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Research Letter

New Perspectives on the Atopic March: Results of a Cross-Sectional Multicenter National Survey and Brief Review of the Literature

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To the Editor,

Atopic march (AM) reflects the sequential appearance of allergic phenomena in predisposed individuals. It typically begins in the first months of life with the onset of atopic dermatitis (AD), followed by later development in childhood of IgE-mediated food allergy (IgE-FA), allergic asthma (AA), allergic rhinitis (AR), and eosinophilic esophagitis (EoE) (Fig. 1).[1] In most cases, AD constitutes the first step. Therefore, several authors have focused on AD as a key therapeutic target for preventing the AM.

In this article, we describe the results of a national multicenter survey conducted among dermatology residents and attending dermatologists in June 2023 on their knowledge and opinions about the AM. We also present a brief review of the literature centered on recent developments related to this entity.

Table 1 illustrates the survey results. A total of 178 participants completed the survey, of whom 159 (89.3%) were attending dermatologists, with the largest proportion being dermatologists with >25 years of clinical practice (37.1%). The autonomous communities with the highest participation were Madrid (n = 39; 23%), followed by Andalusia

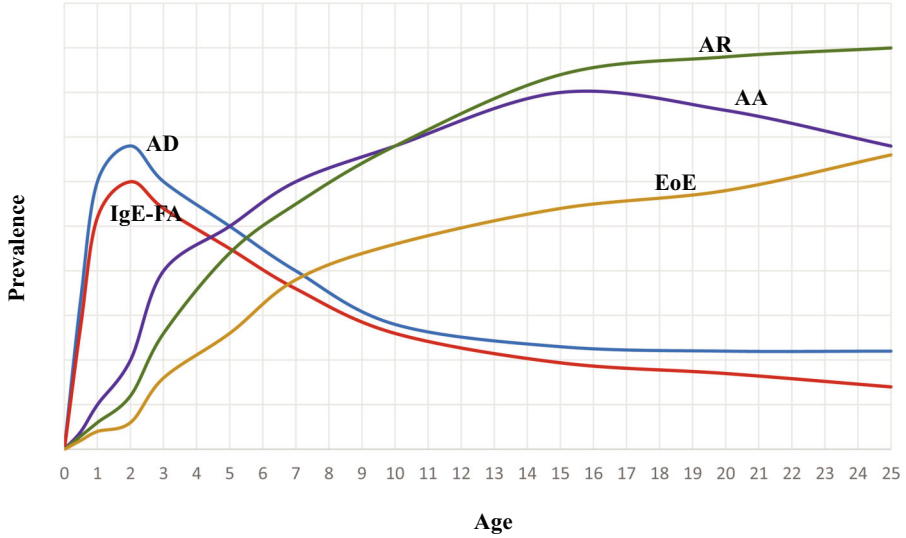

Fig. 1. Atopic march. Atopic dermatitis (AD) typically develops first, followed by IgE-mediated food allergy (IgE-FA), allergic asthma (AA), allergic rhinitis (AR), and eosinophilic esophagitis (EoE). *Source*: authors' own elaboration. AD: atopic dermatitis; IgE-FA: IgE-mediated food allergy; AA: allergic asthma; AR: allergic rhinitis; EoE: eosinophilic esophagitis.

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Table 1
Results of the national survey on the atopic march. Source: data from the national aborDA project survey, conducted between June 20th and June 30th, 2023.

