

CONTACT POINTS

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Immediate cutaneous hypersensitivity response to phytomenadione induced by vitamin K₁ in skin diagnostic procedure

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Key words: eczema; epicutaneous; hypersensitivity; intradermoreaction; Konakion[®]; phytomenadione; prick test; vitamin K.

Case Report

A 64-year-old woman with plaquetopenia and hypoprothrombinaemia caused by chronic hepatitis C virus liver disease started treatment with intramuscular Konakion[®] monthly. 1 week after the third injection, she developed some erythematous, pruriginous maculae with a well-defined outline which grew centrifugally at the site of inoculation on her buttock. By the 3 week, the plaque reached a size of 30 cm in diameter, and a rough desquamation became visible. The skin biopsy disclosed a spongiotic dermatitis. It healed with clobetasol propionate and oral anti-H₁ anti-histaminic. The patch test yielded negative results though a discrete positive reaction after intradermal test with Konakion[®] developed at day +7.

In order to take down the particulars of phytomenadione's direct responsibility, a second immunoallergic study was carried out 2 months later. The positive results yielded by the patch test (+ +) with both Konakion[®], and phytomenadione 10% pet. evidenced a delayed cutaneous hypersensitivity.

Phytomenadione 0.1% pet. and 20 healthy controls who were also patch tested showed negative results.

Phytomenadione 10% pet. prick test resulted positive at 15 min. The biopsy evidenced a massive dermal eosinophilic and neutrophilic infiltrate around the injected material at 30 min. Unlike what had happened 2 months before, Konakion[®] intradermal test disclosed a localized immediate cutaneous reaction at 30 min. From this area, a skin eruption reproducing exactly the same clinical characteristics of the adverse skin reaction developed subsequently. 10 healthy controls that were also pricked and intradermal tested showed negative results.

Comment

Adverse skin reactions induced by vitamin K₁, though exceptional, can be easily disregarded or go unnoticed. The incidence rate of phytomenadione anaphylaxis is 3 per 10 000 intravenous doses (1). Polyethoxylated 'castor oil' used as emulsifier, and vitamin K₁ emulsified by a blend of micelles were held responsible for anaphylactoid reactions. Eczematous reactions and morphea-type plaques are located at the site of injection. Average number of days before evidencing dermatitis is 13. The dose required for the reaction to occur ranges from 10 mg to 410 mg. In some cases, it will take at least 2 months to be solved. The time before the clinical appearance of morphea, with or without fasciitis, and eosinophilia is on average 8.5 months. The responsible dose range is wide (30 mg–208 mg). And it has bad prognosis for resolution (2).

The most extended and trustworthy provocation test to reproduce immediate and delayed hypersensitivity to phytomenadione is intradermoreaction with and without the excipient. Prick test or scarification test sensitivity is lower (3). Going through the literature, we noticed that either the entire vitamin K₁ product or phytomenadione 10%

pet. are normally used for patch test. However, the recommended concentration to patch vitamin K_{1,3,4} is 0.1% in pet.

This cutaneous reaction is peculiar due to its immediate beginning after the second immunoallergic study. The course of the first intradermoreaction and the second patch test showed a delayed hypersensitivity. The prick test and the second intradermoreaction immediately yielded, as expected, an antibody-mediated reaction.

The first vitamin K cutaneous diagnostic procedure could elicit an immediate hypersensitivity. We know that repeated antigen exposure can induce a shift in the time course from a typical delayed-type to immediate-type response followed by a late-phase reaction (4). This phenomenon has been demonstrated with dinitrofluorobenzene and 2,4,6-trinitro-1-chlorobenzene in BALB/c mice (5, 6). Simultaneous type I and IV immunoreactions have also been described by penicillin, contrast media or heparinoids.

The combination of both immediate and delayed hypersensitivity reactions to phytomenadione has not been previously reported. Cutaneous diagnostic procedure could elicit an immediate hypersensitivity reaction. To minimize risk and improve the characterization of phytomenadione adverse reactions, a detailed definition of standard diagnostic protocols is guaranteed.

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Meat protein allergic contact dermatitis: A case report

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Key words: beef; pork; protein contact dermatitis.

Protein contact dermatitis is a term introduced for people with hand eczema demonstrating immediate symptoms after the skin is exposed to food proteins.

We hereby present a case of a food handler that has chronic hand dermatitis diagnosed as protein dermatitis.

Case Report

Our patient is a 27-year-old man with a history of a 11-year-long hand eczema. He had been working as a cook and frequently protected

himself with rubber gloves. His personal history is positive to penicillin allergy and hepatitis A diagnosed during his childhood. 2 of his sons have asthma.

6 years ago, a previous patch test study was performed showing positivity to thiouram mix (+++).

The patient's main complaint was repeated episodes of bilateral hand eczema (Fig. 1), which resolved with topical corticosteroids and potassium permanganate.

