Instant Reference for Health Professionals

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Practice Parameters for Allergy Diagnostic Testing

This practice parameter is based upon current clinical practice and extensive review of the clinical literature and has been developed by the Joint Task Force on Practice Parameters of the American College of Allergy, Asthma & Immunology (ACAAI), the American Academy of Allergy, Asthma and Immunology (AAAAI), and the Joint Council of Allergy, Asthma & Immunology (JCAAI).

This is a summary of practice parameters for the proper use and interpretation of the most important diagnostic tests for allergy. These practice parameters were formulated by expert panels from rigorously evaluated scientific and clinical literature.

Synopsis of Content

- Diagnostic Tests
  - IgE-dependent reactions (immediate hypersensitivity)
  - Cell-mediated immune reactions (delayed hypersensitivity)
- Allergens. Agents to be selected for diagnostic testing.
- Challenge Tests. To establish or confirm clinical sensitivity.
- Controversial and Unproven Tests. Tests to be questioned or avoided.

Tests of IgE Dependent Reactions

Indications

- Confirm IgE-mediated hypersensitivity.
- Determine the allergenic etiology for purposes of avoidance and specific immunotherapy.

In Vivo Skin Tests

Prick/puncture tests: On a per-test basis, the most convenient, *most specific,* least expensive tests for IgE antibodies. *Less sensitive* than intracutaneous (intradermal) tests. Usually performed on the volar surface of forearms, or the upper back.

Reliability: Highly dependent on the skill of the test administrator and quality control of procedures, instruments, and test extracts. Both positive — e.g., (histamine) and negative (diluent) controls must be performed to assure proper interpretation of results.

Interpretation: ***Read*** tests 15-20 minutes post-application; ***Record*** both erythema and wheal in millimeters and compare with diluent control tests; ***Wheal response*** of 3 or more mm (with erythema) than the diluent control usually indicates the presence of allergen-specific IgE.

Drugs that may influence response should be discontinued prior to testing — e.g., H1 antagonists, tricyclic antidepressants, and phenothiazines. (See full Practice Parameters for specific durations.)

Intracutaneous tests: Indicated when *increased sensitivity* is required — e.g., the patient has a negative prick/puncture test despite a suggestive history of clinical sensitivity.

Intracutaneous allergen extract: Starting dose usually a 100 to 1000-fold dilution of concentrated (e.g.1:10w/v) prick/puncture test extract in a patient with a preceding negative prick/puncture test.

Interpretation: ***Read*** and ***Record*** both erythema and wheal; any reaction larger than a negative control *may* indicate specific IgE antibody presence, but *lower specificity* of intracutaneous tests makes small positive reactions difficult to interpret. Late cutaneous reactions that appear several hours after test application and disappear in 24-48 hours are generally of little if any diagnostic significance.

Repetition of skin tests: Regularly repeated (e.g., annual) skin tests are *not* required, but changing symptoms or new exposures may be indications for testing for possible newly developed clinical sensitivity.

In Vitro Tests

Total Serum IgE measurements are useful criteria in the diagnosis of allergic bronchopulmonary aspergillosis, atopic dermatitis and the hyper-IgE syndrome.

Allergen-specific IgE measurements may be preferable: (1) when skin testing is contraindicated by conditions such as severe dermatographism, generalized dermatitis, psychiatric conditions, very young uncooperative children, inability to discontinue drugs such as long-acting antihistamines, or risk of anaphylaxis; (2) as adjunctive tests for allergic bronchopulmonary aspergillosis or parasitic disease; and/or (3) as post-mortem tests to identify allergens responsible for fatal anaphylaxis.

Interpretation of allergen-specific IgE skin or in vitro measurements requires correlation with history and physical examination.

Tests of Cell-Mediated Immune Reactions

In Vivo Tests

Epicutaneous (Patch) Tests: Identify/verify the allergic agents in diagnosis of allergic contact dermatitis and certain drug-induced cutaneous reactions. Patch tests are usually placed on the upper back at least 2.5 cm from the midspinal area.

Screening panel: 20-30 antigens in a standard panel identify 50-75% of clinically relevant agents.

