

LITERATURE REVIEW

European standards and North American practice parameters for skin prick testing panels in allergic rhinitis and asthma

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ABSTRACT

According to the Global Allergy and Asthma European Network (GA²LEN), a pan-European skin prick test panel for the diagnosis of allergic rhinitis and asthma includes 18 aeroallergen extracts, supplemented if necessary for regional or for particular patient needs, while the Allergen Subcommittee and Immunotherapy Committee of the American Academy of Allergy, Asthma and Immunology (AAAAI) selected 36 major clinically relevant aeroallergens for North America.

KEYWORDS: aeroallergen extracts, skin prick tests, allergic rhinitis and asthma

INTRODUCTION

Skin prick testing is an important reliable method to diagnose IgE-mediated allergic rhinitis, rhinoconjunctivitis and asthma. This widely used *in vivo* assessment, indicated, performed and interpreted by allergy practitioners, is minimally invasive, has immediately available and reproducible results, and provides evidence for aeroallergen sensitization. Skin prick tests are highly specific and sensitive for the diagnosis of respiratory allergies. The positive predictive value to diagnose allergic rhinitis increases to 97-99% if allergy skin prick testing is utilized^{1,2}.

According to the Global Allergy and Asthma European Network (GA²LEN), a **pan-European** skin prick test panel for the diagnosis of allergic rhinitis and asthma includes 18 aeroallergen extracts, and these allergens can be supplemented, if necessary, for regional or for particular patient needs². The Allergen Subcommittee and Immunotherapy Committee of the American Academy of Allergy, Asthma and Immunology (AAAAI) previously compiled and selected 36 key aeroallergens in **North America**³.

PARAMETERS FOR SKIN PRICK TESTING PANELS

The **aeroallergen extracts** included in the European standards and North American practice parameters skin prick panels are of plant, fungal and animal origins, as described below¹⁻⁸.

Aeroallergen extracts of animal origin included in these standards belong to *Arthropoda* phylum, *Astigmata* order (house dust mites from the *Pyroglyphidae* family), *Blattodea* order (*Ectobiidae* family from the *Insecta* class), and *Carnivora* order pet animals (*Felidae* and *Canidae* families).

Allergen extracts of fungal origin mentioned in the European and North American recommendations belong to moulds from the phylum *Ascomycota* (*Dothideomycetes* and *Eurothiomycetes* classes).

Pollen from trees or shrubs from *Fagales* order (*Betulaceae* and *Fagaceae* families), *Malpighiales* order (*Salicaceae* family), *Lamiales* order (*Oleaceae* family), *Proteales* order (*Platanaceae* family), *Sapindales* order (*Aceraceae* family), *Rosales* order (*Moraceae* and *Ulmaceae* families), and *Coniferales* order (*Cupressaceae* family), grass pollen from *Poales* order, *Poaceae*

(gramineae) family (*Pooideae*, *Chloridoideae* and *Panicoidae* subfamilies), and pollen from weeds belonging to *Asterales* order (*Asteraceae* / *Compositae* family), *Rosales* order (*Urticaceae* family), *Lamiales* order (*Plantaginaceae* family), *Caryophyllales* order (*Polygonaceae* and *Amaranthaceae* / *Chenopodiaceae* families) are included in these panels.

Weather and climate change the impact of aeroallergens in Europe and North America^{6,9-12}, particularly pollens and moulds. Climatological regimes (warm or cold anomalies, dryer and wetter periods), along with meteorological factors (temperature, wind speed, humidity, rain, thunderstorms), are involved. It is known that human activities increase atmospheric greenhouse gases, such as carbon dioxide. Over the last decades, raised temperatures and atmospheric carbon dioxide concentration have impacted plant and pollen distribution, and induced changes in the quantitative production and dispersion of pollen, pollen season periods and allergen content of pollen grains, which may be region- and species-specific. During the last decades, several changes described below were observed^{6,13-24}. Some anemophilous plants pollinate earlier, the duration of the pollen season is extended in some species, and there are more days with greater airborne pollen grain concentrations. Production of allergenic pollen of some weeds is increased with high ambient carbon dioxide levels. Moreover, higher daily temperatures may increase pollen allergenicity. Climate changes may also lead regionally to the extinction of some plant species and to the proliferation of non-native alien species with allergenic pollens.

According to standardized skin prick testing performed at excellence centres in European countries, the Global Allergy and Asthma European Network (GA²LEN) in association with the European Academy of Allergy and Clinical Immunology (EAACI) suggested a panel of aeroallergens for skin prick testing in all European patients. As mentioned before, allergen extracts can be supplemented if necessary for regional or for particular patient needs². The American Academy of Allergy, Asthma and Immunology (AAAAI) previously selected a double number of key aeroallergens in North America compared with actual European standard. For an individual patient, the choice of allergen extracts for skin prick testing should be guided primarily by the patient's detailed history and physical examination, by the sciences of aerobiology, botany, mycology, arthropod biology, and the contact with companion animals. In North America, it is not possible to elaborate a universal list of appropriate aeroallergens for skin prick testing in all patients. The selection of allergen extracts for *in vivo* testing reflects the physician's knowledge, training and experience³.

