DeNeedle™ Kit
Preventing Surgical Site Infections with Intradermal Antibiotics:
Getting Under the Skin of AMR

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Surgical Site Infection –A Global Burden

Surgical site infections (SSI) are common and burdensome for healthcare. They increase the **readmission rate by a factor of five** and **double mortality rates**[1]. The value to patients and healthcare systems is hugely compromised through costs of re-operation and delayed discharge.[2] The 30-day crude **incidence of SSI is 11%** and varies by anatomical site,[3] duration of surgery and global geography. SSI often occur after discharge, underestimating the true prevalence.[4]

At **15% of the world's antimicrobial consumption**[5], surgical antibiotic prophylaxis (SAP) represents a predictable point of intervention to curtail the global AMR crisis. Skilled antimicrobial stewardship becomes critical since **inappropriate SAP increases SSI rates by a factor of 6.7** and drives antimicrobial resistance (AMR).[6] It is estimated that a staggering **60% of SSI's could be reduced with evidence-based measures.** [7]

Intradermal Antibiotics (IDA) for SSI Prevention

Standard systemic delivery routes of antibiotic administration for SSI prevention are wrought with risks including **adverse events, prescribing errors, stewardship decisions, selection pressure for AMR and detrimental systemic exposure of the microbiome to antibiotics**. As a result, the value we harness from SAP needs improvement.

Cutaneous preoperative **disinfection does not completely mitigate infection, which can be caused by bacteria released from the intradermal space in the skin or surgical equipment (Fig 2 and 4).** The DeNeedle™ antibiotic injection kit (Fig 3) allows novel targeted delivery of antibiotic at microdosed concentrations. Dermal interstitial antimicrobial **tissue levels of 30 to 60 times**[8] greater than systemic routes can be achieved. (Fig 1) Such high local concentrations ensure an effective level at the time of skin closure. Ensuring target **tissue concentrations within the "golden hour" period following incision is vital, as this is when microbes remain antibiotic-susceptible** in the planktonic phase.[9] Beyond this time, microbes are more likely to adopt a biofilm phenotype with a fibrin matrix and are less susceptible to antibiotics.

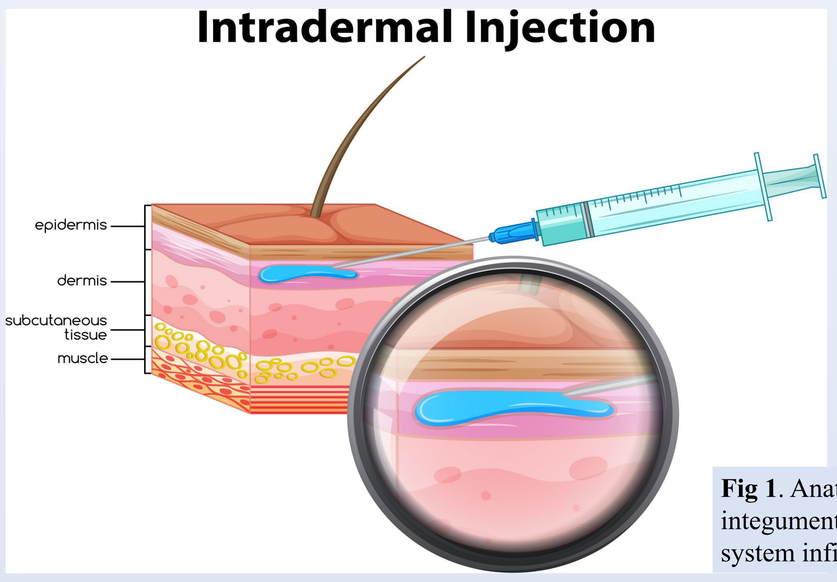

Fig 1. Anatomical layers of the integumentary system. The DeNeedle™ system infiltrates antibiotic to the dermis

Evidence summary for IDA

The documented evidence for IDA started 40 years ago in the UK within general surgery; clear benefits for reducing the burden of SSI were demonstrated. There is now a rich network of evidence across the world and across common surgical procedures which support this approach.

Dermatological cancer surgery is classified as "clean-contaminated" surgery; intradermal antibiotics have a strong evidence base of randomized clinical trials (RCT).

- RCT (n=1133): IDA significantly less SSI vs placebo and significantly more post-op antibiotics required in placebo patients[10]
- Meta-analysis (n-2080): IDA significantly less SSI vs placebo[11]. Test for overall effect z=2.45 (P=0.01)
- Case series (n=11,412); 0.3% SSI rate (10x lower than usual cited prevalence)[12]

General surgery a selection of studies from around the world and in various surgery types.

- RCT (n=120) **cholecystectomy**: Combining with IV Therapy. IV (prevalence 18%) vs IDA +IV (2.5%) $p < 0.05$ [13]
- RCT (n=100) **laparotomy**: Combining with IV Therapy. IV (15%) vs IDA +IV (6%) $p<0.001$ [14]
- RCT (n=100) **hernia repair**: Combining IV therapy. IV (20%) vs IDA+IV (6%) $p<0.05$ [15]
- RCT (n=100) appendectomy: IDA 3.3% vs IV (13.3%) $p<0.05$ [16]