A new patch test study was performed turning out positive to thiouram mix (++) again. The patient explained an itching sensation after handling certain foods, specially meat products. He also referred mouth pruritus after ingesting meat products.

Prick-by-prick test with beef meat and pork loin was positive. Also, commercial prick test to beef meat and pork meat were positives. Immunological studies detected specific IgE against pork (1.19 UI/ml) and beef (3.97 UI/ml). Total IgE was 549 UI/ml.

The patient was diagnosed to have protein allergic contact dermatitis to beef and pork. The recommendations for him included avoiding nude handling of meat and the use of vinyl gloves, with these measures and 10 months after the diagnosis had been made, the patient was free of lesions.

Conclusion

Protein contact dermatitis was first described in 1976 by Hjorth y Roed-Petersen (1) in people who made sandwiches.

Clinically, it is characterized by a chronic eczema with immediate urticarial or vesiculous exacerbations after being in contact with the causative protein agent (2).

The diagnosis is based on the clinical history and the positiveness of the diagnostic tests with the suspected substance.

This condition mostly affects food handlers and people who have direct contact with animals, also bakers, cooks, farmers, veterinarians, florists and health workers such as nurses (3).

On 50% of the cases, an atopic history can be found but not in the other half of the patients.

This irritative dermatitis implies the existence of an alteration in the cutaneous barrier that facilitates the passage of macromolecules, namely proteins, into the inner skin layers.

The clinical examination shows a chronic and recurrent eczema characterized by erythematous and desquamative lesions that can be intermingled with vesicles, it is highly pruriginous and often with urticarial or vesiculous exacerbations after few minutes of being in contact with the allergen.

This allergic contact dermatitis due to proteins also can appear after a recurrent contact urticaria with secondary eczema development (4).

When the allergen is volatile, respiratory and ocular symptoms (rhinitis, asthma and conjunctivitis) can coexist, as it occurs with the bakers that are in continuous contact with flour.

Sometimes, the ingestion of the food can also cause digestive symptoms such as abdominal pain or



Fig. 1. Chronic dermatitis of the hands where we can observe dry lesions.

cramps and diarrhoea, angioedema and/or oral itching (5).

Skin and laboratory tests are the essentials of diagnosis. The best methods are prick test (also prick by prick) and scratch chamber test.

For certain standardized allergens specific IgEs can be dosified by radioallergosorbent test comparing their results with the performed skin tests and the clinical history.

The presence of protein contact dermatitis in meat-handling patients with chronic eczema is not infrequent. However, an accurate early diagnosis could avoid secondary problems or complications associated to this condition.

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Occupational contact dermatitis from simvastatin

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Key words: contact dermatitis; occupational; simvastatin.

Case Reports

Case 1

A 21-year-old male with a history of sensitization to dust mites came to our department in October 2002 because of a facial eruption with desquamative erythema resembling seborrheic dermatitis. (Fig. 1) He explained that these lesions appeared during working hours, being minimal on the 1st day of the week and progressively worsening towards the

last. Each relapse was more intense than the anterior. The patient worked in quality control in simvastatin synthesis.

Case 2

A 31-year-old woman without any relevant history worked in the same pharmaceutical industry as patient no. 1. She came to our department in May 2003 for a facial erythematodesquamative eruption, which

