

Chronic urticaria – which clinical parameters are pathogenetically relevant? A retrospective investigation of 339 patients

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- urticaria
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Summary

Background: Urticaria is a clinical reaction pattern triggered by many factors causing liberation of vasoactive substances such as histamine, prostaglandins and kinins. It presents as transient itching wheals which are either limited to the local stimulus area or more widespread. Urticaria is classified according to its duration into acute (duration < 6 weeks) and chronic (duration ≥ 6 weeks) forms. Various clinical investigations may be initiated to diagnose the cause. This study critically evaluates the relevance of frequently performed laboratory investigations and searches for infectious foci, as well as the results of physical provocation testing and oral provocation with food additives.

Patients and Methods: The laboratory and clinical data of 339 patients who had been treated for urticaria at the Christian-Albrechts-University in Kiel over a period of four years were collected in a data entry form and statistically evaluated. Nominal values were analyzed by their relative and absolute quantities, quantitative parameters with the help of statistical data such as minimum, maximum, median and 25th and 75th percentiles.

Results: Chronic recurrent urticaria was most common, accounting for 52 % of cases. Women were affected 1.8 times more often than men. One-third of the patients also had angioedema. The medians of all laboratory parameters evaluated were within normal values. Only rarely were elevated antinuclear antibody titers, abnormal thyroid function tests or active infections such as hepatitis B or borreliosis detected. The search for infectious foci identified tonsillitis or sinusitis in almost 50 % of analyzed patients. Positive reactions to physical testing occurred in 30 % of patients and in 11 % to oral provocation with various food additives.

Conclusions: This study of a large patient group stresses the relevance of individually- tailored evaluations in patients affected with urticaria rather than an expensive initial broad diagnostic testing. More specific searches should be based on individual clues.

Introduction

Urticaria is a disease which represents a common pathogenetic end result produced by a variety of heterogenous triggers. It presents with variably large, itching or burning transient wheals that can be

localized or widespread and which may be accompanied by swelling in the deeper dermis in the form of angioedema. Chronic urticaria is a subgroup of urticaria presently defined on the basis of a duration longer than six weeks [1].

Depending on the frequency of appearance of wheals it can be further subdivided into a continual form with wheals appearing practically daily or a recurrent form with wheals appearing at intervals of days to weeks. Acute urticaria, in contrast, lasts

less than six weeks; acute intermittent urticaria is characterized by bouts lasting maximally six weeks but recurring after symptom-free intervals of weeks to months [2]. In clinical routine it is often considered as equivalent to chronic urticaria and it is also included in this study. In the etiology-based classification of urticaria, the idiopathic form, where no cause is found, is the most frequent, constituting up to 70 % of cases. Another form is IgE-mediated allergic urticaria often associated with foods or drugs. Further, a pseudoallergic urticaria is defined without an identifiable immunologic sensitization, occurring, for example, after intake of various food additives or nonsteroidal antiinflammatory drugs. After physical exertion as well as mechanical, thermal or electromagnetic stimuli (cold, heat, pressure, water, UV light) various forms of physical urticaria can occur, probably due to unspecific mast cell activation.

Potential causes of urticaria, beyond those mentioned above, can include infections such as syphilis or *Helicobacter pylori* infections, intestinal candidiasis as well as chronic infections such as tonsillitis or sinusitis.

The diagnostic approach to urticaria is very broad and includes a comprehensive clinical chemical and serological laboratory work-up, exclusion of infectious foci and inpatient oral provocation testing with food additives and perhaps with suspected foods, when the history is suggestive, after a pseudoallergen-low or -free diet in a wheal-free phase. Appropriate tests should search for a physical trigger. Rarely a definite cause of urticaria is found, so that these numerous, and in part expensive, tests must be viewed critically. In this study, these parameters are evaluated for their usefulness in determining the cause of urticaria on a large and well-characterized patient collective.

