Is Wheal Size at Age One a Good Predictor of Allergic Sensitization at Age Two?
Cincinnati Childhood Allergy and Air Pollution Study

J.E. Lockey[1], L. N. Anderson[1], J.Khoury[2], ,D. I. Bernstein[1], M. Villareal[1], G. K. Khurana Hershey[2], G. K. LeMasters[1]

[1]University of Cincinnati, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Abstract

RATIONALE: In the U.S. the skin prick test (SPT) is the most commonly utilized procedure for the diagnosis of IgE-mediated sensitivity. Few studies have examined the relationship of wheal size and histamine ratio in young children and its positive predictive value (PPV).

METHODS: In a cohort of infants born to at least one atopic parent, each had an annual SPT to a panel of 15 aeroallergens and two foods at 12 and 24 months of age. Wheal reactions were traced and digitized using the largest diameter from each test measured to the nearest tenth of a millimeter using the computer program AutoCad® 2002. Histamine ratio (HR) was assessed and considered positive if the ratio of the allergen wheal diameter to the histamine wheal was ≥0.5, 0.6 or 0.75.

RESULTS: For 477 infants, aeroallergen sensitization increased from 15.9% to 34.0% between 12 and 24 months while food sensitization decreased from 11.7% to 8.6%, respectively. At 12 months, as the SPT wheal diameter increased from ≥3mm to ≥6mm, the PPV for being aeroallergen SPT+ at 24 months increased from 61.8% to 74.1% and for food allergen it increased from 44.6% to 51.9%. The PPV for an aeroallergen HR of ≥0.5, 0.6 and 0.75 was 65.8%, 65.2% and 72.0% and for food it was 45.0%, 47.3% and 44.4%, respectively.

CONCLUSIONS: Infants can be screened using the standard definition of a positive SPT and as wheal size increases PPV improves while larger histamine ratios has no consistent pattern.

Objectives

- To characterize the natural history of allergic sensitization in high-risk infants
- To compare three definitions of skin prick test (SPT) positivity in high-risk infants

Methods

- Annual medical evaluation performed on infants with one atopic parent
- Skin prick tests (SPTs) conducted with 15 common aeroallergens at age 12 and 24 months
- Positive Control: Histamine Dihydrochloride (10mg/ml)
- Negative Control: Normal saline (0.9%)
- Results read 15 minutes after application
- Wheal and flare reactions traced with ball point pen and transferred with 3M Transpore™ plastic tape
- Reactions were digitized and the diameter measured to nearest tenth of a millimeter using AutoCAD® 2002.

Results

Table I - Twelve and Twenty-four Month Allergen Prevalence Rates[1] (n=477)

	Allergen	12 Month Prevalence (%)	24 Month Prevalence (%)
	Any Aeroallergen	15.9	34.0
Pollen	Meadow Fescue	1.3	1.9
Pollen	Timothy	1.9	6.1
Pollen	White Oak	1.9	2.9
Pollen	Maple mix	1.7	4.0
Pollen	American Elm	0.9	2.3
Pollen	Red Cedar	2.3	7.3
Pollen	Short Ragweed	1.5	2.7
Mold	*Alternaria*	1.5	3.1
Mold	*Aspergillus fumigatus*	1.7	3.4
Mold	*Penicillium* mix	1.1	2.5
Mold	*Cladosporium*	2.1	1.5
Dust	Dust Mite mix	2.3	5.2
Dust	German Cockroach	1.5	3.4
Pet	Cat	2.1	5.7
Pet	Dog	1.7	3.4
	Any Food Allergen	11.7	8.6
	Milk	3.8	1.7
	Egg	9.9	8.0

[1] - Prevalence rates were calculated using the wheal definition of SPT positivity where a wheal diameter 3 mm or greater than the normal saline control was recorded as posititve.

Results (cont'd)

Table II - SPT Conversion, Reversion and Persistence Rates[1] (n=477)

	Allergen	Conversion 12 Month (SPT-) 24 Month (SPT+) (%)	Reversion 12 Month (SPT+) 24 Month (SPT-) (%)	Persistence 12 Month (SPT+) 24 Month (SPT+) (%)
	Any Aeroallergen	28.7	38.2	61.8
Pollen	Meadow Fescue	1.9	100.0	0.0
Pollen	Timothy	5.1	44.4	55.6
Pollen	White Oak	2.4	66.7	33.3
Pollen	Maple mix	3.6	75.0	25.0
Pollen	American Elm	2.3	100.0	0.0
Pollen	Red Cedar	6.2	45.5	54.6
Pollen	Short Ragweed	2.6	85.7	14.3
Mold	*Alternaria*	3.2	100.0	0.0
Mold	*Aspergillus fumigatus*	3.4	100.0	0.0
Mold	*Penicillium* mix	2.5	100.0	0.0
Mold	*Cladosporium*	1.3	90.0	10.0
Dust	Dust Mite mix	5.2	90.9	9.1
Dust	German Cockroach	3.2	85.7	14.3
Pet	Cat	5.6	90.0	10.0
Pet	Dog	3.0	75.0	25.0
	Any Food Allergen	5.9	71.4	28.6
	Milk	0.9	77.8	22.2
	Egg	5.8	72.3	27.7

[1] - Rates were calculated using the wheal definition of SPT positivity.

