

## ORIGINAL PAPERS

# Ambrosia pollen sensitization in allergic rhinitis patients from the central part of the Romanian Plain

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## ABSTRACT

**OBJECTIVE:** Because the prevalence and pattern of IgE-mediated hypersensitivity to inhalant allergens may vary between different European regions, our goal was to evaluate ragweed aeroallergen sensitization in allergic rhinitis patients from the central part of the Romanian Plain, located in the southern part of the country.

**MATERIAL AND METHODS:** In a two-year period we recruited patients with allergic rhinitis symptoms from the mentioned region and skin prick tests were performed using a panel of standardized allergen extracts, including individual tests for Asteraceae weed pollens, *Ambrosia artemisiifolia* var. *elatioides* (common ragweed) and *Artemisia vulgaris* (mugwort).

**RESULTS:** 447 patients with allergic rhinitis were enrolled, and 17.89% presented sensitization to at least one weed pollen. *Ambrosia artemisiifolia* is a prevalent source of weed aeroallergens involved in IgE-mediated sensitization. Patients with allergic rhinitis to common ragweed pollen tend to present more severe and more persistent forms of nasal allergy.

**CONCLUSIONS:** Ragweed is a highly allergenic wind-pollinated weed species with a considerable spreading potential in many European regions, including the Romanian Plain. There is a significant *Ambrosia* pollen sensitization proportion in allergic rhinitis patients from this part of Southern Romania.

**KEY WORDS:** *Ambrosia*, pollen, sensitization, allergic rhinitis

## INTRODUCTION

Allergic rhinitis is a highly prevalent disease in many European Union regions, but there are few epidemiological studies in Romania regarding the sensitization to different aeroallergens, especially in the south of the country<sup>1</sup>.

The Romanian Plain (*Câmpia Română*) is located in southern part of Romania. Part of the historical region of Wallachia, it is bordered by the Danube river in the east, south and west, and by the Getic Plateau and the Moldavian Plateau in the north. Bucharest, the capital city, is located in the central part of the Romanian Plain. This region has a temperate continental climate. The humid continental climate (Köppen climate classification) is a climatic region typified by large seasonal temperature differences, with warm to hot (and often humid) summers, and cold winters<sup>2</sup>.

Recent discussions regarding the climate changes suggest the potential of many significant effects on aeroallergen distribution and exposure, including weed pollens<sup>3</sup>. New allergenic pollen types, such as the common ragweed pollen, might appear in some European countries with allergological consequences<sup>4</sup>.

Common ragweed (*Ambrosia artemisiifolia*) is an annual

weed of North American origin. It has been present in Europe since 1860<sup>5</sup>, arriving probably through contaminated seed grains and hay from North America. *Ambrosia* seeds are very resistant and may remain viable for forty years in the soil seed banks.

The taxonomic name is *Ambrosia artemisiifolia* (Linnaeus), and synonyms include *Ambrosia elata* (Salisbury), *Ambrosia media* (Rydberg), and *Ambrosia artemisiifolia* var. *elatioides* (Descourt). Common names are *annual ragweed*, *common ragweed*, *short ragweed*, *small ragweed*, *bitterweed*, *roman wormwood* (English), *blackweed*, *roman bitterweed* (English-Canada), *petite herbe à poux* (French-Canada), *ambrosie annuelle*, *ambrosie à feuille d'armoise* (France), *ambrosia con foglie di atremisia* (Italy), *aufrechte ambrosie*, *beifußambrosie* (Germany), *aufrechtes traubenkraut* (German-Switzerland), *bynke-ambrosie* (Denmark), *parlagfü* (Hungary), *floarea pusteii*, *iarba pârloagelor* (Romania).

*Ambrosia artemisiifolia* is a herbaceous erect plant with many branches that can reach heights between 1-2 meters. The habitat occupied in Europe is along running waters, roadsides, ruderal sites and cultivated fields.

There are several highly infested European regions with *Ambrosia artemisiifolia*, and in the last decade its

abundance has been increasing in many others. The enormous spread potential of this wind-pollinated neophyte derives from the fact that one plant produces up to three thousand seeds a year, leading to quick invasion and making its control in agriculture difficult<sup>6,7,8</sup>.