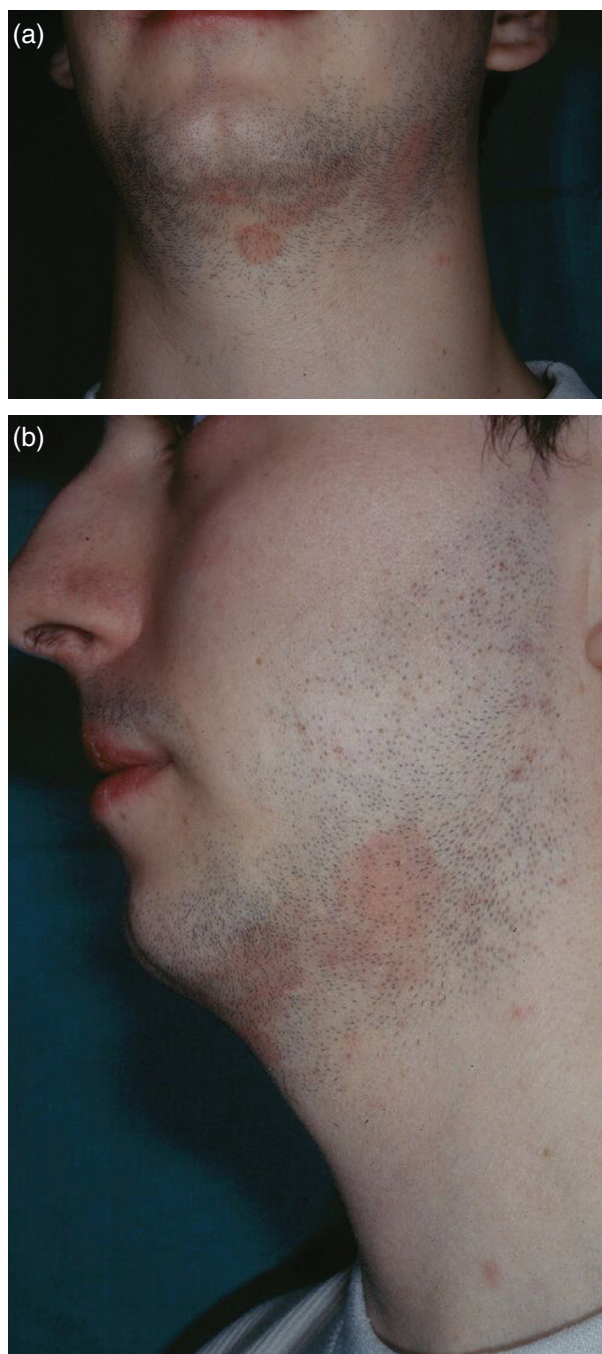


Fig. 1. Clinical appearance of patient no. 1.

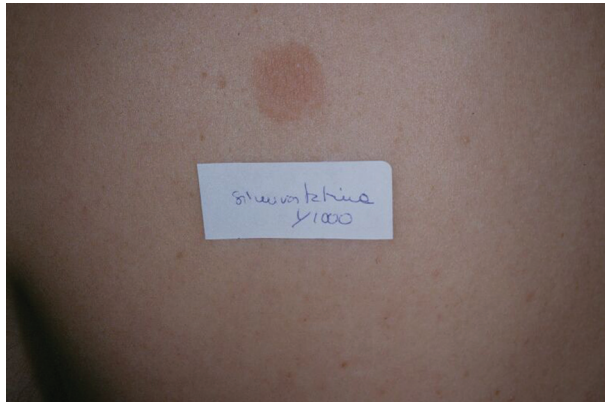


Fig. 2. Positivity of simvastatin 1/1000 in ethanol at 96 hr.

started on the 2nd day of the working week. She had only sporadic contact with the quality control unit.

The European standard series was negative in both patients and we decided to test butyl hydroxyanisole 2% pet. (BHA) and simvastatin.

BHA 2% pet in open and closed test was negative at 48 and 96 hr. Simvastatin 1/1000 in ethanol was positive 48/96 hr ++ (Fig. 2).

We tested 10 controls, all of which were negative.

Discussion

Simvastatin is a competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, commonly used in the treatment of hypercholesterolemia.

HMG-CoA reductase inhibitors are considered safe. However, simvastatin, which is the most widely used statin, has the greatest number of reported side-effects, the most commonly reported including abdominal discomfort, headache, transitory transaminase elevation, hepatitis and cholestatic jaundice, myalgia and myositis (1).

Cutaneous side-effects associated with simvastatin include eczematous skin rash (2, 3), urticaria, angioedema, lichenoid eruption (4), cheilitis (5), chronic actinic dermatitis (6, 7), acute generalized exanthematous pustulosis (8), lichen planus pemphigoides (9), lupus-like syndrome (10), radiation recall reaction (11), photosensitivity (12), dermatomyositis (13), erythema annulare centrifugum (14) and porphyria cutanea tarda (15).

We report two cases of occupational airborne contact allergy to simvastatin affecting the face and neck only.

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Lichen dermatitis in a rock climber

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Key words: allergic contact dermatitis; lichens; rock climbing; usnic acid.

Case Report

A 34-year-old man with a past history of hay fever, pet allergy and mild asthma presented with a recurrent rash occurring 2 to 3 days after outdoor rock climbing. He would develop an itchy, eczematous rash over his face, neck, forearms and hands lasting for approximately 1 week. The rash affected light-exposed areas but was not exacerbated by sunlight and did not occur when climbing indoors. When climbing outdoors, the patient would frequently experience contact with

lichen either directly from the surface of the rock or in an aerosol of plant material created when the rock was scrubbed with a brush to aid grip.

Patch tests were performed to the British Contact Dermatitis Society standard series, plant series, lichen acid mix, the outer sole of his climbing boot and 2 varieties of lichen supplied by the patient. He had a +++ reaction to both varieties of lichen supplied, usnic acid 0.1% pet. (which is an antibacterial substance found in many varieties of lichen), lichen acid mix and fragrance mix. Constituents of fragrance mix were then applied on day 2, and a ++ reaction to oak moss absolute 1% pet. subsequently developed. The diagnosis of lichen dermatitis was made and appropriate avoidance advice given.