Question	Options	*N* (total = 178)	%
Q1. You are a…	Dermatologist with >25 years of practice	66	37.1
	Dermatologist with 15–25 years of practice	39	21.9
	Dermatologist with 5–15 years of practice	38	21.4
	Dermatologist with <5 years of practice	16	9.0
	Dermatology resident	19	10.7
Q2. In which autonomous community do you currently work?	Andalusia	27	16.6
	Aragon	1	0.6
	Balearic Islands	7	4.3
	Canary Islands	5	3.1
	Cantabria	2	1.2
	Castile–La Mancha	6	3.7
	Castile and León	7	4.3
	Catalonia	24	14.7
	Community of Madrid	39	23.9
	Chartered Community of Navarre	17	10.4
	Extremadura	1	0.6
	Galicia	8	4.9
	Basque Country	11	6.8
	Principality of Asturias	3	1.8
	Region of Murcia	4	2.5
	La Rioja	1	0.6
	Ceuta and Melilla	0	0
Q3. Do you have a pediatric dermatology specialty clinic?	Yes	49	30.1
	No	114	69.9
Q4. Do you believe in the existence of the atopic march?	Yes	148	83.2
	No	4	2.3
	Unsure	23	12.9
	Other	3	1.7
Q5. Which of the following factors do you believe may influence the development of the atopic march? (Multiple answers allowed)	Genetic factors	166	93.3
	Immunologic factors	150	84.3
	Environmental factors	163	91.6
	Oxidative free radicals	37	20.8
	Other	6	3.4
Q6. Which of the following statements do you agree with the most?	Atopic dermatitis is always the first sign of the atopic march	5	2.8
	Atopic dermatitis is frequently the first sign of the atopic march	160	89.9
	Atopic dermatitis generally appears after food allergy, rhinitis, or asthma	13	7.3
Q7. In young children with atopic dermatitis, do you recommend any measures to prevent other atopic march-related conditions?	Yes	100	56.2
	No	78	43.8
Q8. Which of the following do you believe could act as preventive measures for other atopic march processes in patients with atopic dermatitis? (Multiple answers allowed)	Emollients	114	64.0
	Topical corticosteroids	78	43.8
	Oral corticosteroids	20	11.2
	Topical calcineurin inhibitors	75	42.1
	Anti-IL-4/13 antibodies	66	37.1
	Anti-IL-13 antibodies	40	22.5
	Janus kinase (JAK) inhibitors	41	23.0
	Prebiotics	33	18.5
	Probiotics	49	27.5
	Early food introduction	48	27.0
	Avoidance of tobacco exposure	95	53.4
	Water softeners	8	4.5
	Other	7	3.9
	None of the above	16	9.0
Q9. In infants at risk of developing atopic dermatitis, should preventive measures be applied in the first weeks or months of life?	Yes	96	53.9
	No	11	6.2
	Unsure	71	39.9
Q10. Which of the following could act as preventive measures for the atopic march in infants at risk of atopic dermatitis? (Multiple answers allowed)	Petrolatum-based emollients	33	20.3
	Emollients with lipid combinations (ceramides, cholesterol, fatty acids)	119	73.0
	Prebiotics	38	23.3
	Probiotics	46	28.2

Table 1
(*Continued*)

Question	Options	*N* (total = 178)	%
	Early food introduction	47	28.8
	Breastfeeding	110	67.5
	Avoidance of tobacco and air pollution	111	68.1
	Pet exposure	60	36.8
	Water softeners	9	5.5
	Other	3	1.8
	None of the above	11	6.8
Q11. Do you believe that the severity of atopic dermatitis is related to later incidence of food allergy, allergic asthma, or allergic rhinitis?	Yes	117	71.8
	No	46	28.2
Q12. Do you believe that the severity of atopic dermatitis is related to later severity of food allergy, allergic asthma, or allergic rhinitis?	Yes	99	60.7
	No	61	37.4
	Other	3	1.8
Q13. Should dermatologists play a central role in managing atopic dermatitis and, when necessary, refer patients for joint management with other specialists?	Yes	157	96.3
	No	1	0.6
	Unsure	4	2.5
	Other	1	0.6

Q, question; IL, interleukin; JAK, Janus kinase.

Table 2
Main studies proposing methods to reduce atopic dermatitis or the atopic march. Source own elaboration.

