# "PATCH TESTING WITH INDIAN STANDARD SERIES TO DETERMINE THE ROLE OF CONTACT ALLERGENS IN PATIENTS WITH HAND AND FOOT ECZEMA"

By

# DR. PUJA SHARMA DISSERTATION SUBMITTED TO THE BLDE UNIVERSITY BIJAPUR, KARNATAKA



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## DERMATOLOGY VENEREOLOGY AND LEPROSY

Under the guidance of

Dr. ARUN C INAMADAR MD, DVD

## **PROFESSOR AND HEAD**

DEPARTMENT OF DEMATOLOGY VENEREOLOY AND LEPROSY

# B.L.D.E UNIVERSITY'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE, BIJAPUR, KARNATAKA.

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Date: Place: Bijapur

### Dr. Arun C Inamadar MD, DVD.

Professor and Head, Department of Dermatology, Venereology and Leprosy BLDEU'S Shri B M Patil Medical College, Hospital and Research Centre, Bijapur.

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#### Dr. Arun C Inamadar MD, DVD.

Professor and Head, Department of Dermatology, Venereology and Leprosy BLDEU'S Shri B M Patil Medical College, Hospital and Research Centre, Bijapur

Date :

Place :

#### Dr. M. S. Biradar M.D.

Principal, B.L.D.E.U.'s Shri B.M. Patil Medical College, Hospital Research Centre Bijapur

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Date:

**Place: Bijapur** 

DR. PUJA SHARMA

# LIST OF ABBREVIATIONS

CD	-	Contact Dermatitis
HE	-	Hand Eczema
ACD	-	Allergic Contact Dermatitis
ICD	-	Irritant Contact Dermatitis
TNF-α	-	Tumor Necrosis Factor-α
IL	-	Interleukin
IFN-γ	-	Interferon-y
GM-CSF	-	Granulocyte Monocyte Colony Stimulating Factor
MHC	-	Major Histocompatiblity Complex
ICDRG	-	International Contact Dermatitis Research Group
ROAT	-	Repeated Open Application Test
ISS	-	Indian Standard Series
CODFI	-	Contact And Occupational Dermatosis Forum of India

#### ABSTRACT

**Background-** Hand and foot eczema is one of the most common disorders. It causes discomfort, embarrassment and loss of working hours in patients. It is an inflammatory condition with etiology being allergic contact dermatitis or irritant contact dermatitis. In allergic contact allergens, the cause of dermatitis can be confirmed by doing the patch test.

**Objectives** - To determine the role of allergens in the causation of hand and foot eczema by patch testing and correlation of occupation and patch test positivity to determine the role of occupational exposure to allergens in the causation of hand and foot eczema.

**Methods-** It is a hospital based, cross-sectional study. Sixty patients above sixteen years, suffering from hand and foot eczema attending the Dermatology, Venereology and Leprosy out patient department of a tertiary care hospital were included in this study. Detailed history of illness, duration, onset, symptoms, recurrence, occupation, family history of atopy and pre-existing medical conditions were recorded. Each patient was subjected to a complete systemic and cutaneous examination. Patients were patch tested with the antigens of Indian Standard Series.

**Results-** A total of 60 patients with hand and foot eczema were examined during the study period. Incidence was more between 21-30 years (35%) of age. Males (61.63%) outnumbered females (38.37%). Hyperkeratotic eczema was most common type seen in 27 (45%) patients. It was seen in housewives (23.33%), followed by mason worker (18.33%), students (13.33%), agriculture laborer (8,33%) and others. Patch testing showed that nickel sulfate and cobalt chloride was most common allergen (18.33%),

followed by potassium dichromate (13.33%), balsam of peru (6,67%), fragnance mix (6.67%), thiuram mix (6.67%) and others.

**Conclusion-** Hand and foot eczema may impose both social and economic burden upon patients. All patients presenting with this disorder should be patch tested with Indian standard series to determine the etiologic allergens.

Keywords- Hand and Foot Eczema, Allergens, Patch Testing

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#### **INTRODUCTION**

Hand and foot eczema is a localized condition clinically characterized by presence of itching, redness, edema, papulovesicles in acute stage; edema and scaling in subacute stage and dry lichenified skin in chronic stage.<sup>1</sup>

It is a common condition affecting people irrespective of age and sex. Various endogenous and exogenous factors contribute to the development of hand and foot eczema. Among endogenous factors atopy and among exogenous factors contact sensitization to different allergens have been found.<sup>2</sup> Contact dermatitis (CD) is an inflammatory response of the skin following exposure to an exogenous substance, which may be either allergen or irritant. Contact allergic dermatitis is a delayed type of hypersensitivity to environmental antigens in a sensitized individual.

The morphological patterns of hand eczema (HE) described are pompholyx, hyperkeratotic eczema, housewives' eczema, discoid eczema, recurrent focal palmar peeling, ring eczema, chronic acral dermatitis, finger tip eczema, interdigital eczema, apron eczema and gut eczema.<sup>3</sup>

HE is the most common form of occupational disease.<sup>4</sup> It is localized to hands, which are important organ of expressions, communication and are necessary for carrying out daily household and work related activity. Impairment in the form or function may result in severe emotional and psychological distress associated with a poor quality of life.<sup>4</sup>

Feet are affected by various eczemas, like nummular eczema, pompholyx, lichen simplex chronicus and allergic contact dermatitis. These are usually chronic, recurrent and difficult to control. These may result in inability to perform daily

1

activities because of pain caused by fissures or secondary infection. These may hamper wearing of shoes, especially when shoes are the cause of the dermatosis.<sup>5</sup>

The diagnosis of contact allergy requires several important and essential steps to recognize the allergen responsible.

As clinical differentiation between chronic allergic and irritant hand eczema is often impossible, patch test becomes an important diagnostic tool for identification of the allergen/allergens responsible for the eczema which is a biologic gold standard test.<sup>6</sup> In a sensitized individual, primed antigen specific T lymphocytes are present throughout the body. Hence, when the allergen is applied on a normal skin it produces a reaction similar to contact dermatitis at the site of application. This is the basic principle of patch testing.<sup>7</sup>

The present study has been planned to detect contact allergens by patch testing in chronic and recurrent cases of hand and foot eczema in adolescents and adults. This may help us to identify the common inducing or aggravating factors for hand and foot eczema and administering appropriate treatment, thus avoiding recurrence.

## **OBJECTIVE OF STUDY**

- 1. To determine the role of allergens in the causation of hand and foot eczema by patch testing.
- 2. Correlation of occupation and patch test positivity to determine the role of occupational exposure to allergens in the causation of hand and foot eczema.

#### **REVIEW OF LITERATURE**

#### Introduction:

Dermatitis of hand and foot is one of the most common disorders encountered by the dermatologists. It causes discomfort and embarrassment and because of its location, interferes significantly with normal daily activities.<sup>8</sup> In significant number of cases hand and foot dermatitis is caused by contact allergens or by irritant agents. In cases caused by contact allergens, the cause of dermatitis can be confirmed by doing the patch test. Patch testing is a well-established "Gold Standard" method of diagnosing allergic contact dermatitis, a delayed type of hypersensitivity reaction (type IV).<sup>9,10</sup>

#### **Definition:**

Hand and foot eczema is defined as an inflammatory reaction clinically characterized by erythema, vesiculation and edema in acute phase; scaling, fissuring and hyperkeratotis in chronic phase<sup>11</sup>

#### **Epidemiology:**

The prevalence of hand dermatitis in general population in Taipei was estimated to be  $2\%-10\%^{12}$  and in Europe it is between  $6.7\% - 10.6\%^{13}$ . The point prevalence of hand eczema among Swedish rural population was estimated to be 2.5%, with a female to male ratio of 2.3:1. Fifty six percent of the cases were estimated to be occupational. In the same study among urban population the point prevalence of hand eczema was 5.4%, with a female to male ratio of 2:1. This female predominance was more in the age group of 20-24 years.<sup>14</sup>

According to a survey conducted by National Health and Nutritional Examination Survey (NHANES), the prevalence of contact dermatitis in United States was 139 per 10,000. In most countries, the reported incidence rate for occupational contact dermatitis varies between 5 to 19 cases per 10,000.<sup>13</sup> In a population-based twin cohort study in Denmark, the crude incidence rate of hand eczema was 8.8 cases per 1000 person-year.<sup>15</sup>

A wide variation in the prevalence of foot dermatitis has been observed in the available literature, ranging from 1.5%-24%.<sup>16</sup> In a study conducted at Kolkata, India, the incidence of foot dermatitis was 24.22%. Females (61.93%) were more commonly affected than males (38.06%).<sup>17</sup>

Nickel allergy is probably the most common cause of contact dermatitis and females (10%) are affected more commonly than males (2%). Frequency of positive patch test reactions with nickel dermatitis varies from 0.5 to 8.5% for males & 43% for female.<sup>18</sup>

#### **Etiology:**

Dermatitis of hand and foot is caused by various exogenous and endogenous factors. Most common exogenous causes of hand and foot eczema are contact allergens and irritant substances giving rise to allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD) respectively. Other causes are systemic allergens (drugs and metals), dissemination from a focus and infective dermatitis involving hands and feet.<sup>1</sup>

