

CONTACT POINTS

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Allergic reaction with persistent hypopigmentation due to temporary tattooing with henna in a baby

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A. Di Landro, R. Valsecchi and L. Marchesi

Clinica Dermatologica, Università degli Studi Milano-Bicocca, Ospedali Riuniti di Bergamo, Bergamo, Italy

Key words: children; hypopigmentation; tattoo.

Recently, temporary paint-on tattoos have become increasingly popular as a safe alternative to permanent tattoos not only in Asia and Northern Africa but also in our countries. The most common dye for such temporary tattoos is henna, a vegetable dye obtained from the dried leaves of a shrub (*Lawsonia inermis*), used for thousands of years to colour the hair and the skin for the ritualistic staining. Allergic reactions to this compound have frequently been reported in adults, rarely in childhood. The most likely causative agent for the eczematous reactions is *p*-phenylenediamine (PPD) present in the commercial

black henna, added to obtain a dark, blackish colour. We describe the case of a little baby who had an allergic contact dermatitis due to temporary paint-on tattoos with a persistent hypopigmentation after the resolution of the eczematous lesions.

Case Report

A 4-year-old girl was referred to us for an eczematous, itchy patch at the site of a henna tattoo made 45 days before on the left arm. Her parents stated that the tattoo was performed during a beach holiday on the Italian Riviera in August 2003. The girl's family and personal history were unremarkable for atopy or allergic reactions. A topical treatment with desoxymethasone 0.25% cream twice a day and oral loratadine 5 mg/day were prescribed with complete resolution after 20 days. In the same area of the allergic reaction, we observed a post-inflammatory hypopigmented area (Fig. 1) that persisted after a 6-month follow up. We performed patch tests with the SIDAPA paediatric series; a positive result (3^{+}) to PPD at 72 hr was observed.

Discussion

Decorating the skin with temporary paint-on henna tattoos has become

increasingly popular in western countries, not only in countries where body painting is a traditional practice (1). They are mostly performed by transient artists in tourist areas, in summer, especially as they are temporary, painless and cheap. However, the addition of chemical agents such as PPD and *p*-toluidenediamine to the traditional mixture may lead to a risk of developing an allergic contact dermatitis (2–5). Allergic contact dermatitis to tattoos has been reported in adults and also in children, although rarely. To our knowledge, only 10 paediatric cases are described in literature (6–9). In our patient, the allergic contact dermatitis developed 1 month after the application of a henna tattoo, and it was followed by hypopigmentation reproducing the tattoo design (Fig. 1). This baby represents the youngest patient reported with an eczematous reaction followed by the persistent hypopigmentation. A positive patch test to PPD confirmed the sensitization to PPD. The subsequent appearance of hypopigmentation at the site of the temporary paint-on henna tattoo is an important concern (10), which seems to be more frequent in childhood (6–9). In fact, it has been reported in 7 of the paediatric cases reported. As 1 of these patients was negative to patch test to PPD, the authors suspected that leucoderma is probably not exclusively due to the presence of PPD in the henna mixture (6). Holiday henna tattoos are becoming increasingly fashionable, but they should be discouraged especially in children, because they are not free of risk, such as a sensitization to such a strong contact allergen as PPD.

References

1. Lestringant G C, Berner A, Frossard P M. Cutaneous reaction to henna and associated additives. *Br J Dermatol* 1999; 141: 598–600.
2. Di Landro A, Valsecchi R, Cainelli T. Temporary henna tattoos: an increasing risk of contact dermatitis. *Contact Dermatitis* 2001; 12(3): 186–187.



Fig. 1. The hypopigmented persistent reaction in the site of Henna tattoo.

