Position paper

EAACI/GA²LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria

This guideline, together with its sister guideline on the management of urticaria [Zuberbier T, Asero R, Bindslev-Jensen C, Canonica GW, Church MK, Giménez-Arnau AM et al. EAACI/GA²LEN/EDF/WAO Guideline: Management of urticaria. Allergy, 2009; 64:1427–1443] is the result of a consensus reached during a panel discussion at the 3rd International Consensus Meeting on Urticaria, *Urticaria 2008*, a joint initiative of the EAACI Dermatology Section, GA²LEN, EDF and WAO. Urticaria is a frequent disease. The life-time prevalence for any subtype of urticaria is approximately 20%. Chronic spontaneous urticaria and other chronic forms of urticaria do not only cause a decrease in quality of life, but also affect performance at work and school and, as such, are members of the group of severe allergic diseases. This guideline covers the definition and classification of urticaria, taking into account the recent progress in identifying its causes, eliciting factors, and pathomechanisms. In addition, it outlines evidence-based diagnostic approaches for different subtypes of urticaria. The correct management of urticaria, which is of paramount importance for patients, is very complex and is consequently covered in a separate guideline developed during the same consensus meeting. This guideline was acknowledged and accepted by the European Union of Medical Specialists (UEMS).


¹Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Germany; ²Ambulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano (MI), Italy; ³Allergy Centre, Department of Dermatology, Odense University Hospital, Denmark; ⁴Allergy and Respiratory Diseases, DIMI – University of Genoa, Genoa, Italy; ⁵Department of Dermatology, Hospital del Mar, IMAS, Universitat Autònoma de Barcelona, Spain; ⁶Dermatology Centre, Norfolk & Norwich University Hospital, Norwich, UK; ⁷Department of Dermatology and Allergology, Hannover Medical University, Germany; ⁸Department of Dermatology, University Hospital RWTH Aachen, Germany; ⁹Clinical Department of Internal Diseases, Allergology and Clinical Immunology, Medical University of Silesia, Poland; ¹⁰Department of Medicine, Johns Hopkins University, Baltimore, MD, USA; ¹¹Allergy and Immunology Department, Centro Medico-Doctor La Trinidad, Caracas, Venezuela; ¹²Allergy Unit, Department of Dermatology, University Hospital, Zurich, Switzerland; ¹³Department of Clinical Epidemiology & Biostatistics, Hamilton, Canada; ¹⁴Department of Dermatology, Johannes Gutenberg-University, Mainz, Germany; ¹⁵Unit of Dermatology, University of Bari, Bari, Italy

Key words: consensus; diagnosis; guideline; urticaria; wheal

Torsten Zuberbier
Charité – Universitätsmedizin Berlin
Allergie-Centrum-Charité
Charitéplatz 1
D-10117 Berlin
Germany

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This guideline is the result of a panel discussion during the 3rd International Meeting on Urticaria *Urticaria 2008*, a joint initiative of the EAACI Dermatology Section, GA²LEN, EDF and WAO.

The wide diversity and number of different urticaria subtypes that have part, our increasing eliciting factors of
cellular mechanisms involved in its pathogenesis. The aim of this guideline is to provide an updated definition and classification of urticaria, thereby facilitating the interpretation of divergent data from different centres regarding eliciting causes and therapeutic responsiveness of subtypes of urticaria. Furthermore, this guideline provides recommendations for diagnostic approaches in common subtypes of urticaria.

Methods
As members of the panel, the authors had prepared in advance their suggestions regarding the definition, classification, and routine diagnosis of urticaria (Table 1). The draft of the guideline took into account all available evidence in the literature (including Medline and Embase searches and hand searches of abstracts at international allergy congresses in 2004–2008) and was based on the existing consensus papers of the first and second symposium in 2000 and 2004 (1, 2). These suggestions were then discussed in detail among the panel and the participants of the meeting and a consensus achieved using a simple voting system where appropriate. The participation of more than 200 specialists in urticaria from 33 countries ensured that this consensus included European and global regional differences in viewpoint and provided a basis for improved comparison of future studies in the field of urticaria.