#### **Pathogenesis:**

ICD is a non immunological, inflammatory reaction occurring on exposure to an irritant agent when applied in a sufficient concentration for an adequate time. It occurs without prior sensitization and involves two different pathogenic mechanisms. Chronic irritant dermatitis is related to a disturbed barrier function and increased epidermal cell turnover leading to lichenification, whereas acute irritant dermatitis is an inflammatory reaction caused by release of inflammatory mediators and cytokines like tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 (IL-1), interleukin-8 (IL-8), interleukin-2 (IL-2), interferon- $\gamma$  (IFN- $\gamma$ ) and granulocyte monocyte colony stimulating factor (GM-CSF). However immunological memory is not involved in irritant contact dermatitis.<sup>19</sup>

ACD is a delayed type of hypersensitivity reaction. It is mediated via two stages, sensitization and elicitation;<sup>7</sup> Flow chart 1 represents pathogenesis of ACD

#### Flow chart 1: Pathogenesis of ACD



(MHC- Major histocompatibility complex, IL- Interleukin, TNF- Tumor necrosis

factor)

a) *Sensitization:* In this stage exogenous antigens are attached to the major histocompatibility complex (MHC) class II molecules on the surface of keratinocytes either directly or by binding to small peptide molecules. Release of various chemokines, IL-1 $\beta$ , TNF- $\alpha$  and GM-CSF occur from damaged keratinocytes. These chemokines result in migration of Langerhans' cells followed by maturation. Langerhans' cells carrying the antigens reach the paracortical areas of regional lymph nodes through an intact afferent lymphatics. In lymph nodes, the antigens are presented to T lymphocytes (antigen recognition), followed by release of various cytokines. These cytokines induce proliferation of antigen specific cytotoxic CD8<sup>+</sup> T cells and CD4<sup>+</sup> lymphocytes. The cytotoxic T cells are disseminated through the efferent lymphatics to result in contact hypersensitivity.

b) *Elicitation:* It may take place as a late reaction after 5-25 days (first exposure) or early reaction within 24-48 hours (in sensitized persons on re-exposure). In this phase both antigen presenting Langerhans' cells and IL-1 secreting keratinocytes release various cytokines augmenting the inflammatory cascade.

#### **Classification:**

Classification of hand and foot dermatitis have been presented in table 1:<sup>4,5</sup>

### Table 1- Classification of hand and foot dermatitis.

	Morphological classification		
Etiological classification	Hand	Foot	
Atopic hand dermatitis	Pompholyx	Nummular eczema	
Irritant dermatitis	Fissured hand eczema	Lichen simplex	
		chronicus	
Allergic contact dermatitis	Hyperkeratotic hand	Allergic contact	
	eczema	dermatitis	
Protein contact dermatitis	Nummular hand eczema	Pompholyx	
	Finger tip eczema	Juvenile plantar	
	(Pulpitis)	dermatosis	
	Interdigital eczema		
	Apron eczema	-	
	Gut eczema	-	
	Recurrent focal palmar		
	peeling		
	House wives' eczema		
	Chronic acral dermatitis		

### **Clinical features:**

Clinically eczematous lesions may be of acute or subacute onset, or may run a chronic course. Hand and foot dermatitis may start at any stage and evolve into another.

Clinical features of various stages of eczema have been described below (Table 2):

*Acute*: It presents as erythema or chapping, or a much more florid dermatitis with edema, inflammation, vesiculation, pain, exudation, bullae formation and tissue necrosis. It is intensely itchy.

*Subacute*: It is a milder reaction characterized by erythema, scaling, fissuring and parched or scalded appearance. Slight to moderate itching is present along with pain, stinging and burning sensation.

*Chronic:* Features of chronic eczema include thickening, scarring and lichenification. Moderate to intense itching is present.

Stage	Primary and Secondary Lesions	Symptoms
ACUTE	Vesicles and intense redness.	Intense itch.
SUBACUTE	Redness, scaling, fissuring,	Slight to moderate itch, pain,
	parched / scalded appearance	stinging hurning
	purched / seurced appearance.	stinging, burning.
	Lichenification	Moderate to intense itch
CHRONIC		

Table 2: Clinical features of various stages of eczema.<sup>8</sup>

Protein contact dermatitis is a chronic or recurrent dermatitis, when skin is exposed to proteins (food-stuff, latex, animal proteins and enzymes) and may result in urticarial or vesicular lesions. The gold standard for diagnosis of this condition is skin prick testing with fresh material.

#### Morphological patterns of hand eczema:

#### Pompholyx (Dyshidrotic eczema):

This is characterized by recurrent crops of tense, "sago-like" vesicles on palms and sides of the fingers. Pompholyx of hands is labeled as cheiropompholyx and that of soles as podopompholyx. It accounts for 5-20% cases of hand eczema. The lesions are intensely pruritic. Atopy is the most common underlying factor.

In an Indian study of 50 patients with pompholyx, patch test was positive to one or more allergens in 20 cases. Nickel sulfate was the commonest allergens (14%), followed by potassium dichromate, phenylenediamine and nitrofurazone (8% each), fragnance mix (6%) and cobalt chloride (4%).<sup>1</sup>

Various etiological factors have been described. The role of sweat glands has been disputed and the term dyshidrosis is a misnomer. Hyperhidrosis is not a constant feature. However it is observed in 36.5% of cases. The role of stress is difficult to define as pompholyx itself causes stress. Various causes of pompholyx are as follows:

1. Atopy

- 2. Contact allergens
- 3. Ingested allergens like nickel, chromium, cobalt, neomycin
- 4. Shoe allergens; rubber allergy may provoke a palmar eruption
- 5. Fungal infection elsewhere (feet) may result in vesicles over palms
- 6. Bacterial infection: pustular bacterid
- 7. Drugs; aspirin, oral contraceptives
- 8. Cigarette smoking

#### Hyperkeratoic hand eczema:

These are well defined, hyperkeratotic plaques on the palms and on the palmar aspects of the fingers. There is no scaling or vesicle formation. This eczema can also be seen on the plantar aspect of the feet.<sup>11</sup> This type of eczema is most common among middle aged men.

#### Nummular eczema:

These are well circumscribed, circular or oval lesions confined to the dorsum of the hand or fingers and characterized by erythema, vesicles, oozing in the acute phase and are intensely pruritic. This form of eczema frequently gets colonized by *S.aureus*. Recently one study identified neurogenic contribution to inflammation in non-atopic nummular dermatitis by showing association between mast cells and sensory nerves and identifying the distribution of neuropeptides in the lesional skin.<sup>20</sup> ACD is relatively common in persistent discoid eczema, with upto 50% of patients being patch test positive.<sup>21</sup> In a study conducted at Banglore, India, patch testing in patients with nummular eczema revealed nickel positivity in a 7.1% cases.<sup>21</sup> Differential diagnosis of nummular eczema are atopic dermatitis, tinea corporis, psoriasis and polymorphous light eruptions.

#### Finger tip eczema ( pulpitis):

This is defined as hyperkeratotic eczema of the fingertips with painful fissures, which may extend to merge with eczematous lesions over the palms. When all fingers, especially those of dominant hand are involved, with aggravation in cold climate, this is possibly a cumulative irritant dermatitis where detergents and trauma

play a role. When non dominant hand is involved vegetables and other items related to cooking are responsible.

#### Housewives' eczema:

It is probably the most common type of contact dermatitis encountered in clinical practice. It is an irritant dermatitis that may occur in any individual who is exposed frequently to soaps, detergents and antiseptics.<sup>22</sup> It also occurs among dishwashers and kitchen-workers in hotels as well as in hospital-cleaning personnel. Atopic individuals are more prone to develop housewives' eczema. It commonly occurs on palmar surface of fingers, web spaces, palms and dorsal aspects of the fingers. The eruption usually begins with mild dryness, redness and scaling that later develop into fissures. In India, where household work is commonly done in squatting position, the feet may also be affected.<sup>1</sup>

#### Apron eczema:

Seen on proximal palmar aspect of two or more adjacent fingers and adjoining palmar surfaces of hands. It is always endogenous in origin.

#### Chronic acral eczema:

It is a chronic, hyperkeratotic, papulovesicular eczema of hand and foot, intensely pruritic and associated with grossly elevated serum IgE levels.

#### Gut eczema:

Workers who eviscerate and clean pig carcasses are at risk of developing vesicular eczema which starts in the finger-webs and spreads to the sides of the fingers. This is a mild, self-limiting condition.

#### Recurrent focal palmar peeling:

It is a mild form of pompholyx. In summer, small areas of superficial, white desquamation develop along the sides of the fingers and on the palms or on the feet.

#### Ring Eczema:

This characteristic pattern of eczema particularly affects young women. An itchy patch appears beneath the finger or toe ring. This type of eczema is due to irritant reaction due to accumulated soap. Patch test may reveal nickel, chromium and cobalt sensitivity. It is also termed as "Black Dermographism".