3. Le Coz C J, Lefebvre C, Keller F, Grosshans E. Allergic contact dermatitis caused by skin painting (pseudo-tattooing) with black henna, a mixture of henna and p-phenylenediamine and its derivatives. *Arch Dermatol* 2002; 136: 1515–1517.
4. Jappe U, Hausen B M, Petzold D. Erythema-multiforme-like eruption and depigmentation following allergic contact dermatitis from a paint-on henna tattoo, due to paraphenylenediamine contact hypersensitivity. *Contact Dermatitis* 2001; 45: 249–250.
5. Chung W H, Wang C M, Hong H S. Allergic contact dermatitis to temporary tattoos with positive paraphenylenediamine reactions: report of four cases. *Int J Dermatol* 2001; 40: 754–756.
6. Chung W H, Chang Y C, Yang L Y et al. Clinicopathologic features of skin reactions to temporary tattoos and analysis of possible causes. *Arch Dermatol* 2002; 138: 88–92.
7. Neri I, Guareschi E, Savoia F, Patrizi A. Childhood allergic contact dermatitis from henna tattoo. *Pediatr Dermatol* 2002; 19: 503–5.
8. Leggiadro R J, Boscamp J R, Sapadin A N. Temporary tattoo dermatitis. *J Pediatr* 2003; 142: 586.
9. Baron S, Baxter K, Wilkinson M. Allergic contact dermatitis to henna tattoo. *Arch Dis Child* 2003; 88: 747.
10. Taylor J S, Maibach H I, Fisher A A, Berfeld W F. Contact leukoderma associated with the use of hair colors. *Cutis* 1993; 52: 273–280.

Address:
Dott.ssa Anna Di Landro
Division of Dermatologia Ospedali
Riuniti
L.go Barozzi 1
24100 Bergamo
Italy
Tel: +39 035 400625
Fax: +39 035 269603
e-mail: aislalomb@tiscalinet.it

Multiple fixed drug eruption due to drug combination

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A. Yokoyama and H. Hara

Department of Dermatology, Nihon
University School of Medicine, 30-1
Oyaguchi-kamicho, Itabashi-ku, Tokyo 173-
0032, Japan

We report the case of a multiple fixed drug eruption (FDE) after taking 1 g

of PL[®] and 100 mg of levofloxacin (Cravit[®]) at the same time. Patch tests with PL[®] alone, levofloxacin alone and the combination of PL[®] and levofloxacin were all negative on the involved and uninvolved sites. Lymphocytic stimulation tests were also negative for PL[®] alone, levofloxacin alone and the combination of PL[®] and levofloxacin. Oral provocation tests with PL[®] alone or levofloxacin alone produced no reactivation. However, we could provoke multiple erythematous plaques on the involved areas by taking a 1/10th dose of the combination of PL[®] and levofloxacin at the same time. Drug eruption due to a drug combination appears to be very rare. This is the first case of multiple FDE caused by taking PL[®]-levofloxacin combination.

Key words: drug combination; multiple fixed drug eruption; PL[®]-levofloxacin; provocation test.

Fixed drug eruption (FDE) can be caused by a variety of drugs. It is characterized by a recurrence at the same site or sites on the skin or mucous membranes, when an offending drug is administered again. Drug eruption due to a drug combination occurs as a reaction when the patient takes multiple drugs at the same time. FDE due to a drug combination was first described by Verbov (1). We describe a case of multiple FDE due to PL[®]-levofloxacin combination.

Case Report

An 80-year-old Japanese woman presented with a sudden onset and widespread rash that had appeared 3 days earlier. She simultaneously took 100 mg of levofloxacin (Cravit[®]; Fig. 1) and a commercially available drug for the common cold, 1 g of PL[®], that contained 150 mg of acetaminophen

(Fig. 2a), 270 mg of salicylamide (Fig. 2b), 60 g of anhydrous caffeine (Fig. 2c) and 13.5 mg of promethazine methylenedisalicylate (Fig. 2d), 12 hr prior to rash onset. She had experienced 4 similar episodes of rashes after taking PL[®] and levofloxacin. Physical examination revealed numerous, red to violaceous, round patches and plaques with central vesicular to bullous changes or erosions with an itching and burning sensation over the trunk and extremities (Fig. 3a). An erythematous, oedematous, eroded area was observed over the upper lip. The results of laboratory tests were not contributory. A clinical diagnosis of FDE was suspected. A skin biopsy obtained from the upper extremity revealed hydropic degeneration of the basal cell layer with necrotic keratinocytes in the epidermis. Mild perivascular infiltration of lymphocytes and eosinophils was observed in the upper dermis. She was treated with oral administration of prednisolone 40 mg per day, leading to rapid improvement within a week, although a slight post-inflammatory hyperpigmentation remained.

