

# Altered Cerebral Dominance in Atopy and in Children of Asthmatic Mothers

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## INTRODUCTION

In a survey of 1092 subjects, Geshwind and Behan<sup>1,2</sup> found left-handed individuals to have an 11.5-fold ratio of self-reported allergy, an increased incidence of other immunologically related diseases, and an increased incidence of developmental learning disorders compared to right-handers. Because childhood allergy and asthma,<sup>3-5</sup> dyslexia,<sup>6</sup> and left-handedness<sup>7</sup> are reported to be more common in males, Geshwind<sup>1,2,6</sup> postulated that both cerebral and immune development are influenced by androgenic hormones.

In that allergy was self-reported in Geshwind's studies, corroborative observation has been warranted. Smith<sup>8</sup> found a confirmatory increase in left-handedness in a survey of patients attending the allergy clinic at St. Mary's Hospital, London, and Weinstein and Pieper<sup>9</sup> found increased left-handedness in atopics on assessing 853 subjects, half from an allergy clinic in Michigan. In the latter study, asthmatic mothers, but not asthmatic fathers, reported a particularly high percentage of their offspring to be left-handed, prompting the following investigation.

## SUBJECTS AND METHODS

One hundred thirty-nine asthmatic mothers completed a written survey regarding handedness in their children and their siblings. Subjects attended one of three

allergy clinics, two in Michigan and one in Washington, DC. Subjects were directly under the care of an allergist who verified the diagnosis of asthma at two clinics. At the third, a university hospital allergy clinic, asthma was verified by the clinic record.

Left-handedness reported by asthmatic mothers in their children was compared to left-handedness reported by the same subjects in their siblings, and to left-handedness previously reported by nonasthmatic, nonatopic mothers in their children and siblings.<sup>9</sup>

The presence of asthma symptoms, and the need for asthma medication during pregnancy, was surveyed in 25 asthmatic mothers, each of whom gave birth to at least one left-handed child.

Differences between groups were assessed by Chi-square analysis.

## RESULTS

Asthmatic women reported a 19.4% (68/351) incidence of left-handedness in their offspring. Left-handedness was numerically, but not statistically greater in sons: 22.6% (42/186) of sons and 15.8% (26/165) of daughters were reported to be left-handed (not significant). No significant differences in like groups existed between locations.

*Left-handedness in children reported by asthmatic women vs. left-handedness in sibs reported by asthmatic women, left-handedness in children reported by nonasthmatic women and left-handedness in sibs reported by nonasthmatic women* (TABLE 1). Compared to the 19.4% incidence of left-handedness reported in their children, asthmatic mothers reported 10.6% (40/378) of their siblings to be left-handed ( $p < 0.001$ ) and 387 nonasthmatic women surveyed earlier<sup>9</sup> reported 11.6% (85/735) of their children to be left-handed ( $p < 0.001$ ) and 9.8% (101/1035) of their siblings to be left-handed ( $p < 0.001$ ).

*Severity of asthma during pregnancy* (TABLE 2). 25 mothers who bore at least one left-handed child were surveyed. 43.4% (10/23) of children of symptomatic pregnancies were left-handed compared to 38.8% (26/67) of children of asymptomatic pregnancies (not significant). In ten symptomatic pregnancies bearing left-handed children, asthma was mild in four, moderate in one, and severe in five pregnancies. Medication was required in only six of thirty-six pregnancies yielding left-handed offspring, sporadically in one and regularly in five. No women required corticosteroids.

**TABLE 1.** Left-Handedness in Children Reported by Asthmatic Women vs Left-Handedness in Siblings Reported by Asthmatic Women, Left-Handedness in Children Reported by Nonasthmatic Women, and Left-Handedness in Siblings Reported by Nonasthmatic Women

Mothers (#)	Children			Siblings		
	% Left	#Left/Total	$p^a$	% Left	#Left/Total	$p^a$
Asthmatic (139)	19.4%	68/351		10.6%	40/378	<0.001
Nonasthmatic (387)	11.6%	85/735	<0.001	9.8%	101/1035	<0.001
Both (526)				10.0%	141/1413	<0.0001

<sup>a</sup> Vs left-handed children reported by asthmatic mothers.

**TABLE 2.** Asthma Symptoms during Pregnancy vs Left-Handedness in Offspring in 25 Asthmatic Mothers of Left-Handed Children

Maternal Asthma	Children		<i>p</i>
	#Left/Total	%	
Symptomatic	10/23	43.4%	NS <sup>a</sup>
Asymptomatic	26/67	38.8%	
Total	36/90	40.0%	

<sup>a</sup> Symptomatic vs asymptomatic pregnancies.

