Clinical Interpretation of Allergy Skin Testing

Fares Zaitoun, MD, ACAAI
American University Hospital
Director: Allergy Asthma & Immunology Center,
Beirut, Lebanon
Consultant, CURE Advanced Diagnostic Center, Abu Dhabi, UAE

WAO-ISC Skin Testing Workshop
Sunday December 5th, 2010
Outline

• Immunopathological basis of allergy skin testing

• Clinical interpretation of allergy skin testing

• Pearls and Pitfalls of allergy skin testing
Nerve Stimulation = **ITCHING**
3-5 min

Degranulated Mast Cell

Antigen

IgE

Other Mediators:
- Prostaglandins
- Tryptase
- Heparin

HISTAMINE

Endothelial Gaping • fluid leakage = **SWELLING**

Vasodilation = **REDNESS**
5-10 min

BLOOD VESSEL

BLOOD VESSEL
Skin prick testing

<table>
<thead>
<tr>
<th>Immediate and late skin reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>late response (at 5 hours)</td>
</tr>
<tr>
<td>immediate response (at 20 minutes)</td>
</tr>
</tbody>
</table>

- 1:10
- 1:100
- 1:1000
- 1:10000
Allergy Skin testing =
Detection of Specific IgE “at work”

• Provides information that the sensitization process has been initiated and that the patient is Atopic

• Along with a positive case history, confirms the suspicion and identifies allergen(s) likely responsible for the Allergic patient’s symptoms

• Without symptoms, may predict the later development of allergic disease

• Identifies environmental and food avoidance strategies as part of the overall treatment

• Directs physician in institution of an effective pharmaceutical and immunomodulating treatment plan
Clinical Indications for allergen skin testing

- To determine if an Ig-E mediated allergic mechanism exists in a clinical setting that is known or suspected to be IgE-mediated.

- To determine type and scope of sensitizations and help identify clinically relevant allergens.

- To help formulate treatment plan: Diagnostic trial with medications, when to start or stop medications, environmental control measure, allergen immunotherapy…

- To obtain possible prognostic information for long-term and follow-up recommendations.
Allergy Skin Test interpretation

Only a clinician who has interviewed and examined a patient can determine the clinical importance of a skin test result

Interpretation of skin tests starts during the Interview process..... First the history, next the history, then the history

- Physical examination
- Think about the differential Dx
- Ordinary lab tests, x-rays and other studies as indicated
- Consider reasons for testing and how will test results be used
- Revise differential Dx; formulate working Dx
Before testing, the Allergy Specialist must know the following:

- Specific clinical history of patient after directed interview
- Type, duration and severity of symptoms and/or affected organ systems
- Current and past medical, family and environmental history
- Known or suspected local or regional indoor & outdoor allergens
- Knowledge of foods, food allergens, food chemistry
- Knowledge of allergen cross-reactivity
- Purpose of testing and clinical action upon test results
- Natural history of disease process
- Prognostic information that tests may provide
Caveats

• Allergy skin tests are best regarded as tests for the presence or absence of specific IgE and not necessarily disease.

• Some patients with the classic “allergic” diseases have easily demonstrable specific IgE Ab, and others do not.

• Even in a symptomatic individual, a positive test result in and of itself is not necessarily clinically relevant.

• IgE is normally present in the body although at very low levels

• Numerous studies of subjects without overt clinical disease have demonstrated specific IgE by skin testing or specific IgE immunoassay in about 15% and up to 30% especially in those with a positive family history
Different interpretations of a positive skin test if clinical scenario is different

- Positive skin test to cat in 8 yo with recurrent cough and wheeze and cat at home
- Positive skin test to cat in a 8 yo with recurrent cough and wheeze and no cat at home
- Positive skin test to cat in an asymptomatic 8 yo with cat at home
- Positive skin test to cat in an asymptomatic 8 yo with no cat at home
Prick skin tests correlate with nasal challenge

Relationship between nasal challenges with pollen grains and skin prick test
Endpoints in patients allergic to *Dactylis glomerata*

\[ R_s = 0.54 \]
\[ p < 0.005 \]

*Bousquet Clin Allergy 1987;17:529-38*
Total IgE levels in atopic patients

- Poor sensitivity

- 30-40% of patients with allergic disease may have “normal” IgE levels

- May be used as a screening test when high suspicion exists

- However, very important in interpretation process
• Setipane et al., noted that positive allergy skin tests were a significant risk factor (2.3 times that of negative skin tests) for the development of hay fever.

