

# Systemic pigmented contact dermatitis to cobalt following ingestion of cobalamin supplement

Thanet Pongcharoensuk<sup>1</sup> and Supitchaya Thaiwat<sup>1</sup>

<sup>1</sup>Phramongkutklao Hospital

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## Abstract

Systemic contact dermatitis (SCD) is a condition occurring in previously sensitized individuals after systemic re-exposure to the same or cross-reacting substance. Pigmented systemic contact dermatitis after intake of cobalt containing diet has never been reported.

## Introduction

Cobalt is an essential element to humans in the form of cobalamin (vitamin B12). The human body contains approximately 1 mg of cobalt, which around eighty percent is a component of vitamin B12. Human dietary intake of inorganic cobalt including green leafy vegetables, dairy products, liver and cereal grains varies between 5 and 50 µg/day, while vitamin B12 represents cobalt only in minute amounts. Cobalt does not accumulate in the body and is rapidly excreted in urine. (1, 2)

We report a case of systemic pigmented contact dermatitis, presenting as hyperpigmented lesions on face, neck and upper back caused by ingesting cobalt (cobalamin, vitamin B12). This patient had a history of ingesting cobalamin (vitamin B12) to treat her neuropathic pain 2 years earlier.

## Case description

A 55-year-old non-atopic woman with an underlying condition of herniated nucleus pulposus presented slate-grey hyperpigmented macules and patches on face, neck and upper back for 2 years (Fig. 1). She had a history of taking vitamin B12 supplement 600 µg daily due to her neuropathic pain for 3 months before onset of hyperpigmented lesion. She denied having direct contact with cobalt, or any other metals and also agents which can induce slate grey hyperpigmentation including fragrances, rubber products or hair dye. Histopathology of the lesions showed focal vacuolar degeneration of the epidermis with superficial perivascular infiltration of lymphocytes and marked increase of dermal melanophages (Fig. 2).

**Fig. 1** . Slate-grey hyperpigmented macules and patches on both cheeks

**Fig. 2** . Histopathology from hyperpigmented lesions showed focal vacuolar degeneration of the epidermis and marked increase of dermal melanophages (black arrows) with superficial perivascular lymphocytic infiltration (H&E x40, x100).

Systemic pigmented contact dermatitis was suspected, so patch testing was performed using the European Society of Contact Dermatitis guideline standard and cosmetic series (3). Readings were performed at 48 and 72 hours according to the International Contact Dermatitis Research Group criteria. Pigmented reactions to cobalt showed positive hyperpigmentation after 48 and 72 hours, while other standard and cosmetic allergens were negative (Fig. 3). We further performed tissue biopsy on the positive pigmented

reaction. Histopathology showed focal parakeratosis with focal vacuolar interface dermatitis at the dermo-epidermal junction and superficial perivascular infiltration with lymphocytes and melanophages consistent with pigmented systemic contact dermatitis similar to her previous active lesions (Fig. 4). The patient was advised to avoid taking oral vitamin B12. One year after diagnosis, the hyperpigmentation gradually faded after discontinuing cobalamin and adjunctive treatment with topical low potency corticosteroid and topical retinoic acid.

**Fig. 3.** Patch test read at 72 hours gave hyperpigmented reactions to cobalt (No.22).

**Fig. 4 .** Histopathology from positive patch test pigmented reaction showed focal vacuolar degeneration of the epidermis with dermal melanophages (black arrows) with superficial perivascular lymphocytic infiltration (H&E x40, x100).

## Discussion

Cobalt is an ingredient of vitamin B12 or cobalamin, reaction to cobalt may cause problems in patients receiving vitamin B12 replacement therapy. Several cutaneous manifestations have been reported in patients with allergic contact dermatitis to cobalt undergoing oral cobalamin replacement including atopic dermatitis, chronic vesicular hand dermatitis, cheilitis, and stomatitis. (4)

Systemic contact dermatitis (SCD) is a condition occurring in previously sensitized individuals after systemic re-exposure to the same or cross-reacting substance. Sensitization occurs due to varying exposures to antigens via multiple routes through the circulatory system, and thereby produces systemic allergic dermatitis, which may result in a variety of skin eruptions and systemic flare. The exact mechanisms behind SCD are not fully understood, but is thought to be a T-cell mediated delayed type hypersensitivity reaction. (5) The common allergens inducing systemic contact dermatitis include nickel, zinc and cobalt. (6-8) Several systemic agents are associated with pigmentation including cytotoxic agents, antimalarial, analgesics and silver but pigmented systemic contact dermatitis after intake of cobalt containing diet has never been reported.

Osmundsen et al. first described pigmented contact dermatitis (PCD) as a non-eczematous variant of contact dermatitis, clinically characterized by hyperpigmentation with little or no signs of dermatitis by observations that the melanosis was due to contact dermatitis caused by an optical whitener containing pyrazoline present in a washing powder. (9) The exact mechanism which allergens induce hyperpigmentation remains unknown. Some experimental studies have shown that allergens having a special affinity for melanin induced cutaneous inflammation increasing the number and size of the melanocytes and enhancing their enzymatic activity (9, 10). The common allergens responsible for pigmented contact dermatitis are listed in Table 1. Related studies have demonstrated cases of pigmented contact dermatitis and histopathological examination revealed focal vacuolar degeneration of the epidermis and increased dermal melanophages with superficial perivascular lymphocytic infiltration. (11, 12) Although the exact mechanism of how cobalt induces systemic contact dermatitis remains unknown (13), one related study revealed the increasing prevalence of cobalt allergy in the general population and the high popularity of food supplements containing cobalt, e.g., vitamin B12 supplement. (14)

## Conclusion

We reported the case as first presenting hyperpigmented macules and patches on the face, neck and upper back after vitamin B12 ingestion. The results of the patch test with the cobalt also showed hyperpigmented reactions consistent with the clinical presentation suggesting the diagnosis of systemic pigmented contact dermatitis resulting from oral administration of cobalamin. The diagnosis was confirmed by histopathological results of the positive patch test results corresponding to the previous active lesions. We suggest investigating systemic pigmented contact dermatitis in reaction to cobalt when patients present unexplained hyperpigmented lesions.

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Cosmetic	Fragrances, Preservative, Hair dyes, Lipsticks
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Fragrances	Benzyl salicylate, ylang-ylang oil, Jasmine, Hydroxy-citronellal, Benzyl alcohol, Cinnamic alcohol, Lavender oi
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Cosmetic	Fragrances, Preservative, Hair dyes, Lipsticks
Textiles	Azo dyes, Optical whiteners
Toiletries	Chromium hydroxide, Fragrances, Nickle oxide
Others	Minoxidil, Nickel sulfate

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**Table 1.** Common allergens causing pigmented contact dermatitis

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### Conflict of interest

The authors have no conflict of interest to report.

### Author contributions

TP: wrote the article, provided pathologic photography and features. ST: corrected the manuscript.

### Ethical approval

We confirm that the manuscript has been read and approved by all named authors. The protection of intellectual property associated with this manuscript had been in our consideration.

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