

3g

GRASS POLLEN ALLERGENS

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BOTANICAL RELATIONSHIP

Grasses are ubiquitous plants in most parts of the world. The grass family (*Poaceae*) includes >600 genera and >11,000 recognized species with a wide distribution. Over 95% of allergy-relevant grass species belong to three sub-families; *Pooideae*, *Chloridoideae* and *Panicoideae* (Figure 1 and 2).

GLOBAL DISTRIBUTION

Depending on climate and geography, grass pollens represent major contributors of airborne allergens during spring as well as summer. They grow on all continents and represent 25% to 35% of the earth's vegetation. *Pooideae* dominate temperate climate zones; *Chloridoideae* cover the North American, African and Australian continents and *Panicoideae* grow in tropical and subtropical environments of Asia, Australia, Africa and South America (Figure 3).

ALLERGENS OF GRASS POLLEN

Grass pollen allergens are grouped according to their protein structure and function (Table 1). They are named according to the official nomenclature (www.allergen.org), i.e.: Phl p 1 = grass group 1 allergen from *Phleum pratense* (timothy grass). Ten designated groups

KEY MESSAGES

- Pollens from diverse grass plants are main contributors to seasonal inhalant allergies worldwide
- Grass group 1 and 5 allergens represent highly cross-reactive and potent major allergens, group 5 present only in temperate climate grasses (*Pooideae*)
- Depending on climate and region, global sensitization rates to grass pollen vary between 1% to 30% of the general population
- Strong evidence supports specific immunotherapy with grass pollen extracts

consist of major (>50% sensitization rate, SR) and minor allergens (<50% SR). Due to their abundance and potency, grass group 1 and 5 allergens are considered immunodominant major *Pooideae* pollen allergens (Figure 4). While group 5 allergens are restricted to the *Pooideae* subfamily, group 1 allergens are present throughout the subfamilies of *Poaceae*. In contrast, pan-allergens profilin (group 12) and polcalcin (group 7) contribute to ubiquitous cross-reactivity between grass, tree and weed pollen in 10 – 15% of grass pollen sensitized subjects. Present concepts of homologous allergen groups, are based on similar biochemical composition, homology and immune cross-reactivity reflecting in most cases their close taxonomic relationship and have

been adopted by the European Medicines Agency (EMA).

CLINICAL ALLERGY BASED ON SENSITIZATIONS

Sensitizations to grass pollen allergens, indicated by grass pollen allergen (extract) positive skin test or specific IgE, reflect regional plant distribution and pollen exposure. Population based sensitization rates are mainly available for Europe and the US and vary considerably between and within countries (Figure 5). Grass pollen allergy is a global problem (Figure 5c). At least half of grass pollen allergen sensitized subjects will suffer from symptoms of allergic rhinoconjunctivitis and/or bronchial asthma, particularly during the warm seasons in moderate climate regions.



Figure 1 Pictures of different grass species and their pollen : a - Timothy grass (*Phleum pratense*), subfamily Pooideae; b-Bermuda grass (*Cynodon dactylon*), subfamily Chloridoideae; c - Bahia grass (*Paspalum notatum*), subfamily Panicoideae.