• A prospective study by Horak examining the development of symptomatic allergic rhinitis among children with sensitivity to inhalant allergens but without any clinical symptoms found that during the follow-up period of 4 years, 53% of the skin positive children manifested allergic rhinitis.
IgE antibodies to food early in life predict later IgE antibodies to inhalants

<table>
<thead>
<tr>
<th>RAST IgEs at six months of age</th>
<th>n</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Specific IgE for egg white</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive finding</td>
<td>54</td>
<td>46</td>
<td>85*</td>
</tr>
<tr>
<td>Negative finding</td>
<td>54</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td><strong>Specific IgE for cow's milk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive finding</td>
<td>31</td>
<td>29</td>
<td>94*</td>
</tr>
<tr>
<td>Negative finding</td>
<td>77</td>
<td>25</td>
<td>32</td>
</tr>
<tr>
<td><strong>Specific IgE for soy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive finding</td>
<td>16</td>
<td>16</td>
<td>100*</td>
</tr>
<tr>
<td>Negative finding</td>
<td>92</td>
<td>38</td>
<td>41</td>
</tr>
</tbody>
</table>

*p<0.001, by chi-square test

Reference: Data from Sasai et al., J Pediatr 1996; 128: 834-840
Asymptomatic skin sensitization to birch may predict development of birch pollen allergy in adults

• **Methods:**

  Asymptomatic adults were followed through use of daily diary cards during 3 consecutive birch pollen seasons
  
  15 +SPT for birch
  
  15 non-atopic controls
  
  6 birch pollen–allergic patients

  At the 3-year follow-up visit, conjunctival and nasal challenges, intradermal late-phase reaction evaluation, and measurement of birch specific IgE were performed.
Asymptomatic skin sensitization to birch may predict development of birch pollen allergy in adults

Results:

– Asymptomatic +SPT subjects had both birch specific IgE levels and positive conjunctival provocation testing.
– Sixty percent (n = 9) of the asymptomatic sensitized subjects developed clinical allergy in the three year period.
– The development of clinical allergic disease was associated with an initial birch skin prick test wheal diameter of >4 mm.
– IgE antibodies ≥ 0.7kU/L (class 2) was 87.5% predictive of allergy development

Conclusion: Positive skin prick test in an asymptomatic patient may indicate potential for development of allergy in the future.

JACI 2003;111:149-54
Keys for successful SPT

- It is imperative that the technician performing the skin tests as well as the clinician ordering/interpreting these tests understands the characteristics of the specific tests they are administering.

- This includes:
  - type of skin testing
  - device used
  - placement of tests (location and adjacent testing)
  - the particular extracts (source, concentration) being used
  - the potential confounder of medications that may suppress skin test response.
Puncture skin testing devices