Common ragweed has a high allergenic potential and *Ambrosia* pollen sensitization in Europe suggests an increasing prevalence<sup>9</sup>. Plants flower from July-August to September-mid October. Flowers are pollinated by wind. One gram of *Ambrosia artemisiifolia* pollen contains about 30-35 million pollen grains, and one well-grown plant can produce more than 45 grams of pollen in one year, depending on the quality of the habitat<sup>10</sup>. About 10 ragweed pollen grains *per* cubic meter of air provoke allergic rhinitis symptoms in sensitive subjects, compared to 50 grass pollen grains<sup>11</sup>. In Hungary, *Ambrosia* generates about half of the total pollen production<sup>12</sup>.

Moreover, a new allergen from *Ambrosia artemisiifolia* pollen, *Amb a 4*<sup>13</sup>, has homology to the major pollen allergen of *Artemisia vulgaris*, *Art v 1*, suggesting discussions regarding cross-reactivity or co-sensitization in some patients. Ragweed is easily mistaken with mugwort species *Artemisia vulgaris* and *Artemisia verlotiorum*, and the temporal distribution of pollen seasons is similar.

## MATERIALS AND METHODS

### Study design and patients

This clinical research performed in the Allergy Department, Hospital "Nicolae Malaxa" Bucharest, Romania, included patients with a history of rhinitis symptoms, with or without asthma and/or conjunctivitis concomitant manifestations. This two-year study, covering two consecutive *Ambrosia* pollen seasons for Central Europe, recruited patients with allergic rhinitis who lived for the last ten years predominantly in the central part of the Romanian Plain, especially in Bucharest and in places belonging to *Bucureștilor Plain*, a central subdivision of the Romanian Plain, including Târgoviștei, Ploieștilor, Mizil, Titu, Gherghiței, Călnăului and Vlășiei Plains. Written informed consent for allergy skin *prick* testing in the clinic was obtained for all patients.

### Allergen extracts and reagents

The following aeroallergen extracts were selected as standard *prick* testing panel: house dust mites from the *Pyroglyphidae* family (Order *Astigmata*): *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*; pet animals epithelia (Order *Carnivora*): cat (*Felis domesticus*), dog (*Canis familiaris*); moulds from the Phylum *Ascomycota*: *Alternaria*, *Cladosporium*, *Aspergillus*, *Penicillium*, and *Zygomycota*: *Mucor*; spring tree pollens from the *Betulaceae* family (*Betula*, *Alnus*, *Corylus*); humid-zone tree pollens from *Salicaceae* family: *Salix*, *Populus*, and *Oleaceae* family: *Fraxinus*; grass (*Poaceae*/*Gramineae*) pollens, including *Agrostis stolonifera*, *Anthoxanthum odoratum*, *Arrhenatherum elatius*, *Dactylis glomerata*, *Festuca rubra*, *Holcus lanatus*, *Lolium perenne*,

*Phleum pratense*, *Poa pratensis*, *Secale cereale*; weed pollens from the *Asteraceae/Compositae* family: *Ambrosia elatior* (*Ambrosia artemisiifolia* var. *elatior*), *Artemisia vulgaris*, and from other plant families: *Rumex*, *Plantago*, *Urtica*.

Standardized cutaneous extracts for *prick* tests were applied. Histamine hydrochloride (10 mg/mL) was used as a positive control, while a phenolated glycerosaline solution as a negative control.

### Allergy skin prick tests

The allergy *prick* testing consisted of pricking the volar forearm skin with adequate lancets through individual drops of allergen extracts. The mean wheal size was recorded after 15 minutes and a skin *prick* test was considered positive when the induced wheal size is minimum 3 mm larger than the negative control. Skin tests were performed by specialists on healthy patient skin in order to avoid not interpretable results. Because antihistamine treatment may significantly reduce responses to skin *prick* tests, rapid acting antihistamines were withdrawn for at least 48 hours, while ketotifen, hydroxyzine, and tricyclic antidepressants for at least two weeks before testing. The administration of glucocorticosteroids, when the dose was limited to a maximum daily dose equivalent to 30 mg prednisolone, or leukotriene modifiers does not significantly modify reaction to skin tests.

Statistical analysis and data collection were performed using Microsoft Office Excel.

## RESULTS

We recruited 447 patients with allergic rhinitis, from which 245 presenting only rhinitis symptoms without asthma, and 202 having the combined allergic rhinitis and asthma syndrome.

House dust mites (*Dermatophagoides pteronyssinus* and/or *Dermatophagoides farinae*) and grass pollens are the most relevant aeroallergens in these subjects, being involved in sensitization of 48.99% and 47.42% of patients respectively.