We performed patch test with 12.5%, 25% and 50% petrolatum of PL[®] alone, levofloxacin alone and the combination of PL[®] and levofloxacin on the previously involved and uninvolved sites 21 days after the resolution of the drug eruption. All test substances were applied using Finn Chambers[®]. Readings were performed after D2 and D3 according to ICDRG criteria. Patch tests were all negative.

Lymphocytic stimulation tests (LSTs) with PL[®] alone, levofloxacin alone PL[®]-levofloxacin combination were then performed. The peripheral blood mononuclear cells were incubated for 72 hr with or without serially diluted them at concentrations from 3.2 µg/l to 1 mg/l. Cell proliferation

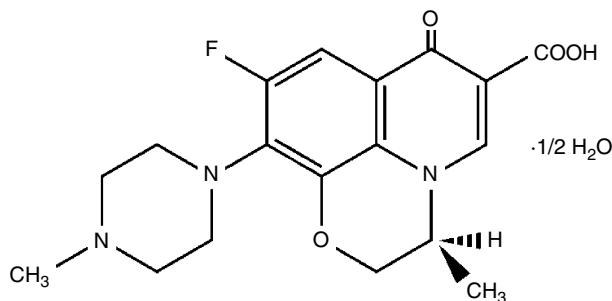


Fig. 1. Chemical structure of levofloxacin (Cravit[®]).

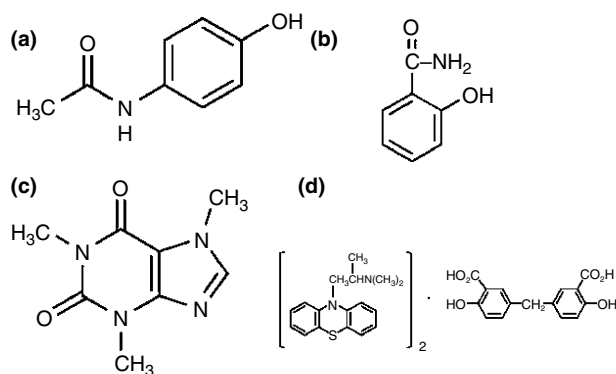


Fig. 2. Chemical structure of PL (a) acetaminophen, (b) salicylamide, (c) anhydrous caffeine, (d) promethazine methylethylendimalicylate.

was evaluated by tritium thymidine incorporation. The ratio of the counts of the drug-responded samples to the control counts was described as stimulation index. The cutting-off index of LST was 180%. LST for PL[®] alone was 122%. LST for levofloxacin alone was 123%. LST for the combination of PL[®] and levofloxacin was 124%. Therefore, LSTs were all within normal level.

Then the patient was subjected to oral provocation test with PL[®] alone, levofloxacin alone and the combination of PL[®] and levofloxacin, respectively. The provocation test with PL[®] alone and the following day, the provocation test with levofloxacin alone was performed. Both the provocation test produced no reactivation. Finally, 2 days after the provocation test with levofloxacin alone, oral challenge test with PL[®]-levofloxacin combination at the same time was then carried out. The dose used was 100 of PL[®] and 10 of levofloxacin, which were both 1/10th of a single

dose. Within 1 hr, multiple erythematous plaques developed on the back and extremities, where similar provoked lesions at old sites occurred (Fig. 3b). Oral challenge test with the combination of PL[®] and levofloxacin confirmed multiple FDE as the causative drugs. Consent for oral challenge test with a combination of its ingredients and levofloxacin could not be given by the patient.

Discussion

We describe a case of multiple FDE due to PL[®]-levofloxacin combination. The lesions of FDE could only be reproduced at the same sites after the simultaneous ingestion of both agents. Patch tests on involved areas and uninvolved areas were negative. Oral provocation test was carried out, and FDE was induced by PL-levofloxacin combination, but not by PL[®] alone or levofloxacin alone.

