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*A World Federation of Allergy Asthma
and Clinical Immunology Societies*



ALLERGY TESTING Interpretation In-Vivo

Sandra N. González-Díaz, MD, PhD

FAAAAI, FACAAI, SLAAI 2010-2012



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Sandra Nora González Díaz, MD, PhD



- **Current President of the Latin American Society of Asthma, Allergy and Clinical Immunology (SLAAI) 2010-2012**
 - **Director of the Residency Program in Allergy and Clinical Immunology, Regional Centre of Allergy and Clinical Immunology, University Hospital of Monterrey, NL since 1990**
 - **Head of Regional Centre of Allergy and Clinical Immunology, University Hospital, Monterrey, NL since 2000**
 - **Professor of Regional Centre of Allergy and Clinical Immunology, University Hospital, Monterrey, NL since 1990**
 - **Director of Fundraising Department, University Hospital since 2007**
 - **Director General, Department Fundraising at the Autonomous University of Nuevo Leon**
 - **Researcher Level 1 CONACYT**
 - **Past President of the Mexican Association of Allergy and Clinical Immunology (CMICA) 2005-2007**
 - **Past President Chapter of the Latin American Society Mesoamerica Asthma, Allergy and Clinical Immunology (SLAAI) 1997-1999**
 - **Past president UNASMA (International Asthma Foundation) M2007-2011**
 - **Member of CAICNL , CMICA, SLAAI, AAAAI, ACAAI, WAO, EAACI**
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- **Faculty of Medicine, U.A.N.L 1977-1983. Monterrey, NL Mexico**
 - **Specialty of Internal Medicine, University Hospital, UANL Monterrey, N.L.1986 – 1988**
 - **Fellowship in Pediatric Allergy and Immunology Clínica, UCSD, University of San Diego, California, USA, 1987-1988**
 - **Subspecialty in Allergy and Clinical Immunology, University Hospital UANL , Monterrey, N. L.1988 – 1990**
 - **Doctor of Medicine, Hospital Universitario UANL , Monterey, N.L.1991 - 1997**



MEDICAL TEAM CRAIC 2012



FELLOW IN TRAINING CRAIC 2012



Background

- Confirmation of allergy and identification of causative allergens are crucial for correct disease management
- Clinical suspicion is confirmed by means of investigation of IgE antibodies *in vivo* (skin tests) or *in vitro*
 - **Skin tests are regarded as the gold standard for detection of IgE antibodies**

Skin Test

- Skin Tests are used to confirm clinical sensitivity induced by aeroallergens, foods, some drugs, a few chemicals, and hymenoptera venom

IgE-mediated diseases:

- AR
- Asthma
- Food Allergy
- AD
- Hymenoptera hypersensitivity

Skin testing in allergy diagnosis

Skin testing is the diagnostic cornerstone for allergies

- **Skin tests are convenient, simple, biologically relevant, reproducible, easy and rapid to perform, with low cost and high sensitivity**
- **May confirm or rule-out the diagnosis of IgE-mediated allergy**



VARIETY OF SKIN TEST



- **Epicutaneous**
- Cell-mediated delayed hypersensitivity



- **Percutaneous**
- IgE-mediated immediate hypersensitivity



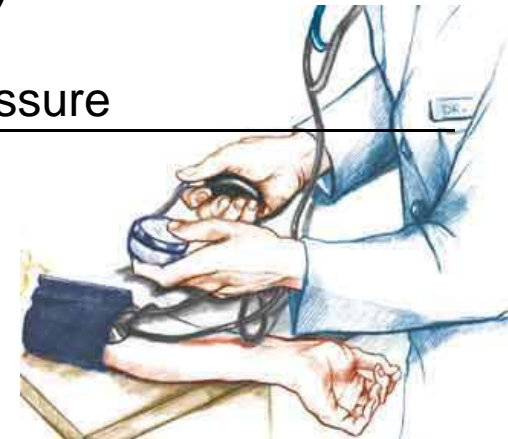
- **Intradermal**
- Mediated hypersensitivity cells and IgE

Prior to Perform Skin Test...