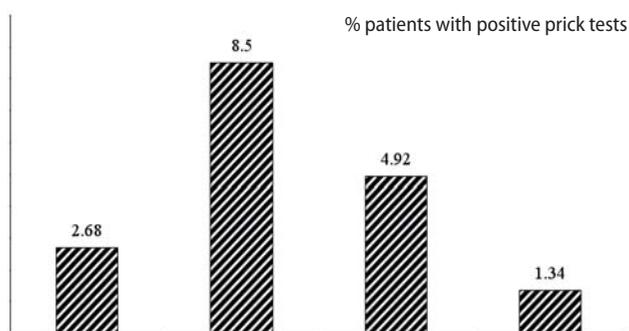
Sensitization to at least one weed pollen (17.89%) and to cat epithelia (23.71%) is also important.

Allergic sensitization to moulds (11.4%), tree pollens (10.96%) and dog epithelia (6.04%) is less frequent.

Regarding IgE-sensitization to weed pollens, *Artemisia vulgaris* and *Ambrosia artemisiifolia* var. *elatior* were the most prevalent aeroallergens among allergic rhinitis patients, being responsible in 13.42% and 11.18% of patients. Several cases of sensitization to *Plantago lanceolata* and *Rumex acetosa* pollens were recorded (Figure 1).

*Ambrosia* pollen sensitized patient characteristics are presented in Table 1. There was no significant difference between male and female patients in the rate of sensitization to *Ambrosia artemisiifolia*.

An important aspect revealed by our study is represented by the fact that patients with allergic rhinitis sensitized to this weed pollen tend to present more severe and more persistent forms of nasal allergy.



**Figure 1** Sensitization to weed pollens in patients with allergic rhinitis

Regarding allergic comorbidities, from patients with positive skin *prick* tests to *Ambrosia* pollen, 60% had rhinitis without asthma, 38% presented allergic rhinitis and asthma symptoms, and 34% had concomitant allergic conjunctivitis. Only two patients presented associated pollen-food syndrome.

Finally, we have to discuss the aspects of polysensitization in patients with positive *prick* test to *Ambrosia* pollen extract. 76% of patients present also positive tests to another *Asteraceae* weed pollen, *Artemisia vulgaris*, data that raise questions regarding cross-reactivity versus co-sensitization. Other important concomitant sensitizations in these patients are represented by positive *prick* tests to other outdoor aeroallergens (grass pollens, 62%; tree pollens, 36%) and to indoor allergens (*Pyroglyphidae* house dust mites, 26%; cat epithelia, 28%).

## DISCUSSIONS

Many studies have reported the prevalence of aeroallergen sensitization using skin *prick* testing<sup>14</sup>. Allergy skin *prick* testing is the standard method to assess IgE-mediated sensitization to inhalant allergens, commonly used because it is rapid, accurate and reproducible<sup>15</sup>. But we have to recognize that patient groups studied in clinical studies are not very representative of the general population, reflecting patterns of referral and differences in health services.

Variation in the rates of sensitization in various European regions is probably an important factor for different rates of allergic disease in some European countries. Climatic and agricultural changes are also influencing sensitization to pollen aeroallergens from weeds that have expanded in recent years<sup>16</sup>. Allergenic pollen of *Ambrosia artemisiifolia* can interact with environmental aspects, such as pollution and climate changes, in a synergic way, increasing the risks to public health.

Among the more than thirty species of the genus *Ambrosia* from *Asteraceae* family, widely spread around the world, *Ambrosia artemisiifolia*, *Ambrosia trifida* and *Ambrosia psilostachya* were reported in Europe<sup>17</sup>. *Ambrosia artemisiifolia* is the most invasive of all the species, being included on The Official List of Quarantine Weeds. Besides the fact that this weed causes significant agricultural damages, the aeroallergens spread during the quite long pollen

**Table 1**  
**Ambrosia pollen sensitized patient characteristics**

Age range	5-62 years
Age group most affected	31-40 years (30%)
Gender Female (%) vs Male (%)	52 % vs 48 %
Location Urban (%) vs Rural (%)	80 % vs 20 %
Evolutionary forms of allergic rhinitis (%)	Intermittent (8%); Persistent (92%)
Severity forms of allergic rhinitis (%)	Mild (22%); Moderate-severe (78%)

season may cause severe respiratory allergies.

