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Case Report

# Delayed-Type Hypersensitivity to Henna Tattoo Components: 2 Case Reports

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**Abstract**

The fashion of temporary henna tattoos has become an increasingly diffuse habit in Western countries, but it may have undervalued consequencies such as a contact hypersensitivity to paraphenylenediamine, a strong sensitizer added to henna tattoo dye so turning red henna in black henna, without considering the damage to public health consumers, because paraphenylendiamine sensitization may be a permanentside-effect of a temporary whim.

**Keywords:** Cotrimoxazole; Cross-reactivity; Maculo-papular rash; Contact dermatitis paraphenylenediamine; Henna tattoo

## Introduction

Henna tattoos may be responsible of allergic contact dermatitis (ACD) because paraphenylenediamine (PPD) is frequently added to henna paste to increase brightness, duration and quality of the temporary tattoo. Such reactions might develop up to 45 days after the application of the tattoos because PPD is responsible of active sensitization [1]. Furthermore PPD is a potent hapten showing a potential cross-reactivity with a wide range of substance, which include drugs, hair and texile dyes and rubber additives too [1]. Because its widespread use , it is quite difficult for the sensitized patients to avoid any contact to p-phenylendiamine or related crossreacting substances.Hereby we describe two patients who have developed hypersensitivity reactions to PPD following the application of a henna tattoo.

## Case A

A 26-year-old woman with a history of allergic asthma to olive-pollen, presented with a severe pruritic papulo-vesicular reaction on her right hand. Such lesions had the flower-like shape of the original henna tattoo that a street vendor in Morocco applied at this site about 20 days earlier (see Picture 1). The patient stated that the dye of the tattoo disappeared 10 days before the appearance of the dermatitis that arised 2 days after she used a pair of rubber gloves to perform housework. It was the first time patient carried out a temporary henna tattoo application. The lesions were itching and so painful patient was unable to clench her fist.

Treatment with topic clobetasol ointment 0.05% in a twice daily application was performed for 1 week, associated to the administration of 5 mg levocetirizine dihydrochloride once daily for 2 weeks. The dermatitis completely healed in 1 month.

Three months after the complete resolution of the dermatitis, the patient was patch tested with the baseline S.I.D.A.P.A. (Italian Society of Allergological, Occupational and Environmental Dermatology) standard series (FIRMA® Inc., Florence, Italy), with the rubber series and with henna dust 10% pet. Patch tests were applied on the back and left in occlusion for 2 days using Finn Chambers® (Ø 8 mm; SmartPractice, Phoenix, USA) technique on Scanpor® tape (Norgesplaster A/S, Vennesla, Norway) and readings were made at 48 hours and 96 hours. The reactions showed positive result to para-phenylenediamine (PPD) (+++), diaminodiphenylmethane (++), carba mix (++) at 48 hours. Prick test with latex (Lofarma Inc. – Milano Italy) turned out negative.

## Case B

A 21 years-old male patient with an itching maculo-papular rash on the trunk, upper limbs and face was referred to our consultation by First Aid Center of Civil Hospital Vito Fazzi in Lecce. The rash has appeared on the third day following an antibiotic treatment with Bactrim Forte® (cotrimoxazole: sulfamethoxazole/trimethoprin 400 mg/80 mg-Roche Inc. Milan, Italy) tablets assumed for an acute febrile dysentery form. At the moment of evaluation, physical examination excluded bullous skin lesions or mucosal involvement. Medical history included a seasonal allergic rhinitis to ragweed pollen, a previous anaphylactic shock after taking oral amoxicillin/clavulanic acid and an urticaria following an unspecified oral cephalosporin.

**Figure 1:** Sample Text.


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Because of the previous drug adverse reactions, the patient had always taken macrolides only. Patient reported that he had never taken Bactrim Forte® tablets before that episode. We suspended Bactrim Forte® administering Rifaximin as alternative treatment, introducing 2 tablets of prednisone 25 mg onve daily for a week and levocetirizine 5 mg pills.

After 45 days from lesions' resolution, the patient underwent patch tests with SIDAPA (Italian Society of Dermatology and Allergology Environmental Professional) series and cotrimoxazole 10% in petrolatum (F.I.R.M.A Inc.- Florence-Italy). The patch tests gave positive results with reading at 48 hours and 72 hours to paraphenylenediamine (PPD) 1% in petrolatum (+++), to nickel sulfate 5% in petrolatum (+) and to cotrimoxazole (++). Apparently, these positive results seemed without a clinical relevance, because the patient reported that he had never dyed his hair nor had ever used condoms containing benzocaine. However, he remembered that two years before, during a short holiday in Greece, he had made a temporary henna tattoo on his left arm that was responsible for a painful bullous skin lesion after a few days in the site of tattoo. Patient reported the skin lesion regressed with steroids and macrolides therapy, although a hyperpigmented area persisted for few months. The patient declined an oral challenge test with increasing doses of cotrimoxazole.