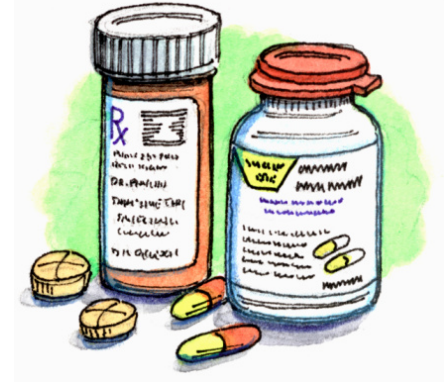
Preparation prior to skin testing



- Perform skin tests when the patient is stable, controlled or with minimal symptoms of allergic process (evaluate asthma control)
- Use objective measures to define the degree of stabilization/ decompensation of the patient allergic process (flowmetry, spirometry, ACT)
- Prior a skin tests you should register a baseline blood pressure



Prior to Perform Skin Test...



Stop taking drugs before skin tests

- Stop H1 antihistamines second-generation seven days before performing skin tests, tricyclic antidepressants and H2-blockers, a day before
- It is not necessary to suspend the leukotriene antagonists
- Avoid use of topical steroids three weeks before, in places where skin testing is applied
- If local anesthetics are applied, do not take account of the erythema, papule only in the interpretation of results

Suppressant Effects of Drugs on Immediate Skin Test*

Drugs	Generic drug	Days suppressed
Antihistamine First generation	Chlorpheniramine Clemastine Cyproheptadine Dexchlorpheniramine Diphenhydramine Hydroxyzine Promethazine Tripeleminamine	2-6 5-10 9-11 4 2-5 5-8 3-5 3-7
Second generation	Azelastine nasal Ebastine Cetirizine Fexofenadine Loratadine Desloratadine Levocetirizine Levocabastine nasal Levocabastine Opth	3-10 3-10 3-10 2 7-10 3-10 3-10 0 0
Tricyclic antidepressants and tranquilizers	Desipramine Imipramine Doxepin Doxepin topical	2 >10 6-11 11
Histamine ₂ antihistamines	Ranitidine	1
Cysteinyl leukotriene antagonists	Monteleukast Zafirleukast	0 0
Short-term oral corticosteroids Long-term and relatively high dose corticosteroids Potent topical corticosteroids**	30 mg of prednisone daily for 1 week >20mg/d >3 week	Do not suppress skin tests Suppression of immediate skin test reactions Suppress immediate skin tests over areas where they have been applied
Local anesthetic	EMLA (Eutectic Mixture of Local Anesthetics) cream	1 hour before test suppression only the erythema

Don't forget

Skin Testing Form

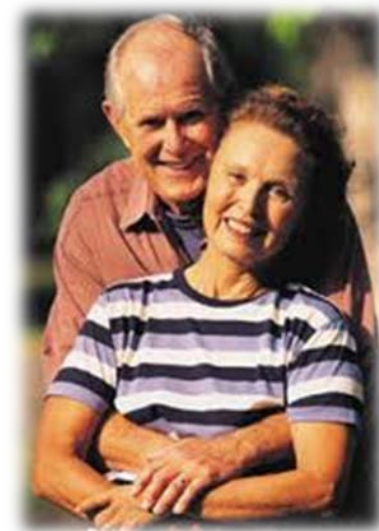
Have a consent signed by the patient, and explaining the risks and benefits of performing the skin test



VARIABLES THAT MAY AFFECT THE SKIN TEST REACTIVITY

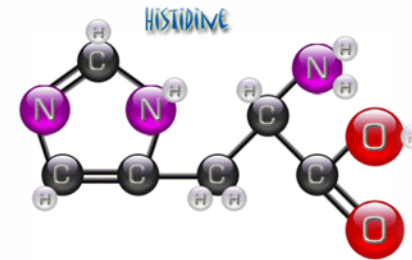
- **Age**

Reactivity decreases with age, peaks at the end of adolescence and the beginning of the 20s, then declines with time after 65 years



VARIABLES THAT MAY AFFECT THE SKIN TEST REACTIVITY

- **Histamine sensitivity**
- Inherent innate sensitivity may increase or decrease the reactivity of the skin test
- **Body location**
- Upper vs lower back
- Arm vs back