Patients and methods

The charts of 339 patients with known chronic urticaria who were treated either as in- or outpatients at the Department of Dermatology, Venereology and Allergy of the Christian-Albrechts-University of Kiel, Germany, over the course of four years were evaluated retrospectively. Data were collected on a specially developed form which included relevant epidemiological patient information such as age and duration of symptoms. Based on

course of the disease and its duration, classification into chronic continual, chronic recurrent and acute intermittent urticaria was undertaken. In addition, routine laboratory parameters including complete blood count, serum electrolytes, hepatic and renal function parameters were documented, along with immunologic, allergologic and infectious disease test results (cryoproteins, antinuclear antibodies, C1 esterase inhibitor, rheumatoid factor, thyroid autoantibodies, serum immunoglobulins, *Borrelia* and hepatitis serology and tests for parasites and yeast in the stool). Further consultations to search for infectious foci included ultrasonography of the abdomen, chest X-ray, ENT, dental and gynecologic consultations as well as a C13 urea breath test to diagnose *Helicobacter pylori* infection. To exclude physical urticaria, sweat testing in a foil wrap, cold exposure to forearm with ice cubes, application of a hot-water bottle and of weights and mechanical stroking of the skin for dermatographism were performed. During a wheal-free interval, prick and intracutaneous testing of inhalation allergens as well as oral, single-blind, placebo-controlled provocation testing were undertaken. The food additive blocks consisted of the following:

- Block I: bisulfites
 - Block II: tartrazine, sodium benzoate, mafenamic acid, beer yeast
 - Block III: paracetamol, 4-hydroxybenzoic acid methyl ester, dye mix I (quinoline yellow E 104, sunset yellow E 110, azorubine E 122, amarant E 123, cochineal red A E 124)
 - Block IV: sorbic acid, sodium benzoicum dye mix II (erythrosine E 127, patent blue E 131, indigo carmine E 132, brilliant black E 151)
 - Block V: indomethacin, balsam of Peru
- In addition to these blocks oral provocation with acetylsalicylic acid (ASA) was performed.

Nominally scaled parameters such as gender were analyzed on the basis of their absolute and relative frequencies. Valuation of quantitative parameters such as erythrocytes or thyroid-stimulating hormone was done using statistical data such as minimum, maximum as well as 25th and 27th percentile.

Results

The frequencies of the individual urticaria forms are listed in Table 1. The male :

female ratio among all urticaria subgroups was about 1 : 2. The average age in all urticaria categories was 40.9 years. Angioedema, mainly of the face or tongue, was reported as an isolated or additional symptom by 36 % of patients. A history of atopy was given by 23 %.

Table 2 shows an analysis of serologic parameters. In 12 of 279 patients (4 %) thyroid-stimulating hormone (TSH) decreased; of these, 3 had known and treated hypothyroidism, the rest was untreated. Four patients (1 % of the collective) had positive thyroid antibodies, but only one patient had a manifest Hashimoto thyroiditis. Stool samples showed growth of *Candida albicans* in 71 of 298 cases (24 %), but only < 10⁶ colony forming units per gram. *Yersinia* was found in only one case; parasite eggs in none. Occult blood was found in 3 % of examined stool samples, but gastroenterologic work-up found no infectious or malignant gastrointestinal disease in these cases. Positive bacterial cultures of urine despite lack of clinical symptoms were found in 7 % of tested samples. In the majority of cases *E. coli* was found at a level $\geq 10^5$ /ml. All other laboratory parameters were in the normal range.

In searching for an infectious focus at least one site of infection possibly causing urticaria was found in 134 patients (52 % of those examined, 40 % of the total collective, respectively). An acute or chronic tonsillitis was found in 9 % of the total collective, sinusitis in 4 %, dental caries in 7 % and further infections in 68 cases (20 %), including dental problems such as pulpitis and parodontitis or gynecologic problems such as vaginitis. Chest X-rays and ultrasonography of the abdomen revealed no sites of infection. Of 20 patients undergoing testing for *Helicobacter pylori*, 16 (80 %) were positive. Physical provocation testing was performed in 172 patients and 106 (62 %) displayed positive reactions. Of patients tested, 8 % (of these 85 % out of the group of cholinergic urticaria) reacted to sweat testing in a foil wrap, 9 % to cold challenge, 1 % (1 patient) to warmth, 2 % to weight exposition; urticarial dermatographism occurred in 42 % of those provoked.

Of 123 patients tested, 3 (2 %) showed an intolerance of sodium bisulfite (food additive block I). In 136 patients, oral provocation testing with food additives of blocks II, III, IV and V were performed.

Table 1: Frequency of various urticaria forms in absolute numbers.