- Several different devices available for skin testing.
- Varying degrees of trauma to the skin with differing levels of skin test reaction.
- Physician should be familiar with the characteristics of the device used, as each require different criteria for what constitutes a positive or negative reaction.
<table>
<thead>
<tr>
<th>Device</th>
<th>Wheel Size, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devices for which a 3mm wheal would be significant</td>
<td></td>
</tr>
<tr>
<td>Quintest (HS) puncture</td>
<td>0</td>
</tr>
<tr>
<td>Smallpox needle (HS) prick</td>
<td>0</td>
</tr>
<tr>
<td>Duotip (Lincoln) prick</td>
<td>1.5</td>
</tr>
<tr>
<td>Lancet (HS) puncture</td>
<td>2.0</td>
</tr>
<tr>
<td>Lancet (ALK) puncture</td>
<td>3.0</td>
</tr>
<tr>
<td>DermaPICK II (biomedixs)</td>
<td>0</td>
</tr>
<tr>
<td>Devices for which &gt;3mm wheal would be significant</td>
<td></td>
</tr>
<tr>
<td>DuoTip (Lincoln) twist</td>
<td>3.5</td>
</tr>
<tr>
<td>Bifurcated needle (ALO) prick</td>
<td>4.0</td>
</tr>
<tr>
<td>MultiTest (Lincoln) puncture</td>
<td>4.0</td>
</tr>
<tr>
<td>Bifurcated needle (ALO) puncture</td>
<td>4.0</td>
</tr>
<tr>
<td>Quick Test (Pantrex)</td>
<td>4.0</td>
</tr>
<tr>
<td>Greer Track (Greer)</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Nelson et al., Evaluation of devices for prick skin testing. JACI 1998;101:153-156
Are skin tests easy to interpret?
Reproducibility of skin test scoring and interpretation by Board-certified/eligible allergists

• Methods:
  – Series of SPT were digitally photographed

• 22 tests with controls
  – a questionnaire regarding interpretation was sent to 70 allergists to assess
    • positive, negative or intermediate
    • positive or whether a ICT test was desired

McCann Ann Allergy Asthma Immun 2002;89:368-71
Reproducibility of skin test scoring and interpretation by Board-certified/eligible allergists

• Results:
  – 33 interpretable responses
• 24 relied on a grading scale (0-4+);
  • 2 measured in mm,
  • 7 provided only interpretation with no grading
  – Greatest agreement with median/mode score 4+
  – Least agreement with median/mode score 1-2+
  – Range of requested ICT test was 0-11 tests

• Conclusion:
  – Significant variability in scoring and interpreting skin tests
  – Reinforces the need to report skin test reactions by measuring and recording reaction size in mm
  – Reinforces the need for individualized history and clinical evaluation

McCann Ann All Asthma Immun 2002;89:368-71
## Inter-individual variation in SPT

<table>
<thead>
<tr>
<th>Test result</th>
<th>Nurse 1</th>
<th>Nurse 2</th>
<th>Nurse 3</th>
<th>Nurse 4</th>
<th>CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative control</td>
<td>0.1 mm</td>
<td>0.4 mm</td>
<td>0.2 mm</td>
<td>0.2 mm</td>
<td>55.9%</td>
</tr>
<tr>
<td>Histamine</td>
<td>11.7 mm</td>
<td>9.7 mm</td>
<td>12.9 mm</td>
<td>14.5 mm</td>
<td>16.6%</td>
</tr>
<tr>
<td>Grass</td>
<td>2.1 mm</td>
<td>2.5 mm</td>
<td>4.7 mm</td>
<td>5.2 mm</td>
<td>42.8%</td>
</tr>
<tr>
<td>Mugwort</td>
<td>7.7 mm</td>
<td>4.8 mm</td>
<td>7.4 mm</td>
<td>9.1 mm</td>
<td>24.7%</td>
</tr>
<tr>
<td>Dog</td>
<td>1.5 mm</td>
<td>1.1 mm</td>
<td>3.0 mm</td>
<td>2.5 mm</td>
<td>43.3%</td>
</tr>
<tr>
<td>House dust mite</td>
<td>1.7 mm</td>
<td>2.2 mm</td>
<td>1.6 mm</td>
<td>2.8 mm</td>
<td>26.5%</td>
</tr>
</tbody>
</table>

*CV = inter-individual coefficient of variation, Target < 25%; Voblonen I et al. Allergy 1989; 44: 525-531*
Intradermal Testing Procedure

- Use upper arm.
- Use 26 or 27 gauge needle.
- Bevel down.
- Space at 1-2 inches apart.
- Inject same volume for each test (0.02 ml; 3 mm bleb).
- No air in syringe.
Indications for Intradermal skin testing

- When SPT is negative and there is a strong clinical history for sensitization, a positive ID test might provide evidence of sensitization.