Aeroallergens of animal origin, such as those from house dust mites, domestic pets and insects, are important indoor allergens involved in allergic rhinitis and asthma as discussed below^{1-3,6-8,17,25-30}. Spending more time inside buildings (at work and at home) creates conditions for more exposure to multiple indoor aeroallergens. House dust includes various organic and inorganic matter, including dust mites, animal dander, cockroach debris and other insect parts, natural and synthetic fibers, but also moulds, pollen grains and inorganic debris. House dust mites are the most common and important indoor allergens.

House dust mites belong to the phylum of *Arthropoda* (class *Arachnida*, subclass *Acari*), *Astigmata* order, *Pyroglyphidae* family, and the most important species are *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, and this is the reason why allergen extracts of these domestic mites are included in European standards and North American practice parameters skin prick panels. Pyroglyphid mites are highly cross-reactive, but they seem to have a limited cross-reactivity with storage mites found in farms, and *Blomia tropicalis*, significant mite species in tropical or subtropical areas. These non-pyroglyphid mite extracts are used only in selected cases, and are not included in pan-European and North American screening panels.

The most important urban indoor inhalant insect allergens in Europe and North America derive from domestic **cockroach** species, especially *Blattella germanica* (German cockroach), this one being included in North American and European standard panels.

Aeroallergens of small **mammal pets** from the *Carnivora* order (epithelia/dander) belong to the *Felidae* family: *Felis catus* syn. *Felis domesticus* (domestic cat) and *Canidae* family: *Canis lupus familiaris* syn. *Canis familiaris* (dog). Both are included in European and North American practice parameters skin prick panels. In selected cases, other mammalian allergen extracts may be used (horse, domestic guinea pig, hamster, rabbit).

Aeroallergens of fungal origin involved in allergic sensitization in rhinitis and asthma^{1-3,6-8,17,31-34} are moulds belonging to the phylum *Ascomycota*, class *Dothideomycetes*, *Pleosporaceae* family: *Alternaria alternata* syn. *Alternaria tenuis*, *Davidiellaceae* family: *Cladosporium herbarum*, *Cladosporium cladosporioides* (both types being predominantly outdoor moulds, with dry spores), and class *Eurothiomycetes*, *Trichocomaceae* family: *Aspergillus fumigatus* (predominantly indoor mould). *Alternaria alternata*, *Cladosporium* spp and *Aspergillus fumigatus* are included in North American and European standard panels. The North American practice parameters skin prick panel includes in addition fungi belonging to class *Eurothiomycetes*, *Tricho-*

comaceae family: *Penicillium chrysogenum* syn. *Penicillium notatum*, *Penicillium expansum*, and dematiaceous fungi from class *Dothideomycetes*: *Bipolaris/Curvularia/Drechslera spicifera* syn. *Helminthosporium spiciferum*, and *Epicoccum nigrum* syn. *Epicoccum purpurascens* (predominantly indoor moulds).

Pollens of anemophilous plants (wind-pollinated plants) are important outdoor sources of aeroallergens, exposure to pollen grains depending of the type of plant, wild spread or cultivation, geographic area, altitude, air currents, temperature, precipitation and other weather events, and pollen extracts for European and North American skin testing panels are discussed below^{1-3,6-8,17,35-39}.

In the European standard panel, pollen extracts from **trees** (mostly) or shrubs (some) belong to the class *Magnoliopsida* (dicotyledons), *Betulaceae* family: *Betula pendula* syn. *Betula verrucosa* (European silver birch) or *Betula pubescens* syn. *Betula alba* (European white birch), *Alnus glutinosa* (European black alder) or *Alnus incana* (grey alder), and *Corylus avellana* (European hazel); the *Oleaceae* family: *Olea europaea* (common olive) or *Fraxinus excelsior* (European ash); *Platanaceae* family: *Platanus acerifolia* syn. *Platanus vulgaris* (London plane tree or maple leaf sycamore); and to the class *Coniferopsida* (gymnospermae) from the *Cupressaceae* family: *Cupressus sempervirens* (Mediterranean cypress). In the North American list of major clinically relevant aeroallergens, *Magnoliopsida* trees/shrubs pollen extracts belong to the *Betulaceae* family: *Betula papyrifera* (paper birch), *Alnus rubra* (red alder); *Fagaceae* family: *Quercus alba* (white oak), *Quercus rubra* (Northern red oak); *Juglandaceae* family: *Juglans nigra* (black walnut), *Carya illinoensis* (pecan tree); *Salicaceae* family: *Populus deltoides* (Eastern cottonwood); *Oleaceae* family: *Fraxinus americana* (white ash), *Olea europaea* (common olive); *Platanaceae* family: *Platanus occidentalis* (American sycamore); *Aceraceae* family: *Acer rubrum* (red maple) or *Acer negundo* (boxelder maple); *Moraceae* family: *Morus rubra* (red mulberry); and *Ulmaceae* family: *Ulmus americana* (American elm), *Ulmus pumila* (Siberian elm) or *Ulmus parvifolia* (Chinese elm). *Juniperus ashei* (mountain cedar) pollen extract included in the North American list is a standard of the *Cupressaceae* family.