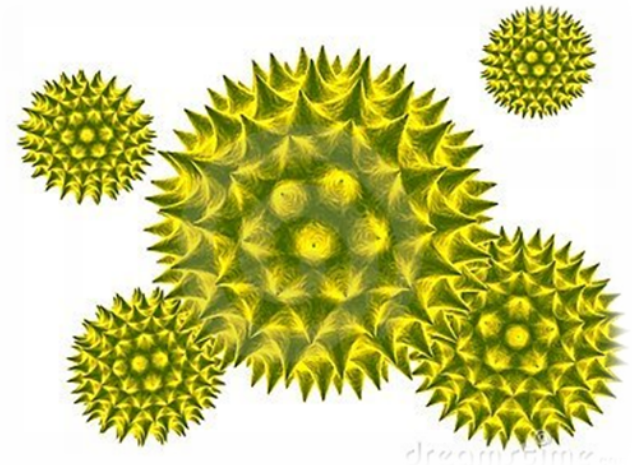
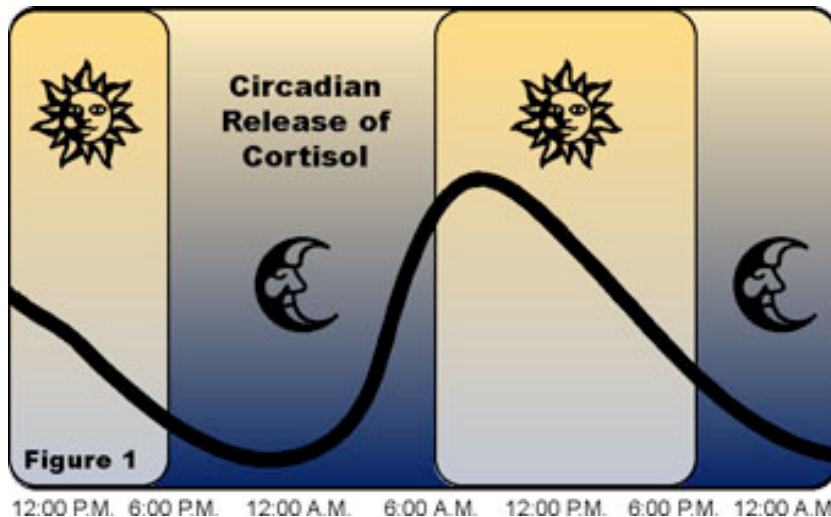
VARIABLES THAT MAY AFFECT THE SKIN TEST REACTIVITY

- Skin tests should not be conducted in areas with severe **dermatitis or dermatographism**
- **Damage caused by the sun on the skin**
 - Affects the number of mast cell and may explain the loss of skin test reactivity with aging and decreased IgE with age
- **Other diseases**
 - may suppress skin test reactivity: Skin cancer, Chronic renal failure, diabetic neuropathy, immunosuppressed



VARIABLES THAT MAY AFFECT THE SKIN TEST REACTIVITY

- **Chronobiology**
- Circadian rhythms and annual variability



VARIABLES THAT MAY AFFECT THE SKIN TEST REACTIVITY

- **Allergen immunotherapy**
 - Immunotherapy effectively decrease the skin test reactivity to allergens treated
- **Allergen extract quality**
 - Weak extracts can produce false negative results



VARIABLES THAT MAY AFFECT THE SKIN TEST REACTIVITY

- **Near the positive control to other allergens**
- When placing an allergen extract near a strongly positive allergen extract can produce false positive results

- **Medications**
- Some can increase (eg B-blockers) and
- Others may decrease the skin test reactivity (eg, antihistamines, tricyclic antidepressants)