#### **Investigations:**

#### Histopathology:

In acute stage spongiosis is the feature, which leads to stretching and eventual rupture of intercellular attachment with formation of vesicles. In subacute stage, acanthosis is associated with formation of parakeratotic horny layer. It often contains layers of coagulated pyknotic nuclei of the inflammatory cells. In chronic stage, parakeratosis, prominent acanthosis and dermal changes are seen. Rete ridges become elongated and broadened.

#### Patch test:

Jadasshon in 1895 first introduced patch testing as a diagnostic procedure of contact dermatitis. <sup>23</sup> It is a biological gold standard test to identify contact allergen.<sup>6</sup>

In a sensitized individual, primed antigen specific T lymphocytes are present throughout the body. Hence, when the allergen is applied on a normal skin it produces a reaction similar to contact dermatitis at the site of application. This is the basic principle of patch test.<sup>7</sup>

Patch test is contraindicated in patients with active disease at test site or at a distant site, in patients on systemic steroids or other immunosuppressive drugs or on phototherapy. If patient has been treated with systemic corticosteroids, patch testing should be delayed for at least 2 weeks.<sup>24</sup>

In an institution-based study on morphological pattern of hand eczema, male to female ratio was 2:1, in age group of 21-40 years. Most of the women were housewives (81.8%) and men were masons (32.8%). Fourteen percent of the patients had pompholyx, 10% had housewives' eczema, 9% had hyperkeratotic eczema, 5% had finger tip eczema, and 62% of the patients could not be placed into any specific category. Patch test was positive in 65 patients out of which 44 were men and 21 were women, 30 were atopic and 35 were non atopic. Potassium dichromate was the most common allergen (25%), followed by fragrance mix (16%), nickel sulphate (14%) and PPD (13%).<sup>2</sup>

In a study conducted at PGIMER, Chandigarh, 560 patients (M=303, F=257) of suspected allergic contact dermatitis, age ranging from 9 to 85 years were recruited. Out of them, 90 patients had hand dermatitis and 51 patients had footwear dermatitis. Hand and foot dermatitis together was seen in 22 patients. Nickel sulfate (17.5%) was the most common sensitizing agent in females followed by potassium dichromate (7%) and fragrance mix (7%). In males, potassium dichromate (16.8%) was the most common allergen, the next being nickel sulfate (7.26%).<sup>25</sup>

In another study conducted at Allahabad, India, 1000 patients (M=566, F=434) presenting with signs/symptoms of suspected ACD were patch tested from

May, 1997 to April, 2006. Positive results were seen in 590 patients to one or more allergens. In this study nickel (43%) was the commonest allergen found in females and potassium dichromate (30%) in males. Other important allergens found in this study were neomycin (7%), mercaptobenzothiazole (6.6%), nitrofurazone (6%), colophony (5.7%), fragrance mix (5.5%) and cobalt chloride (5.4%).<sup>26</sup>

In a hospital-based study conducted at Jaipur, India, 100 patients with hand eczema were registered. Patch test was done in 21 patients (M=13, F=8) with Indian Standard Series (ISS). Age of the patients ranged from 23 to 55 years. Patch test was positive in seven out of the 21 patients. Of the seven patients, only three (two positive for potassium dichromate and one for nickel and formaldehyde) had definite occupational exposure. Two housewives were positive for nickel, a possible source of exposure might have been detergents and soaps. The other two patients were positive for wool alcohol and paraben mix and fragrance mix and wool alcohol respectively. No occupational or environmental exposure could be established in these patients.<sup>27</sup>

In a study conducted at JIPMER, Pondicherry, India, 36 cases (M=30, F=6) of hand eczema, age ranging from 19-65 years were examined. Patch test was positive in 19 cases (52.78%). Potassium dichromate was the most common sensitizer seen in 10 cases, followed by colophony, black rubber mix, balsam of peru, fragrance mix and neomycin.<sup>28</sup>

In a hospital-based study conducted at Mangalore, India, 50 patients (M=28, F=22) with hand eczema attending the out patient's department (OPD) for a period of 15 months were included. A positive patch test was seen in 82% of patients. Potassium dichromate was the commonest sensitizer (26%), followed by nickel (18%).<sup>29</sup>

#### **Principles of patch testing:**

- Patient should be tested only with known substances in "standard" concentrations. In doubtful cases, open or "use" tests with controls should be done. Patch test should not be done with industrial substances of unknown concentrations.
- 2. In acute stage of dermatitis patch test should not be done. The test site must be completely free of dermatitis.
- 3. The patient must be instructed to leave the patches for 48 hours. If any patch test site burns and itches severely, the patient should immediately report to the doctor and that patch has to be removed carefully without disturbing the others.
- 4. The patient is instructed not to take shower, bath or engage in sports while the patches are in place. Certain types of heavy works are contraindicated as well, especially if the patient sweats considerably.
- Patch test can be read initially at 48 hours after allowing the tape reaction to subside (approximately 1 hour), but an additional reading should be taken after 72 hours.

#### Technique of patch testing:

The present standard test methods involve a device and patch test material. The patch test material consists of allergens incorporated usually in petrolatum base and acetone. The device used for application of allergens is Finn chamber, which consists of small aluminum discs on scanpor tape that should be non-occlusive, nonirritant and non-allergenic.

Recording of patch test reaction is done according to the scale suggested by International Contact Dermatitis Research Group (ICDRG):<sup>9</sup> Table 3: Recording of patch-test reactions according to the InternationalContact Dermatitis Research Group.7

Recording	Interpretation
-	Negative
?+	Doubtful reaction; faint erythema only
+	Weak positive reaction; palpable erythema, infiltration, possibly papules
++	Strong positive reaction; erythema, infiltration, papules, vesicles
+++	Extreme positive reaction; intense erythema and infiltration and coalescing vesicles
IR	Irritant reaction of different types
NT	Not tested

Various causes of false positive and false negative patch test reactions are listed in table4.

### Table 4: Causes of false positive and false negative patch test reactions:

False positive reactions	False negative reactions
• Excessive concentration	Insufficient concentration
• Impure substance	• Insufficient amount applied
• Irritant vehicle	• Poor adhesion of patches
• Application of excess allergen	• Patches applied at wrong site
• Uneven dispersion	Inappropriate vehicle
• Current (or) recent dermatitis at	• Readings taken too early
patch test site	• Substance degraded
• Current dermatitis at distant sites.	• Pretreatment of patch test site
• Pressure effect of hard materials.	with topical corticosteroid or
• Adhesive tape reactions	ultra violet rays.
• "Angry back" reaction causing	• Systemic treatment with
intensification of weak irritants.	immunosuppressants.

Several adverse reactions may follow patch test, as follows:

- Active sensitization
- Irritant patch test reactions
- "Ectopic" flare of dermatitis
- Koebner phenomenon
- Persistent positive reaction
- Anaphylactic reactions

- Hyper and hypo pigmentation at the sites of positive patch test reactions
- Pustular patch test reactions
- Pressure effects
- Bacterial and viral infections
- Necrosis, scarring and keloids

#### Other tests for allergic contact dermatitis:

#### **Open test:**

The allergen is dropped on an area of skin measuring about 1 cm in diameter and the solution is allowed to dry. No occlusion is used. Test site should be checked at regular intervals during 30-60 minutes after application. Second reading should be taken at 3-4 days.<sup>9</sup> The reaction is often weaker and consists of isolated papule only. It is used as a preliminary screening procedure.

#### Repeated open application test (ROAT):

ROAT in a standardized form was introduced by Hannuksela and Salo.<sup>9</sup> The substances are applied twice daily on atleast 5 cm<sup>2</sup> area on the upper arm for seven days or until positive eczematous reaction develops. It helps to determine the relevance of doubtful positive patch test reactions.

#### Usage test:

This test is helpful either in final confirmation of contact hypersensitivity of hapten or in assessment of clinical relevance of a equivocal result of patch test. These are useful in suspected cosmetic and clothing dermatitis.

#### Intradermal testing:

It is used only for investigative purposes. It is reliable for detecting nickel and corticosteroid allergy.

#### Photo patch testing:

Antigens are applied in duplicate parallel to each other and covered with an opaque material. The patches are read as usual. One set is then irradiated with UVA. When the allergic reaction occurs only on the irradiated side and not on the control site, it is recorded as a positive photo allergic patch test. It is important to distinguish phototoxic from photo allergic reactions.

#### **Treatment:**

Treatment of acute stage of hand and foot eczema constitutes rest to the part and bland applications, it should be soaked three or four times a day in either Burrows solution (aluminum acetate 1%) or potassium permanganate solution ( diluted 1:8000). Occlusive ointments should not be used at this stage. In the subacute stage, creams may be used and in chronic stage ointments are preferred.

Systemic antibiotics should be given for secondary bacterial infections.

Chronic hand and foot eczema is multifactorial and particular attention must be paid to the causative factors including allergens, irritants or secondary infections. The main principles of treatment include:

- Avoidance of allergens and irritants,
- Frequent applications of emollients,
- Use of topical steroid sparingly.