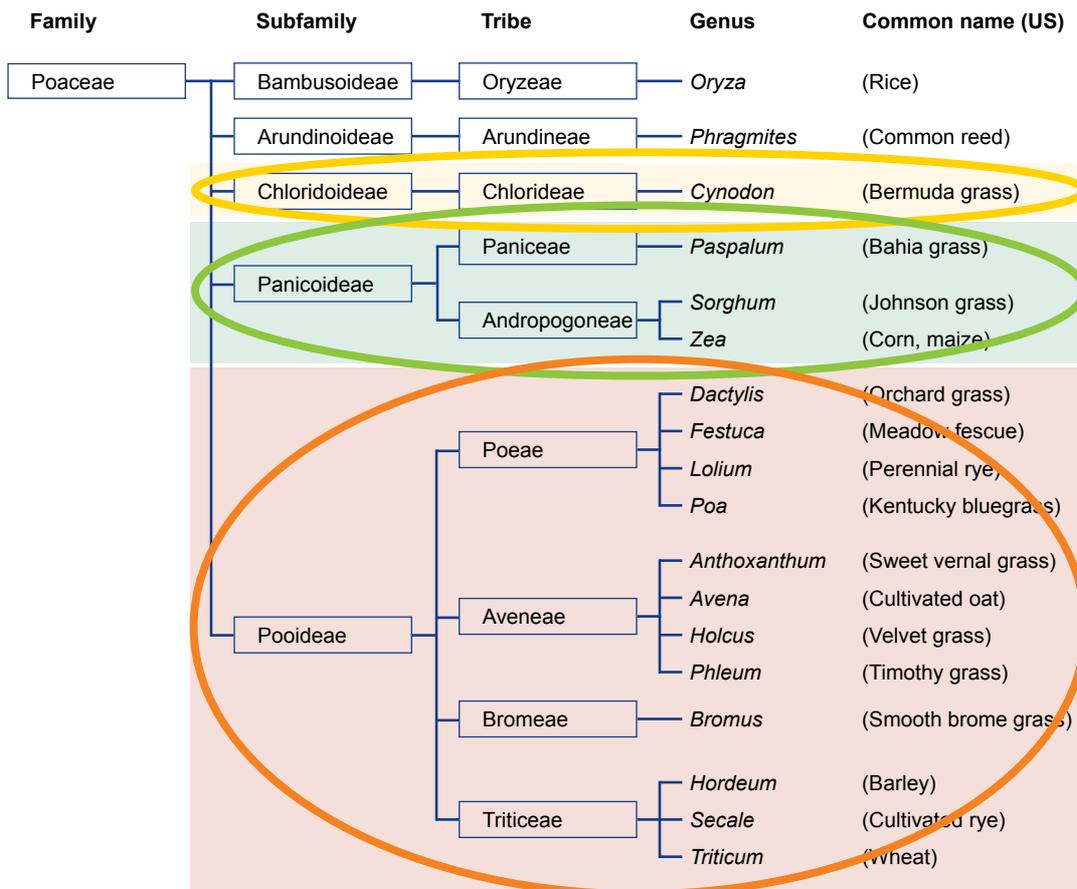


Figure 2 Taxonomy of grasses (important subfamilies within colored boxes). Overlapping circles (colored lines) indicate partial cross-reactivity between neighboring subfamilies (modified from (2), (4) and (10)).

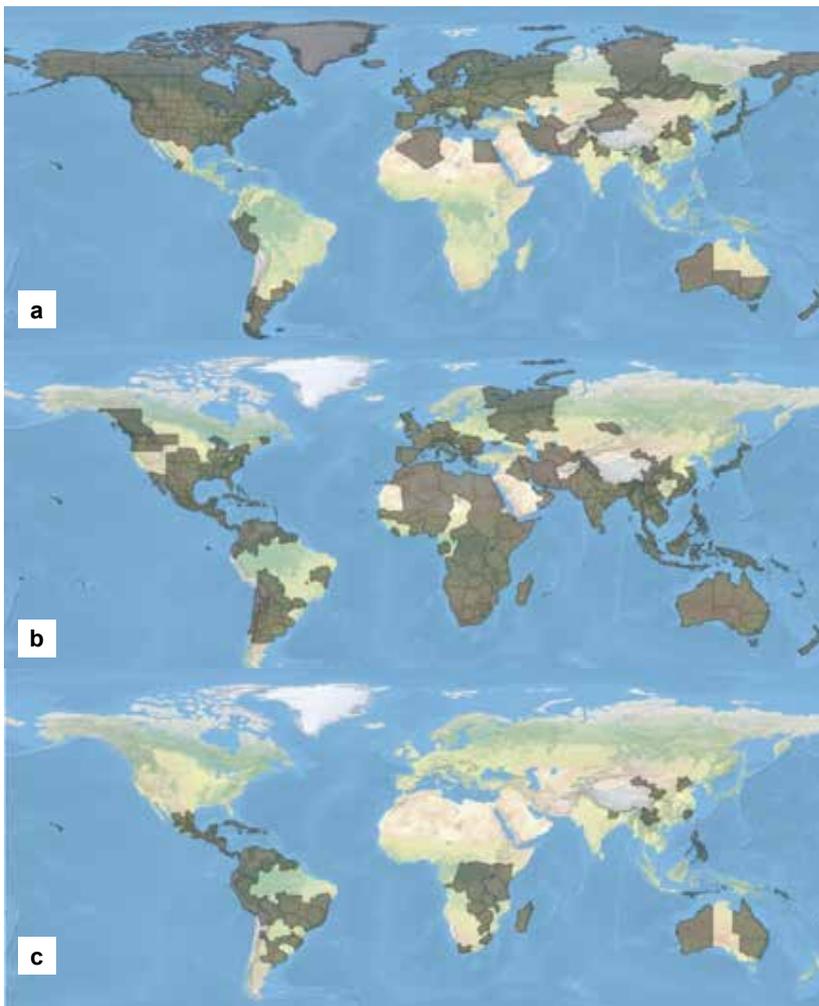


Figure 3 Global distribution of selected grass species (10): a- Timothy grass (*Phleum pratense*), subfamily Pooideae; b-Bermuda grass (*Cynodon dactylon*), subfamily Chloridoideae; c-Bahia grass (*Paspalum notatum*), subfamily Panicoideae.