Grass pollen is produced in Europe by wild or cultivated herbaceous plants belonging to class *Liliopsida* (monocotyledons), *Poales* order, *Poaceae* family (gramineae). The European standards for the skin prick testing recommend a pollen mix of five grasses belonging to *Pooideae* subfamily. *Phleum pratense* (timothy grass), *Dactylis glomerata* (orchard grass or cock's foot grass), *Poa pratensis* (smooth meadow grass or bluegrass), *Lolium perenne* (perennial ryegrass) and *Anthoxanthum odoratum* (sweet vernal grass) are wide-

spread in the temperate zone; their pollen represents a substantial proportion of grass pollen grains to which European and American rhinitis patients are sensitized, and their pollen extracts are included in the grass pollen mixes used for skin prick testing. Other *Pooideae* grasses included in some mixes are *Festuca pratensis* syn. *Festuca elatior* (meadow fescue), *Holcus lanatus* (velvet grass or Yorkshire fog), *Agrostis capillaris* syn. *Agrostis vulgaris* (bent grass), and *Arrhenatherum elatius* syn. *Helictotrichon elatius* (oat grass). Allergists should also consider that the grass pollen individual extracts or mixes selected for warm temperate and subtropical areas in Europe should cover the regionally most dominant grasses, including those which are not cross-reactive with *Pooideae*, such as *Paspalum notatum* (Bahia grass) or *Cynodon dactylon* (Bermuda grass). In the panel of clinically relevant aeroallergens of North America, grass pollen extracts belong to the *Pooideae* subfamily: *Phleum pratense* (timothy grass), *Lolium perenne* (ryegrass), *Festuca elatior* (meadow fescue), *Chloridoideae* subfamily: *Cynodon dactylon* (Bermuda grass), and *Panicoideae* subfamily: *Sorghum halepense* (Johnson grass), *Paspalum notatum* (Bahia grass).

In Europe, the skin prick panel includes the most important **weed** pollen extracts involved in allergic rhinitis belonging to herbaceous plants from the class *Magnoliopsida* (dicotyledons), *Asterales* order, *Asteraceae* / *Compositae* family: *Ambrosia artemisiifolia* var. *elatior* (short ragweed or common ragweed), *Artemisia vulgaris* (mugwort or common wormwood), and *Rosales* order, *Urticaceae* family: *Parietaria officinalis* (wall pellitory or lichwort) or *Parietaria judaica* (wall pellitory or sticky weed). Weed pollen from *Amaranthaceae/Chenopodiaceae* family, *Chenopodium album* (lamb's quarter or fat hen white goosefoot) and *Salsola kali* (Russian thistle or common saltwort) are important pollen aeroallergens in Spain and semi-arid areas. Some experts mention adding *Plantago lanceolata* (narrow-leaved plantain) from *Plantaginaceae* family, to *Chenopodium* sp and *Salsola kali*, for routine aeroallergen regional panels in countries like Turkey, Spain, Italy and Greece. It is important to test these allergens depending on local climate, but possibly not to use them in a pan-European skin test battery. Moreover, the GA²LEN skin tests may be extended to other parts of the world to assess the common panel for skin testing. The North American Practice Parameters skin prick panel includes weed pollen extracts belonging to *Asterales* order, *Asteraceae* family: *Ambrosia artemisiifolia* (short ragweed), *Artemisia vulgaris* (mugwort); *Lamiales* order, *Plantaginaceae* family: *Plantago lanceolata* (narrow-leaved plantain); *Caryophyllales* order, *Polygonaceae* family: *Rumex acetosella* (sheep sorrel) and *Amaranthaceae* family: *Amaranthus retroflexus* (redroot pigweed), *Salsola kali* (Rus-

sian thistle or common saltwort) and *Bassia scoparia* syn. *Kochia scoparia* (burning bush).

It is important to underline that the American Academy of Allergy, Asthma and Immunology (AAAAI) selected the above mentioned 36 major clinically relevant aeroallergens for North America³, while in the United States, according to the third National Health and Nutrition Examination Surveys (NHANES), few aeroallergen extracts were previously used for skin testing screening: *Dermatophagoides* spp (dust mites), *Blattella germanica* (German cockroach), *Felis domesticus* (cat), *Alternaria alternata*, and pollen from *Quercus alba* (white oak), *Lolium perenne* (perennial rye), *Cynodon dactylon* (Bermuda grass), *Ambrosia eliator* (short ragweed), *Salsola kali* (Russian thistle)⁴⁰.

CONCLUSIONS

In **conclusion**, allergists and ENT specialists from the Northern Hemisphere must be informed regarding the European standards and North American practice parameters for skin prick panels of aeroallergens of plant, fungal and animal origins, used in the diagnosis of allergic rhinitis with asthma. The GA²LEN position statement and AAAAI practice parameters regarding skin prick testing to aeroallergens were received with great interest by specialists interested in the updated diagnosis of respiratory allergies.

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