Proposed measure	Evidence	*N*	Proposed mechanism of action	Results	Reference
Emollients	Phase 3 clinical trials (results from 3 trials)	1394	Skin barrier restoration	Daily emollient use in high-risk newborns reduced AD prevalence at age 3 years	Chalmers et al.
	Prospective study	160	Skin barrier restoration	No significant differences in AD incidence rate at age 2 between high-risk newborns treated with emollients vs placebo	Kottner et al.
	Systematic review and meta-analysis	11 studies, >10,000 patients	Skin barrier restoration	Early emollient application is effective for preventing AD in high-risk infants; emulsions are the optimal vehicle	Liang et al.
Prebiotics	Prospective study	459	Cutaneous homeostasis regulation	Use of synbiotics and/or emollients within the first year of life did not reduce incidence rate of AD or FA	Dissanayake E et al.
Probiotics	Prospective study	459	Cutaneous homeostasis regulation	Use of synbiotics and/or emollients within the first year of life did not reduce incidence rate of AD or FA	Dissanayake E et al.
	Phase 1/2 clinical trial	15	Cutaneous homeostasis regulation	Topical *Roseomonas mucosa* significantly reduced AD severity, topical steroid use, and *S. aureus* colonization	Myles I et al.
Feeding, early food introduction, and breastfeeding	Prospective cohort	4089	Cutaneous homeostasis regulation	Breastfeeding > 4 months reduced AD and other AM outcomes at age 4 years	Kull I et al.
	Prospective cohort	2252	Cutaneous homeostasis regulation	When breastfeeding is not possible, the use of hydrolyzed formulas in infants aged 0–4 months reduces the incidence of AD (whey and casein hydrolysates) and of allergic rhinitis and allergic asthma (casein hydrolysates).	Von Berg A et al.

Table 2
(*Continued*)

Proposed measure	Evidence	*N*	Proposed mechanism of action	Results	Reference
	Real-world clinical trial	640	Cutaneous homeostasis regulation	In children at risk for AD, early (before 11 months of age) and regular peanut consumption through 6 years of life decreases the prevalence of this allergy.	Du Toit G et al.
	Systematic review and meta-analysis	27 prospective studies, >10,000 patients	Cutaneous homeostasis regulation	No association was found between AD and breastfeeding. However, in patients with an atopic genetic predisposition, exclusive breastfeeding may offer a protective benefit vs the development of AD	Lin et al.
Avoidance of tobacco, pollution, and climate factors	Prospective study	100,303	Cutaneous homeostasis regulation	Cold temperatures, low humidity, and low atmospheric pressure increased AD incidence rate	Yokomichi et al.
	Retrospective study	53,505	Cutaneous homeostasis regulation	Pre- and post-natal smoking significantly increased risk of AD and allergic asthma	Yoshida S et al.
Pet exposure	Meta-analysis	>10,000 patients	Cutaneous homeostasis regulation	Cat exposure slightly protective for asthma; dog exposure, on the other hand, slightly increases asthma; no effect on allergic rhinitis	Takkouche B et al.
	Cohort study	84,478	Cutaneous homeostasis regulation	Dog exposure slightly protective for AD and asthma; bird exposure slightly increases asthma	Pinot de Moira A et al.
Immunotherapy	Systematic review and meta-analysis	15 RCTs with 2703 patients	Cutaneous homeostasis regulation	Not conclusively effective for preventing the AM; small benefit in reducing asthma in patients with allergic rhinitis	Paller AS et al.
Water softeners	Prospective study	1303	Cutaneous homeostasis regulation	In children with filaggrin mutations, hard-water exposure increased AD risk ×3; softeners may help	Jabbar-López JK et al.
Vitamin D	Systematic review	1 RCT + 3 uncontrolled studies	Cutaneous homeostasis regulation	The evidence supporting sun exposure or vitamin D supplementation for the prevention of atopic dermatitis and other atopic signs is limited; therefore, these measures should not currently be recommended.	Yepes-Nuñez JJ et al.
Topical corticosteroids	Prospective study	74	Reduction of cutaneous immune response	Topical corticosteroid therapy normalized cytokine signatures in the peripheral blood of children with AD, suggesting a protective role vs other features of the atopic march.	McAleer MA et al.
Oral corticosteroids	—	—	—	No studies have evaluated the prevention of the atopic march with oral corticosteroids. Moreover, these agents may exacerbate disease flares.	Drucker AM et al.
Topical calcineurin inhibitors	Prospective study	1091	Reduction of cutaneous immune response	Pimecrolimus did not reduce AD or AM signs vs placebo	Schneider L et al.
Anti-IL-4/13 antibodies	Clinical trial meta-analysis	2296 dupilumab; 1229 placebo	Reduction of cutaneous immune response	Dupilumab significantly reduced allergic events; may help block the AM	Geba G et al.
Anti-IL-13 antibodies	Phase 2 trial	224	Reduction of cutaneous immune response	Tralokinumab did not significantly reduce eosinophilic inflammation in the bronchial lamina propria, blood, or sputum compared with placebo, although it did lower FeNO and IgE levels. These findings suggest that IL-13 is not a key driver of airway inflammation.	Russell RJ et al.