DIAGNOSIS AND TREATMENT

Positive skin prick tests and elevated specific serum IgE to grass pollen preparations indicate allergic sensitizations, being clinically relevant only in case of corresponding symptoms. Measuring IgE to major allergens (i.e. Phl p 1 and 5) increases analytical specificity for temperate grass pollen allergy, particularly in case of sensitizations to cross-reactive pollen-panallergens. Specific immunotherapy is most successfully applied for at least three years by subcutaneous injections or sublin-

gual home use of droplets or tablets with monopreparations of one grass species, but also grass mixes (mainly Pooideae), with or without adjuvants.

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TABLE 1

| Grass pollen allergen groups | | | | | |
|------------------------------|--|------------------------|----------------------------------|--|----------------------|
| Allergen group | Biochemical function | Molecular-weight [kDa] | Member in <i>Phleum pratense</i> | Features | IgE reactivity |
| 1 | β-expansin | 27 - 35 | Phl p 1 | Glycoprotein, major grass pollen allergen, produced by every grass species | >90% 85-99% |
| 2 | Unknown | 11 | Phl p 2 | highly homologous to group 3 and C-terminal portion of group 1 allergens | 35 - 50% 40-60% |
| 3 | Unknown | 11 - 14 | Phl p 3 | highly homologous to group 2 and C-terminal portion of group 1 allergens | 35 - 70% 57-67% |
| 4 | Oxidoreduc-tase | 50 - 60 | Phl p 4 | Glycoprotein, Berberine bridge enzyme family member, plant pathogen response system | 50 - 75% 45 - 88% |
| 5 | Unknown | 27 - 35 | Phl p 5 | found in Pooideae grass species, associated with submicronic cytoplasmic starch particles | 65 - 85% 50 - 88% |
| 6 | Unknown | 12 - 13 | Phl p 6 | homologous to internal group 5 sequences, only in <i>Anthoxanthum odoratum</i> , <i>Phleum pratense</i> and <i>Poa pratensis</i> | 60 - 70% 45 - 70% |
| 7 | Polcalcin, Ca ⁺⁺ -binding protein | 8 - 12 | Phl p 7 | Panallergen, dimer assembly in grass pollen, broad pollen-related crossreactivity | 5 - 35% 2 - 12% |
| 11 | Ole e 1-related protein | 16 - 20 | Phl p 11 | Glycoprotein, similar structure to pollen allergens from olive tree pollen (Ole e 1) and lamb's quarter (Che a 1) | 18 - 56% |
| 12 | Profilin | 13 - 14 | Phl p 12 | Panallergen, highly conserved, broad pollen and plant food-related crossreactivity | 10 - 40% 9 - 32% |
| 13 | Polygalacturo-nase | 45 - 60 | Phl p 13 | Glycoprotein, susceptible to protease degradation | 30 - 40% 36 - 56% |

Modified from (1). Due to their taxonomic and biochemical relationship, many grasses contain similar allergens grouped according to shared amino acid sequences. Specific allergens from timothy grass (*Phleum pratense*, see middle column) are given as examples of the listed grass allergen groups.

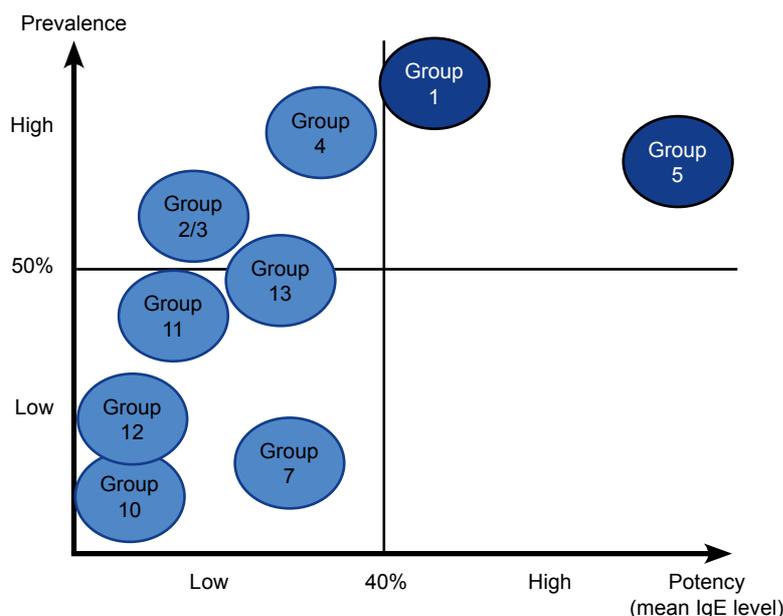


Figure 4 Involvement of grass pollen allergens in patient sensitization (3).