Table 1. Box of recommendations and suggestions for the diagnosis of urticaria

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend adhering to the definitions of urticaria types and subtypes provided by these guidelines in order to avoid misunderstandings both in patient care as well as in publications.</td>
</tr>
<tr>
<td>We recommend following the classification of urticaria as outlined in Table 2 in clinical trials, publications, and routine daily practice.</td>
</tr>
<tr>
<td>We suggest using the urticaria activity score (UAS) in routine daily practice to assess disease severity and monitor success of treatment in patients with spontaneous urticaria.</td>
</tr>
<tr>
<td>Furthermore, we strongly recommend the use of this validated score in clinical trials to allow comparison with others.</td>
</tr>
<tr>
<td>We recommend a stepwise diagnostic approach as outlined in Table 5.</td>
</tr>
<tr>
<td>We suggest using the same procedure in children.</td>
</tr>
</tbody>
</table>

Definition
Urticaria is a heterogeneous group of diseases. All types and subtypes of urticaria share a common distinctive skin reaction pattern, i.e. the development of urticarial skin lesions and/or angioedema. Urticaria needs to be differentiated from other medical conditions where wheals can occur as a symptom, e.g. skin prick test or acute anaphylaxis without symptoms in daily life.

Clinical appearance
Urticaria is characterized by the sudden appearance of wheals and/or angioedema (Fig. 1).

A wheal consists of three typical features:
1. a central swelling of variable size, almost invariably surrounded by a reflex erythema
2. associated itching or, sometimes, burning sensation
3. a fleeting nature, with the skin returning to its normal appearance, usually within 1–24 h

Angioedema is characterized by:
1. a sudden, pronounced swelling of the lower dermis and subcutis
2. sometimes pain rather than itching
3. frequent involvement below mucous membranes
4. resolution that is slower than for wheals and can take up to 72 h

Histological aspects
On histology, the classical fleeting wheal demonstrates edema of the upper and mid dermis, with dilatation of the postcapillary venules and lymphatic vessels of the upper dermis. In angioedema, similar changes occur primarily in the lower dermis and the subcutis. Skin affected by wheals virtually always exhibits upregulation...
of endothelial adhesion molecules and a mixed inflammatory perivascular infiltrate of variable intensity, consisting of neutrophils and/or eosinophils, macrophages, and T-cells (3). A mild to moderate increase of mast cell numbers has also been reported by some authors. In delayed pressure urticaria, the infiltrate is typically located in the mid to lower dermis. In some subtypes of urticaria, upregulation of adhesion molecules (4) and altered cytokine expression are also seen in uninvolved skin (5).

These findings underline the complex nature of the pathogenesis of urticaria which has many features in addition to the release of histamine from dermal mast cells (6, 7).

These changes are also seen in a wide variety of inflammatory reactions and are thus not specific or of diagnostic value. A search for more specific histological markers for different subtypes of urticaria is desirable.

Classification of urticaria on the basis of its duration, frequency, and causes

The spectrum of clinical manifestations of different urticaria subtypes is very wide. Additionally, two or more different subtypes of urticaria can coexist in any given patient. Table 2 presents a classification for clinical use. It is clear that there are some inconsistencies in this classification, e.g. physical urticarias are also chronic conditions but they are grouped separately due to the special nature of their eliciting physical factors, whereas in typical acute and chronic spontaneous urticarias wheals arise spontaneously without external physical stimuli. However, it should be noted to avoid confusion that the commonly used abbreviation for chronic urticaria remains chronic urticaria even if the full term is chronic spontaneous urticaria. This expression is chosen only for classification purposes.

Urticaria pigmentosa (cutaneous mastocytosis), urticarial vasculitis, familial cold urticaria and nonhistaminergic angioedema (e.g. hereditary or acquired C1 esterase inhibitor deficiency) are no longer considered as subtypes of urticaria, due to their distinctly different pathomechanisms, but are listed in Table 3 for reference. Wheals are features of several eponymous syndromes (Table 3).