Discussion

Allergic contact dermatitis to lichen is unusual even in those who regularly come into direct contact with lichen, such as gardeners, forestry workers and lichen pickers (1). Sensitization may also occur through contact with various cosmetic products that contain lichen extracts, particularly men's perfumes containing oak moss (2). Reports of non-occupational sensitization via direct exposure to lichens are rare. Lichen dermatitis has previously been reported in a young girl who was sensitized via direct contact with lichens when tree climbing (3). To our knowledge, this is the first reported case of allergic contact dermatitis to lichen arising in a rock climber. As leisure and outdoor activities become more popular and lichen abundance increases as a consequence of environmental changes (4), we may see an increase in lichen sensitization distinct from the traditional occupational and cosmetic routes.

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Sensitization to para-phenylenediamine in a streetside temporary tattoo artisan

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Key words: allergic contact dermatitis; henna; para-phenylenediamine; tattoo; skin dye.

Henna temporary tattooing is a costume among Islamic and Oriental cultures. This costume has been imported to Western cultures as a leisure activity in touristic areas, attraction parks and festivals. Due to the slow drying of henna, which can take up to an hour, other substances such as essential oils, coffee, tea, indigo, azoic dyeing or para-phenylenediamine (PPD) are added in order to accelerate the process of dyeing. 'Black Henna' is commonly referred to as henna with other dyeing elements such as indigo (derived from the plant *Indigofera argentea*) or PPD.

A 24-year-old woman, leisure assistant at a hotel in Gran Canaria (Canary Islands, Spain), presented chronic dermatitis on her hands the previous

year, which became severe when she worked as a streetside temporary tattoo artisan. On one occasion, she applied to herself a temporary tattoo, in which an inflammatory skin reaction was remarkable. The dye that she used was a dark brown powder, which was purchased at a flea market as 'Natural Henna Imported from Morocco'. The dye is made by mixing the powder with an equivalent portion of water, and the paste obtained is applied with a brush. 15 min is enough for drying in order for the tincture to set. The patient frequently bleaches her hair, and on some occasions, she has dyed it without remarkable reactions.

Patch test with the GEIDC standard series and hairdressing series (Chemotechnique Diagnostics[®], Tygelsë, Sweden) was positive to PPD after 48 (+++) and 96 hr (+++). The open test, applying a paste made with water and the aported powder on her forearm, demonstrated an eczematous reaction 8 hr after application. Pure original henna from India, grayish green colour, was applied as a mixture with water in open and, 48 h, closed test without reaction. The high resolution liquid chromatography study of the powder used by the patient, extracted in acetonitrile-phosphate buffer at pH 7 (1), demonstrated the presence of 23.5% of PPD and 5% of 2-hydroxy-1, 4-naphthoquinone.

Comment

Henna is a natural product derived from the leaves of the shrub *Lawsonia inermis*, and its active component is the hydroxy-naphthaquinone. It is recommended as an alternative for hair dyeing to women sensitized to PPD (2). It is usually commercialized as a greenish powder obtained by dried and grinded leaves, which is mixed with water or oils in order to obtain a paste. This paste is used to apply decorative motifs on the skin or for hair colouring use.

In the past few years, PPD reactions in patients exposed to temporary tattoos, in theory applied with natural henna, have been described (3–7). These cases refer to transient painters' clients who presented lichenoid, eczematous or erythema-multiforme-like eruptions in the painting site. Our case is the first case of sensitization to PPD in a streetside temporary tattoo artisan. Our

patient was not aware of the possible sensitization risk of a 'natural' product. The maximum concentration of PPD in the final product allowed in Europe is under 6% (4), and our patient used a mixture of water and powder with an approximate final concentration of PPD of 12%. This level of concentration and the fact of application on hairless skin would justify the increase of sensitization cases described, including childhood cases (6, 8). These people are not aware of PPD consequences and consider they are using 'natural', traditional and safe products.

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The baboon syndrome – report of two first cases in Poland

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Key words: amoxycillin; baboon syndrome; nickel; systemic contact allergy.

Systemic contact dermatitis is a contact allergy reaction provoked by allergens administered through a systemic route (ingestion, inhalation and intravenous administration). It develops generally in patients previously sensitized by topical exposure to chemical agents; although, according to some authors, it may represent a recall of any form of dermatitis that had developed in the past in the same areas as present skin lesion (unrelated to the drug currently in question) (1). Contact dermatitis triggered through systemic exposure to topical allergens, such as metals (nickel, cobalt, mercury and gold) has been well documented in the literature (2–5). Medicines administered systemically such as amoxycillin, terbinafine, 5-aminosalicylic acid and roxithromycin are also known to provoke haematogenous contact eczema (6–8). Here, we present, to the best of our knowledge, the two first cases of the baboon syndrome reported in Poland.

Case Reports

Case 1

A 25-year-old woman with a previously proven contact allergy to nickel developed painful, pruritic, generalized rash. Several days before admission she had inhaled vapours of water-based paints, she had eaten canned beans and had drunk tap water, all of which are known to be rich in nickel metal she was allergic to. She had also worn continually a wristwatch containing nickel.

