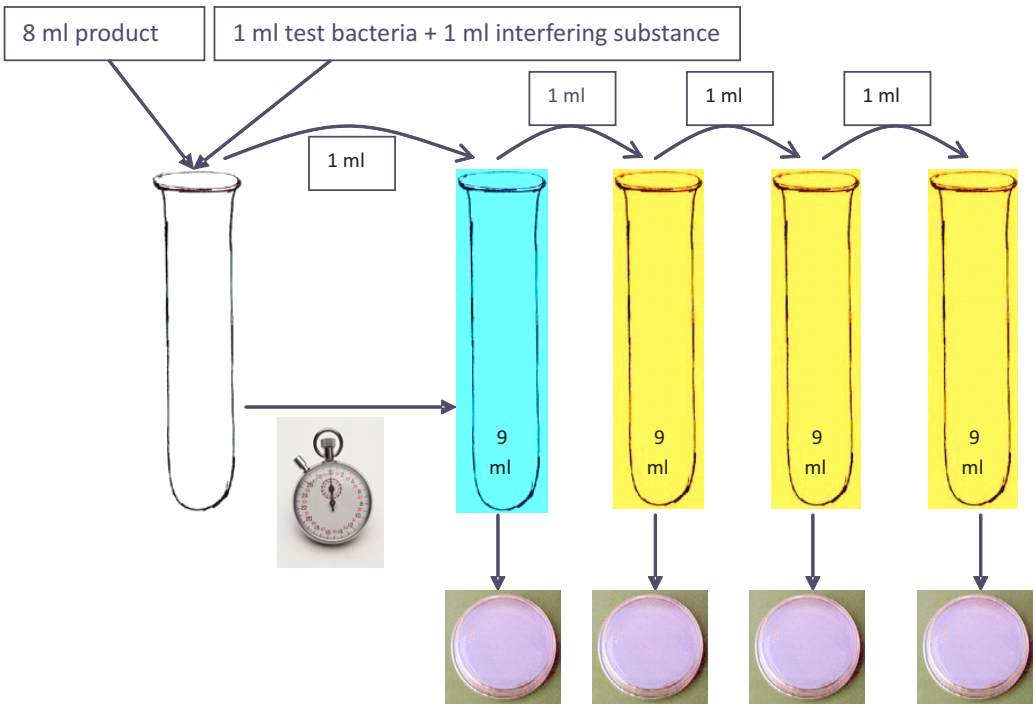

Fig. 1. Test principle of a suspension test, e.g. according to EN 13727; in published studies with chlorhexidine the sampling fluid vial (blue), dilution fluid vials (yellow) and surface agar plates do not always contain neutralizing agents.

is measured before and after exposure to the preparation allowing the extent of reduction to be described (primary endpoint). The efficacy is always measured after a specific exposure time or application time. That is why it is crucial to make sure that the number of surviving test organisms can accurately be determined. If the true number of surviving test organisms can not be found the measured "efficacy" is scientifically highly doubtful.

Chlorhexidine gluconate (CHG) is used in many countries as an active agent in hand hygiene preparations, both in liquid soaps as a single active agent but also in alcohol-based hand rubs as a second active agent. It is a non-volatile agent which is considered to have bacteriostatic activity beginning at a concentration of 1 mg/l and bactericidal activity at a concentration of $\geqslant$20 mg/l. [1] CHG is assumed to have "residual activity", especially in surgical hand disinfection. [2] The validity of the assumed "residual activity" has been questioned before. [1] That is why it appears necessary to scrutinize if there are valid data to support this claim.

The effect of inadequate neutralization

Neutralizing any residual activity in the sampling fluid after exposure is only a technical detail of the efficacy test but has a tremendous effect on the primary outcome. If there is no evidence that neutralization was successfully carried out the measured and calculated efficacy is very likely to be significantly overestimated. This will now be looked at in detail.

Suspension tests (e.g. EN 13727)

The test principle of suspension tests is to expose specific test organisms to the antiseptic for a specific exposure time and to measure the mean $\log_{10}$ reduction that can be achieved within the exposure time (Figure 1). For hand antiseptics the typical exposure time is 30 s (hygienic hand disinfection) or longer, up to 5 min (surgical hand disinfection). [3] After the exposure of the test organisms to the antiseptic it is crucial that any remaining bactericidal or bacteriostatic activity of the antiseptic is stopped immediately to make sure that all test organisms can be found which survived the exposure to the hand antiseptic. That is why at least the first dilution step should always contain valid neutralizing agents, which ensure to stop any ongoing activity at the end of the exposure (Figure 1). The additional dilution steps and the corresponding agar plates may also contain the same neutralizing agents, which increases the chance to obtain valid data. [4] If this is not done the antiseptic agent can continue to kill test bacteria beyond the 30 s exposure time in the sampling fluid or can express bacteriostatic activity on the agar plates which does not allow the survivors to form