The rule of 4 R's can be applied in the management of hand and foot eczema;<sup>4</sup>

- Recognition of the culprit irritant or allergen
- Removal of the irritant or allergen
- Reduction of the skin inflammation
- Restoration of the skin barrier

Various treatment modalities for hand and foot eczema have been presented in table5:

Table 5: Treatment modalities of hand and foot eczema:<sup>4</sup>

Topical	Systemic	Physical Therapy
1. Emollients and barrier	1. Corticosteroids	1. Photochemotherapy: with
creams		broad and narrow band
		UVB, PUVA, UVA1
2. Kertolytics (salicylic acid	2. Cyclosporine	2. Iontophoresis
20%), urea 5-10%		
3. Topical corticosteroid	3. Azathioprine	
ointments		
4. Topical calcineurin inhibitors	4. Retnoids	
(tacrolimus, pimecrolimus)	(acitretin,	
	alitretinoin)	
5. Wet wraps	5. Methotrexate	
6. Topical retinoids- bexarotene		
7. Tar based products ( coal tar)		
8. Radiotherapy: X rays/Grenz		
rays		
9. Boutilinum toxin		
#### **Emollients and barrier creams:**

Emollients and moisturizers help to restore the barrier. These should be applied frequently on the skin as a thin smear. These facilitate the hydration of stratum corneum and improve the barrier function of skin.

#### Keratolytics:

These include salicylic acid up to 20% and urea 5-10%. Urea softens the horny layer and increases its water-binding and penetration-enhancing capabilities.

#### **Topical steroids:**

Steroids along with emollients are the mainstay of therapy in hand and foot eczema. Potent topical steroids are used daily for about 4 weeks and then tapered. Potent topical steroids are more effective and reduce the risk of recurrences as compared to moderately-potent preparations. Many adverse effects of long term topical steroids are known. Alternatively a moderately-potent topical steroid with a topical calcineurin inhibitor reduces side effects and is clinically found to be effective. Topical tacrolimus is reported to be as effective as mometasone furoate in dyshidrotic palmar eczema.<sup>30</sup> Wet wrap dressings have also been found to be effective in atopic eczema.

## **Photochemotherapy:**

Phototherapy improves the skin barrier. Topical psoralen + UVA (PUVA) has been found to be superior to phototherapy with UVB. PUVA should be considered first for hyperkeratotic eczema as it is relatively safe. Broad and narrow band UVB and UVA1 have also been reported to be beneficial.

### Topical retinoids:

Topical bexarotene gel, a retinoid has been reported to be effective although irritation, stinging, burning and a flare of dermatitis has been reported.<sup>31</sup>

## Coal tar:

Coal tar-based products are effective in sub-acute and chronic eczema and have an anti-inflammatory, anti-pruritic and anti-proliferative effect.

### **Radiotherapy:**

Grenz ray therapy may act by reducing Langerhans' cell numbers. <sup>12</sup> These are safer than X-rays since penetration is only skin deep and risk of cancer is quite small as compared to phototherapy.

Superficial X-rays are found to be more effective than Grenz rays, possibly due to deeper penetration.

#### Systemic corticosteroids:

It is used in short term management of acute hand and foot eczema or during exacerbation of chronic hand and foot eczema (0.5-1mg/kg/day).

## **Oral retinoids:**<sup>4</sup>

Acitretin 40mg oral dose daily showed 50% improvement at 4 weeks in a study of patients with hyperkeratotic hand eczema

## Alitretinoin (9-cis-retinoic acid):<sup>32</sup>

It is an isomer of isotretinoin and is an endogenous physical retinoid. It binds to both RARs and RXRs. It has become the only licensed systemic agent for severe chronic hand eczema. The BACH study (Benefit of Alitretinoin in Chronic Hand Eczema) is currently the largest-controlled trial of this drug in hand eczema.<sup>33</sup>

#### Azathioprine:

Hand eczema due to parthenium responds well to azathioprine(2mg/kg/day). Atopic hand eczema also shows good response to this drug.<sup>34</sup>

## Methotrexate:

Low dose methotrexate (5-20mg weekly) has been reported to be effective in chronic hand eczema.<sup>35</sup> It has been found effective in parthenium dermatitis in atopic patients presenting with hand eczema.

## **Botulinium toxin:**

Intradermal injection of botulinium toxin has been used successfully for treating dyshidrotic eczema.<sup>36</sup>

## Avoidance advice:

This is an important component of management, once a diagnosis of contact dermatitis has been made. The possible allergens should be identified by a detailed history, examination and patch testing.<sup>37</sup> Examples of specific avoidance are the use of plastic instead of rubber gloves, use of medications free of an identified allergen, protective measures like gloves for hands in case of exposure at work. Education regarding minimal use of irritants like soap and detergents is important at home.

## **Conclusion:**

Thus from the review of literature it is evident that hand and foot eczema affect an individual's life adversely. Various allergens are implicated in the causation or aggravation of hand and foot eczema and avoidance of these agents may reduce the chronicity and recurrence of these disorders. Patch testing of patients with hand and foot eczema is helpful to detect the common allergens involved in the causation of this disorder.

## **METHODOLGY**

A total of 60 patients of with hand and foot eczema who attended the Dermatology, Venereology and Leprosy OPD of B.L.D.E.U's Shri. B. M. Patil Medical College Hospital and Research Centre, Bijapur, Karnataka, during the period of October 2011 to August 2013 were taken in the present study.

### **SELECTION OF PATIENTS:**

## **Inclusion criteria:**

Adolescents (16 years onwards) and adults with hand and foot eczema of more than three months duration were included for the study.

## **Exclusion criteria:**

Following patients with chronic hand and foot eczema were excluded from the study:

- 1) Children below 16 years of age.
- 2) Patients with definite history and clinical features of ICD of hand and foot.
- Patients with active dermatitis on back (patch test site). These patients were enrolled on a further visit when the back was free of dermatitis.
- 4) Patients on treatment with systemic steroid or immunosuppressive drugs. These patients were enrolled when the systemic steroid was tapered to a minimal dose or immunosuppressive drugs were stopped.
- Patients with major systemic illnesses like uncontrolled diabetes, hypertension, neurological disorders were excluded.

#### **HISTORY AND EXAMINATION:**

A detailed history of each patient was recorded in the proforma about the onset and duration of symptoms, recurrence, family history of atopy, preexisting medical condition. A detailed occupational history was taken including the agents used routinely like detergents, gloves, artificial ear-rings, cement etc..

A complete clinical examination and cutaneous examination was done in all patients. Clinical diagnosis of the type of eczema was recorded. The baseline hematological investigation was done. Patch test was performed in these patients after obtaining their consent.

#### **PATCH TEST:**

Patients were patch tested with ISS (SYSTOPIC LABORATORIES) containing 20 antigens approved by Contact and Occupational Dermatosis Forum of India (CODFI). Before performing the patch test, patients were counseled in their colloquial language regarding the non-invasive and painless nature of the technique.

The ISS of 20 antigens consists of:

- 1. Vaseline
- 2. Wool alcohols (30%)
- 3. Balsam peru (25%)
- 4. Formaldehyde (1%)
- 5. 2-Mercaptobenzothiazole (2%)
- 6. Potassium dichromate (0.5%)
- 7. Nickel sulfate hexahydrate (5%)
- 8. Cobalt (II) chloride hexahydrate (1.0%)
- 9. Epoxy resin (1%)

- 10. Colophony (20%)
- 11. Paraben mix (15%)
- 12. 4-Phenylenediamine base (1.0%)
- 13. Neomycin sulfate (20%)
- 14. Benzocaine (5.0%)
- 15. Parthenium
- 16. Fragrance mix (8%)
- 17. Nitrofurazone (1%)
- 18. Thiuram mix (1%)
- 19. Black rubber mix (0.6%)
- 20. Chlorocresol

#### **Procedure employed:**

Part or area (viz:back) is prepared by shaving with sterile blade. The test site was cleaned with swabs soaked in rectified spirit and it was allowed to evaporate. Antigens were placed into aluminium chambers (optimal quantity:3mm length from the nozzle). In case of liquid antigens, one drop of the antigen was poured on a round piece of tissue paper (of diameter less than the chamber) placed on the aluminium chamber. Antigen impregnated chambers was placed sequentially from left to right side on patient's back sparing the midline and reinforcement was done by using 2" micropore tape. Patients were instructed to avoid exercise, sunbathe or scratch the test site for subsequent 2 days. In case intense irritation or pruritus occurs, patients were instructed to report to the investigator immediately.

First reading was done at 48 hours. The strips were removed gently. The sites of antigen application were marked by a circle with water resistant marker pen. After

an interval of minimum 1 hour, readings were taken and recorded. Following 1st reading, patients were sent home with further advice as previously, not to tamper the patch test site. At 72 hours the second reading was taken and recorded. Patch test results are interpreted as per ICDRG guidelines.<sup>7</sup>

## **ICDRG guidelines:**

- ?+ Doubtful reaction; faint erythema only
- + Weak positive reaction; erythema, infiltration, possibly papules.
- ++ Strongly positive reaction; erythema, infiltration, papules, vesicles.
- +++ Extreme positive reaction; intense erythema, infiltration and coalescing vesicles.
- -- Negative reaction
- IR Irritant reactions of different types.
- NT Not tested.

