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RESEARCH ARTICLE

PATCH TEST - A GOLD STANDARD IN DIAGNOSIS OF CONTACT ALLERGIES

*Karthik, R. and Mohan, N.

Department of Oral Medicine and Radiology, Vinayaka Missions sankarachariyar Dental College, Salem, India

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ABSTRACT

Patch test (epicutaneous test) is the gold standard in the diagnosis of Contact Allergies and Allergic contact Dermatitis: Performing the test significantly increases probability of accurate diagnosis, reduces costs of treatment, and leads to improved patients' quality of life. Patch test results may be influenced by patient's medication and health status, and interpretation requires due knowledge and experience.

INTRODUCTION

Contact allergy is alteration of immune response with readiness to develop an inflammatory reaction against a specific substance of low molecular weight (hapten). Allergic Contact Dermatitis refers to clinical symptoms of such inflammatory reaction in the skin. Jadassohn introduced the Patch test in 1895 is considered as the Father of Patch Testing (Trautmann, 2006).

Principle of patch testing

Patch test is used for the demonstration of delayed contact hypersensitivity (Type IV Hypersensitivity) reactions in cases of suspected contact dermatitis. Allergens are applied in a patch to the upper back/outer arm/outer thighs in that order of preference. The patch is removed after 48 hours and then read for any reaction.

Kits for patch test

Indian standard series

Devised by contact dermatitis Forum of India (CODFI), these Kits contain allergens including plant allergens required in the Indian settings.

*Corresponding author: Karthik, R.

Department of Oral Medicine and Radiology, Vinayaka Missions Sankarachariyar Dental College, Salem, India.

Additional cosmetic and footwear series allergens are also available. Aluminium Finn chambers mounted on micro pore tape are available with this kit.

True Test Kit

TRUE Test is an acronym for Thin-layer Rapid Use Epicutaneous test and was devised by Fischer and Maibach. Its main advantage is that the allergens are available ready to use form. It has a standard set of 20 allergens coated onto polyester patches in a hydrophilic vehicle. The major disadvantage is that some of the allergens like Parthenium are missing in this series.

Chemotechnique Diagnostics Patch test kit

This kit has hypoallergenic polyethylene plastic chambers that are mounted on tape. More than 25 different series are available with this kit including the International standard series and the European standard series.

METHODS OF PATCH TEST

- **AI TEST:** Made of Aluminium foil covered with polythene. Allergens are adsorbed onto a centrally placed filter paper disc of 10 mm diameter.

- **FINN CHAMBERS:** Made of aluminium wells of 8 mm diameter and 0.5 mm depth. Plastic coated Finn chambers are preferred for testing sensitivity to metals like Nickel, cobalt, Mercury as these interact with aluminium.

FINN chambers for patch test



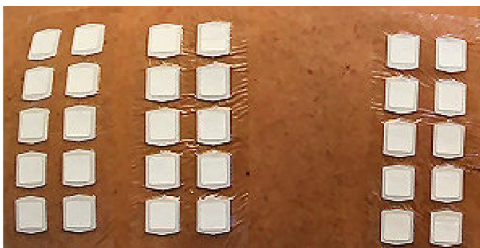
- **PLASTIC CHAMBERS** are of 10-15 mm diameter accommodating 15-100 micro litre of allergen.
- **TRUE TEST**-In this the allergens are available ready to use form coated onto polyester patches in a Hydrophilic vehicle.

In the absence of these standardized kits, Patch test can still be done using simple gauze piece and sticking plaster. However the chance of false negative or false positive reactions is higher.

Procedure

The most common site of Patch testing is the Para median Juxtrascapular area or outer arms or anterolateral thigh. Patch strips are applied over back and have to be retained in place for 48 hours without wetting them. The Patch is removed after 48 hours and the first reading is taken half an hour after removal. Two late readings are usually taken for allergens which react late like nickel, cobalt, formaldehyde resins. The first late reading is taken after 48-72 hours and the second late reading after 4-7 days of applying the test patch.

