

Intradermal tests in dermatology-II: Tests for noninfectious diseases

Sushil Pande, Rahul Nagar, Uday Khopkar

Department of Dermatology, Seth GS Medical College and KEM Hospital, Mumbai, India.

Address for correspondence: Dr. Uday Khopkar, Department of Dermatology, Seth GS Medical College and KEM Hospital, Parel, Mumbai - 12, India. E-mail: drkhopkar@gmail.com

INTRODUCTION

Intradermal tests are widely used to support the diagnosis of dermatological and nondermatological diseases. They are mainly indicated for the detection of immediate (Type I hypersensitivity) and delayed type hypersensitivity (DTH, Type IV hypersensitivity) towards exogenous or endogenous antigens. Intradermal tests for the diagnosis of noninfectious diseases and of other uses in dermatology are discussed in this section.

Before undertaking an intradermal test, it is advisable to stop or avoid systemic steroids, immunosuppressive agents at least three days before the procedure and antihistamines at least seven days prior to the test.

Types of intradermal test for the diagnosis of noninfectious diseases are described in Table 1.

INTRADERMAL SENSITIVITY TEST FOR COMMON ALLERGENS

In cases of acute urinary, intradermal antigens can be used to detect immediate hypersensitivity. Sensitivity to different agents can be identified by using preformed purified antigens, which are commercially available.

Different antigens can be checked at the same time, positive (histamine solution) and negative control (normal saline) are applied for the comparison. Reading is taken 20-30 min following intradermal injection. Alternatively, similar

antigens can also be applied on to the skin surface and skin prick testing (SPT) can be performed. Common allergens that are tested in skin prick test are food, fungi, epithelia, pollens and mites. Intradermal tests can be done for similar indications but is rarely advocated as there is more risk and they do not offer added advantages for the prediction of hypersensitivity.

INTRADERMAL SENSITIVITY TEST FOR DRUG^[1-3]

Intradermal testing is a rapid, convenient and reproducible method of detecting drug hypersensitivity (drug-specific IgE antibodies). It is commonly performed for penicillin, general and local anesthetic agents, tetanus toxoid, iodinated radiocontrast media, insulin, heterologous sera, collagen chymopapain etc.

Intradermal testing is in general safe with few reactions and does not appear to result in sensitization. However, resuscitative measures and epinephrine injections should be kept ready as there remains possibility of anaphylaxis.

Penicillin intradermal skin tests should be carried out using major determinant (benzylpenicilloyl polylysine, PPL) and minor determinant mixture (benzyl penicillin, benzyl penicilloate and benzyl penilloate) antigens, these are commercially available. The test can also be performed using 2-10 units of fresh penicillin. Negative intradermal test does not rule out penicillin sensitivity. Other agents are tested similarly for detection of immediate and delayed type of hypersensitivity.

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Table 1: Intradermal tests for the diagnosis of non-infectious diseases

Intradermal test	Remarks
Intradermal test in acute urticaria	Detects Type I hypersensitivity to drugs (penicillin, general and local anesthesia, radiocontrast media, sera, collagen) or other allergens responsible for acute urticaria
Autologous serum skin test	For the diagnosis of autoimmune urticaria
Kveim-Siltzbach test	Detects sensitivity to endogenous antigen i.e., sarcoid antigen. Useful for the supportive diagnosis of sarcoidosis, positive test indicates activity of disease, antigen is not commercially available
Pathergy test	Detects nonspecific hypersensitivity as observed mainly in pyoderma gangrenosum and Behçet's disease
Autoerythrocyte sensitization test	Useful for the diagnosis of autoerythrocyte sensitization syndrome or Garder-Diamond syndrome
Pilocarpine test	Detects integrity of dermal nerves responsible for axon reflex, helpful in detecting hypohidrosis or anhidrosis over the lesions of leprosy
Histamine test	Detects integrity of dermal nerves responsible for axon reflex, detects neural deficit over the lesions of leprosy

Intradermal skin tests have no predictive value in nonIgE-mediated reactions such as serum sickness, hemolytic anemia, drug fever, interstitial nephritis, contact dermatitis, maculopapular exanthemata or exfoliative dermatitis. Skin testing is contraindicated where there is a history of exfoliative dermatitis, Stevens-Johnson syndrome or TEN.