Another important factor in classifying urticaria is disease activity. In physical urticaria and in cholinergic urticaria, as well as exercise-induced urticaria/anaphylaxis, the threshold of the eliciting factor(s) should be determined, e.g. critical temperature and stimulation time thresholds for cold provocation in cold urticaria. These thresholds allow both patients and treating physicians to evaluate disease activity and response to treatment. For acute and chronic spontaneous urticaria, assessing disease activity is more complex. Several scoring systems have been proposed using scales from 0–3 or up to 10 points. A unified and simple scoring system, the urticaria activity score (UAS), was proposed in the last version of the guidelines. Use of the UAS facilitates comparison of study results from different centres. The UAS (Table 4) is based on the assessment of key urticaria symptoms (wheals and pruritus). It is suitable for the evaluation of disease activity by urticaria patients and their treating physicians. Furthermore, this scoring system has been validated (8). As urticaria symptoms frequently change in intensity, overall disease activity is best measured by advising patients to document 24-h self-evaluation scores for several days. The UAS, i.e. the sum score of 7 consecutive days, should be used in routine clinical practice to determine disease activity and response to treatment of chronic urticaria patients. As CU-Q2oL, a disease specific questionnaire

<table>
<thead>
<tr>
<th>Types</th>
<th>Subtypes</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous urticaria</td>
<td>Acute spontaneous urticaria</td>
<td>Spontaneous wheals and/or angioedema &lt; 6 weeks</td>
</tr>
<tr>
<td></td>
<td>Chronic spontaneous urticaria</td>
<td>Spontaneous wheals and/or angioedema &gt; 6 weeks</td>
</tr>
<tr>
<td>Physical urticaria</td>
<td>Cold contact urticaria</td>
<td>Eliciting factor: cold objects/air/fluids/wind</td>
</tr>
<tr>
<td></td>
<td>Delayed pressure urticaria</td>
<td>Eliciting factor: vertical pressure</td>
</tr>
<tr>
<td></td>
<td>Heat contact urticaria</td>
<td>(wheals arising with a 3–12 h latency)</td>
</tr>
<tr>
<td></td>
<td>Solar urticaria</td>
<td>Eliciting factor: localized heat</td>
</tr>
<tr>
<td></td>
<td>Urticaria factitia/dermographic urticaria</td>
<td>Eliciting factor: UV and/or visible light</td>
</tr>
<tr>
<td></td>
<td>Vibratory urticaria/angioedema</td>
<td>Eliciting factor: mechanical shearing forces</td>
</tr>
<tr>
<td></td>
<td></td>
<td>e.g. pneumatic hammer</td>
</tr>
<tr>
<td>Other urticaria types</td>
<td>Aquagenic urticaria</td>
<td>Eliciting factor: water</td>
</tr>
<tr>
<td></td>
<td>Cholinergic urticaria</td>
<td>Elicitation by increase of body core temperature due to physical exercises, spicy food</td>
</tr>
<tr>
<td></td>
<td>Contact urticaria</td>
<td>Elicitation by contact with urticariogenic substance</td>
</tr>
<tr>
<td></td>
<td>Exercise induced anaphylaxis/urticaria</td>
<td>Eliciting factor: physical exercise</td>
</tr>
</tbody>
</table>
Table 3. Diseases related to urticaria for historical reasons and syndromes that include urticaria/angioedema

<table>
<thead>
<tr>
<th>Diseases related to urticaria for historical reasons</th>
<th>Syndromes that can be associated with urticaria/angioedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urticaria pigmentosa (mastocytosis)</td>
<td>Muckle-Wells syndrome (Urticaria-deafness-amyloidosis), sensorineural deafness, recurrent urticaria (hives), fevers, arthritis</td>
</tr>
<tr>
<td>Urticarial vasculitis</td>
<td>Schnitzler’s syndrome monoclonal gammopathy, recurrent fever, arthritis</td>
</tr>
<tr>
<td>Familial cold urticaria (vasculitis)</td>
<td>Gleich’s syndrome (episodic angioedema with eosinophilia), IgM gammopathy, eosinophilia</td>
</tr>
<tr>
<td>Nonhistaminergic angioedema (e.g. HAE)</td>
<td>Well’s syndrome (Eosinophilic cellulitis), granulomatous dermatitis with eosinophilia</td>
</tr>
</tbody>
</table>