- Dermatographism or irritant reaction can give false + reaction.

- Concentration to produce + test about 1000 - 30,000 less than SPT.

- More sensitive than SPT, but less specific.

- Absolute necessity to do ID testing, when the SPT is negative, for drugs and venoms.
Intracutaneous skin testing (ICT)

• **ICT should be interpreted cautiously.** Many positive reactions (up to 70% according to some published reports) are not clinically relevant.

• Because ICT uses larger volumes of injected allergen preparations, there may be some **irritant reactions** not mediated by an allergic mechanism. Many drugs may directly stimulate mast cells to release mediators.
Evidence based medicine

• Likelihood ratio:
  – the ratio of post-test odds after a test result to the pre-test odds indicates how much the odds change after a test

• Likelihood ratios (positive – negative)
  – >5.0 or < 0.2 generate moderate to large shifts in disease probability
  – 1.0 to 2.0 and 0.5 to 1.0 generate very small and often clinically insignificant changes in disease probability

Jaeschke JAMA
1994;271:703-7
### SPT vs ICT comparison using evidenced based medicine

<table>
<thead>
<tr>
<th>Test</th>
<th>Allergen</th>
<th>+ Likelihood</th>
<th>- Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPT</td>
<td>Cat</td>
<td>4.93</td>
<td>0.08</td>
</tr>
<tr>
<td>IDT</td>
<td>Cat</td>
<td>0.89</td>
<td>1.24</td>
</tr>
<tr>
<td>SPT</td>
<td>Grass</td>
<td>6.82</td>
<td>0.28</td>
</tr>
<tr>
<td>IDT</td>
<td>Grass</td>
<td>1.05</td>
<td>0.98</td>
</tr>
</tbody>
</table>

**Conclusion:**
SPT relate closely to disease, while ICT do not (there are presently no available data in children or in allergens other than cat and grass).

*Gendo Ann Int Med 2004;140:278-89*
Quantification of IgE antibodies in diagnosing food allergy

**Objective:** Compare results of CAP system FEIA to outcome of SPTs and Double Blind Placebo Controlled Food Challenge (DBPCFC)

**Population:** 196/320 well characterized pediatric patients; Age: mean 5.2 years [range: 0.6-18 years] Gender: 117 male; 79 female

**Evaluation:** IgE mediated reactions by history, SPTs, DBPCFC and open challenges

Sampson and Ho 1997 100: 444-51
Performance characteristics of ImmunoCAP® at cut-off 0.35 kU/L

<table>
<thead>
<tr>
<th></th>
<th>egg</th>
<th>milk</th>
<th>peanut</th>
<th>soy</th>
<th>wheat</th>
<th>fish</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. pts pos/neg</td>
<td>145/51</td>
<td>95/101</td>
<td>136/60</td>
<td>34/162</td>
<td>23/173</td>
<td>52/144</td>
</tr>
<tr>
<td>sensitivity</td>
<td>98</td>
<td>100</td>
<td>97</td>
<td>94</td>
<td>96</td>
<td>94</td>
</tr>
<tr>
<td>specificity</td>
<td>45</td>
<td>30</td>
<td>38</td>
<td>25</td>
<td>20</td>
<td>65</td>
</tr>
<tr>
<td>Positive Predictive value</td>
<td>84</td>
<td>57</td>
<td>78</td>
<td>21</td>
<td>14</td>
<td>49</td>
</tr>
<tr>
<td>Negative Predictive value</td>
<td>88</td>
<td>100</td>
<td>85</td>
<td>95</td>
<td>97</td>
<td>97</td>
</tr>
</tbody>
</table>