On examination, she presented with maculopapular, erythematous patches affecting buttocks, anogenital and sacral area, major flexures and groins.

Tense blisters on her left wrist, where she had worn a watch before the tests for contact allergy were performed, were observed. Particularly, exacerbated lesions, occurring as tense blisters, were located on her left wrist, in the place where she used to wear the wristwatch before the hypersensitivity to nickel developed. After the course of intravenous hydrocortisone (5 days, from 200 mg to 50 mg), systemic antihistaminics and mild topical corticosteroids skin eruptions had markedly improved within 3 days, and the patient with complete recovery left the ward after 7 days of the treatment.

Diagnostic patch testing was performed 3 weeks later and revealed strong positive reaction to 1% nickel sulphate. Other details of the patient's history were reported elsewhere (9).

Case 2

A 72-year-old man was referred to our department because of diffuse pruritic skin eruptions that he had developed within the previous 24 hr after the second dose of oral amoxycillin applied for a periodontal abscess.

On examination, he presented with oedematous erythema of the buttocks, anogenital area and major flexures, inner thighs, axillae and feet with the overlying tense bullae and blisters on the forearms and the buttocks. There was no mucosal involvement.

On admission, the patient gave a history of contact allergy after topical application of penicillin ointment on his eyelids in the childhood. Afterwards, he had developed erythematous oedema of the eyelids and the whole face. As a young adult, he accidentally poured on his forearms fluid penicillin (the entire content of an ampoule) with a consequent oedematous erythema and maculopapular rash in the area of the contact to the chemical. Approximately 10 years ago in the out-patient-clinic, he experienced a heavy dyspnoea due to accidental inhalation of the penicillin vapour.

After intravenous injections of hydrocortisone (3 days, from 300 mg to 200 mg) and topical administration of 3% boric acid and mild steroids, the patient developed generalized erythrodermia with tense blisters and maculopapular eruptions on the buttocks, on the feet and around the groins. The corticoid therapy was changed

to methylprednisolone intravenously (two pulses, 500 mg), what resulted in marked clinical improvement within successive days. Complete recovery was observed after 10 days of therapy.

Discussion

The baboon syndrome is a form of systemic contact dermatitis with skin eruptions in the area of buttocks and major flexures. The catchword 'baboon syndrome' has been used to denote a characteristic clinical picture reminiscent of the red gluteal region of a baboon (9). The flexural predilection of the lesions is unclear, and it could be only partially explained by local occlusion and sweating (10). Histopathology of the skin lesions reveals mainly unspecific features of an inflammation (9). Thus, delayed T-cell type hypersensitivity mechanisms play a key role in evolutions of characteristic flexural eruptions.

Hypersensitivity to nickel is one of the most frequently observed contact allergies in the population. Despite high frequency of nickel-provoked contact dermatitis, its generalized form is very rare, and according to the literature, it was elicited mainly by some internal systemic routes, such as inhalation, oral intake, transfusion and implantation of metal medical devices (i.e. orthodontic appliances) in patients previously exposed to subjects containing nickel of which quite often are metal buttons and belt-buckles (11). Some studies showed (12) that a permanent contact with nickel-containing objects may result in a local soluble nickel salts formation, followed by its diffusion into the skin or circulatory system. This phenomenon may explain an induction of systemic allergic reaction.

Amoxycillin and other oral synthetic penicillins are commonly used antibiotics for their low toxicity and relatively small amount of adverse reactions. Although they are considered safe, they provoke a considerable number of skin reactions including urticaria, morbilliform and maculopapular exanthema (13). There are only few reports of flexural eruptions caused by synthetic penicillins. First was Andersens's in 1984, presenting a patient who had developed a flexural rash after topical administration

of penicillin to the ear. All described cases are characterized by congruent course of the disease (acute onset, ranged from several hours to 6 days, similar appearance and evolution of the skin lesions).

The frequency of the baboon syndrome is unknown. Patients with suggestive medical history should undergo patch testing, which could be helpful in differential diagnosis of erythematous eruptions and help to avoid the allergen in the future.

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Two cases of occupational allergic contact dermatitis to *p*-aminophenol in pharmaceutical workers manufacturing paracetamol

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Key words: paracetamol; *p*-aminophenol; occupational; break down products.

A 41-year-old man was referred to the Contact Dermatitis Investigation Unit with a 6-month history of an intermittent facial dermatitis. There was no past history of skin disease or atopy. He had worked as a powder blender for a pharmaceutical manufacturer for 18 months and was involved in the production of paracetamol. The work environment was extremely dusty. The dermatitis improved when he took time off work or when he went on holiday.