Preoperative scrubbing does not eradicate intradermal bacteria

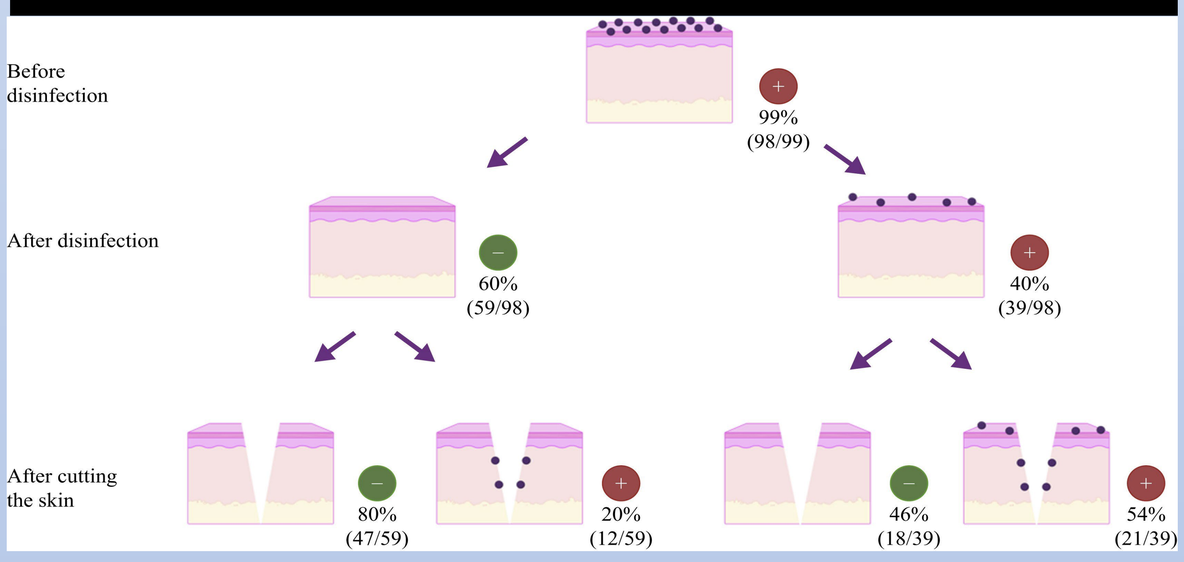

Figure 2- Percentages and numbers of patients (n=99) with positive or negative cultures before disinfection (swab 1), after disinfection (swab 2) and after cutting the skin (swab 3). Purple dots represent micro-organisms. Ref. Guarch-Perez C, et al. Journal of Hosp Inf. 2023 May; Vol 140:62-71. https://doi.org/10.1016/j.jhin.2023.07.014

Intradermal cultures remain positive after surgical scrub

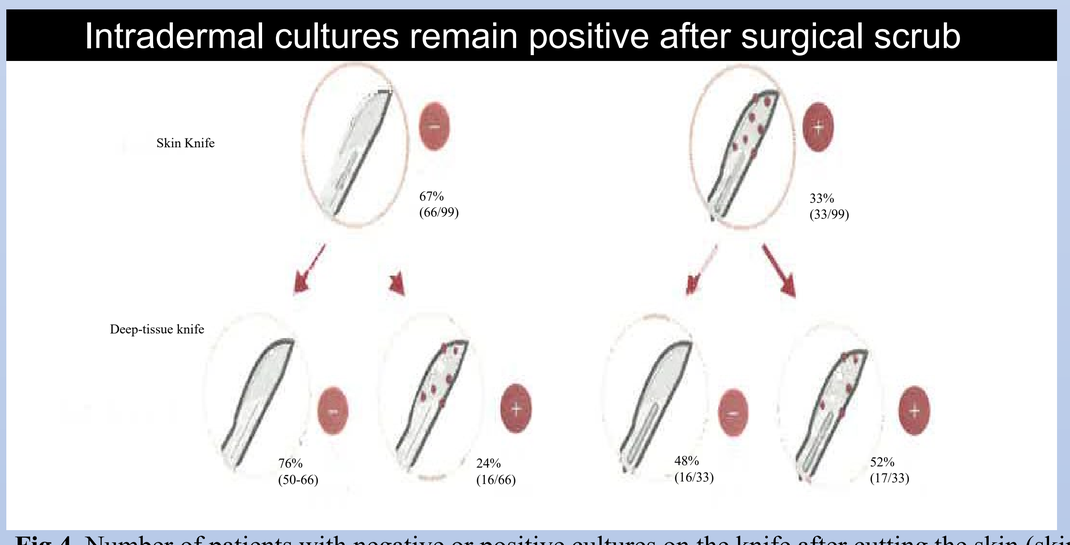

Fig 4. Number of patients with negative or positive cultures on the knife after cutting the skin (skin knife), and on the second knife after cutting the deeper tissue layers (deep-tissue knife). Ref. Guarch-Perez C, et al. Journal of Hosp Inf. 2023 May; Vol 140:62-71 https://doi.org/10.1016/j.jhin.2023.07.014

Intradermal antibiotics for SSI embraces and empowers the surgical team to act as stewards in the fight against AMR, to truly value antimicrobials and reduce inappropriate use. Together, we aim to revolutionize surgical outcomes

Fig 3. The DeNeedle™ injection kit for reconstitution of antibiotic components includes a sterile vial of antibiotic, adapter device, a diluent (e.g., lidocaine), a syringe, specialized 2.5 mm needle for intradermal delivery

DeNeedle™ Benefits

1. Preoperative antibiotic administration tailored to the onset of the surgical procedure
2. Nausea associated with oral administration of antibiotics is eliminated
3. Compliance issues are eliminated
4. Major organ systems of the body, including renal and CNS, are not exposed
5. The gastrointestinal microbiome is not altered. Emergence of colitis is minimized.
6. Higher tissue levels with greater efficacy.
7. Less risk of medical errors and IV mishaps
8. The development of resistant organisms are minimized
9. A theoretical possibility to decrease systemic drug interactions
10. Cost and environmental impact of plastic use
11. Multiple new indications possible

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