Our patient has unique features in that he had multiple FDE due to the

combination of two chemically unrelated drugs. Cross-sensitivity reactions occur with chemically related drugs [i.e. phenylbutazone and oxyphenbutazone (2), piroxicam and tenoxicam (3), tetracyclines and sulphonamides (4)]. Polysensitivity, in which 2 or more chemically unrelated drugs cause FDE at the same sites in a single patient, also occurs (5). However, our case seems to be distinct from either the case of cross-sensitivity or the case of polysensitivity. In the most cases of FDE by multiple drugs, each drug reactivates different lesions separately (6), whereas in this cases, there is the particularly that the association of the drugs reactive all lesions at the same time. The etiopathogenic mechanism of FDE due to a drug combination is not yet understood. Recent studies have demonstrated that FDE is considered by some to be a T-lymphocyte-mediated disease (7–9) and that the rapid release of performed cytokines, such as tumour necrosis factor- α from mast cells, provides a localized initiating stimuli for the activation (10). It is noteworthy that 11 out of 24 previously reported cases due to drug combination in Japan were FDE (11). 7 out of 11 FDE cases were due to a combination of xanthine, such as anhydrous caffeine or theophylline, and other drugs (12). Imagawa et al. (12) postulated that xanthine is involved in the development of drug eruption due to a drug combination. PL[®], as one of the causative drugs in our case, includes both xanthine and acetylsalicylic acid. In summary, multiple FDE in the present case is considered to be caused by the combination of levofloxacin and the ingredients of PL[®]. Further investigations will provide information about the mechanisms and pathogenesis of FDE due to drug combination.

References

1. Verbov J. Fixed drug eruption due to a drug combination but not to its constituents. *Dermatologica* 1985; 171: 60–61.
2. Bernand W, Scheidegger E P, Dummer R, Burg G. Multifocal fixed drug eruption to paracetamol, tropisetron and ondansetron induced by interleukin 2. *Dermatology* 2000; 201: 148–150.



Fig. 3. (a) Clinical appearance of the fixed drug eruption on the patient's back at presentation. (b) After the provocation test, erythema reappeared in the previously involved areas.

3. Gonçalo M, Oliveira H S, Fernandes B, Cordeiro M R, Figueiredo A. Topical provocation in fixed drug eruption from nonsteroidal anti-inflammatory drugs. *Exogenous Dermatol* 2002; 1: 81–86.
4. Tornero P, De Barrio M, Baeza M L, Herrero T. Cross-reactivity among p-amino group compounds in sulphonamide fixed drug eruption: diagnostic value of patch testing. *Contact Dermatitis* 2004; 51: 57–62.
5. Pastricha J S, Shukla S R. Independent lesions of fixed drug eruption due to two unrelated drugs in the same patient. *Br J Dermatol* 1979; 101: 361–362.
6. Ozkaya-Bayazit E. Independent lesions of fixed drug eruption caused by trimethoprim-sulfamethoxazole and tenoxicam in the same patient: A rare case of polysensitivity. *J Am Acad Dermatol* 2004; 51: S102–S104.
7. Komatsu T, Moriya N, Shiohara T. T cell receptor (TCR) repertoire and function of human epidermal T cells: restricted TCR Va-Vβ genes are utilized by T cells residing in the lesional epidermis in fixed drug eruption. *Clin Exp Immunol* 1996; 104: 343–350.
8. Teraki Y, Shiohara T. IFN-γ-producing effector CD8+ T cells and IL-10-producing regulatory CD4+ T cells in fixed drug eruption. *J Allergy Clin Immunol* 2003; 112: 609–613.
9. Mizukawa Y, Yamazaki Y, Teraki Y, Hayakawa J, Hayakawa K, Nuriya H, Kohara M, Shiohara T. Direct evidence for interferon-γ production by effector-memory- type intraepidermal T cells residing at an effector site of immunopathology in fixed drug eruption. *Am J Pathol* 2002; 161: 1337–1347.
10. Teraki Y, Moriya N, Shiohara T. Drug-induced expression of intercellular adhesion molecule-1 on lesional keratinocytes in fixed drug eruption. *Am J Pathol* 1994; 145: 550–560.
11. Toyama K, Hattori N, Nakabayashi Y. Fixed drug eruption due to drug combination: Report a Case. *Rinsho Derma (in Jap)* 2002; 44: 747–750.
12. Imagawa H, Ono K, Okuda T, Oh-I T. Fixed drug eruption due to an allylisopropyl-acetylurea-anhydride caffeine combination but not to either drug separately. *Jpn J Dermatol* 2002; 7: 18–23.