Sampson, Ho. JACI, 1997;100
Performance characteristics of SPT at 3mm vs DBPCFC

<table>
<thead>
<tr>
<th></th>
<th>egg</th>
<th>milk</th>
<th>peanut</th>
<th>soy</th>
<th>wheat</th>
<th>fish</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. pts pos/neg</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sensitivity %</td>
<td>90/34</td>
<td>53/53</td>
<td>20/219</td>
<td>29/78</td>
<td>19/659</td>
<td>11/7</td>
</tr>
<tr>
<td>specificity %</td>
<td>98</td>
<td>96</td>
<td>90</td>
<td>76</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td><strong>Predictive value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>85</td>
<td>66</td>
<td>55</td>
<td>35</td>
<td>35</td>
<td>77</td>
</tr>
<tr>
<td>Negative</td>
<td>90</td>
<td>93</td>
<td>75</td>
<td>84</td>
<td>94</td>
<td>80</td>
</tr>
</tbody>
</table>

*Sampson, Ho, JACI, 1997;100*
Tests for diagnosis of food allergy
skin tests vs challenge test

• PPV of positive SPT - <50% vs DBPCFC

• NPV of negative SPT - >95% vs DBPCFC
Size of SPT with 100% likelihood of positive open challenge in children with pre-existing food allergy

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Milk</th>
<th>Egg</th>
<th>Peanut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 0-2 yrs</td>
<td>≥ 6mm</td>
<td>≥ 5mm</td>
<td>≥ 4mm</td>
</tr>
<tr>
<td>Children all ages</td>
<td>≥ 8mm</td>
<td>≥ 7mm</td>
<td>≥ 8mm</td>
</tr>
</tbody>
</table>

*Sporik et al Clin Exp Allergy 2000;30*
Prick-prick test
Skin testing with natural foods in subjects suspected of having food allergy

- 22 patients with highly suspected food allergies but with negative SPT to commercial extracts had positive prick-prick skin tests with fresh natural foods:
  - 7 fish and seafood
  - 4 fruit and vegetable
  - 9 peanut and tree nuts
  - 1 milk
  - 1 egg

Prick-prick test reactions
• Infants & young children: cow’s milk, eggs, peanuts, soy and wheat account for 90% of food allergens

• Older children & adolescents: additional foods include chicken meat, tree nuts, legumes, fish & shellfish, spices, fruits & vegetables

• Extensive cross-reactivity exists among food allergens or between seemingly unrelated food and pollen allergens
Cross-reactivity among allergens exists if 2 or more different proteins are recognized by the same IgE antibody, or in other words an IgE antibody binds to different, seemingly unrelated proteins.

Cross-reactivity may be clinically silent (specific IgE detected in testing without any clinical significance), or may result in clinical symptoms (OAS, Food & Pollen allergy/exercise induced anaphylaxis).
Molecular level or Component-resolved diagnosis (CRD) provided by ISAC® (Immuno Solid-phase Allergen Chip) is a biochip-based test system that facilitates the identification of possible cross-sensitizations to allergens in unrelated biological sources.
Allergy or tolerance in children sensitized to peanut: Prevalence and differentiation using component-resolved diagnostics

Nicolaos Nicolaou, MD, MPhil, a Maryam Poorafshar, PhD, b Clare Murray, MD, a Angela Simpson, MD, a Henric Winell, MSc, b Gina Kerry, RN, a Annika Härlin, MSc, b Ashley Woodcock, MD, FMedSci, a Staffan Ahlstedt, PhD, c and Adnan Custovic, MD, PhD, FRCP a Manchester, United Kingdom, and Uppsala and Stockholm, Sweden

Background: Not all peanut-sensitized children develop allergic reactions on exposure.
Objective: To establish by oral food challenge the proportion of children with clinical peanut allergy among those considered peanut-sensitized by using skin prick tests and/or IgE measurement, and to investigate whether component-resolved allergy. Component-resolved diagnostics may facilitate the diagnosis of peanut allergy. (J Allergy Clin Immunol 2010;125:191-7.)