Interpretation: Tests should be read at 48 and 96 hours and results must be correlated with the patient's history, habits, and environment.

Intracutaneous Delayed Tuberculin-like and Recall Tests: Evaluate the presence and level of cell-mediated immunity. ***Intracutaneous tuberculin-like skin tests*** for delayed-type reactions predict host's cellular immunocompetence; ***Recall antigen skin tests*** predict survival of immunocompromised patients (e.g., pre-transplantation screening), detect disease-related changes in immunity, follow outcomes of therapy; recall skin tests use antigens of mumps, trichophyton, *Candida albicans,* tetanus toxoid.

Interpretation of recall antigen: ***Measure*** reaction size 48 hours after test challenge; ***For recall immunity the minimum reaction*** should either be a single ≥5 mm palpable, firm, indurated site or two or more palpable, firm, indurated ≥2 mm areas; ***Anergy*** (no reaction) is evidence of impaired cellular immunity and/or lack of prior sensitization.

In Vitro Tests

Assess (1) cellular function in patients with recurrent or multiple infections, (2) depressed cellular immunity — e.g., AIDS, sarcoidosis, cancer, (3) certain instances of drug hypersensitivity, e.g. phenytoin, and (4) chemical hypersensitivity — e.g., toluene diisocyanate, beryllium.

Nonspecific, cost-effective in-vitro screening tests for cellular immune competence

- Absolute lymphocyte count
- Total T-cells measured by anti-CD3 surface markers
- CD4+ helper cell populations and CD8+ suppressor-cytotoxic cell populations
- T-cell lymphocyte activation by IL-2 secretion or fluorescent anti-CD25 and/or anti-HLA-DR monoclonal antibodies
- Relative percentage of CD45RO+ CD29+ T-cell lymphocytes as indication of number of memory T-cells

Allergens

Accurate allergy diagnosis depends upon the correct choice of allergens for testing in the patient. Allergy extracts are available for many allergic agents.

Categories

Aeroallergens (inhalants)

- pollens, molds, animal emanations (e.g., dander, urine), acarids (e.g., house dust mites), insects (e.g., cockroach), drugs (e.g., psyllium, pancreatic dornase), chemicals (e.g., acid anhydrides, polyisocyanates)

Foods

- nearly any food can be allergenic; patient history is suggestive (most common are milk, egg, peanuts, shellfish, fish)

Stinging Insect Venom and Whole-Body Extracts

Antibiotics, Other Drugs, Chemicals

- penicillin and its determinants
- biologies (insulin, heparin)
- enzymes

Contactant Allergens

Occupational Allergens

- >200 substances used in industry can cause respiratory and/or dermatologic symptoms

Effective use of aeroallergens for testing requires knowledge of:

- recent, reliable aerobiologic data for indigenous pollens, molds, etc.
- correlation of patient symptoms with aerobiologic data
- clinical significance of local and regional allergens
- cross-reactivity patterns between allergens — e.g., pollens of tree families, grass families, etc.

Challenge Tests

Challenge tests sites include conjunctivae, nares, gastrointestinal tract, and bronchi. Only a physician with relevant knowledge about and experience with such challenges should order, administer and interpret organ challenge tests — e.g., bronchoprovocation. Challenge tests can be used to evaluate new allergens or confirm the role of allergens in patients with significant symptoms but no immediate skin test response. All challenge tests should be preceded by a control test; if possible, the procedure should be conducted on a double-blind basis.

Controversial and Unproven Allergy Tests

Procedures invalid for any allergy diagnostic purpose:

- cytotoxic test
- provocation-neutralization
- electrodermal diagnosis and applied kinesiology
- "reaginic pulse" test
- chemical analysis of body tissues — e.g., hair

Valid procedures inappropriate for diagnosis of IgE-mediated allergic disease:

- measurement of (1) circulating allergen-specific IgG or IgG4 antibodies, (2) circulating immune complexes to foods, and (3) serum immunoglobulins, complement and lymphocyte subsets

Valid tests inappropriate to general use due to cost, sensitivity/specificity issues, or general availability:

- in vitro histamine release
- in vitro lymphocyte transformation
- serial endpoint titration

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