Table 2
(*Continued*)

Proposed measure	Evidence	*N*	Proposed mechanism of action	Results	Reference
JAK inhibitors	Narrative review	Not defined	Reduction of cutaneous immune response	A pathophysiological review proposing JAK inhibitors as a potential preventive therapeutic strategy for the atopic march. Real-world studies are still lacking.	Hee Kim Kim J et al.
Anti-IgE antibodies	Real-world clinical trial	Not defined	Reduction of cutaneous immune response	Assessment of asthma development in high-risk patients aged 2–4 years on omalizumab at standard doses for 2 years, followed by an additional 2-year observation period. Results are not yet available.	Phipatanakul W et al.
Anti-TSLP antibodies	Phase 2 trial	251	Reduction of cutaneous immune response	Target EASI not achieved on week 12; mechanism suggests possible role in AM prevention	Spergel J et al.
Holistic educational prevention programs	Real-world clinical trial	2226	Multidisciplinary intervention on various aspects of the etiopathogenesis of AD	Study designed to evaluate the effectiveness of a holistic prevention program (educational, pharmacologic, etc.) for atopic dermatitis in Chinese mothers. Results are not yet available.	Zhao M et al.

AD: atopic dermatitis; IL: interleukin; Ig: immunoglobulin; FeNO: fractional exhaled nitric oxide; TSLP: thymic stromal lymphopoietin.

(n = 27; 16.6%), and Catalonia (n = 24; 14.7%). Most respondents supported the existence of the AM (n = 148; 83.2%) vs 12.9% who had doubts and 2.3% who did not believe in its existence. In addition, nearly 90% agreed that AD is frequently the first sign of the AM. When asked about contributing factors in the AM, the most frequently cited were genetic factors (n = 166; 93.3%), followed by environmental (n = 163; 91.6%) and immunologic factors (n = 150; 84.3%). More than half of respondents (56.2%; n = 100) supported the use of preventive measures in young children with AD to reduce the risk of developing additional components of the AM. The most widely endorsed preventive measures were emollients (64%), avoidance of tobacco exposure (53.4%), and topical corticosteroids (43.8%). On the other hand, in infants without AD but at risk of developing it, 53.9% (n = 96) supported the use of preventive measures. In this scenario, the most frequently endorsed interventions were emollients with lipid combinations (73%), avoidance of tobacco and environmental pollution (68.1%), and breastfeeding (67.5%). Approximately two-thirds of respondents believed that greater AD severity increases both the likelihood and severity of AM signs. Finally, nearly all respondents (n = 157; 96.3%) agreed that dermatologists should play a central role in the management of AD and, when necessary, be responsible for referral to other specialists (allergists, pulmonologists, etc.). Since AD precedes other AM components, preventing AD—and, when present, initiating early treatment—may serve as a strategy to prevent the AM. Table 2 illustrates the main studies proposing methods to reduce AD or the AM.[2–5]

Therefore, according to the results of our survey, the main measures to limit AD and the AM would be emollients, breastfeeding, and avoidance of tobacco smoke. Evidence regarding emollients for preventing the AM is contradictory.[2,3] In contrast, several studies support breastfeeding and tobacco avoidance for AM prevention.[3,4] Regarding other potential preventive strategies, there is uncertainty on the utility of probiotics and prebiotics, early pet exposure, immunotherapy, or topical calcineurin inhibitors.[6] These variable findings mirror our survey results, in which only 20–40% of respondents indicated they would use probiotics, prebiotics, topical or oral corticosteroids, or biologic therapies targeting IL-4 or IL-4/13 to prevent the AM.

We are currently in a period of rapid expansion in knowledge related to the pathophysiology of AD and the AM. This knowledge has led to the development of new therapeutic targets (Supplementary Table 1).[7] The next major challenge is the ability to determine each patient's specific genotype and, consequently, to select individualized therapies.[8] It is anticipated that such targeted treatment will reduc AD and the associated processes of the AM.

In conclusion, most Spanish dermatologists believe in the existence of the AM and support the need for early preventive interventions. The main preventive measures identified were "plus" emollients, breastfeeding, and avoidance of tobacco exposure.

Conflict of interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ad.2025.104545.

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