Chronic urticaria							Other urticaria forms n = 25					
	Acute intermittent	Recurrent angioedema	Chronic recurrent	Chronic continual	Urticaria factitia	Cold urticaria	Cholinergic urticaria	Contact urticaria	Deep urticaria	Heat contact urticaria	Pressure urticaria	Urticarial vasculitis
Patient collective n = 339	38	24	175	40	21	16	11	4	3	1	4	2
Cases with additional cholinergic urticaria n = 13	-	-	1	-	-	1	11	-	-	-	-	-
Cases with additional urticaria factitia n=72	8	2	27	5	21	1	6	1	-	-	1	-
Cases with additional angioedema n = 122	15	24	70	5	1	3	2	1	1	-	-	-

Positive clinical reactions with wheals and/or angioedema occurred in 15 patients (11 %), all of whom had acute intermittent or chronic recurrent urticaria. Testing of the individual components of the additive blocks II, III and IV was performed in 91 % and remained negative in all cases.

Only in testing the individual components of block V did 4 patients react to indomethacin and 2 to balsam of Peru. An intolerance of ASA could be demonstrated in 17 of 134 patients challenged (13 %). Table 3 lists the results of the oral provocation testing.

Discussion

Chronic urticaria is a frequent disease that can persist or recur over a long period of time up to years causing distress and at times being life-threatening. As a cause is often not found, it presents the physician with a diagnostic and therapeutic challenge. To evaluate the role of a comprehensive diagnostic approach at a university clinic, a retrospective analysis of data collected from a relatively large number of patients (339) presenting over the course of four years was performed. The central issue was the actual relevance of each diagnostic method in finding the cause of urticaria.

Epidemiology

Classification into chronic recurrent, chronic continual and acute intermittent urticaria was done on the base of the course of the disease over time [1, 2]. Due to the tendency of the acute intermittent form to persist for months to years despite long symptom-free intervals, this form clinically imitates chronic urticaria and is thus included in this study, but as a separate subgroup.

As to the frequency of the urticaria subgroups, our study finds 14 % acute intermittent and 86 % chronic urticaria, a ratio of 1 : 6. On comparison, reports in the literature range from 16 % acute (continual and intermittent) and 84 % chronic urticaria [3] up to 46 % acute (continual and intermittent) and 54 % chronic cases [4]. Hardly any references exist on the frequency of acute intermittent urticaria alone: in a study by Häcki-Hermann [5] a ratio of 47 % acute intermittent versus 53 % chronic urticaria was found. Women constituted 65 % of patients, confirming observations of a female predominance in the literature [6]. Average age was 41 years with a minimum of 4 and a maximum of 86 years, corresponding to the literature [3, 7]. About one-third of patients developed deep swelling or angioedema, all located

in the face such as lips, eyelids and throat, the typical sites reported [8, 9]. A positive history of atopy was found in 23 % of the collective, corresponding to the prevalence of atopic diseases in the general population [10]. Total serum IgE was elevated in 60 % of the tested patients and was on average 149.90 U/ml. Grattan et al. [11] and Wüthrich [12] report similar results.

Autoimmune diseases

A positive rheumatoid factor was found in 5 % of tested patients, equivalent to the rate in the general population [13]. A significant titer of antinuclear antibodies was found in 3.5 %, but there was no indication of an underlying autoimmune disease. According to a recommendation by Zuberbier and Henz [14], testing for rheumatoid factor and antinuclear antibodies is advisable only if a history or clinical features are suggestive.

In the literature a connection between urticaria and autoimmune disease is often suggested. For example, it has often been reported as a phenomenon in the course of autoimmune thyroid disease, and anti-IgE antibodies and anti-IgE-receptor antibodies are often found in patients with chronic urticaria [15, 16]. Isolated associations with vitiligo and

Table 2: Results of serological tests.