## STATISTICAL ANALYSIS:

- The observations pertaining to the parameters under study group was expressed in percentage.
- > Collected data was presented with mean  $\pm 2$ SD.
- To find the correlation between occupation and patch test positivity Fischer's exact test were applied.

## **ETHICAL CLEARANCE:**

Institutional ethical committee clearance was undertaken for the study.



Figure 1: Palmar peeling



Figure 2: Fingertip Eczema



Figure 3: Hyperkeratotic eczema of foot



Figure 4: Hyperkeratotic eczema of hand



Figure 5: Unclassified Eczema



Figure 6: Indian Standard Series allergens.



Figure 7: Finn chamber laid out on Scanpor tape.



Figure 8: A 5-mm ribbon of petrolatum-based allergen is placed into the Finn

chamber.



Figure 9: Application of a filter paper disk into the Finn chamber to hold liquid allergens.



Figure 10: Finn chambers in place on the upper portion of the back.



Figure 11: +/- Macular erythema



**Figure 12:** + = Weak reaction (erythema with few papules)



Fig 13: ++ = strong (vesicular) reaction



**Figure 14:** +++ = An extreme bullous positive reaction

## **RESULTS**

A total of 60 cases with hand and foot eczema were examined during the study period. Out of them 27 (45%) patients were affected with hyperkeratotic type, 4 (6.67%) with pompholyx, 3 (5%) with nummular eczema, 2 (3.33%) with palmar peeling, 1 (1.67%) with fingertip eczema and chronic acral erythema (CAE) each and 22 (36.66%) with unclassified eczema (Table 6 and figure 15)

Types	No.	%
Hyperkeratotic	27	45
Pompholyx	4	6.67
Nummular eczema	3	5
Palmar peeling	2	3.33
Fingertip eczema	1	1.67
CAE	1	1.67
Unclassified eczema	22	36.66
Total	60	100

Table 6: Clinical types of hand and foot eczema



Figure 15: Clinical types of hand and foot eczema

## Age incidence and sex distribution of hand and foot eczema

The age of the patients with hand and foot eczema ranged from 19 years to 64 years (mean 35.86 years). Incidence of hand and foot eczema was highest 21 (35%) among patients with 21-30 years, followed by 14 (23.33%) with 31-40 years. Males (61.63%) outnumbered females (38.37%). The age and sex distribution of the patients is shown in Table7 and figure 16

Age (years)	male		(years) male Female		Total	
	No.	%	No	%	No.	%
17-20	3	5	3	5	6	10
21-30	11	18.3	10	16.67	21	35
31-40	10	16.6	4	6.7	14	23.33
41-50	8	13.4	1	1.6	9	15
51-60	2	3.33	3	5	5	8.33
>60	3	5	2	3.4	5	8.34
Total	37	61.63	23	38.37	60	100

 Table 7: Age incidence and sex distribution of hand and foot eczema

Figure 16: Age incidence and sex distribution



## Distribution of hand and foot eczema according to duration of the disease

Duration of hand and foot eczema ranged from 4 months to 240 months (mean 42.45 months). Most common duration of disease period observed was between 6-24 months with 34 patients (56.7%) . Distribution of hand and foot eczema according to the duration is shown in table 8 and figure 17

 Table 8: Distribution of hand and foot eczema according to duration of the

 disease

Duration	No. of patients	Percentage
4-6 Months	4	6.6 %
6-24 Months	34	56.7%
> 24 Months	22	36.7%

Figure 17: Distribution of hand and foot eczema according to the duration



### Distribution of cases according to their occupation

Maximum patients in this study were housewives 14 (23.33%), followed by mason workers 11 (18.33%), students 8 (13.33%), agriculture laborer 5 (8.33%), teachers 4 (6.67%). Small number of patients were businessmen, drivers, goldsmith, retiree, laborer, mechanic, dentist, sweeper, servant, gardener and others. Distribution of cases according to occupation is shown in table 9 and figure 18

Occupation	Males		Fe	males	Total		
	No.	%	No.	%	No.	%	
Housewives	-	-	14	23.33	14	23.33	
Mason	11	18.33	-	-	11	18.33	
Student	5	8.33	3	5	8	13.33	
Agriculture	4	6.67	1	1.67	5	8.33	
laborer							
Teacher	3	5	1	1.67	4	6.67	
Businessmen	2	3.33	-	-	2	3.33	
Driver	2	3.33	-	-	2	3.33	
Goldsmith	2	3.33	-	-	2	3.33	
Retiree	1	1.67	1	1.67	2	3.33	
Laborer	1	1.67	1	1.67	2	3.33	
Mechanic	1	1.67	-	-	1	1.67	
Dentist	1	1.67	-	-	1	1.67	
Sweeper	1	1.67	-	-	1	1.67	
Servant	1	1.67	-	-	1	1.67	
Gardener	1	1.67	-	-	1	1.67	
Others	2	3.33	1	1.67	3	5	
Total	38	63.33	22	36.67	60	100	

## Table 9: Distribution of cases according to their occupation



Figure 18: Distribution of cases according to their occupation

## Association with atopy in hand and foot eczema

Only 2 (3.33%) patients were found to be atopic. Relation with atopy is shown in table 10 and figure 19

Atopy	No of cases	Percentage
Positive	2	3.33
Negative	58	96.67
Total	60	100

## Table 10 : Association with atopy in hand and foot eczema



## Figure 19: Association with atopy in hand and foot eczema

## Allergens with positive patch test

Allergens showing positive patch test in hand and foot eczema is shown in table 11. In males potassium dichromate was more common (11.67%), followed by cobalt chloride (10%) whereas in females, nickel was most common allergen (11.67%).

S.No	Allergens	Μ	ale	Fer	nale	Τα	otal
		No.	%	No.	%	No.	%
1	Vaseline	-	-	2	3.33	2	3.33
2	Balsam of peru (25%)	4	6.67	-	-	4	6.67
3	Formaldehyde (1%)	2	3.33	1	1.67	3	5
4	Potassium	7	11.67	1	1.67	8	13.33
	dichromate(0.5%)						
5	Nickel sulfate	4	6.67	7	11.67	11	18.33
	hexahydrate(5%)						
6	Cobalt (II) chloride	6	10	5	8.33	11	18.33
	hexahydrate (1.0%)						
7	Epoxy resin (1%)	2	3.33	-	-	2	3.33
8	Colophony (20%)	2	3.33	1	1.67	3	5
9	Paraben mix (15%)	3	5	-	-	3	5
10	4-Phenylenediamine base	1	1.67	-	-	1	1.67
	(1.0%)						
11	Benzocaine (5.0%)	1	1.67	-	-	1	1.67
12	Parthenium	3	5	-	-	3	5
13	Fragrance mix (8%)	3	5	1	1.67	4	6.67
14	Nitrofurazone (1%)	1	1.67	1	1.67	2	3.33
15	Thiuram mix (1%)	4	6.67	-	-	4	6.67
16	Black rubber mix (0.6%)	1	1.67	-	-	1	1.67

## Table 11: Allergens with positive patch test

## Figure 20 : Various allergens with positive patch test



## Distribution of patients with positive patch test results according to their occupation:

Positive patch test was higher in mason group 8 (13.33%) followed by housewives (11.66%), students (10%) and agriculture labourer (5%). (Table 12 and figure 21)

# Table 12: Distribution of patients with positive patch test results according to their occupation:

Occurretion	Patch test results						
Occupation	No of cases	Positive reaction	%				
Housewives	14	7	11.66				
Mason	11	8	13.33				
Agriculture laborer	5	3	5				
Student	8	6	10				
Teacher	4	2	3.33				
Businessmen	2	1	1.67				
Driver	2	1	1.67				
Goldsmith	2	1	1.67				
Retiree	2	2	3.33				
Laborer	2	0	0				
Mechanic	1	0	0				
Dentist	1	0	0				
Sweeper	1	0	0				
Servant	1	1	1.67				
Gardener	1	1	1.67				
Others	3	2	3.33				
Total	60	35	58.33				

Figure 21: Distribution of patients with positive patch test results according to their occupation:



## Correlation of positive patch test results with occupation:

In correlation of positive patch test with occupation mason worker out of 11 patients 7 had positive to potassium dichromate allergen (p<0.0001) which is highly significant and 4 were positive to cobalt (p=0.1044) which was not significant (Table 13).

