Early life risk factors for chronic sinusitis: A longitudinal birth cohort study

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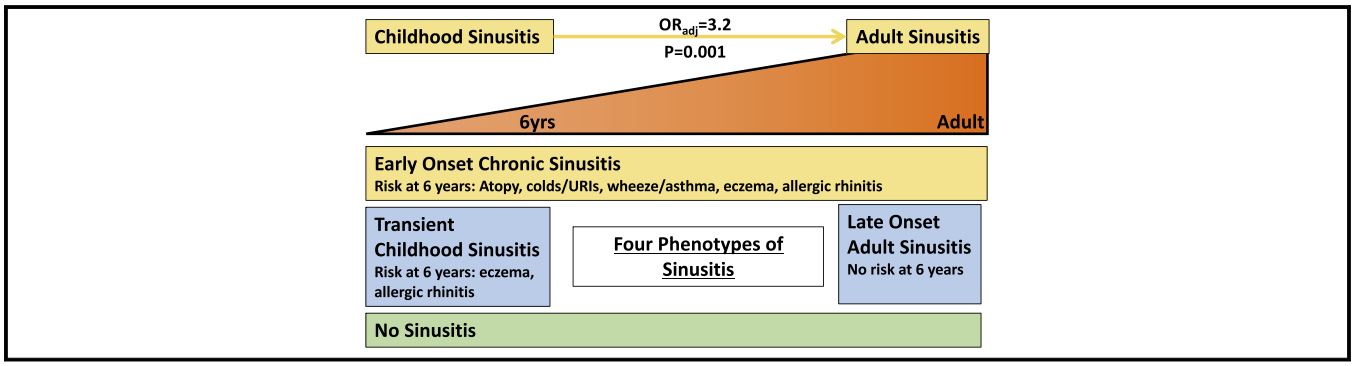
GRAPHICAL ABSTRACT



Background: Chronic sinusitis is a commonly diagnosed condition in adults who frequently present with late-stage disease and irreversible changes to the sinus mucosa. Understanding the natural history of chronic sinusitis is critical in developing therapies designed to prevent or slow the progression of disease.

Objective: We sought to determine early life risk factors for adult sinusitis in a longitudinal cohort study (Tucson Children's Respiratory Study).

Methods: Physician-diagnosed sinusitis was reported at age 6. Adult sinusitis between 22 and 32 years was defined as self-reported sinusitis plus physician-ordered sinus radiologic films. Atopy was assessed by skin prick test. Individuals were grouped into 4 phenotypes: no sinusitis (n = 621), transient childhood sinusitis only (n = 57), late-onset adult sinusitis only (n = 68), and early onset chronic sinusitis (childhood and adult sinusitis, n = 26).

Results: Sinusitis was present in 10.8% of children and 12.2% of adults. Childhood sinusitis was the strongest independent risk factor for adult sinusitis (odds ratio = 4.2; 95% CI: 2.5-7.1; $P < .0001$; n = 772). Early onset chronic sinusitis was associated with increased serum IgE levels as early as at 9 months of age, atopy (assessed by skin prick test reactivity), childhood eczema and allergic rhinitis, frequent childhood colds, maternal asthma, and with increased prevalence of concurrent asthma. No association was found between late-onset adult sinusitis and any of the early life risk factors studied.

Conclusions: We identified an early onset chronic sinusitis phenotype associated with a predisposition to viral infections/colds in early life, allergies, and asthma. Elucidation of the molecular mechanisms for this phenotype may lead to future therapies to prevent the progression of the disease into adult sinusitis. (J Allergy Clin Immunol 2018;141:1291-7.)