He was patch tested to our standard series, face series and the pharmaceutical powders he came into contact with at work. He had ++ allergic reactions to *p*-phenylenediamine (PPD, 1% pet), *p*-aminophenol (PAP, 1% pet) and *m*-aminophenol (1% pet).

There was no reaction to paracetamol itself.

A 35-year-old man who worked for a different pharmaceutical manufacturer was referred because of a 2-year history of a dermatitis affecting his hands, forearms and face. He was employed as a process worker in the production of paracetamol powder. There was a consistent relationship between his symptoms and being at work. He was patch tested and had a ++ allergic reaction to PPD (1% pet), + allergic reaction to PAP (1% pet), *p*-aminoazobenzene (0.25% pet) and Disperse orange 3 (1% pet). There was no reaction to paracetamol itself.

Dry pure paracetamol is a white odourless bitter tasting crystalline powder and is very stable at temperatures up to 45°, but under humid conditions hydrolysis to PAP takes place (1). The PAP is then degraded through oxidation characterized by colour change to pink, then brown and eventually black. The presence of aspirin, codeine and magnesium stearate facilitates this change.

Delayed hypersensitivity to paracetamol has been reported in four cases where systemic allergic contact dermatitis appears to have been caused by either oral or rectal administration of the drug. Patch tests with paracetamol in these cases showed allergic reactions (2, 3).

The PAP allergy was felt to be relevant, as it is a breakdown product of paracetamol under moist or wet conditions at room temperature. The other positive results were felt to be cross-reactions.

p-Aminophenol is a 'para amino' compound structurally related to PPD but less allergenic. Both these men denied previous exposure to hair dyes. *p*-Phenylenediamine and PAP have a common hapten, benzoquinone (4, 5). One can hypothesize that PPD more readily forms this hapten, and this may explain the stronger patch test reaction to PPD than PAP in the second case.

Interestingly, despite working in different sites, both these men reported that the factory floors where the paracetamol was processed had a black discolouration. This is supportive of there being significant quantities of para-amino compounds present in the working environments of these individuals.

Allergic contact dermatitis due to paracetamol is rare, and it is

important to consider breakdown products as responsible allergens in individuals who are exposed to paracetamol in the pharmaceutical industry.

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Hand dermatitis among a complete cross-section of Chinese physicians

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Key words: hand dermatitis; physicians; Epidemiology; risk factor; hand-washing; occupational contact dermatitis.

Hand dermatitis (HD) is a common occupational disease, which may affect between 5% and 10% of the population over the course of a year (1). Occupational exposure is very important, with particularly high prevalence rates seen among health care workers (1–3). Despite this fact, few authors have investigated

HD among physicians. Some previous research included doctors as part of a larger survey, although their exact prevalence rate was not elucidated (4, 5). Where HD rates were documented among physicians, it was usually as part of a larger community (6) or hospital survey (7). To our knowledge, no authors have yet investigated HD among a complete cross-section of medical doctors working across multiple hospital departments. Occupational health studies of this nature have also been scarce in China for a number of years. Therefore, we considered it necessary to undertake the first HD investigation of hospital physicians in Mainland China. A previously validated questionnaire methodology was utilised (8), as this has been shown to be convenient and effective when surveying large groups in China (3) and elsewhere (1, 2).

Subjects and Methods

Our study involved a cross-sectional epidemiological analysis of HD among Chinese physicians, with data gathered by means of a self-reporting questionnaire (8). All information was collected anonymously, and informed consent was implied when physicians completed and returned their questionnaires. Our Chinese-language survey included questions on specific HD symptoms (such as erythema, itching, vesiculation and scaling) (1–3, 8) and the presence or history of systemic allergies (3, 9). HD was registered when two or more symptoms occurred in the past 12 months and had persisted for more than 3 weeks or reoccurred (1–3, 8). Information regarding latex allergy symptoms was also requested (10). Data was analysed by statistical software, with logistic regression performed to elucidate possible HD correlations. Results were expressed as odds ratios (OR), 95% confidence intervals (95% CI) and probability (*P*) values. Probability values below 0.05 were regarded as statistically significant throughout the analyses.

Results and Discussion

We recruited an entire cohort of 361 physicians from all departments of a university teaching hospital in Shijiazhuang City, Mainland China (response rate: 79.2%). Using

previously defined criteria (8), their HD prevalence ranged from 2.7% in the miscellaneous departments to 21.4% in the gynaecology department (P for trend = 0.0177) (Table 1). With an overall prevalence of 12.9%, HD among our Chinese physicians was comparable to the rate previously described among doctors in Norway (4.5% to 17.6%) (7) and Sweden (13.3%) (6), suggesting that 10% to 15% may be an average background level in their profession. If so, it is higher than community surveys conducted in the Netherlands (5.2% to 10.6%) (1) and Sweden (11.8%) (6), but lower than HD rates previously documented among American (55.6%) (5), Dutch (28.8%) (2) and Italian (21.2%) (4), hospital staff. Although HD within our Chinese cohort was lower than a recent survey of Japanese physicians (where 25.1% reported contact dermatitis) (9), the Japanese response rate was only 34.3%, suggesting incomplete coverage and a possible responder bias. Interestingly, a previous Italian study showed that HD was more common among cleaners and nurses, when compared to physicians in the same hospital (4). This suggests that medical doctors may have a lower HD prevalence when compared to other health care workers.