Mason	Potassium dichromate						
	Yes No Total						
Yes	7	4	11				
No	1	48	49				

## Table 13:Correlation of positive patch test results with occupation:

Mason	Cobalt						
	Yes No Total						
Yes	4	7	11				
No	7	42	49				

## Distribution of patients according to causes of allergens showing positive patch test results:

Out of 60 patients, 35 showed positive patch test results. Out of them 22 were males and 13 were females. Patch test positivity to one allergen was seen in 15 (42.86%) patients, two allergens in 13 (37.14%) patients, three allergens in 4 (11.43%) patients and four allergens in 3 (8.57%) patients. (Table 14 and figure 22)

 Table 14: Distribution of patients according to causes of allergens showing

 positive patch test results:

Single & multiple allergens positive	Μ	ale	Female		Total	
	No	%	No	%	No	%
One	6	17.14	9	25.71	15	42.86
Two	10	28.58	3	8.57	13	37.14
Three	4	11.43	-	-	4	11.43
Four	2	5.71	1	2.86	3	8.57
Total	22	62.86	13	37.14	35	100

Figure 22: According to single and multiple allergen positivity



## DISCUSSION

Contact dermatitis is a significant public health concern.<sup>13</sup> It is an increasing problem all over the world and accounts for 4-7% of all dermatological consultations.<sup>25</sup> In day to day life a person is obliged to handle several types of agents everyday, CD of hand and foot is a common problem.<sup>38</sup> It is a chronic disorder with high socioeconomic burden and often results in long-term sick leave or unemployment.<sup>39</sup> Patch testing is a definite tool for diagnosing allergic contact dermatitis.<sup>26</sup>

In the present study according to morphology hyperkeratotic type was seen in 27 (45%) patients. Our finding did not match with study conducted by Handa et al <sup>2</sup> in which only nine patients had hyperkeratotic eczema and in study by Laxmisha et  $al^{28}$  four cases had positive results. It showed low rates when compared to present study.

Pompholyx accounted 4 (6.67%) patients in the present study. In study conducted by Laxmisha et  $al^{28}$  only one case had pompholyx, in contrast study by Handa et  $al^2$  showed 14% patients with pompholyx, which was higher than the present study may be due to more number of patients with atopy which is an endogenous factor.

Unclassified eczema, where lesion were not fitting into known morphological types of eczema, it accounted 22 (36.66%) patients positivity in the present study. In comparison a study conducted by Handa et  $al^2$  showed 62% of patients positivity, which was higher than the present study. This emphasizes the fact that morphological classification of all patients of hand and foot eczema is not always possible.

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Other morphological types were nummular eczema 3 (5%), palmar peeling 2 (3.33%), fingertip eczema 1 (1.67%) and chronic acral erythema 1 (1.67%). Study by Handa et al <sup>2</sup> showed 5% of patients with fingertip eczema which was high compared to present study.

In the present study 35% of patients were between 21 to 30 years of age. Similar observation was done in a study by Huda et al<sup>38</sup> where most of cases were between 21 to 30 years.<sup>38</sup> High percentage of this disease in young adults may be due to their more active life styles resulting in frequent exposure to various irritants and allergens in the environment. A low incidence of this disease is noted in other age groups in study by Huda et al<sup>38</sup> including present study. Less environmental exposure among these age group may be responsible for this variation. Our finding did not match with study by Handa et al<sup>2</sup> where most of cases (54%) were between 21 to 40 years.<sup>2</sup>

Hand and foot eczema occurs in both males and females, however male predominance (61.63%) was seen in the present study, which was similar to other study by Bajaj et al<sup>26</sup>, Handa et al<sup>2</sup>, Jindal et al<sup>25</sup>, Kishore et al<sup>29</sup>, Agarwal et al<sup>27</sup> and Laxmisha et al.<sup>28</sup> On other hand, a female predominance was seen in study by Huda et al<sup>38</sup> and Davoudi et al.<sup>40</sup>

Male predominance is generally high. It could be due to more exposure to various allergens as most of them are involved in out door activities. But in few studies females predominance was seen. In India females are specially more involved in household work. Therefore, it could be concluded that different incidence in two groups is not due to gender difference but rather due to difference in exposure to allergens.

Duration of hand and foot eczema differ depending upon chronic course of disease, mode of exposure and ignorance about the contact allergens. The absence of social security system in India results in continuous exposure of patients to the occupational allergens because of their inability to change their professions easily.

In the present study duration of illness ranged from 4 months to 20 years. Most common duration of disease period at the time of presentation was between 6 to 24 months, in almost 56.7% of patients. In other studies <sup>2, 25,40</sup> the duration ranged from few months to few years.

Patients with atopic diathesis are more prone to develop hand and foot eczema. In present study history of atopy was found in only 2 (3.33%) patients. Similar observation was seen in study by Laxmisha<sup>28</sup> where only one case had atopy history. The present study finding did not match with study by Jindal et al<sup>25</sup> were 186 (30%) patients had positive history of atopy, however there was no statistically significant difference in contact sensitization between atopics and non-atopics.

Hand and foot eczema is a common health problem in persons with both indoor and outdoor occupational group. Persons who are at risk to develop this disorder include occupation like housewives, mason workers, laborers, students etc. Here the patient comes in contact repeatedly with the allergen or irritant, and the chances of developing this disorder increases. Housewives constituted a large number 14 (23.33%) in the present study followed by mason workers 11 (18.33%), students 8 (13.33%) and agriculture laborer 5 (8.33%). High incidence of housewives positivity was also reported in study by Kishore et al<sup>29</sup> (68.2%), Huda et al <sup>38</sup> (23.75%) and Handa et al<sup>2</sup>. Indian housewives tend to develop hand eczema at younger age as compared to those in developed countries. This is because of variety of agents that they come in contact which may act either as irritants or allergens in addition to trauma of rubbing and scrubbing.<sup>41</sup>

Contact allergic dermatitis is a delayed type of cell-mediated hypersensitivity reaction. Patch testing is a "gold standard" for identification of contact allergens.<sup>6</sup> In the present study a total of 60 patients with hand eczema with or without foot eczema were patch tested, among which 58.33% showed positive results to one or more antigens. Most common sensitizers were nickel sulfate (18.33%) and cobalt chloride (18.33%) followed by potassium dichromate (13.33%) etc. which was similar in studies conducted by Bajaj et al<sup>26</sup>, Narendra et al<sup>42</sup> where nickel was most common sensitizer followed by potassium dichromate but cobalt chloride was in lower percentage compared to our study.

Antigen	Narendra et al <sup>42</sup>	Shenoi et al	Bajaj et al <sup>26</sup>	Present
	2002)	(mampai- 1994)	(Ananabad- 2007)	study
Nickel sulfate	15	10.8	12.9	18.33
Potassium	13.5	11.3	11.1	13.33
dichromate				
Cobalt chloride	8.75	7.1	5.4	18.33
Balsam of peru	2.5	3.3	2.3	6.67
Fragnance mix	7.5	6.1	5.5	6.67
Thiuram mix	7.5	2.4	3.3	6.67
Paraben mix	3.75	2.4	2.4	5
Formaldehyde	0	3.8	1.1	5
Parthenium	-	-	14.6	5

Table 15: Comparison of sensitivity to allergens at different centers

Chromates are abundantly presently in the environment. Exposure occurs usually through which a person gets contact in his day to day activities. The common sources in which it is present is cement, leather, bleaches, matches, photography material, electroplating, rubber and printing industries. Cement contains high amount of chromate and cobalt.<sup>44</sup> In the present study 8 patients (13.33%) showed positivity to potassium dichromate of which 7 were males and 1 was female. Patients in our study had significant occupational exposure to chromates, there by increasing the risk of contact sensitivity to chromates, which could explain the high number of positive patch test reaction to potassium dichromate and cobalt chloride noted by us. Similar observation was made in study by Bajaj et al<sup>26</sup>, Narendra et al.<sup>42</sup> The present study finding did not match with study conducted by Handa et al<sup>2</sup>, Shenoi et al<sup>43</sup> and Kishore et al<sup>29</sup> where the percentage was higher than the present study, may be due to more number of patients involved.

Nickel sulphate positivity was seen in 11 (18.33%) patients in our study. Seven (11.67%) of females and six (6.67%) of males were positive. This metal is present everywhere and exposure to this can occur while handling with artificial jewellery, bangles, pins, buttons, coins, zips, hooks, door handles, scissors, watches, cooking acidic food in stainless-steel. First quart of tap water drawn from any faucet in the morning contains nickel. Industrial exposure to nickel occurs in electroplating, electrical wiring, ceramics and paints for glass. Similar observation was seen in study by Kishore et al<sup>29</sup> with 18% positivity to nickel sulfate and other two study by Narendra et al<sup>42</sup> Jindal et al<sup>25</sup> and Bajaj et al.<sup>26</sup>

Cobalt chloride is another frequent sensitizer found in mainly in cement and other like adhesives, pottery, clay, hair dyes. In present study it was positive in 11 (18.33%) patients. Six (10%) were males and five (8.33%) were females. Study

conducted by Narendra et al<sup>42</sup>, Shenoi et al<sup>43</sup>, Bajaj et al<sup>26</sup> and Jindal et al<sup>25</sup> found lower members of positivity when compared to present study.

Few cosmetics also accounted for sensitivity in 9 cases of hand and foot eczema in the present study. They were fragnance mix 4 (6.67%) patients, balsam of peru 4 (6.67%) patients and PPD in 1 (1.67%) patient. Similar observation for fragnance mix was seen in Shenoi et al  $^{43}$ (6.1%) and little higher in Narendra et al $^{42}$  (7.5%) and Jindal et al $^{25}$  (7.1%). This positivity may be due to wide use of cosmetics, perfumes and deodorants. Toothpaste, soft drinks china painting and oil painting may also add to this list.