Key words: *Sinusitis, asthma, allergy, viral, natural history*

The prevalence of chronic rhinosinusitis (CRS) is estimated to be 10% of the US population, with expenditures accounting for approximately 4.5% of total US health care dollars[1] ($60 billion annually).[2] Nevertheless, approximately 25% of individuals with maximal medical and surgical treatment fail to show significant clinical improvement.[3] This may be in part attributable to irreversible structural changes in the sinus mucosae, which perpetuate symptoms and hamper response to therapy. There is thus a critical need to develop strategies for the primary and secondary prevention of CRS, but very little is known about the natural history of the disease, the timing of the inception of the different subphenotypes of the disease, and the factors that determine its persistence.

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Abbreviations used
AR: Allergic rhinitis
CRS: Chronic rhinosinusitis

Allergic rhinitis (AR), asthma, and CRS often co-occur in the same individuals, and although the link between these disorders is multifactorial, there is evidence that AR and CRS can be risk factors for the development of asthma. In a longitudinal cohort study of 1655 households, AR was independently associated with a 3-fold increase in the development of adult-onset asthma, and when AR was present with sinusitis this predictive value was further increased.[4] CRS and asthma frequently coexist: approximately 20% to 33% of patients with CRS have concomitant asthma, a prevalence 4-fold greater than that of the general population.[5,6] Nearly 80% of patients with severe asthma will have concomitant CRS.[7] Moreover, treatment of AR and CRS has been shown to improve asthma symptoms, suggesting a common pathway.[8,9] The concomitant expression of these conditions is believed to be driven by type 2 mediated inflammation resulting in elevated IgE, eosinophilic inflammation, and airway remodeling.[10]

TABLE I. Early life risk factors for childhood sinusitis

		MD sinusitis at age 6 y				
Characteristic	**Category**	**n**	**Percent**	***P* value***	**OR**	**95% CI**
	All	772	10.8			
Sex	Male	366	10.4			
	Female	406	11.1	.753	1.08	0.68-1.70
Race/ethnicity	NHW	506	10.9			
	HW	172	8.1		0.73	0.39-1.34
	Other	94	14.9	.233	1.44	0.76-2.70
Maternal						
Asthma	No	680	9.6			
	Yes	83	20.5	**.002**	2.44	1.35-4.40
Smoking	No	657	10.7			
	Yes	115	11.3	.836	1.07	0.57-2.00
Education	≤12 y	186	10.2			
	>12 y	585	10.9	.781	1.08	0.63-1.85
Age	≤26	326	10.7			
	>26	446	10.8	.991	1.00	0.63-1.59
Paternal						
Asthma	No	636	9.6			
	Yes	94	16.0	.059	1.79	0.97-3.30
Smoking	No	551	10.3			
	Yes	211	10.9	.823	1.06	0.64-1.77
Education	≤12 y	177	11.3			
	>12 y	581	10.3	.712	0.90	0.53-1.55
Age	≤26	203	10.3			
	>26	559	10.6	.933	1.02	0.60-1.73
Child at 6 years						
Atopy	No	375	7.7			
	Yes	239	12.6	**.048**	1.71	0.99-2.93
Alternaria sensitization	No	511	8.6			
	Yes	102	14.7	.057	1.83	0.98-3.43
Bermuda sensitization	No	445	9.0			
	Yes	169	11.2	.397	1.28	0.72-2.28
Eosinophilia	<4%	307	8.8			
	≥4%	113	12.4	.271	1.47	0.74-2.91
Active asthma	No	697	9.8			
	Yes	69	20.3	**.007**	2.35	1.24-4.46
Active wheeze	No	577	8.7			
	Yes	190	16.8	**.002**	2.13	1.32-3.44
Ever eczema	No	648	9.6			
	Yes	117	18.0	**.007**	2.07	1.21-3.55
Ever hay fever	No	492	3.9			
	MD allergic	278	23.0	**<.001**	7.44	4.35-12.7
Colds*	0	24	8.3			
	1-3	581	8.6		1.04	0.24-4.53
	4-5	132	17.4		2.32	0.51-10.6
	6-9	29	27.6	**.001**	4.19	0.80-22.1

Boldface values are statistically significant.
HW, Hispanic white; *NHW*, non-Hispanic white.
**P* value from chi-square statistic.