Key words: Peanut allergy, oral food challenge, component-resolved diagnostics, Ara h 2, microarray, birth cohort

Nicolaos N, et al., JACI 2010;125:191-7
Higher reactivity to CCD’s and Timothy grass component if tolerant to peanuts while allergic subjects had higher fold changes to rAra h1-3

FIG 2. Empirical cumulative distribution functions. Green and yellow lines represent peanut tolerant subjects and subjects with peanut allergy, respectively. n. Native; r. recombinant.
Predictive value of skin prick tests using recombinant allergens for diagnosis of peanut allergy

Catherine Astier, PhD, MD, Martine Morisset, MD, Olivier Roitel, PhD, Fanny Codreanu, MD, Sandrine Jacquenet, PhD, Patricia Franck, PharmD, Virginie Ogier, PhD, Nicolas Petit, MD, Barbara Proust, PharmD, PhD, Denise-Anne Moneret-Vautrin, MD, A. Wesley Burks, MD, Bernard Bihain, MD, Hugh A. Sampson, MD, and Gisèle Kanny, MD, PhD

Nancy, France, Durham, NC, and New York, NY

Background: Current diagnosis of peanut allergy relies on natural extracts that lack standardization. Recombinant DNA technology allows production of pure biochemically characterized proteins. Their usefulness for peanut allergy diagnosis is not established.

Objective: This study aimed to evaluate the diagnostic value of the 3 major recombinant peanut allergens.

Methods: Recombinant (r) Ara h 1, rAra h 2, and rAra h 3 were produced according to the recommendations of good manufacturing practice for recombinant allergens. Skin prick tests to individual recombinant peanut allergens appear to be a safe and effective diagnostic tool. Cosensitization to rAra h 2 and rArah 1 and/or rAra h 3 is predictive of more severe reactions.

Clinical implications: Recombinant peanut allergens can be used by SPTs for diagnosis and evaluation of allergy severity. (J Allergy Clin Immunol 2006;118:250-6.)

Key words: Food allergy, peanut, diagnosis, recombinant allergens

Astier C et al., JACI 2006;118:250-6
• All patients with peanut allergy showed **positive SPT results to rAra h 2**; 40% reacted with rAra h 1 and 27% with rAra h3

• Cosensitization to rAra h2 and rArah 1 and/or rAra h3 is predictive of more severe reactions

• Recombinant peanut allergens may be used by SPTs for diagnosis and evaluation of allergy severity
Allergy skin testing

• On arm or back
  – Back more sensitive than arm
  – Lower back more sensitive than upper back

• Different grading systems depending on technique

• In general, the higher the grade, the higher the clinical sensitivity
Table 2. Semiquantitative Reporting of Skin Test Results*

<table>
<thead>
<tr>
<th>Criteria to read test results</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin prick or puncture tests</td>
<td>No reaction or no different from control</td>
</tr>
<tr>
<td>Negative</td>
<td>Erythema less than a nickel in diameter</td>
</tr>
<tr>
<td>1+</td>
<td>Erythema greater than a nickel in diameter</td>
</tr>
<tr>
<td>2+</td>
<td>Wheal with surrounding erythema</td>
</tr>
<tr>
<td>3+</td>
<td>Wheal with pseudopods and surrounding erythema</td>
</tr>
<tr>
<td>Intracutaneous tests when control ≥2 mm</td>
<td>No different from control</td>
</tr>
<tr>
<td>Negative</td>
<td>Wheal 1 to 2 times control or definite erythema greater than a nickel in size</td>
</tr>
<tr>
<td>1+</td>
<td>Wheal 2–3 times control</td>
</tr>
<tr>
<td>2+</td>
<td>Wheal &gt;3 times control</td>
</tr>
<tr>
<td>3+</td>
<td>Wheal with pseudopods</td>
</tr>
<tr>
<td>Intracutaneous tests when control &lt;2 mm</td>
<td>No difference from control</td>
</tr>
<tr>
<td>Negative</td>
<td>3- to 4-mm wheal with erythema or erythema greater than a nickel in size</td>
</tr>
<tr>
<td>1+</td>
<td>4- to 8-mm wheal without pseudopods</td>
</tr>
<tr>
<td>2+</td>
<td>&gt;8-mm wheal without pseudopods</td>
</tr>
<tr>
<td>3+</td>
<td>Wheal with pseudopods and erythema</td>
</tr>
</tbody>
</table>