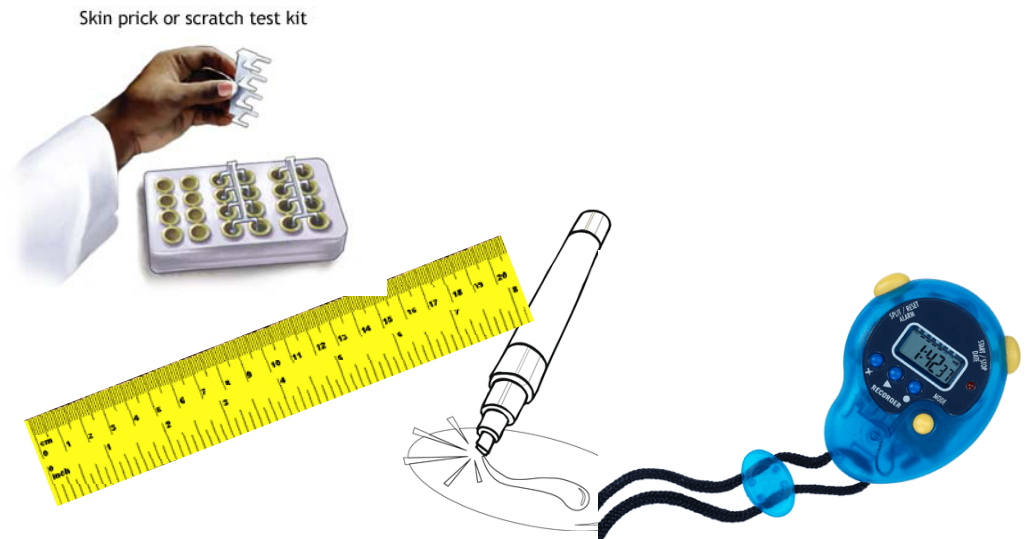
Skin Testing

Materials

- Test allergens
- Positive control (histamine 10mg/mL)
- Negative control (saline or 50% glycerinated HSA–saline)



- Device of choice
- Alcohol swabs
- Clock
- Ruler to measure
- Marker



Selections of allergens

Allergen product	Epicutaneous test concentration	Intradermal test concentration
Standardized short ragweed	1:20 w/v	1:1000 w/v
Standardized cat hair	10,000 BAU/mL	200 BAU/mL
Standardized grass pollens	10,000-100,000 BAU/mL	200 BAU/mL
Standardized Hymenopteran venoms	1.0 ug/mL protein	0.1-10 ug/mL protein
Standardized mites	10,000 AU/mL	200 AU/mL
Nonstandardized allergens	1:40-1:20 w/v	1:1000 w/v

Adapted from Dolen WK, MD. Immunology and Allergy Clinics of North America. Volume 21, number 2. May 2001. Saunders. Selection of allergen products for skin testing by Robert E. Esch, PhD