In addition to HD, almost one-quarter of the physicians in our group reported some kind of reaction immediately following contact with latex products. Their overall prevalence of symptoms was as follows: any symptoms (23.1%), skin rash (17.1%), hives (3.1%), allergic rhinitis (2.8%) and asthma or wheezing

(0.7%). As such, this result is very similar to a previous study conducted in a Canadian dental school, where 24% reported symptoms consistent with immunoglobulin E-mediated responses to latex (10).

A statistical examination of risk factors among our Chinese physicians showed some interesting results. Firstly, HD prevalence was quite similar between the genders (female doctors: 14.5% and male doctors: 11.4%). This is contrary to previous studies, where marked differences in HD prevalence by gender were documented among Norwegian (7) and Swedish physicians (6). Alternatively, we found that HD prevalence varied significantly between the hospital departments, with highest rates seen in the gynaecology department. Despite this fact, department of employment was not shown to be a statistically significant HD risk factor when analysed in a combined regression model. Systemic allergic disease was also not shown as a HD risk factor, despite numerous other reports documenting an association in China (3), as elsewhere (4). No correlations between hand washing frequency and HD were elucidated, which again, is contrary to some previous research (5). Nevertheless, Chinese physicians who reported regular surgical scrubbing of the hands were almost 5 times as likely to suffer HD, when compared to their colleagues who did not (OR 4.9, 95% CI 1.3–19.1, $P = 0.0189$) (Table 2). As such, this suggests that surgical scrubbing may predispose Chinese physicians to HD, a finding which is consistent with observations from other countries (5, 9).

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Table 1. Hand dermatitis (HD) prevalence

Department	n ^a	n ^b	(%) ^c
Gynaecology	28	6	(21.4)
Internal medicine	78	15	(19.2)
Intensive care	28	4	(14.3)
Surgical unit	43	6	(14.0)
Orthopaedics	36	4	(11.1)
Miscellaneous	73	2	(2.7)
All departments ^d	286	37	(12.9)

^aNumber of physicians in each department.

^bNumber of HD cases per department.

^cHD prevalence by department.

^dOverall HD prevalence (P for Tend = 0.0177).

Table 2. Hand dermatitis risk factors

	OR ^a	(95% CI)	P
Personal factors			
Female gender	0.8	(0.3–2.1)	0.6442
Increasing age	0.1	(0.002–7.9)	0.3023
Childhood allergy	0.9	(0.3–2.6)	0.9496
Adult allergy	1.2	(0.5–2.6)	0.7405
Family allergy	0.5	(0.2–1.2)	0.1423
Workplace factors			
Domestic soap	1.4	(0.5–4.2)	0.4939
Disinfectant	2.2	(0.8–6.0)	0.1160
Surgical scrub	4.9	(1.3–19.1)	0.0189
Hand wash/Shift	0.9	(0.22–5.0)	0.9351
Total work years	8.7	(0.2–340.6)	0.2522

^aEvaluated simultaneously as a combined model and expressed as odds ratios (OR), with 95% confidence intervals (95% CI) and probability (P) values

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Unusual allergen in nurse uniform trousers

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Key words: allergic contact dermatitis; clothing dermatitis; cobalt.

Case Report

A 20-year-old student nurse presented with a history of a pruritic rash on her lower limbs occurring 2 days after wearing blue nursing uniform trousers. The rash occurred on the inner thighs and posterior calves. Symptoms resolved on avoidance of the trousers. Patch testing to the British standard series revealed ++ reaction to cobalt chloride. Patch tests to clothing series were negative. Patch tests to trouser fabric revealed ++ positive reaction.

The company responsible for manufacturing the trousers in question was contacted. It was revealed that cobalt

0.32 mg/kg was contained in the dye used in the nursing uniform trousers. Cobalt was the likely allergen responsible for allergic dermatitis in this patient as patch tests were negative to the blue dyes including Disperse Blue 3, Disperse Blue 124 and Disperse Blue 106. The manufacturing company was unaware of other cases of allergic contact dermatitis to nursing uniform trousers (Fig. 1).

Discussion

Cobalt is a silvery metal which belongs, together with nickel and chromium, to the transition elements (1). It is found naturally in soil, dust and seawater. Sources include pottery, ceramics, blue paints, metal plated objects and vitamin B12. It is also found in metallic dyes. The incidence of dye dermatitis varies from 1% to 15.9% depending on the country, patient sample and the number of dyes in the patch test series. Disperse Blue 106 and Disperse Blue 124 are the strongest clothing dye sensitizers to date (2).