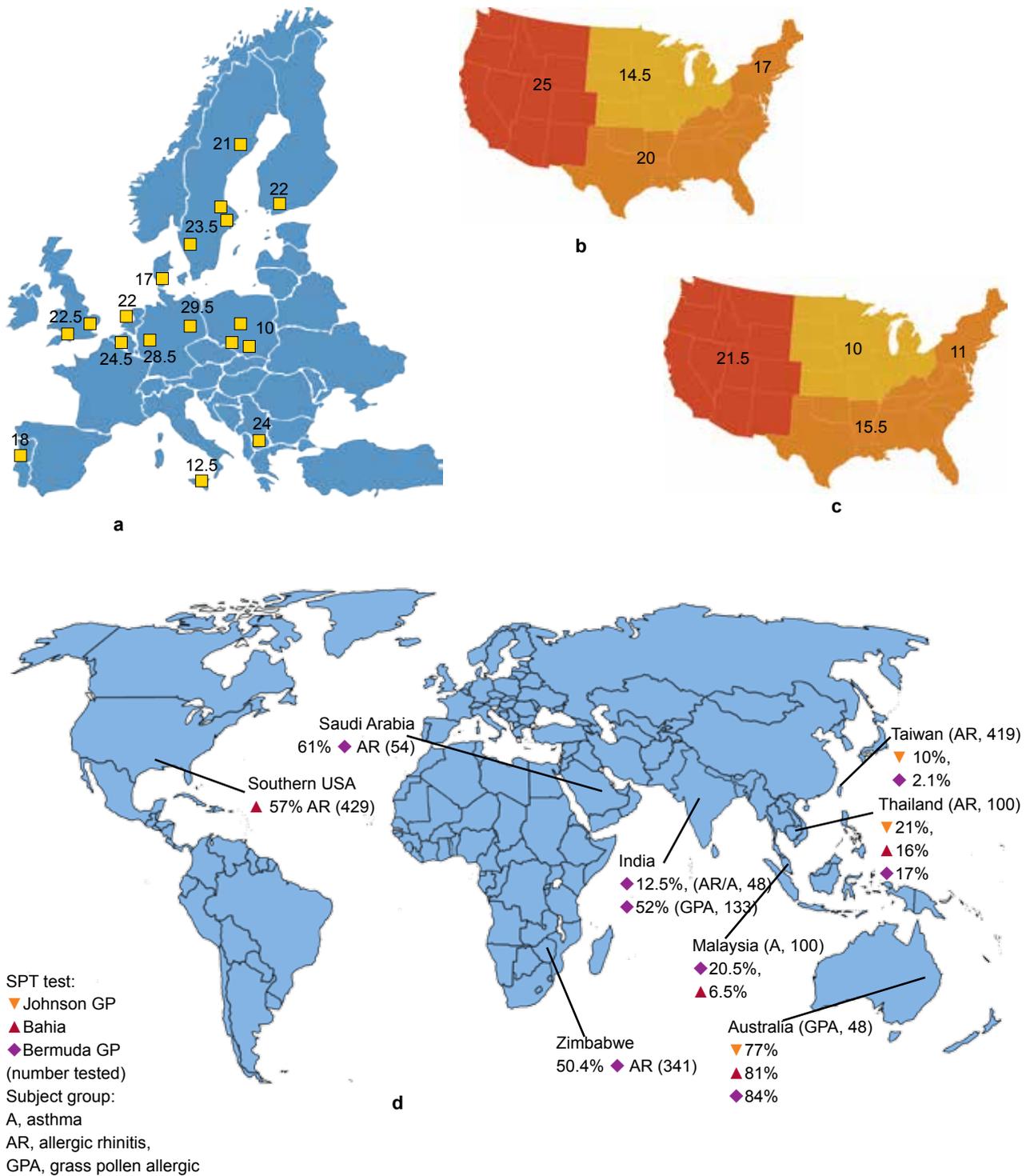


Figure 5 Sensitization rates to grass pollen (*Pooideae*) in Europe (a: modified from (7)), to Ryegrass (b) and Bermuda grass (c) in the US (b and c: modified from (8)) and to Johnson, Bahia and Bermuda grass pollen elsewhere (d: limited information, modified from (9)).