## DISCUSSION

Although handedness would appear far afield from allergy, Geshwind's hypothesis has intriguing conceptual implications regarding the pathogenesis and nature of the atopic state. In assessing 853 subjects, 424 from an allergy clinic and 429 from a health screening clinic, Weinstein and Pieper found increased left-handedness in atopic participants; mean laterality quotient measured by modified Edinburgh Handedness Inventory was  $66.4 \pm 51.6$  in atopics vs  $79.4 \pm 42.1$  in nonatopic controls ( $p < 0.001$ ) and the incidence of left-handedness was 12.1% vs 6.8%, respectively ( $p < 0.02$ ).<sup>9</sup> Results were in agreement with those of Smith<sup>8</sup> in a similar study comparing 313 allergy clinic patients with 350 age- and sex-matched controls.

The association between allergy and handedness remains controversial by virtue of negative studies.<sup>10-14</sup> In comparing 325 patients who attended the allergy clinic at Pellegrin Hospital, Bordeaux, France to age and sex matched controls, Betancor *et al.*<sup>10</sup> noted a tendency toward left-handedness in patients whose allergy symptoms began before puberty but were otherwise unable to relate allergies and left-handedness. In other studies in which an association could not be found, allergy was identified either by self-report<sup>11-13</sup> or by review of a general health survey,<sup>14</sup> as opposed to study of a known atopic population.

Asthmatic subjects previously surveyed by Weinstein and Pieper<sup>9</sup> reported a particularly high percentage of left-handed children ( $16.7 \pm 26.3\%$ ) compared to nonatopic parents ( $10.3 \pm 21.2\%$ ) ( $p < 0.002$ ), the increase attributable to offspring reported by asthmatic women ( $18.6 \pm 29.0\%$ ), but not asthmatic men. In the present study asthmatic mothers reported a correspondingly high incidence of left-handed children, significantly greater than the incidence of left-handed children previously reported by nonasthmatic mothers, or left-handed siblings reported by asthmatic mothers or nonasthmatic mothers.<sup>9</sup> Findings were similar in independent survey at each of three locations minimizing sample bias favoring inclusion of left-handed subjects or families with left-handed members or due to locality. The incidence of left-handedness reported by asthmatic women in their children represents a 2.4-fold increase compared to the 7.96% incidence of left-handedness documented by Oldfield,<sup>7</sup> in 1100 students ( $p < 0.001$ ) and a 2.9-fold increase compared to the 6.8% incidence of left-handedness found in a nonatopic population by Weinstein and Pieper ( $p < 0.001$ ).<sup>9</sup>

Our understanding of the inheritance of allergy as well as left-handedness, is uncertain. It has long been appreciated that allergic children are born into households in which other family members suffer from allergy. An autosomal recessive mode of inheritance of basal IgE level has been suggested.<sup>15</sup> However, more boys than girls suffer from these disorders,<sup>3-5</sup> the concordance for asthma in twins, even

monozygotic twins, is low,<sup>16</sup> and mother's allergic status, rather than father's, has been found to correlate with the age of onset of children's symptoms.<sup>17</sup> Allergic disorders other than asthma occur more frequently in relatives of extrinsic than intrinsic asthmatics<sup>18</sup> suggesting that independent factors might control the inheritance of asthma and IgE formation.

Arguing for maternal and hormonal influences shaping the development of atopy, umbilical cord serum IgE, a predictor of atopy, appears to be influenced more by maternal than paternal IgE.<sup>19</sup> Cord IgE has been found to be elevated if progesterone is taken during pregnancy.<sup>19</sup> Correlative of our finding of increased left-handedness in children of asthmatic mothers, beta-antagonists taken by non-asthmatics during pregnancy increase cord serum IgE and result in a high incidence of allergic offspring.<sup>20</sup>

Both neural and immune dysfunction are associated with allergy.<sup>21</sup> The inclusion of such diverse clinical entities as atopic dermatitis, nasal polyposis, allergic rhinitis, extrinsic asthma and intrinsic asthma into the same disease category can be reconciled by viewing allergy as a spectrum of immunologic and neuroautonomic disorders, each variably expressed in any affected individual.

Since asthmatics represent the subset of atopics most affected by neuroautonomic dysfunction, one might hypothesize an operant relationship between adrenergic message and the pregnant asthmatic's endocrinologic milieu resulting in left-handed offspring. Our results do not suggest severity of asthma, fetal oxygen deprivation or asthma medication taken during pregnancy to be major pathophysiologic considerations.

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