Number of skin tests



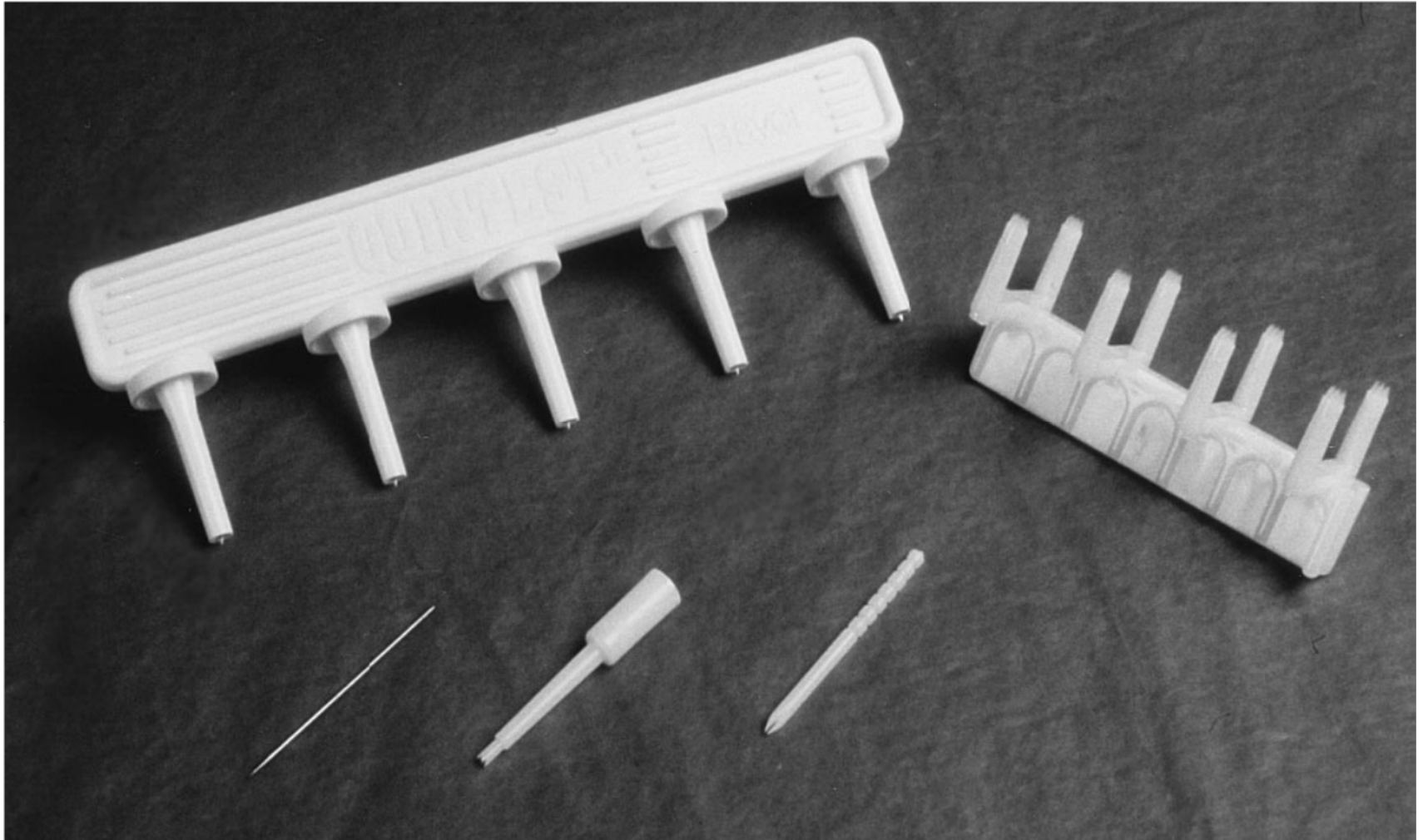
Recommended

- Include skin test allergens relevant to each region
- Standardized allergen products should be used for skin testing whenever possible
- Reduce the number of allergens used in skin testing, taking into account cross-reactions and eliminating allergens with little presence in that region

Anatomical site for testing



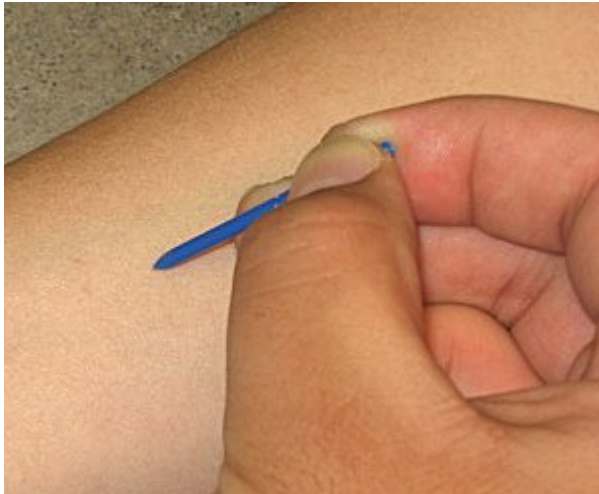
Available devices for skin testing



Preparing equipment

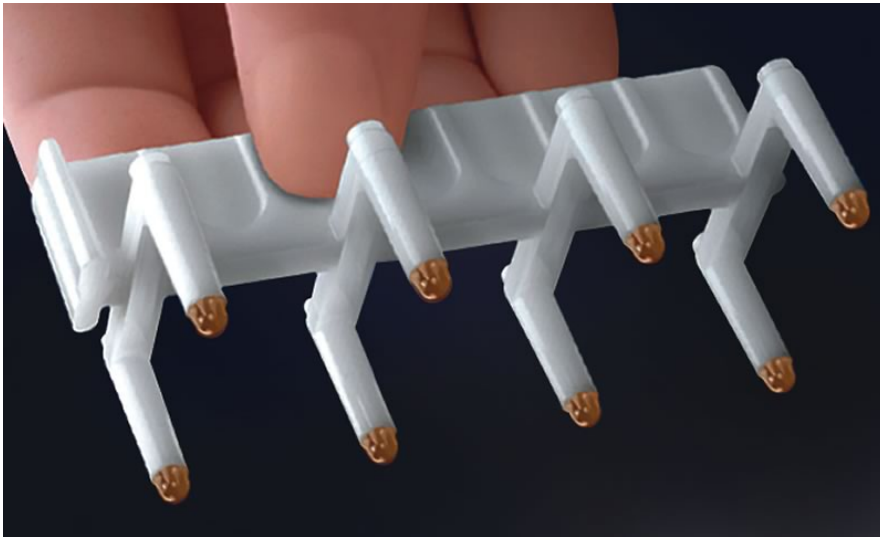


Skin Prick Testing Technique



**A drop of a solution containing a possible allergen is placed on the skin
Then a series of scratches or needle pricks lets the solution enter the skin**

Skin Puncture Test Technique



Positive control (histamine phosphate 10mg/mL)
Negative control (saline or 50% glycerinated HSA-saline)