* Data are from Vanselow.28
• Criteria for a positive skin prick test to dog

<table>
<thead>
<tr>
<th>criteria</th>
<th>sensitivity</th>
<th>specificity</th>
<th>overall efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥3-mm wheal diameter</td>
<td>0.98</td>
<td>0.82</td>
<td>0.89</td>
</tr>
<tr>
<td>≥5-mm wheal diameter</td>
<td>0.66</td>
<td>0.98</td>
<td>0.84</td>
</tr>
<tr>
<td>3+ histamine reference</td>
<td>0.92</td>
<td>0.93</td>
<td>0.93</td>
</tr>
</tbody>
</table>
Grading/Scoring skin test results

• Traditional:
  – Positive test = 3mm above negative control
  – Negative test = No reaction or same as negative control

• Other scoring systems (depending on method/device used)
  – Ex.  | Wheal Size            | Erythema   |
         | 0 = No reaction        | + = 10-15 mm |
         | 1 = 1/3 of positive control | ++ = > 15 mm |
         | 2 = 1/2 to 2/3 of positive control |
         | 3 = Same as positive control |
         | 4 = Larger than positive control |
         | 5 = Pseudopod              |
Recording skin test responses

Results of both SPT and ICT skin tests should be reported in the most quantitative terms possible.

• Reports of minimal usefulness include:
  – Positive or negative
  – 0 to 4+ (unless accompanied by an indication of what these numbers represent).
• Useful to report both wheal and flare measurements in mm:
  – A superior method is to measure the reaction in mm across the cross-diameter
  – Area (cross-diameter in mm) of the wheal and erythema is the most accurate way to present results.
  – Measurements of:
    • the product of the orthogonal diameters
    • the sum of the orthogonal diameters
    • the longest diameter
  – Correlate very well with area (r values greater than 0.9).

Ownby JACI 1982:69:536-8
Potential pitfalls of skin testing

- Assumption that skin testing is easy to do
- Testing by inexperienced personnel; failure to assess and document proficiency
- Failure to store extracts properly
- Failure to test for relevant allergens
- Testing for non-relevant allergens
- Testing first, case history second
- Testing in clinical situations that don’t need testing
- Failure to establish clinical relevance of positive or negative tests
Skin test form developed by the Immunotherapy committee of AAAAI
<table>
<thead>
<tr>
<th>Allergen: Concentration: Extract Manufacturer. *</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Percutaneous</strong></td>
</tr>
<tr>
<td><strong>W (mm) F</strong></td>
</tr>
<tr>
<td><strong>Trees</strong></td>
</tr>
<tr>
<td>1. American Elm 1:20 AL</td>
</tr>
<tr>
<td>2. Mountain Cedar 1:10 AL</td>
</tr>
<tr>
<td>3. Paper Birch 1:20 G</td>
</tr>
</tbody>
</table>

* Extract manufacturer abbreviations: G=Greer, AL=Allergy Labs, Ohio, LO Allergy Labs, Oklahoma, AK=ALK, HS=Hollister-Stier, C=Center, NE=Nelco, AM=Allermed
• Physician name, address.
• Patient name, testing date, medications.
• Location of testing (back or arm).
• Method used (prick-puncture, intradermal).
• Device used (prick, puncture).
• Reactions measured or scored with key.
• Results of positive & negative controls.
• Specify name of all allergens used.
Summary

- **Allergy skin testing** is a manual technique that requires training, skill and expertise.

- Various systems used to report results. **Results** from one allergy practice **not interchangeable** with results from another allergy practice.

- Allergy skin testing with **recombinant allergens** is a promising development for use in future clinical practice.

- Allergy testing and its clinical interpretation is both **an art and a science**.

- Probably the most reliable, clinically valuable and cost-effective “allergy test” is **consultation with a board-certified allergist-immunologist**.
“…..the fact that skin testing has not turned out to be a simple and completely reliable technics [sic] does not detract from the fact that when it is intelligently and skillfully performed, it remains the most effective diagnostic procedure in reaginic allergic disorders.”

1947 by Dr M. Walzer

Questions?