Clothing dye dermatitis usually occurs when the patient is subject to hyperhidrosis which 'bleeds' dye from fabrics. This bleeding is extremely rare in today's fabrics because of superior methods of fixing the dyes. It is usually the various other chemicals used in conjunction with the dyes that cause sensitization (3).

Cobalt should be considered in clothing dermatitis, especially fabrics coloured with metallic dyes as in this case.

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Detection of sensitivity to cardol in north-eastern and south-eastern Brazil

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Key words: contact dermatitis; cardol; sensitization; cashew nut shell liquid.

Cardol is a C-15 side chain resorcinol-type phenol found in the cashew nut shell liquid (CNSL) of a north-eastern Brazilian tree (*Anacardium occidentale* L.). This substance has been associated with several clinical pictures, especially contact dermatitis among cashew nut workers in the cashew nut processing industry (1) and perioral contact dermatitis (2). *A. occidentale* is a member of the Anacardiaceae family, which include the mango (*Mangifera indica*), lacquer tree (*Rhus vernicifera*), Indian marking nut tree (*Semecarpus anacardium*), the poison ivy, oak, sumac genera (*Toxicodendron*) and the Brazilian pepper tree (*Schinus terebinthifolius*)



Fig. 1. Nursing uniform trousers.

(3). Allergic contact dermatitis has been reported from all of these plants, and they are the most frequent cause of this malady worldwide. These plants share similar chemicals in their oleoresin that cross-react immunologically. Therefore, an individual who is sensitive to one member of the Anacardiaceae family is susceptible to allergic contact dermatitis from another member of the family (4). The possibility of cardol performing an important role as a causal sensitizing contact dermatitis agent in Brazil led us to include this substance as a potentially relevant compound in the standard series of patch tests. Patch tests were performed in 294 patients with contact dermatitis, using the standard series augmented by cardol (1% in ethanol 70%) supplied by FDA-Allergenic Ltda. Laboratory (Rio de Janeiro, Brazil). Among these patients, 51 were dermatology out-patients at the Hospital of São Paulo Medicine School, 104 were dermatology out-patients at the Clinical Hospital of Minas Gerais Federal University and 139 were dermatology out-patients at Walter Cantidio University Hospital, in Fortaleza, Ceará, Brazil.

Cardol was extracted from technical CNSL that was obtained from Sione cashew nut processing factory, Ceará. Technical CNSL (a mixture of anacardic acid, cardanol and cardol) was heated for about 2 hr for total decarboxylation that transforms the constituent anacardic acid into cardanol. Treated CNSL (50 g) was mixed with silica gel 60 (50 g) and deposited on the top of a chromatographic column filled with silica gel 60 (500 g) immersed in hexane, then eluted

with the solvents hexane (200 ml), chloroform (200 ml), chloroform : ethyl acetate 1 : 1 (200 ml), chloroform : ethyl acetate 1 : 2 (200 ml), chloroform : ethyl acetate 1 : 3, ethyl acetate (200 ml), ethyl acetate : methanol 3 : 1 (200 ml), ethyl acetate : methanol 2 : 1 (200 ml), ethyl acetate : methanol 1 : 1 (200 ml) and methanol (200 ml). Cardol is obtained mainly from fractions eluted with ethyl acetate : methanol 3 : 1 and ethyl acetate : methanol 2 : 1. The solvents of these fractions were eliminated using a rotary evaporator and cardol (2.5 g, 5% yield) was obtained. In the patch tests, 1% cardol solution (0.5 ml) was applied on patients using Finn Chambers on the back, with readings taken after 2, 3 and 4 days, in accordance with internationally accepted guidelines.

All patients completed forms with identity data, history and clinical examination, to permit clinical correlation.

In the patients of Fortaleza city, Ceará state, the positivity to cardol was 9%; in Belo Horizonte city, Minas Gerais state, the positivity was 8% and in São Paulo city, state of São Paulo, the positivity was 4%. In this last city, the positive readings (4 days) showed weak reactions (+), apparently without relation to the clinical picture. In Belo Horizonte, the results were more significant (++ to +++), apparently without relation to the clinical picture although with domestic occurrence. In relation to the patients of Fortaleza, results varied from + to +++ showing stronger dermatitis on the hands and arms of cashew nut processing workers, as well

as periungual and perioral regions, as previously described (1, 2, 5).

The positive results in 8.3% of the total patients tested is high enough to justify the inclusion of cardol in the allergens that constitute the standard series of patch tests in Brazil, even taking into account the lower percentage results in São Paulo (4%), which is also of interest. Nevertheless, the studied group was not statistically significant and further studies including people of all Brazilian states should be performed, using a larger number of persons to ensure a more general conclusion.

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