Intradermal Test Technique



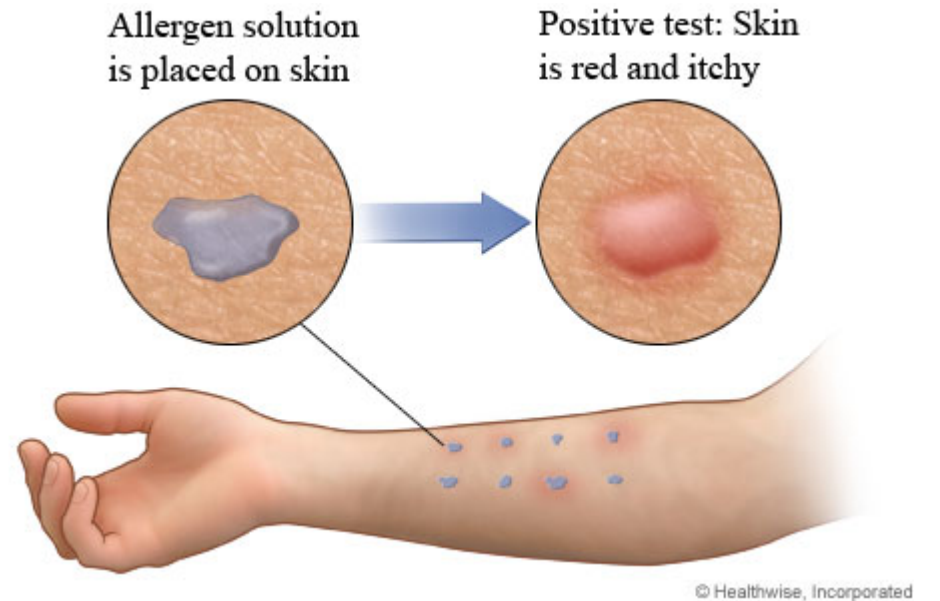
Prick vs Intradermal testing

	Prick test	Intradermal test
Simplicity	+++	++
Speed	++++	++
Interpretation of positive and negative reactions	++++	++
Discomfort	+	+++
False-positive reactions	Rare	Possible
False-negative reactions	Possible	Rare
Reproducibility	+++	++++
Sensitivity	+++	++++
Specificity	++++	+++
Detection of IgE antibodies	Yes	Yes
Safety	++++	++
Testing of infants	Yes	Difficult

















Results Skin Test

- After 15min
- Wheal
- Erythema
- Itching

- Positive Test
- Wheal \geq 3mm than the Negative control



Interpretation of results in skin tests

INTERPRETACION	Control negativo	Alergeno 1	Alergeno 2	Control positivo
Sensibilidad a Alergeno 2	 D* = 1 mm	 D* = 3 mm Alergeno 2	 D* = 6 mm	 D* = 5 mm
Sensibilidad a Alergeno 1 y 2	 D = 2 mm	 D* = 7 mm	 D* = 6 mm	 D* = 5 mm
Prueba negativa, no sensibilidad cutánea a ningún alergeno probado	 D = 2 mm	 D* = 2 mm		 D* = 5 mm
Prueba no válida Falso negativo				



With permission of patient. Regional Center of Allergy and Clinical Immunology, Monterrey, Mexico

Common Errors in Prick Testing

- 1.** Tests are placed too close together (<2 cm), and overlapping reactions cannot be separated visually
- 2.** Induction of bleeding, possibly leading to false-positive results
- 3.** Insufficient penetration of skin by puncture instrument, leading to false-negative results.
- 4.** Spreading of allergen solutions during the test or when the solution is wiped away

Potential side effects of skin tests

- **Usually the side effects, if any, are itching and a mildly red skin**
- **This can last for a minutes, a couple of hours to a day**



Allergen immunotherapy: A practice parameter second update

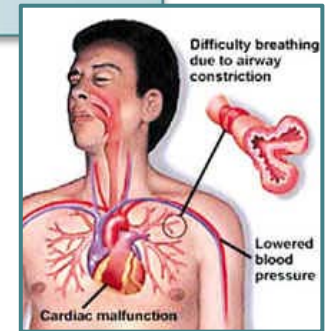
AAAAI, ACAAI

J Allergy Clin Immunol
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Supplement Editor: Linda Cox, MD