In Europe, some areas are heavily infested, such as the Rhone Valley and the Burgundy, expanding towards the northwestern regions of France<sup>18</sup>, and in the Po Valley, mainly the Lombardy region, in Italy<sup>19</sup>. In Belgium, Switzerland, Bavaria in southeastern Germany, Czech Republic and Austria, many foci, mainly in urban areas, were reported. It seems that ragweed is not yet fully established in many of these countries<sup>6,7,8</sup>. In Hungary, *Ambrosia* became instead the most important agricultural weed during the last twenty years. Almost 80% of the agricultural surface is infested<sup>20</sup>. This country has shown great spreading of ragweed since the early nineties, when the abandonment of large collective agriculture resulted in uncultivated fields with *Ambrosia* invasion<sup>9</sup>. In Serbia, ragweed is a dominant weed in soybean and sunflower crops, while in Croatia, *Ambrosia* is abundant in Slavonia (a region in eastern part of the country<sup>21</sup>).

In Romania, *Ambrosia artemisiifolia* was first identified in Banat (at Orșova railway station) in 1908<sup>22,23,24</sup>. Years later it was reported in 1943 in Transilvania, in Donat-Cluj, Maramureș<sup>25</sup>, Oltenia<sup>26</sup>, Moldova<sup>27</sup> Muntenia<sup>28</sup>, Crișana<sup>29</sup>, and Dobrogea<sup>30</sup>. Although until now the presence of ragweed it was indicated in all Romanian regions, the spread of this species through the country is still incompletely known<sup>31</sup>. Recently, *Ambrosia artemisiifolia* was studied in Bihor<sup>32</sup>. As a consequence of the invasive character of the species and the spread along the roads, *Ambrosia* has been more extensively spreading towards the south and the centre of Romania, the last reports coming from Bărăgan and the Southern part of Moldova<sup>33</sup>. Analysis of the ragweed pollen counts using a volumetric method in Timișoara, in the season of 2004, revealed that the highest concentration was 220 pollen grains per cubic meter of air per day. In September, 65.71% of the total aeropollen concentration is due to *Ambrosia*<sup>34</sup>.

Our findings regarding the proportion of sensitization using skin *prick* tests in allergic rhinitis patients from the central part of the Romanian Plain are in concordance with reported data from studies performed in other regions of Central Europe<sup>16</sup>. *Ambrosia* pollen has reached at this moment the threshold for high prevalence allergen in the European Union. The prevalence for ragweed pollen sensitization is above 2.5% in many European countries,

except Finland (2.4%). While Hungary is expected to show high prevalence of ragweed sensitization, several central and western European countries, such as Germany and the Netherlands show unexpectedly high sensitization rates (14.2% and 15.2% respectively). Denmark is also heavily affected, with a prevalence of 19.8%<sup>9</sup>.

Because ragweed and mugwort have nearly identical flowering periods, and clinical and serological studies show that ragweed and mugwort sensitization are often associated, there are questions regarding co-sensitization or co-recognition, and possible decision problems in patients for whom allergen specific immunotherapy is indicated<sup>35</sup>. In addition, concomitant sensitization to mugwort pollen could lead to overestimation of the sensitization rate to ragweed pollen due to cross-reactivity<sup>36</sup>.

Moreover, high sensitization rates to *Ambrosia* pollen found in patients from one region may be due hypothetically either to the weed dissemination in that area or to a long distance travel of the ragweed pollen. Several Italian studies regarding this aspect must be discussed. Ragweed was first found in Italy in the regions of Piemonte and Liguria in 1902. The most affected regions of Italy in our days are Lombardia and Friuli Venezia-Giulia, in the northeast<sup>37,38</sup>. No published data exist on the distribution of *Ambrosia* plants in the central part of Italy, but *Ambrosia* pollen data were collected in Florence and Pistoia, for a six-year period, and the relationship between pollen counts and local ground prevalent wind directions was evaluated. Weather conditions were also evaluated on a large-scale circulation pattern, using air mass trajectories and weather maps. This study suggested as a possible source of *Ambrosia* pollen, an area in southern Hungary<sup>39</sup>. The Pannonian Plain is also a source of ragweed pollen in the Balkan Peninsula<sup>40,41</sup>. But recent findings in 2010 revealed that long-distance transport of ragweed pollen does not induce new sensitizations in the short term<sup>42</sup>.

## CONCLUSIONS

Common ragweed (*Ambrosia artemisiifolia*) is a highly allergenic wind-pollinated weed species with a considerable spreading potential in many European regions, including the Romanian Plain. There is a significant ragweed pollen sensitization proportion in allergic rhinitis patients from this part of Southern Romania.

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