Table 4. Assessment of disease activity in urticaria patients

<table>
<thead>
<tr>
<th>Score</th>
<th>Wheals</th>
<th>Pruritus</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Mild (&lt;20 wheals/24 h)</td>
<td>Mild (present but not annoying or troublesome)</td>
</tr>
<tr>
<td>2</td>
<td>Moderate (20-50 wheals/24 h)</td>
<td>Moderate (troublesome but does not interfere with normal daily activity or sleep</td>
</tr>
<tr>
<td>3</td>
<td>Intense (&gt;50 wheals/24 h or large confluent areas of wheals)</td>
<td>Intense (severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep</td>
</tr>
</tbody>
</table>

Sum of score: 0–6.

Diagnosis of urticaria

Chronic spontaneous urticaria is a disease with a high burden for patients (11) and high direct and indirect healthcare costs (24) with large socio-economic implications due to a reduction in performance of 20–30%. Due to the heterogeneity of urticaria and its many subtypes, a routine patient evaluation, which should comprise a thorough history and physical examination, and the ruling out of severe systemic disease by basic laboratory tests, should be performed first. Specific provocation, e.g. with a pseudoallergen rich diet, and laboratory tests are helpful for the identification of underlying causes of chronic spontaneous urticaria, whereas this is very unlikely in physical and other inducible urticarias. Extended diagnostic procedures in patients with the latter two types of urticaria should therefore only be carried out on an individual basis, i.e. in patients where the routine patient evaluation has uncovered a specific potential cause of urticaria. Extended diagnostics aimed at the identification of underlying causes should be performed in patients that suffer from longstanding, severe and/or persistent urticaria symptoms (Table 5).

Of all the diagnostic procedures, the most important is to obtain a thorough history including all possible eliciting factors and significant aspects of the nature of the urticaria. Questions should be asked regarding the following items (17):

1. Time of onset of disease
2. Frequency and duration of wheals
3. Diurnal variation
4. Occurrence in relation to weekends, holidays, and foreign travel
5. Shape, size, and distribution of wheals
6. Associated angioedema
7. Associated subjective symptoms of lesion, e.g. itch, pain
8. Family and personal history regarding urticaria, atopy
9. Previous or current allergies, infections, internal diseases, or other possible causes
10. Psychosomatic and psychiatric diseases
11. Surgical implantations and events during surgery
12. Gastric/intestinal problems (stool, flatulence)
13. Induction by physical agents or exercise
14. Use of drugs (NSAIDs, injections, immunizations, hormones, laxatives, suppositories, ear and eye drops, and alternative remedies)
15. Observed correlation to food
16. Relationship to the menstrual cycle
17. Smoking habits
18. Type of work
19. Hobbies
20. Stress (eustress and distress)
21. Quality of life related to urticaria and emotional impact
22. Previous therapy and response to therapy

Possible mechanisms in urticaria

In the last two decades, many advances have been made in identifying causes of different types and subtypes of urticaria, e.g. in chronic spontaneous urticaria (reviewed in (13) and (14)). Among others, acute or chronic infections (e.g. Anisakis simplex or Helicobacter pylori), nonallergic hypersensitivity reactions to foods and drugs (pseudoallergic), and autoreactivity including autoimmunity mediated by functional autoantibodies directed against the IgE receptor have been described (15–23). The concept of autoimmune urticaria is increasingly being recognized but has still to be defined. However, there are considerable variations in the frequency of underlying causes in the different studies. This may reflect differences in patient selection, emphasizing the need for a consensus on the classification of urticaria subtypes that will allow the comparison of results from different centres.

for assessing quality of life in patients with chronic spontaneous urticaria is becoming available and validated in several languages; this instrument should be used to assess disease activity in chronic urticaria patients (9–12).
The second step is the physical examination of the patient. This should include a test for dermographism (NB: antihistamine therapy should be discontinued for at least 2–3 days). Subsequent diagnostic steps will depend on the nature of the urticaria subtype, as summarized in Table 5.