Table III - SPT Positivity Definition Comparison using 12 Month Prevalence Rates (n=477)

	Allergen	Wheal[1] (%)	Wheal and Flare[2] (%)	0.5 Histamine Ratio[3] (%)	0.6 Histamine Ratio[3] (%)	0.75 Histamine Ratio[3] (%)
Pollen	Meadow Fescue	1.3	1.3	1.3	1.3	1.3
Pollen	Timothy	1.9	1.9	2.1	1.9	1.9
Pollen	White Oak	1.9	1.9	2.1	2.1	2.1
Pollen	Maple mix	1.7	1.5	1.3	1.1	0.8
Pollen	American Elm	0.8	0.8	0.8	0.6	0.0
Pollen	Red Cedar	2.3	2.3	2.1	1.7	1.1
Pollen	Short Ragweed	1.5	1.5	1.5	1.3	0.8
Mold	*Alternaria*	1.5	1.5	1.1	0.6	0.2
Mold	*Aspergillus fumigatus*	1.7	1.5	1.5	1.3	0.4
Mold	*Penicillium* mix	1.1	1.1	1.1	0.8	0.6
Mold	*Cladosporium*	2.1	1.9	2.1	1.9	1.7
Dust	Dust Mite mix	2.3	2.3	2.3	1.7	0.8
Dust	German Cockroach	1.5	1.5	1.5	1.5	1.3
Pet	Cat	2.1	2.1	2.1	1.7	1.3
Pet	Dog	1.7	0.8	1.7	1.7	1.3
	Milk	3.8	3.4	4.4	4.0	2.9
	Egg	9.9	9.6	10.1	9.4	7.8

[1] Wheal - A SPT was recorded as positive when the wheal diameter was 3 mm or greater than the normal saline control.
[2] Wheal and Flare - A SPT was recorded as positive when the wheal diameter was 3 mm or greater than the normal saline control and the corresponding flare reaction was greater than the wheal.
[3] Histamine Ratio - A SPT was recorded as positive when the ratio of the allergen specific wheal diameter to the histamine wheal diameter was ≥ a predetermined cut off point. We examined three cut off points: 0.5, 0.6, and 0.75.

Table IV - Prediction of 24 Month Aeroallergen Sensitization[1] from 12 Month Wheal Diameters (n=477)

Wheal diameter[2] (mm)	Aeroallergen n	Sens[3]	Spec[4]	PPV[5]	NPV[6]	Food n	Sens	Spec	PPV	NPV
≥3	76	29.0	90.8	61.8	71.3	56	15.4	90.2	44.6	67.5
≥4	60	23.5	93.0	63.3	70.4	47	13.6	92.1	46.8	67.4
≥5	41	16.7	95.6	65.9	69.0	42	12.4	67.4	47.6	67.5
≥6	27	12.4	97.8	74.1	68.4	27	8.6	95.9	51.9	67.1

Table V - Prediction of 24 Month Aeroallergen Sensitization[1] from Histamine Ratios at 12 months (n=477)

Histamine Ratio	Aeroallergen n	Sens[3]	Spec[4]	PPV[5]	NPV[6]	Food n	Sens	Spec	PPV	NPV
≥0.5	73	29.6	92.1	65.8	71.8	60	16.7	89.5	45.0	67.6
≥0.6	69	27.8	92.4	65.2	71.3	55	16.1	90.8	47.3	67.8
≥0.75	50	22.2	95.6	72.0	70.5	45	12.4	92.1	44.4	67.1

[1] Sensitization to ANY aeroallergen at 24 months.
[2] Classify SPTs as positive or negative and compared 12 months wheal diameters ≥ 3mm to ≥ 6mm in 1mm increments to 24 month wheal diameter of ≥ 3mm
[3] Sensitivity = True Positives/(True Positives+False Negatives)
[4] Specificity = True Negatives/(True Negatives+False Positives)
[5] Positive Predictive Value = True Positives/(True Positives+False Positives)
[6] Negative Predictive Value = True Negatives/(True Negatives+False Negatives)

Conclusions

- Food allergen and indoor and outdoor aeroallergen sensitization begin in infancy
- Specific allergen sensitization was largely transient at 12 months
- Overall, aeroallergen sensitization, however, persisted at 24 months
- Wheal size improved the PPV of SPT while histamine ratio showed no consistent pattern.

Funded by NIEHS Grants: ES11170