Patch Test



EBS (European Baseline Series) is recommended by the European Society of Contact Dermatitis (ESCD) and European Environmental Contact Dermatitis Research Group (EECDRG) as the first choice for testing patients with the suspicion of contact allergy. IQ Ultra Chambers are made of chemically inert polyethylene, which does not react with the haptens and does not sensitize patients. The shape of the test

chamber may also influence the final reading: IQ Ultra Chambers and TRUE Test are squaric, which allows a better discrimination between allergic and irritant reactions. In allergic reaction, inflammatory infiltrate typically expands beyond the borders of the contact area, which can be seen as "rounding" of the testing areas' corners. In contrast, irritant reaction is typically restricted to the area of contact, so that the shape of the inflamed area remains sharp.

IQ ultra chambers



Reading patch test (international contact dermatitis research group, ICDRG Guidelines)

Clinical signs	Reading of test	Interpretation of test
Faint erythema only	+/-	Doubtful Reaction
Erythema, edema, discrete Papules	+	Weak/Non-vesicular
Erythema, edema, Papules and vesicles	++	Strong/ vesicular
Intense erythema, edema and coalescing vesicles	+++	Extreme / Bullous

+ Positive reaction
-Negative reaction

Reaction of skin to an allergen in patch test



False Positive Reactions (Trautmann, 2006)

- Excited Back Syndrome/angry back syndrome/status eczematicus-false positive reactions to multiple allergens.
- Misreading of irritant reactions as positive reactions.
- Too much amount of concentration of allergen.
- Scratching of the site.
- Malingering
- Rarely sensitivity to the vehicle in a patch(control Patch shows reaction).

False Negative Reactions (Trautmann, 2006)

- Inappropriate selection of allergens
- Too little amount or concentration of allergen in a test strip.
- Loosening of patch

- Lack of natural contributing factors like moisture etc. required for the elicitation of allergic reaction.
- Systemic steroids taken in a dose greater than 20 mg/day or any other systemic immunosuppressants.

Contraindications

Contraindications for patch testing include immune deficiencies, immunosuppressive treatment and autoimmune diseases. Pregnancy and lactation are conditional contraindications, as there are no data on the safety of the test for the mother and child (leukocyte migration inhibition test, 2011).

Photopatch Test

In Photo Allergic Contact Dermatitis (PACD), the additional factor required for the development of skin symptoms is the light, typically this is ultraviolet (UV) light. Under photo activation, precursors are converted into offending haptens, or energy carried by the photons is necessary for initiation of binding between hapten and carrier protein. Diagnosis of photoallergic contact dermatitis requires respective modification of patch test called Photo Patchtest i.e. irradiation of tested skin area with UV. Typically, UVA (wavelength 320-400 nm) is used; in rare cases UVB (290-320 nm) is necessary for the initiation of allergic reaction. The UVA dose used at photopatch testing is 5-10 J/cm² or, alternatively, of Minimal Erythema Dose (MED) determined individually for the tested person [53]. The haptens tested are applied in double sets, with only one being irradiated. While interpreting photo patch test results, both sets of haptens are compared: the "bright" side (patch tests irradiated with UV) with "dark" side (not exposed to UV). A positive result on the "bright" side with a negative result on the "dark" side suggests photo allergy, equal responses on both sides "classical" contact allergy.⁷

Other tests for contact allergic dermatitis

1) Open test: The Allergen is applied on skin and left to dry and read as for a standard patch test. Used for screening purpose.

2) Repeat Open Application Test (ROAT) (Hannuksela, 1986): Allergen is applied repeatedly daily once or twice over antecubital fossa for fixed duration for 5-7 days or until elicitation of positive reaction. This test is employed to determine the relevance of doubtful positive reactions (Hannuksela, 1986).

3) Usage test: Suspected product is used in its usual manner for several days and the sites of application observed. Employed in cases of negative patch test but with strong history suggestive of contact allergic dermatitis.

4) Prophetic patch test / Repeat insulin patch test: Test agent is applied repeatedly in 10-14 applications under occlusion. After a 1 week of test free period, individual is challenged with the test again by application of test agent and readings for erythema, edema and vesiculation is taken at 24, 48 and 72 hours after removal of patch. If the test is positive at anytime during repeat application but does not show

reaction after challenge, then it implies that the test agent is a mild irritant the contrary if the reaction develops after challenge then it implies that the agent tested is an allergen. Hence this test gives prediction of possible allergenicity of the test agent before it is used or marketed widely.