Address:

Ai Yokoyama, MD
 Department of Dermatology
 Nihon University School of Medicine
 30-1 Oyaguchi-kamicho
 Itabashi-ku, Tokyo 173-0032
 Japan
 Tel: +81-3-3972-8111x2502
 Fax: +81-3-5995-9841
 e-mail: ayoko@med.nihon-u.ac.jp

Allergic contact gingivitis due to eugenol present in a restorative dental material

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J. F. Silvestre, M. P. Albares, M. Blanes,
 J. C. Pascual and N. Pastor

Dermatology Department, Hospital General
 Universitario de Alicante, Alicante, Spain

Key words: eugenol; gingivitis.

Case Report

A 45-year-old female patient, who was working as a nurse was presented to us in June 2003 with an itchy generalized macular exanthema. The clinical appearance was consistent with cutaneous drug eruption. She referred 2 dental procedures during the last month. She was using a dental liquid with menthol and triclosan in its composition. The lesions cleared up within a month.

Patch tests were performed with the Spanish standard (GEIDC) and the dental screening (Chemotechnique®, Malmö, Sweden) series and with triclosan 2% petrolatum and menthol 2% pet. We found positive reactions to palladium chloride 2% pet. (+ +) and eugenol 2% pet. (+ +). There was no previous history of metallic implants.

In November 2003, the patient consulted with inflammation in a gingival mucosal area close to a metal-ceramic dental bridge which had been placed in August 2003. The dentist informed us that it had been sealed using IRM caps®. IRMcaps® is a temporary cement which is obtained by mixing IRM powder® (polymethacrylate and zinc oxide) and IRM liquid® (99% eugenol and 1% acetic acid). After the replacement of this restorative dental material, the lesions cleared up.

Discussion

Eugenol is a phenolic compound extracted from cloves and cinnamon which is used in cosmetics, food and restorative dental materials. In Dentistry, eugenol is used because of its anaesthetic and antiseptic

properties. It is used as impression material, periodontal dressing and in several cements. Combination of eugenol with zinc oxide (ZOE cement) is usual. After contact with the saliva, eugenol can be dissolved (1).

Eugenol is both a primary irritant and sensitizer. Allergic contact dermatitis due to eugenol often affects hands of dentistry workers. More rarely, allergic stomatitis has been described in two patients, one using a mouthwash (2) and one using a preparation in the treatment of lichen planus (3). To our knowledge, our case is the first case of gingivitis due to the eugenol present in a dental implant.

It is difficult to demonstrate that the exanthema in our patient was due to eugenol as well. However, the patient had undergone 2 dental procedures, and eugenol could have been employed. The rich vascularization of the oral mucosa would have allowed the access to the systemic circulation, causing the generalized lesions.

References

1. Kanerva L, Estlander T, Jolanki R. Dental nurse's occupational allergic contact dermatitis from eugenol used as a restorative dental material with polymethylmethacrylate. *Contact Dermatitis* 1998; 38: 339.
2. Vilaplana J, Grimalt F, Romaguera C, Conellana F. Contact dermatitis from eugenol in mouthwash. *Contact Dermatitis* 1991; 24: 223–224.
3. Fujita Y, Shimizu T, Nishie W, Shimizu H. Contact dermatitis due to eugenol used to treat oral lichen planus. *Contact Dermatitis* 2003; 48: 285.

Address:

J. F. Silvestre
 Dermatology Department
 Hospital General Universitario of
 Alicante
 Avenue/Pintor Baeza s/n
 03010 Alicante
 Spain
 e-mail: silvestre_jfr@gva.es

Allergic reaction to hydroxyethyl-methacrylate following intradermal filler injection

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J. P. Thyssen and T. Menné

Department of Dermatology, University of Copenhagen, Gentofte Hospital, Niels Andersensvej 165, 2900 Hellerup, Denmark

Key words: acrylate; allergic contact dermatitis; allergy; DermaLive; filler; HEMA; intradermal.

Case Report

A 55-year-old woman presented with perioral cutaneous inflammation. Two years earlier, DermaLive[®], a dermal filler substance containing 40% hydroxyethylmethacrylate (HEMA) and ethylmethacrylate (EMA) suspended in 60% hyaluronic acid, was injected during corrective surgery. Months later, she experienced palpable nodules in both cheeks. The responsible aesthetic surgeon evacuated the filler leaving the areas of swelling (Fig. 1). Afterwards, three dermal injections of corticosteroids were performed with good result, although perioral inflammation persisted. In our department, she was patch tested to an extended European standard series supplemented with HEMA 2% in pet. and EMA 2% in pet. Finn chambers[®] were used for occlusion and were fixed with Scanpor[®] tape to the skin. The test showed a positive reaction to HEMA (+) but negative to EMA. Unfortunately, the patient was not asked about previous occupational or dental exposure to HEMA. She was informed that HEMA had been responsible for the allergic cutaneous reaction.