Co-editors: James T. Li, MD, Harold Nelson, MD, and Richard Lockey, MD

- **Systemic reactions can occur from skin testing in a highly sensitive individual**



Immediate systemic reactions are more common with **intradermal than with the prick or puncture tests**



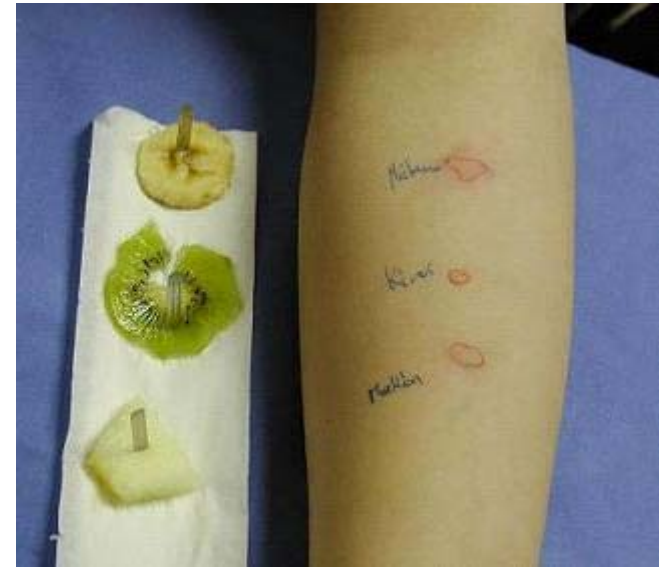
Lin MS, Tanner E, Lynn J, Friday GA Jr. Nonfatal systemic allergic reactions induced by skin testing and immunotherapy. Ann Allergy 1993; 71:557-62. III

Valyasevi MA, Maddox DE, Li JT. Systemic reactions to allergy skin tests. Ann Allergy Asthma Immunol 1999;83:132-6. III

Allergic reactions during allergy skin testing

**Although very rare...
In most patients, occur after
Prick to Prick testing**

**Anaphylaxis has been described with
milk, egg, wheat, or fish P-P testing,
during infancy**



Fortunately...

**No deaths due to food allergy testing have been
reported since 1984**

Those reported until then had occurred following intradermal testing

Intradermal skin tests with food extracts are not used anymore

Recommended equipment and medications to treat anaphylaxis

TABLE VI. Recommended equipment and medications to treat anaphylaxis

Adequate equipment and medications should be immediately available to treat anaphylaxis, should it occur. This should include at least the following equipment and medications:

- stethoscope and sphygmomanometer;
 - tourniquet, syringes, hypodermic needles, and large-bore needles (14-gauge);
 - aqueous epinephrine HCL 1:1000 wt/vol;
 - equipment to administer oxygen by mask.
 - intravenous fluid set-up;
 - antihistamine for injection (second-line agents for anaphylaxis, but H₁ and H₂ antihistamines work better together than either one alone);
 - corticosteroids for intravenous injection;
 - vasopressor;
 - equipment to maintain an airway appropriate for the supervising physician's expertise and skill.
-

Recommendations to reduce the risk of systemic reactions

1. The prick method is to precede the application of intradermal tests
2. Avoid foods intradermal testing
3. Exclude the use of beta blockers
4. Caution in infants with eczema who underwent prick tests with fresh foods
5. Have the training to recognize early symptoms and anaphylaxis
6. Have emergency equipment

Skin Testing Summary Precautions

- 1. Skin tests should never be performed unless a physician is available immediately to treat systemic reactions.**
 - 2. Have emergency equipment readily available, including epinephrine.**
 - 3. Be careful with patients having current allergic symptoms.**
 - 4. Determine the value of allergenic extracts used and assess their stability.**
 - 5. Be certain that the test concentrations are appropriate.**
 - 6. Include a positive and a negative control solution.**
 - 7. Perform tests in normal skin.**
 - 8. Evaluate the patient for dermographism.**
 - 9. Determine and record medications taken by the patient and time of last dose.**
 - 10. Record the reactions at the proper time.**
-

Conclusions

- Confirmation of allergy and identification of causative allergens are crucial for correct disease management.
- Skin tests are regarded as the gold standard for detection of IgE antibodies
- Is a simple and safe method which is reliable in skilled hands
- Skin tests should include relevant allergens and use standardized allergen extracts
- To avoid false positives and false negatives, it is necessary to proper conduct and interpretation of skin tests by the doctor who performs.