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**A case of immediate hypersensitivity to chlorhexidine.**

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Short running title: Type 1 hypersensitivity to chlorhexidine

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### **A case of immediate hypersensitivity to chlorhexidine.**

#### **Abstract**

Chlorhexidine is a widely used and effective antiseptic agent. Although skin contact is usually well tolerated, it may cause both immediate and delayed hypersensitivity reactions. We report a case of immediate hypersensitivity to chlorhexidine causing both skin and respiratory symptoms, following occupational exposure in a healthcare worker.

**Keywords:** chlorhexidine, immediate hypersensitivity, type I hypersensitivity, healthcare.

#### **Learning Points**

- Chlorhexidine is an effective antiseptic agent that is also a rare allergen.
- Chlorhexidine has the potential to cause both immediate and delayed hypersensitivity reactions.

#### **Introduction**

Chlorhexidine is a commonly used antiseptic agent within the healthcare setting and is present in community based medical products and personal care items. Chlorhexidine is present as the diacetate or digluconate salt and is effective against a range of gram positive and gram negative bacteria, viruses and fungi.<sup>1</sup>

Since chlorhexidine's introduction in 1954, it has proved to be a key antimicrobial in reducing infection rates, as a result of its superior antiseptic properties compared to povidone-iodine and alcohol.<sup>2</sup> It is routinely used as part of hand hygiene, as a skin or mucosal disinfectant prior to surgical procedures, in skin asepsis prior to vascular access, as a lubricant for urological procedures and is often impregnated within wound dressings and central venous catheters.

Chlorhexidine has the propensity to cause a range of hypersensitivity reactions such as delayed type hypersensitivity, causing allergic contact dermatitis (ACD).<sup>1</sup> We recently reported our experience of ACD to chlorhexidine.<sup>3</sup> In our clinic population, the rate of relevant chlorhexidine induced ACD was found to be at least 0.24% and in healthcare workers, as high as 2%.<sup>3</sup> Chlorhexidine has also been reported to cause immediate hypersensitivity, with reports of both contact urticaria<sup>4-7</sup> and anaphylaxis.<sup>6,8</sup> Damage to the epidermal barrier or application to mucous membranes seems to enhance the likelihood of an immediate hypersensitivity reaction occurring, however the incidence is unknown.

### Case

A 49-year-old female endoscopic technician presented with a six-month history of urticaria occurring on the hands and arms. This occurred 5-10 minutes after entering the endoscopy suite and more recently had been associated with respiratory symptoms including chest tightness and dyspnoea. She also had a two-year history of hand, wrist and arm dermatitis.

As an endoscopy technician for four years, her duties included maintenance and cleaning of endoscopes. More specifically her job entailed exposure to Rapid-Zyme™, an endoscopic enzyme cleaner. Whilst handling this substance, she used protective clothing including long nitrile gloves, an apron and face shield. Prior to entering the endoscopy suite, she washed her hands with chlorhexidine containing hand rubs (Debug® and/or Avagard®).

Her symptoms were completely restricted to the workplace, with improvement away from work. She found antihistamines helpful in controlling her symptoms.

Medical history was limited to an allergy to aspirin, contact dermatitis to cheap metal jewellery and a family history of atopic eczema. She had previously been assessed by both an allergist and occupational physician, but no diagnosis had been made.

The patient was patch tested to the Australian Baseline Series, rubber chemicals, various antiseptics including chlorhexidine diacetate 0.5% in aqueous solution and chlorhexidine digluconate 0.5% in aqueous solution and her own samples. There was a positive reaction to nickel, which was consistent with her past history of issues with jewellery. Patch testing to all other allergens, including both forms of chlorhexidine was negative.

Given the immediate nature of her symptoms, she underwent a targeted prick test to chlorhexidine digluconate 0.5% in aqueous solution and Debug®, positive control (histamine) and negative control (normal saline). The patient developed sizable wheals to both the chlorhexidine and Debug®, as well as to the positive histamine control. There was no reaction to the negative control.

The diagnosis was assessed as immediate hypersensitivity to chlorhexidine and deemed to be the cause of both her urticaria and respiratory symptoms. Allergen avoidance was recommended and subsequently she tolerated a chlorhexidine-free alcohol based hand gel (Aqium®) without recurrence of her symptoms.

### **Discussion**

This case illustrates immediate hypersensitivity to chlorhexidine manifesting as contact urticaria, which was associated with respiratory symptoms including dyspnoea. There have been reports of urticarial eruptions following mucosal exposure to chlorhexidine via the oral,<sup>4</sup> vaginal,<sup>5</sup> urethral route<sup>6</sup> and also from skin exposure when used pre-operatively.<sup>7</sup>

The majority of the recent literature on immediate hypersensitivity to chlorhexidine has focused on anaphylaxis predominantly in the perioperative

setting.<sup>6,8</sup> The reports of anaphylaxis have followed mucosal exposure from the intraurethral use of chlorhexidine containing gel for urinary indwelling catheter insertion,<sup>6,8</sup> intravenous exposure via chlorhexidine impregnated central venous catheters<sup>6</sup> or the use of chlorhexidine skin preparation prior to epidural insertion.<sup>8</sup>

In Japan and Denmark, there is growing awareness of chlorhexidine as a potential allergen, albeit a rare one. In 1984 following a cluster of 15 cases of anaphylactic shock attributed to chlorhexidine, the Japanese Ministry of Welfare prohibited the use of chlorhexidine on mucous membranes and restricted its use to the lowest bacterial concentration (0.05%) on wound surfaces.<sup>9</sup> This also led to the withdrawal of all chlorhexidine impregnated central venous catheters in Japan.<sup>9</sup> More recently in a Danish study, 228 patients with a suspected perioperative allergy were investigated using specific IgE, histamine release, skin prick and intradermal tests.<sup>10</sup> In this study, 9.6% of patients were diagnosed with a chlorhexidine allergy.<sup>10</sup>

However this concern is not widespread. As chlorhexidine is not a pharmaceutical product, it is not standard practice to document its use during simple investigations or surgical procedures and therefore it may be overlooked as an allergen. As allergy may initially be unsuspected, there is risk of re-exposure with potentially fatal consequences. It is present in a wide array of hospital, community based medical and personal care products (see Table 1). It is therefore important that healthcare professionals are aware of chlorhexidine's potential to cause severe immediate hypersensitivity reactions.

### **Conclusion**

Chlorhexidine is a rare allergen: however it is capable of causing both immediate and delayed allergic reactions and affecting both patients and healthcare workers. It is often not suspected as a culprit allergen, as in our case. Healthcare professionals should be aware of its propensity to cause allergic reactions and the types of products chlorhexidine is found in.

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**Tables**

Table 1 Potential chlorhexidine containing products

<b>Hospital</b>	<b>Community medical</b>	<b>Personal care</b>
Central venous catheters	Wound dressings	Teeth whitener
Antiseptic hand wash/rub	Antiseptic cream	Throat gargle
Antiseptic hand lotion	Antiseptic powder	Mouth wash
Catheter lubricant gel	First aid cream	Toothpaste

Gynaecological disinfectant or lubricant	Acne wash	Antiseptic dental drops
Surgical hand wash	Acne lotion	Hair conditioner
Surgical skin preparation	Nasal cream	Hair dye
Hospital grade surface disinfectant		Hair gel
Hospital grade disinfectant wipes		Deodorant
Antiseptic swab		Aftershave
Wound disinfection solution		Lip balm
Irrigation solution		Make up remover
		Face masks