Rubber material frequently used in day to day life, is responsible for contact dermatitis in many individuals. Its products such as thiuram mix and black rubber mix is seen in a number of products such as latex gloves, rubber slippers, fungicides, disinfectants, soaps and animal repellents. In present study, 4/60 (6.67%) patients showed sensitivity to thiuram mix and 1/60(1.67%) patient to black rubber mix. Similar observations were seen in study by Narendra et al.<sup>42</sup> However, low percentages were seen in Shenoi et al al<sup>43</sup>, Bajaj et al<sup>26</sup> and Jindal et al<sup>25</sup> compared to present study.

Out of the 60 patients considered under present study for allergen positivity: 3 (5%) had formaldehyde, 3 (5%) parthenium, 3 (5%) paraben mix, 3 (5%) colophony and 2 (3.33%) epoxy resin sensitivity. In a study conducted by Shenoi et  $al^{43}$ , formaldehyde positivity was seen in 3.8%, paraben mix in 2.4%, and no patients were positive to parthenium, which was less when compared to our study. In a study by Bajaj et  $al^{26}$  14.6% of patients were positive to parthenium, which was higher than our study.

The percentage of positive patch test to multiple allergens in present study was 35/60 (58.33%). Positivity to one allergen was seen in 15/60 (42.86%), two allergens in 13/60 (37.14%), three allergens in 4/60 (11.43%) and four allergens in 3/60(8.57%). However, positive patch test to multiple allergens were in the range of 46.7% to 82% in various studies.<sup>29,45,46</sup> Our finding was much higher than the positivity rate of 32.3% reported recently from a study done at Turkey.<sup>47</sup>
## CONCLUSION

- The higher incidence among patients belonging to second and third decade of life is because this is the vocational age group where the chances of exposure to various allergens is high.
- There was a slight preponderance of males.
- The higher incidence among housewives, mason workers are probably due to persistent exposure to the allergens.
- Only 2 patients had history of atopy.
- Patch testing, was positive in more than 50 % of cases and hence it was very useful in the diagnosis of hand and foot eczema. Consequently is helpful in reducing its recurrence, which is not only an occupational hazard but also a socioeconomic problem.
- In some situations, a change of occupation can be advised, however if it is not possible, patients can be asked to take proper preventive measures.
- In chronic hand and foot eczema, patients are unable to perform daily activities because of the pain and cosmetically unpleasant appearance. The patients who have this disorder suffer from stigma, which could be greatly reduced by detecting the causative agents, treating the problem and taking proper precautionary measures. Therefore good diagnosis, proper treatment and advice can help all sufferers of this disease to have a better quality of life.

#### SUMMARY

A hospital based, cross-sectional study on patch testing with Indian Standard Series was done during the period October 2011 to September 2013.

It was done to determine the role of contact allergens in patients with hand and foot eczema. Adolescents above 16 years were included and detailed history of onset and duration of symptoms, recurrence, family history of atopy, occupational history was recorded.

Each patient was subjected to a complete clinical and cutaneous examination. Relevant information about agents used routinely like detergents, gloves, artificial ear-rings, cement etc was taken into account.

Following are the salient findings of this study:

- Clinical types of hand and foot eczema:45% had hyperkeratotic type, 6.67% had pompholyx and 36.66% with unclassified eczema.
- Hand and foot eczema was more common between 21-30 years of age which accounted for 35% of the cases.
- Males (61.63%) outnumbered females (38.37%) in the ratio of 1.6:1.
- Occupation of patients in the present study varied. Commonest being housewives (23.33%) followed by mason workers (18.33%), students (13.33%), agriculturalists (8.33%), teachers (6.67%) and others.
- History of atopy was not a significant association (positive only in two patients).
- Patch testing revealed positive results to multiple allergens in 35 patients. Among them, 22 were males and 13 were females.

- Positivity to single allergen was seen in 42.86% of patients, two allergens in 37.14%, three allergen in 11.43% and four allergens in 8.57%.
- Nickel sulfate (18.33%) and cobalt chloride (18.33%) were the most common allergens, followed by potassium dichromate (13.33%), balsam of peru (6.67%), fragrance mix (6.67%), thiuram mix (6.67%).
- Correlation of positive patch test with occupation was seen in mason workers.

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## ANNEXURES

### **PROFORMA:**

### SCHEME OF CASE TAKING

# B.L.D.E.U'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR

## Department of Dermatology, Venereology and Leprosy

SL.NO:	Date:	Sex: Male/Female
Name:		Age:
Father's/Husband's name:		
Address :		
Occupation : (H/O handling following things)		
1. Complaints with duration	:	
2. Presenting features		
a) Symptoms with duration	n :	
b) Itching	: Mild / modera	te / severe
c) Number of episodes/ Recurrence	:	
e) Family history of atopy Hand and foot eczema	/ : First degree fa Second degree Yes / No	amily members / e family members.

3.	General Physical Examination	:	
	Pallor-	Cyanosis-	Clubbing-
	Icterus -	Edema -	
	Lymphadenopathy-		
4. Cut	taneous examination :		
	a) Site of lesion	: Hand or foot or both	
	b) Type of lesion	: Papule / plaque / vesicle / b	olisters.
	c) Distribution of lesion	: Localized Symmetrical / asymmetrica	1
	d) Scaling	: Yes / No	
	e) Pigmentation	: Yes / No	
	f) Lichenification	: Yes / No	
5. Sys	stemic Examination	:	
	Respiratory system	:	
6. Clir	ical diagnosis	:	
7. Inve	estigations	:	
	Hemoglobin %	:	
	Total leucocyte count	:	
	Differential count	:	
8. Pato	ch testing Results	:	
	Positive to	:	

## **B.L.D.E.** Association's

## SHRI B.M.PATIL MEDICAL COLLEGE., SPECIALITY HOSPITAL, BIJAPUR DEPARTMENT OF DERMATOLOGY

## **PROFORMA FOR PATCH TEST RESULT**

Name:

Age/Sex:

Date:

Sl.No	Allergen	Reading at 48hours	Reading at 72
			hours
1	Vaseline		
2	Wool alcohols (30%)		
3	Balsam peru (25%)		
4	Formaldehyde (1%)		
5	2-Mercaptobenzothiazole (2%)		
6	Potassium dichromate (0.5%)		
7	Nickel sulfate hexahydrate (5%)		
8	Cobalt (II) chloride hexahydrate (1.0%)		
9	Epoxy resin (1%)		
10	Colophony (20%)		

11	Paraben mix (15%)
12	4-Phenylenediamine base
	(1.0%)
13	Neomycin sulfate (20%)
14	Benzocaine (5.0%)
15	Parthenium
16	Fragrance mix (8%)
17	Nitrofurazone (1%)
18	Thiuram mix (1%)
19	Black rubber mix (0.6%)
20	Chlorocresol

## SAMPLE INFORMED CONSENT FORM BLDEU'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE.

#### **BIJAPUR – 586103**

#### **RESEARCH INFORMED CONSENT FORM**

TITLE OF THE PROJECT : PATCH TESTING WITH INDIAN STANDARD SERIES TO DETERMINE THE ROLE OF CONTACT ALLERGENS IN PATIENTS WITH HAND AND FOOT ECZEMA.

PG GUIDE	: DR. ARUN C. INAMADAR
PG STUDENT	: DR. PUJA SHARMA

#### **PURPOSE OF RESEARCH :**

I have been informed that this project will study to know the incidence and detect the contact allergens of hand and foot eczema in adolescents and adults.

#### **BENEFITS:**

I understand that my participation in this study will help the investigator to understand the disease better and will help in the management of the disease.

#### **PROCEDURE :**

I understand that relevant history will be taken and detailed clinical examination after which necessary investigation (patch test) will be done whenever required.

#### **RISK AND DISCOMFORTS:**

I understand there is no risk involved and i will experience minimal side effects during the procedures performed.

#### **CONFIDENTIALITY:-**

I understand that medical information produced by this study will become a part of hospital records and will be subjected to the confidentiality and privacy regulation of the said hospital. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file.

If the data are used for publication in the medical literature or for teaching purposes no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand I may see the photographs, videotapes and hear the audiotapes before giving this permission.

#### **REQUEST FOR MORE INFORMATION:-**

I understand that I may ask more questions about the study at any time concerned. The researcher is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which may influence my continued participation.

#### **REFUSAL OR WITHDRAWAL OF PARTICIPATION:-**

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in this study at any time without prejudice. I also understand that the researcher may terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician if this is appropriate.

#### **INJURY STATEMENT:-**

I understand that in the unlikely event of injury to me resulting directly from my participation in this study and if such injury were reported promptly, then medical treatment will be available to me, but no further compensation will be provided. I understand that by my agreement for my participation in this study, I am not waiving any of my legal rights.

I have explained to (patient's / relevant guardian's name) the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in patient's own language.

Investigator / P. G. Guide

Date

I confirm that .....(Name of the PG guide / chief researcher ) has explained to me the research, the study procedures that I undergo, and the possible risks and discomforts as well as benefits that I may experience. I have read and I understand this consent form. Therefore, I agree to give my consent for my participation as a subject in this research project.