1) Atopic Patch Test (APT): The mode of application of APT is similar to "classical Differences are in the test substances used (high molecular weight protein allergens – "atopens" instead of haptens), and the morphology of the positive patch test reaction (e.g. contact urticarial lesions, or papules at the orifices of sweat glands, which are the possible entrance for big protein allergens into the epidermis) especially in the diagnosis of airborne dermatitis (caused e.g. by plant pollen or mites) and eczema related to food allergy (Wüthrich, 1993).

Invitro Tests

1) Leukocyte migration inhibition test (migration inhibition assay)

An immune function test that measures MIF (monocyte/macrophage inhibitory factor) and LIF (leukocyte inhibitory factor) production after lymphocyte stimulation with common antigens- e.g., streptokinase-streptodornase, Candida antigen, PPD, concanavalin A, phytohemagglutinin, pokeweedmitogen, etc. In this test, peripheral lymphocytes are harvested from peripheral blood, spleen or lymph nodes, washed, and then separated from the plasma by centrifugation; the cells are then exposed to the mitogen, washed again, and then incubated. The supernatant is then used to determine the inhibition of migration on a sample of naïve macrophages (e.g., from guinea pigs). The MIA correlates well with immune competence, and is one of the best tests for delayed-type hypersensitivity. MIF production is lost or markedly decreased in immunodeficiency states such as AIDS, DiGeorge syndrome and Wiskott-Aldrich syndrome (Hannuksela, 1986).

2) Lymphocyte transformation test (Pichler and Tilch, 2004)

The lymphocyte transformation test (LTT) measures the proliferation of T cells to a drug in vitro--from which one concludes to a previous in vivo reaction due to a sensitization. This concept of the LTT has been confirmed by the generation of drug-specific T-cell clones and the finding that drugs can directly interact with the T-cell receptor, without previous metabolism or need to bind to proteins (Pichler and Tilch, 2004).

Spot Tests

Dimethyl Glyoxime Test

This test is recommended by the European committee for standardization. This test helps in the determination of nickel in 10 ppm. A few drops of Dimethylglyoxime 1% in ethanol and ammonium hydroxide 10% in water are applied to a cotton applicator tip which is rubbed against the metal object to be investigated. Dimethylglyoxime reacts with nickel ions in the presence of ammonia giving a red salt.¹

Disodium-1-Nitroso-2-Naphthol-3, 6-Disulfonate test

This test developed by Thyssen *et al.* to determine cobalt release at 8.3ppm in cobalt allergic patients (Thyssen *et al.*, 2010).

Diphenylcarbazine Test

Used as a reagent for detection and estimation of chromium when present as chromate or dichromate. The reagent produces a violet or reddish violet colour with exceedingly small amounts of dichromate (Norman, 1928).

Lutidine Test

Used for detection of formaldehyde. A yellow colour reaction occurs in presence of diacetyldihydrolutidine from acetylacetone and formaldehyde in the presence of ammonium salt (Nash, 1952).

Prick test (Bruster, 1959)

The first publication about SPT by Helmtraud Ebruster in 1959, who extensively researched this diagnostic test, it has been used as a primary diagnostic tool to detect type I hypersensitivity reactions. This test is done using predissolved antigens for the diagnosis of respiratory allergies and chronic urticarial mediated by immediate or Type I hypersensitivity reactions. The Prick testing kit consists of the following

- Allergens in the solution form in small bottles.
- Blood Lancets to introduce the allergen in the superficial skin.
- Stencil for the measurement of erythema /wheal.

Procedure

Prick test is usually done in the flexor aspect of forearm. It can also be done over the back in younger children.

Reading	Results	Interpretation
+	No wheal, Flare 3mm more than negative control	Mild sensitivity
++	2-3 mm wheal	Moderate sensitivity
+++	3-5 mm wheal	Severe sensitivity
++++	>5mm wheal	Very severe sensitivity

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