Table 5. Recommended diagnostic tests in frequent urticaria subtypes

<table>
<thead>
<tr>
<th>Types</th>
<th>Subtypes</th>
<th>Routine diagnostic tests (recommended)</th>
<th>Extended diagnostic programme* (suggested)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous urticaria</td>
<td>Acute spontaneous urticaria</td>
<td>None</td>
<td>None†</td>
</tr>
<tr>
<td></td>
<td>Chronic spontaneous urticaria</td>
<td>Differential blood count and ESR or CRP (omission of suspected drugs (e.g. NSAID)</td>
<td>Test for (i) infectious diseases (e.g. Helicobacter pylori); (ii) type I allergy; (iii) functional autoantibodies; (iv) thyroid hormones and autoantibodies; (v) skin tests including physical tests; (vi) pseudoallergen-free diet for 3 weeks and tryptase‡; (vii) autologous serum skin test, lesional skin biopsy</td>
</tr>
<tr>
<td>Physical urticaria</td>
<td>Cold contact urticaria</td>
<td>Cold provocation and threshold test (ice cube, cold water, cold wind)</td>
<td>Differential blood count and ESR/CRP cryoproteins rule out other diseases, especially infections</td>
</tr>
<tr>
<td></td>
<td>Delayed pressure urticaria</td>
<td>Pressure test (0.2-1.5 kg/cm² for 10 and 20 min)</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Heat contact urticaria</td>
<td>Heat provocation and threshold test (warm water)</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Solar urticaria</td>
<td>UV and visible light of different wave lengths</td>
<td>Rule out other light-induced dermatoses</td>
</tr>
<tr>
<td></td>
<td>Dermograph urticaria/urticaria factitia</td>
<td>Elicit dermographism</td>
<td>Differential blood count, ESR/CRP</td>
</tr>
<tr>
<td>Other urticaria types</td>
<td>Aquagenic urticaria</td>
<td>Wet cloths at body temperature applied for 20 min</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Cholinergic urticaria</td>
<td>Exercise and hot bath provocation</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Contact urticaria</td>
<td>Prick/patch test read after 20 min</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Exercise-induced anaphylaxis/urticaria</td>
<td>According to history exercise test with/without food but not after a hot bath</td>
<td>None</td>
</tr>
</tbody>
</table>

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NSAID, nonsteroidal anti-inflammatory drugs.
*Depending on suspected cause.
†Unless strongly suggested by patient history, e.g. allergy.
‡As indication of severe systemic disease.

Guideline: classification of urticaria

The second step is the physical examination of the patient. This should include a test for dermographism where indicated by history (NB: antihistamine therapy should be discontinued for at least 2–3 days). Subsequent diagnostic steps will depend on the nature of the urticaria subtype, as summarized in Table 5.

Intensive and costly general screening programmes for causes of urticaria are strongly advised against. Type I allergy is a rare cause of chronic spontaneous urticaria in patients who present with daily or almost daily symptoms, but must be considered in chronic spontaneous urticaria patients with intermittent symptoms. In contrast, nonallergic hypersensitivity reactions to food or food additives may be more relevant for chronic spontaneous urticaria with persistent symptoms. Diagnosis should be based on an easy-to-follow diet protocol. Food challenge test for type I allergy should be preceded by an appropriate elimination diet. In exercise-induced urticaria/anaphylaxis both allergic and nonallergic hypersensitivity reactions to food should be taken into account, especially type I allergy to wheat and gliadin as well as nonspecific reactions to alcoholic beverages. Chronic persistent bacterial, viral, parasitic, or fungal infections, e.g. with *H. pylori*, *streptococci*, *staphylococci*, *yersinia*, *Giardia lamblia*, *mycoplasma pneumonia*, *hepatitis virus*, *norovirus*, *parvovirus B19*, *anisakis simplex*, *entamoeba spp*, *blastocystis spp*, have been suggested to trigger urticarial symptoms in patients with chronic spontaneous urticaria. The frequency and relevance of infectious diseases varies between different patient groups and different geographical regions. For example, *Anisakis simplex*, a sea fish nematode, has been discussed as possible cause of recurrent acute spontaneous urticaria in areas of the world where uncooked fish is eaten frequently (25). The relevance of dental or ENT infections appears to vary between patient groups. Altogether more research is needed for in order to make definitive recommendations regarding the role of infection in urticaria. In contrast to previous recommendations to screen for malignancies in the diagnosis of chronic spontaneous urticaria, this is no longer suggested since there is no evidence available for a correlation of urticaria with neoplastic diseases.