Discussion

Allergic contact dermatitis (ACD) is a well-known adverse health effect of methacrylates monomers, especially documented in dental personnel (1–3). One case report described a dental patient with an intraoral lichenoid reaction suspected of being an allergic reaction to a HEMA-containing restoration (4). Subcutaneous exposure to epoxy has caused an allergic reaction (5).

To our knowledge this is the first report of ACD following an

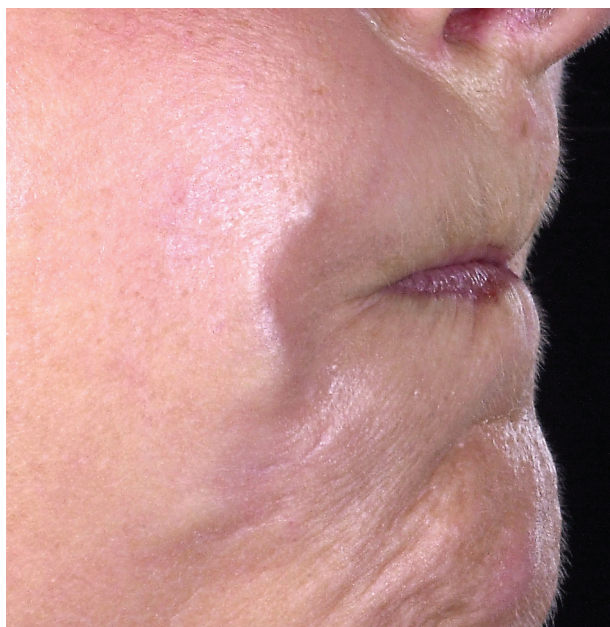


Fig. 1. Areas of swelling following dermal filler injection.

intradermal injection of a HEMA-containing filler used in cosmetic surgery. Because no previous exposure to HEMA was recorded, a possible connection to occupational or dental exposure can not be outruled. However, the patch test showed no other positive reactions besides HEMA. We therefore conclude that the content of HEMA in the dermal filler is not coincidental and that it was responsible for the allergic cutaneous reaction. At present, DermaLive[®] is used in the long-term correction of natural as well as acquired skin depressions. Long-term side-effects have been reported in 1.2/1000 patients (6). They appear mainly as delayed hypersensitivity reactions, appearing a few weeks to several months after the injection and as palpable nodules occurring about 6 months after injection (6). In our case, a localized granulomatous reaction can not be outruled although not histologically confirmed.

Our case shows that intradermal injection of HEMA may cause ACD. Consequently, aesthetic surgeons and dermatologists should be aware of this potential side-effect when patients injected prior with, e.g. DermaLive[®], present with dermatitis.

References

1. Sood A, Taylor J S. Acrylic reactions: a review of 56 cases. *Contact Dermatitis* 2003; 48: 346–347.
2. Kanerva L, Rantanen T, Aalto-Korte K et al. A multicenter study of patch test reactions with dental screening series. *Am J Contact Dermat* 2001; 12: 83–87.
3. Kanerva L, Alanko K, Estlander T, Jolanki R, Lahtinen A, Savela A. Statistics of occupational contact dermatitis from (meth)acrylates in dental personnel. *Contact Dermatitis* 2000; 42: 175–177.
4. Moore M M, Burke F J, Felix D H. Allergy to a common component of resin-bonding systems: a case report. *Dent Update* 2000; 27: 432–434.
5. Andersen K E. Cutaneous reaction to an epoxy-coated pacemaker. *Arch Dermatol* 1979; 115: 97–98.
6. Bergeret-Galley C, Latouche X, Illouz Y G. The value of a new filler material in corrective and cosmetic surgery: DermaLive and DermaDeep. *Aesthetic Plast Surg* 2001; 25: 249–255.

Address:
Jacob Pontoppidan Thyssen
P.D. Løvs. Allé 12
2.th., 2200 København N
Denmark
Tel: +45 61 71 73 61
e-mail: pthyssen@hotmail.com