PREDICTIVE SENSITIZATION TESTS^[4]

Sensitization index is the relative capacity of a given agent to induce sensitization in a group of humans or animals. Predictive sensitization tests are used to compare the sensitizing properties of new products or chemicals with those of known substances. Both in guinea-pigs and humans, an estimate of the sensitizing potential can be performed using intradermal route. Draize test and Freund's complete adjuvant test are intradermal methods of testing sensitization potential.

AUTOLOGUS SERUM SKIN TESTING (ASST)^[5-7]

About 25-45% of patients of chronic idiopathic urticaria have autoantibodies against the high affinity IgE receptor FcεRI or IgE that are capable of histamine release. These antibodies, if present in serum, can cause wheal and erythema following intradermal serum injection. This reaction forms the basis of the ASST.

The test is performed by injecting 0.05 ml of the patient's own serum intradermally into the left flexor forearm two inches below the antecubital crease and a saline control into the right forearm. The optimum combined sensitivity and specificity of the ASST was obtained if a positive test is accepted as a red wheal with a diameter of ≥ 1.5 mm than control. Serum is obtained after withdrawing 5 ml of venous blood and standing for about 45 min for separation. The process can be hastened up by centrifugation of the blood.

The cases of idiopathic urticaria which are ASST positive are designated as autoimmune urticaria.

KVEIM-SILTZBACH TEST^[8-10]

It is a valuable intradermal test for the diagnosis of sarcoidosis. The test can be utilized to differentiate from other causes of diffuse pulmonary mottling, uveitis and erythema nodosum.

The antigen is prepared from the splenic tissue obtained from a proven case of sarcoidosis either after splenectomy or during autopsy.

About 0.1-0.15 ml of this antigen is injected intradermally, a nodule develops after four to six weeks, which can be biopsied for histopathological confirmation of the diagnosis. False positive reactions were found in an appreciable proportion of patients with Crohn's disease, ulcerative colitis and tuberculous lymphadenitis, but only with few batches of commercially available antigens.

PATHERGY TEST^[11-15]

Pathergy is the development of a papulopustular lesion around a puncture site on the skin, 24-48h after the injection of a sterile substance like normal saline intradermally. This phenomenon forms the basis of the pathergy test. The test is used as a diagnostic criterion for Behçet's disease.

Results of the test depend upon the type of needle used; reactivity varies with the diameter and sharpness of needle. The sensitivity and intensity of the reaction is considerably less with sharp needles and needles with smaller diameter.

Pathergy is also a reported phenomenon in pyoderma gangrenosum, in hairy cell leukemia, Hodgkin's lymphoma and in chronic myeloid leukemia treated with interferon alpha.

Histopathological evaluation of the test is not found to be more sensitive than the clinical evaluation.

AUTOERYTHROCYTE SENSITIZATION TEST

The intradermal test for the diagnosis of autoerythrocyte sensitization syndrome is done with washed RBCs of the patient in the intrascapular region with a saline control on the opposite side.^[16] Patient develops a painful ecchymotic reaction within two hours at the site of the injection indicating positive test. The control site does not show reaction.

HISTAMINE TEST^[17]

When histamine is injected intradermally, it causes bright red histamine flare due to capillary vasodilatation. However, this effect is due to axon reflex within dermal nerves. Thus the histamine test can be used to test integrity of dermal nerves in cases of tuberculoid leprosy. One drop of histamine acid diphosphate 1 in 1000 (1 mg/ml) is placed on the skin surface. Superficial prick is made through the drop and bright flare will appear within a minute if dermal nerves are intact. Response takes little longer on the extremities.

PILOCARPINE TEST^[17]

Similar to the histamine test, the pilocarpine intradermal test is used to detect the integrity of dermal nerves in suspected cases of tuberculoid leprosy. About 0.2 ml of 1 in 1000 solution of pilocarpine nitrate is injected intradermally into the lesion, the injection site is then painted with tincture of iodine and then dusted with starch powder. Sweating, if present, causes blue discoloration of the powder. Alternatively, quinizarin powder can be used in place of starch powder with the advantage that there is no need for painting the test site with tincture of iodine.

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