Currently, the only generally available test to screen for autoantibodies against either IgE or the high affinity IgE receptor is the Autologous Serum Skin Test (ASST), a nonspecific screening test which evaluates the presence of serum histamine-releasing factors of any type, not just...
histamine-releasing autoantibodies. General experience, including that of the panel, is that healthy controls and patients without chronic spontaneous urticaria do not have positive ASST responses as defined by an inflammatory red wheal response (26–35). In contrast to most previously published studies, some studies have demonstrated a relatively high prevalence of positive ASST reactivity in 30–50% of adult patients with allergic or nonallergic respiratory symptoms, reaching up to 80% in childhood populations (36–40). In two of these studies, 40–45% of healthy individuals also had a positive ASST although the criteria used to define positivity were adopted from those that had been validated only for chronic urticaria. The meaning of these discrepancies is unclear.

The ASST should be performed with utmost care since infections might be transmitted if, by mistake, patients were injected with someone else’s serum. A more refined laboratory test evaluates the in vitro histamine release from basophils. The subject is further elucidated in a separate EAACI/GA²LEN position paper (41).

In physical urticaria the routine diagnosis is mainly aimed at the identification of the subtype by the appropriate physical stimulation tests and to the determination of trigger thresholds. The latter is important as it allows for assessing disease severity and response to treatment. For most types of physical urticaria no validated tools for provocation testing exist. Exceptions include cold urticaria, where a peltier element-based provocation device (TempTest®) is available (42, 43), and symptomatic dermographism urticaria facticia, for which a dermographometer has been developed (44). In other physical urticarias or cholinergic urticaria, graded provocation tests with office-based methods, e.g. ergometer provocation in cholinergic urticaria, should be standardized in the single practice setting to allow comparison of disease activity at different time points in the same patient.

In some subjects with active chronic spontaneous urticaria, several groups have noted blood basopenia and that blood basophils exhibit suppressed IgE receptor-mediated histamine release to anti-IgE. Blood basophils are detected in skin lesions and in nonlesional skin of chronic spontaneous urticaria patients. Chronic spontaneous urticaria remission is associated with increases in blood basophil numbers and IgE receptor triggered histamine response (45, 46). This finding, however, needs to be examined in future research and currently does not give lead to diagnostic recommendations. However, it should be noted that a low basophil blood count should not result in further diagnostic procedures.

**Diagnosis in children**

Urticaria can occur in all age groups. The underlying causes of chronic urticaria appear not to be different between children and adults (47) except possibly in infants (48). However, there appear to be differences in the frequency of some of the underlying causes (49). In general, further epidemiological studies in children are needed. However, it is becoming apparent that the differences between the underlying causes of urticaria in children and adults are only small indicating that the diagnostic approach should, therefore, be the same as in adults (50, 51).

**Need for further research**

The panel and participants identified several areas which need further research.