Participant / guardian

Date

Witness to signature

Date

## ETHICAL CLEARANCE CERTIFICATE



aommitte. JAPUR- 585103 OUT WARD

Dermatolog

## B.L.D.E. UNIVERSITY'S SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103 INSTITUTIONAL ETHICAL COMMITTEE

## INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on <u>20-10-2011</u> at <u>10-30 ampto</u> scrutinize the Synopsis/Research projects of postgraduate/undergraduate student/Faculty members of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis/Research project has been accorded Ethical Clearance.

Title Patch testing nith Indian Standard Series the gole of contact allergens detis with hand and in patients foot eczeona "

Name of P.G./U.G. student/Faculty member\_ Ar. Duja Sharma reat of Dermate

Name of Guide/Co-investigator Dr. A.C. Inamadah 1000+ 8-

> DR.M.S.BIRADAR, CHAIRMAN INSTITUTIONAL ETHICAL COMMITTEE BLDEU'S, SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR. Chairman Ethical Committee BLDEA'S Shri. B.M. Patil Madical College Bijapur-586103

Following documents were placed before E.C. for Scrutinization 1) Copy of Synopsis/Research project. 2) Copy of informed consent form

3) Any other relevant documents.

## **KEY TO MASTER CHART**

М	-	Male
F	-	Female
HW	-	Housewife
A.L	-	Agriculture Labourer
HK	-	Hyperkeratotic
POM	-	Pompholyx
CAE	-	Chronic acral eczema
FTE	-	Fingertip eczema
NE	-	Nummular eczema
РР	-	Palmar peeling
UE	-	Unclassified eczema
C.grass	5-	Congress grass
2MBT	-	Mercaptobenzothiazole
4-PD	-	4-Phenylenediamine base
BRM	-	Black rubber mix

				(su		At	ору		Site	es																		Pa	tch te	sting
S.no	Age (yrs)	Sex	Occupation	Duration (Mont)	Episodes	Personal	Family	Suspected contactants	Hand	Foot	Morphology	Vocalina			Wool alcohol	Doloom Dom	baisam reru		Formaldehyde	2.MRT	1011-7	Potassium	Dichromate	Wished Culubate		71-7-22	CODAL	Thory resin	ment fenda	
1	20	F	HW	4	2	-	-	DETERGENT	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	32	м	MASON	4	2	-	-	CEMENT	-	+	UE	-	-	-	-	-	-	-	-	-	-	-	I	-	-	-	-	-	-	-
3	60	М	A.L.	4	2	-	-	SUNFLOWER	+	-	НК	-	-	-	-	-	-	+	+	-	-	-	-	+	+	-	-	-	-	-
4	45	F	TEACHER	12	4	-	-	DETERGENT	+	+	нк	-	-	-	-	-	-	+	+	-	-	-	-	+	+	-	-	-	-	-
5	42	м	BUSINESS	120	6	-	-	PLASTIC	+	+	POM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-
6	40	F	A.L.	240	7	-	-	C. GRASS	+	+	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	25	F	HW	120	5	-	-	DETERGENT	+	+	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	36	М	MASON	120	3	-	-	CEMENT	+	+	UE	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-
9	36	М	MASON	6	10	-	-	CEMENT	+	+	CAE	-	-	-	-	-	-	-	+	-	-	+	+	-	-	+	+	-	-	-
10	22	М	STUDENT	6	7	-	+	GLOVES	+	-	НК	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-
11	22	F	HW	6	3	-	-	DETERGENT	+	-	FTE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
12	24	F	HW	180	6	-	+	DETERGENT	+	+	НК	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
13	56	F	HW	12	6	+	-	DETERGENT	+	-	НК	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
14	42	М	TEACHER	6	4	-	-	CHALK	+	+	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
15	33	М	DRIVER	60	5	-	-	FRUITS	+	+	НК	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+
16	59	F	HW	6	4	-	-	DETERGENT	+	+	НК	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
17	24	м	STUDENT	36	5	-	-	INSTRUMENTS	+	-	NE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
18	61	м	MECHANIC	24	6	+	+	GREECE	+	+	NE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
19	38	м	TEACHER	12	6	-	-	CHALK	+	+	НК	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
20	23	F	STUDENT	6	5	-	-	SOAP	+	-	POM	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-

				(su		At	ору		Sit	es																		Pa	tch te	sting
S.no	Age (yrs)	Sex	Occupation	Duration (Mont)	Episodes	Personal	Family	Suspected contactants	Hand	Foot	Morphology	Vocalina			Wool alcohol	Doloom Dom	baisam reru		Formaldehyde	2.MRT		Potassium	Dichromate	Wished Culubate	NICKEI Sulphate	71-7-22	CODAL	Thory resin	nton tran	كماساسي
21	64	F	RETIRED	5	3	-	-	paper	+	+	НК	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
22	40	М	MASON	6	6	-	-	CEMENT	+	-	нк	-	-	-	-	+	+	-	-	-	-	-	+	-	-	+	-	-	-	+
23	38	М	GOLDSMITH	6	6	-	-	CHEMICAL	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
24	25	м	TEACHER	36	3	-	-	CHALK	+	-	НК	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
25	25	м	STUDENT	24	4	-	+	FOOTWEAR	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	_	-	-
26	48	м	BUSINESS	6	2	-	-	FLOUR	+	+	POM	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
27	30	м	NURSE	6	10	-	-	GLOVES	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-
28	38	м	A.L.	6	1	-	-	CEMENT	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
29	61	м	MASON	180	4	-	-	CEMENT	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30	46	м	MASON	24	3	-	-	CEMENT	+	+	UE	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-
31	30	м	MASON	8	5	-	-	CEMENT	+	+	UE	-	-	-	-	-	-	-	-	-	-	-	+	-	-	+	+	-	-	-
32	21	м	STUDENT	24	5	-	-	INSTRUMENTS	+	+	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
33	23	F	STUDENT	7	2	-	-	SOAP	+	-	РР	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	-	-	-
34	34	F	SALESGIRL	6	3	-	-	STEEL	-	+	нк	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-
35	19	м	STUDENT	180	5	-	-	SOAP	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-
36	43	м	ELECTRICIAN	12	5	-	-	WIRE	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
37	44	м	MASON	180	3	-	-	CEMENT	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
38	52	F	HW	240	5	-	-	SOAP	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
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				(St		At	ору		Sit	es																		Pa	atch te	esting
S.no	Age (yrs)	Sex	Occupation	Duration (Montl	Episodes	Personal	Family	Suspected contactants	Hand	Foot	Morphology	Vocalina			Wool alcohol	Dolcom Down	baisam reru		r ormalgenyde	2-MRT		Potassium	Dichromate	oto quipto forte in	INICKEL DUIDINALE	71-1-52	Cobait	T-court marin	Epoxy resu	
41	40	F	HW	6	3	-	-	SOAP	+	+	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+
42	26	F	LABOURER	24	5	-	-	C. GRASS	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
43	44	М	GARDNER	24	4	-	-	PLANTS	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	I	-	-	-
44	34	м	SERVENT	12	6	-	-	DETERGENT	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-
45	30	F	HW	12	4	-	-	SOAP	+	+	нк	-	-	-	-	-	-	-	-	-	-	+	+	+	+	+	+	-	-	-
46	19	М	MASON	8	5	-	-	TILES	+	-	UE	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-
47	29	М	GOLDSMITH	6	4	-	-	GOLD	+	-	POM	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-
48	19	F	STUDENT	12	3	-	-	JEWELRY	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-
49	42	М	MASON	6	5	-	-	CEMENT	+	-	НК	-	-	-	-	+	+	-	-	-	-	+	+	-	-	-	-	-	-	-
50	62	F	HW	240	7	-	-	DETERGENT	+	-	НК	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
51	22	F	HW	7	4	-	-	SOAP	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-
52	19	F	HW	6	3	-	-	SOAP	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+	+	-	-	-
53	28	М	MASON	8	4	-	-	CEMENT	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
54	19	М	SWEEPER	6	2	-	-	SOAP	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
55	25	М	LABOURER	24	4	-	-	SOAP	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
56	25	М	DRIVER	24	4	-	-	STEARING	+	+	NE	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
57	55	М	A.L.	6	3	-	+	PLANTS	+	-	UE	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
58	62	М	RETIRED	144	2	-	-	PAPER	+	-	нк	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
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result	s (48	Hrs/72	2 Hrs	)																
cotopnony		Paraben mix		4-PD	-	Neomycin		Benzocaine		Partnemum		Fragrance mix		Nuronurazone		1 hiuram mix		DIAM		Chlorocresol
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result	ts (48	Hrs/72	2 Hrs	)																
cotopnony		Paraben mix		4-PD		Neomycin		Benzocaine	-	Parthenium		Fragrance mix		Nitrofurazone		Thiuram mix		BKM		Chlorocresol
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cotopnony		Paraben mix		4-PD		Neomycin		Benzocaine		Farthemum		Fragrance mix	•	Nitrofurazone		Thiuram mix		BKM		Chlorocresol
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