## Discussion

Temporary henna tattoos have been used for decades in Muslim and Hindu populations for religious, cultural and cosmetic reasons, but they have become very popular in Western society too. Nowadays, these tattoos are well accepted and considered fashionable even among Western tourists in view of their non-permanent character, even if are frequently performed by street vendors on beaches or in summer resorts with low sanitary standards [2]. Unfortunately, PPD is frequently added and mixed to henna solution, sometimes in high percentage, as showed by Brancaccio et al. [3]. They evidenced, by high-performance liquid chromatography (HPLC) on different commercial samples of black henna mixtures, that PPD could reach high concentrations of 15, 7% [4].

Furthermore, White et al. have demonstrated for the first time in a recent study that, over the time period tested, the allergenic metabolites of PPD accumulate in the skin. Hence, intermittent exposure to lower concentrations of PPD may be equivalent to a higher concentration in a one-off exposure [4].

Chung et al. identified 2 groups of patients sensitized to PPD contained in henna tattoos: the first group developed an acute cutaneous response to temporary tattooing, typically presenting with intense eczematous responses within two days after tattooing; the second one manifested a subacute response slowly developing as a lichenoid eruption into 1 or 2 weeks [5]. From the comprehensive reviews of literature [1-6] it is possible to speculate that there is a third group of patients, i.e, patients who undergone an henna tattoo developing a latent sensitization to PPD, without eliciting any skin next application of PPD, usually contained in an hair dye or in a new henna tattoo [1-6]. The reaction may appear few hours, usually within 24 hours, after the second exposure to PPD and it can be highly severe. Jasim et al. describe the cases of two teenagers which developed redness and swelling on the face and neck few hours after an application of hair dye. In one patient the reaction was so violent he developed respiratory difficulties and was admitted to intensive care for intubation and treated with intravenous steroids and antibiotics. Both the patients had developed a strong skin reaction towards a henna tattoo in the previous two years. Furthermore, PPD was removed from standard series few hours after its application because of the strong reaction in the patch test site [7].

In the first case, the use of rubber gloves might have favored the onset of the ACD, possibly because of the occlusive effect of the glove and the presence of PPD as rubber additive in the gloves have induced an inflammatory flare-up of the original henna drawing, Surprisingly, patch tests showed a positive reaction to carba mix, while thiuram mix turned out negative. Patch tests positive to Thiuram mix and Black Rubber mix are frequently associated to PPD sensitization [6], even in pediatric age [8].

Such evidence might be explained by the presence, in tattoo inks, of some rubber accelerants as contaminants, inducing a concomitant contact allergy. Nevertheless, we cannot rule out that our patient had been sensitized to carbamates in the past.

Interestingly, cutaneous lesions were so severe and painful to cause a temporary functional inability of the painted hand, as already described for other henna tattoo blistering reaction involving extremities [9].

As far as the second patient is concerned, because PPD shows a wide spectrum of cross-sensitivity with a lot of substances as azo-dyes [10,11], various para-amino compounds, including some drugs as local anesthetic benzocaine [11], mesalazine [12] and hydrochlorothiazide [13]. Due to the short latency between cotrimoxazole assumption and the onset of skin rash, we suspect patient had developed a sensitization to PPD in the henna tattoo, but the generalized skin reaction has been elicited by the ingestion of cotrimoxazole, that is a potential cross-reactive compound.

Previously, in a patient with a personal history of contact allergic sensitization towards different para-compounds (e.g.: sulphonamides and benzocaine), the application of henna containing PPD caused allergic contact reactions on the site of tattoo [14], but the possibility to induce a generalized cutaneous rah in a PPD-sensitized patient assuming sulphonamides has never been reported in literature yet.

However, there are some doubtful points in the case B. Firstly, maculopapular exanthema are frequently reported as drug rash associated to cotrimoxazole, especially in HIV positive patients [15]. Although patient declared not to have assumed previously cotrimoxazole or other sulpha drugs, the ingestion of other cross-reactive substances cannot be excluded completely. The Sunset Yellow FC&C No.6 (or E110, according to the European nomenclature of food and drug additives), for instance, is used as dye in pharmaceutical preparations and it can induce a worsening of eczema or a generalized skin rash after the ingestion of iron tablets and antihistamine pills in PPD-sensitized patients [16,17]. The culprit agent was a dye metabolite, the sulfanilic acid (4-amino-benzene sulfonic acid) produced by the intestinal flora through the dye degradation, which is cross-reacting with PPD [16,17].

Alternatively, patient could have been sensitized to yellow sunset even and the cross-reactive phenomenon should be attributed to

common metabolites of cotrimoxazole, PPD and Sunset Yellow.

At anyway, it is necessary to consider patch tests to cotrimoxazole may result a good diagnostic tool in drug induced skin eruption, since they have been used successfully even in maculopapular exanthema induced by betalactams [18], although an oral challenge test that patient refused, could be required to confirm the diagnosis [19].

Lastly, in our opinion, PPD should be considered a "super-hapten", because some studies *in vitro* have showed that, although PPD is a contact allergen, it is able to interact directly with T-cell receptor through a processing independent pathway [20], according to the immune model of pharmaceutical-interaction (p-i) proposed by Pichler for drug hypersensitivity [21].

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