These include but are not limited to:

- epidemiology of urticaria
- the socio-economic consequences
- identification of mast cell basophil activating factors
- identifying new histological markers
- standardized procedures for testing physical urticaria
- standardized procedures for testing serum autoreactivity in chronic spontaneous urticaria
- determination of minimal important differences for instruments in quantifying a relevant response (e.g. UAS, CU-QoL)
- clarification of the role of coagulation/coagulation factors in chronic spontaneous urticaria
- how to score angioedema reliably
- characterization of the relevance of nickel and food as possible triggering factor in chronic spontaneous urticaria

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References


### Appendix

Physicians and specialists who contributed on diagnosis and management of urticaria in the democratic process and discussion within the 3rd International Consensus Meeting on Urticaria, *Urticaria 2008*:

- Abd El Fattah, Ahmed (Dubai)
- Abdal Karim Mualem, Mohamad Gyas (Abu Dhabi)
- Abdallah, Mahmoud (Egypt)
- Abdollahnia, Mandana (Germany)
- Aber, Werner (Austria)
- Alborova, Alena (Germany)
- Al Harthy, Aseela (Dubai)
- Altmayer, Anita (Hungary)
- Altrichter, Sabine (Germany)
- Altunay, Ilknur Kivanc (Turkey)
- Ardelean, Elena Angelica (Germany)
- Astner, Susanne (Germany)
- Atakan, Nilgun (Turkey)

- Ayala, Fabio (Italy)
- Aydemir, Ertugrul (Turkey)
- Badiardini, Ilaria (Italy)
- Balazs, Anna (Germany)
- Baranov, Alexander (Russia)
- Bendandi, Barbara (Italy)
- Berberoglu, Harun (Turkey)
- Bergmann, Karl-Christian (Germany)
- Biedermann, Tilo (Germany)
- Bielsa, Isabel (Spain)
- Blazek, Claudia (Germany)
- Blaziene, Audra (Lithuania)
- Blume-Peytavi, Ulrike (Germany)
Onder, Meltem (Turkey)  Soost, Stephanie (Germany)
Opper, Britta (Germany)    Sorensen, Eva Valbjørn (Denmark)
Ozturkcan, Serap (Turkey)  Ständter, Harmut (Germany)
Pawliczak (Poland)        Ständter, Sonja (Germany)
Pereira, Celso (Portugal)  Stefaniak, Richard (Germany)
Philipp, Sandra (Germany)  Steinhoff, Matthias (Germany)
Pigatto, Paolo Daniele (Italy)  Stenmark, Särhammar Gunnel (Sweden)
Popescu, Florin-Dan (Romania)  Stockfleth, Eggert (Germany)
Raap, Ulrike (Germany) Szakos, Erzsébet (Hungary)
Ramadan, Rana (Lebanon)  Szalai, Zsuzsanna (Hungary)
Rasche, Claudia (Germany) Szegedi, Andrea (Hungary)
Rzany, Berthold (Germany)  Taskapan, Oktay (Turkey)
Romanska-Gocka (Poland)  Teebi, Zaid (Malta)
Rosen, Karin (USA)        Teichler, Angela (Germany)
Rueff, Franziska (Germany)  Terzi, Seyma (Spain)
Saarialho, Henna (Finland)  Trautinger, Franz (Austria)
Sabato, Vito (Italy)        Trefzer, Uwe (Germany)
Sanjiv, Kandhari (India)   Treiber, Nicolai (Germany)
Santa, Marta Cristina (Portugal)  Trosien, Julia (Germany)
Schäfer, Torsten (Germany)  Van der Valk, P.G.M. (Netherlands)
Schäfer-Hesterberg, Gregor (Germany)  Varszegi, Dalma (Hungary)
Schmidt, Ute (Germany)      Vestergaard, Christian (Denmark)
Schoepke, Nicole (Germany) Vieira dos Santos, Rosaly (Germany)
Scholz, Elisabeth (Germany)  Weller, Karsten (Germany)
Seefluth, Robina (Germany) Wieczorek, Dorothea (Germany)
Seymons, Katy (Belgium)    Wöhrl, Stefan (Austria)
Sharma, Rajeev (India)     Wölner, Kristina (Germany)
Silvestre Salvador, Juan Francisco (Spain)  Worm, Margitta (Germany)
Sitkauskiene, Brigita (Lithuania)  Wozniacka, Anna (Poland)
Skov, Per Stahl (Denmark)  Zuberbier, Martina (Germany)
Sommerfeld, Beatrice (Sweden)