Parameter	Number of positive results in relation to number of tested patients	Comments
Cryoagglutinins	0/339	
Cryofibrinogen	0/339	
Cryoglobulins	0/339	
Rheumatoid factors	15/300 (5.0 %)	No further clinical or serological indications of autoimmune diseases
Antinuclear antibodies ($\geq 1:320$)	11/313 (3.5 %)	
Borrelia antibodies	3/269 (1.1 %)	IgM positive with specific bands
	6/269 (2.2 %)	IgM positive without specific bands
Viral hepatitis	1/300 (0.3 %)	Active hepatitis B
	25/300 (8.3 %)	Past hepatitis A
	4/300 (1.3 %)	Past hepatitis A and B
	4/300 (1.3 %)	Past hepatitis B
	0/300	Active or past hepatitis C
<i>Treponema pallidum</i> hemagglutination test	0/339	
Anti-staphylolysin ($> 1:200$)	1/300 (0.3 %)	No further indication of focus of infection
Anti-streptolysin ($> 1:200$)	27/300 (9.0 %)	In four of these cases tonsillitis/sinusitis
Anti-streptodornase ($> 1:200$)	17/300 (5.6 %)	In three of these cases tonsillitis/sinusitis
Total serum IgE (> 100 U/ml)	197/322 (61.2 %)	

insulin-dependent diabetes have been reported [17]. In 4 patients in our study (1.4 %) thyroid autoantibodies were detected, but in only one case could Hashimoto thyroiditis be confirmed. All other patients displayed no clinical abnormalities at the time of examination, but they could not be followed over time.

Infectious diseases

Urticarial reactions can be associated with bacterial infections such as borreliosis [2]. In three patients of the Kiel collective, all out of the subgroups acute in-

termittent and chronic recurrent urticaria, positive IgM antibodies including specific bands were found despite a lack of history for borreliosis. Antibiotic therapy was initiated, but the clinical course of urticaria was not followed. Only one patient had active hepatitis B. In the literature, urticaria is reported as a frequent prodromal symptom of acute hepatitis B in about 20 % to 30 % of cases [18, 19]. A *Helicobacter pylori* infection has in the past been discussed controversially as a causal factor for urticaria [20], recent recommendations are that it should be excluded when sus-

pected [1]. It is quite common in the general population and its prevalence approximately corresponds to age [21]. Wedi and Kapp observed a disappearance of urticaria in 91 % of affected patients after *Helicobacter pylori* eradication [22]. Cribier and Noacco [23], on the other hand, found no difference in the prevalence of *Helicobacter pylori* in urticaria patients in comparison to the general population. Reported healing of urticaria after *Helicobacter pylori* eradication has not been followed sufficiently to prove definite success. Due to the small case numbers in regard to *Helicobacter pylori* infections in this study, no conclusions can be made.

A significant intestinal candidiasis was found in 24 % of tested patients, while the relationship between candidiasis and urticaria remains controversial [17, 24]. Detection of *Yersinia*, parasite eggs, occult blood in stool, positive syphilis serology (TPHA) or positive urine bacterial culture was made in only isolated cases without clinical correlation. These parameters, too, are either irrelevant or only important in few individual cases and are of only minor pathogenetic relevance. The median of all other clinical chemistry laboratory parameters in all subgroups of urticaria corresponded to that of the healthy population. On medical and economic grounds it therefore appears prudent to perform comprehensive laboratory diagnostics only to exclude a particular, individually suspected causative factor and, in routine cases, limit laboratory work-up to basics such as complete blood count, transaminases, renal function parameters and parameters of inflammation.

Focus search

Consultations to identify an infectious focus suspicious findings occurred in 134 of 258 patients (52 %), especially in the ENT and dental examinations, with tonsillitis and dental cavities being most common. Anti-staphylolysin (AStA), anti-streptolysin (ASL) and anti-streptodornase (ASD) antibodies can serve as indicators for such a focus. A corresponding focus could be found in only a small portion of 15 % (4 of 27) of ASL-positive and 18 % (3 of 17) ASD-positive patients. On the other hand, only few patients suspected of harboring a focus tested positive for AStA, ASL or ASD antibodies. Tanphaichitr reports

Table 3: Oral provocation with food additives in 136 patients.

	Acute intermittent urticaria	Chronic recurrent urticaria	Chronic continual urticaria	Urticaria factitia (dermographism)	Cold urticaria	Recurrent angioedema	Other urticaria forms
Block II	1	3	-	-	-	-	-
Block III	1	2	-	-	-	-	-
Block IV	1	6	-	-	-	-	-
Block V	3	8	-	-	-	-	-
Patients with positive reaction n = 15 (11 %)	3 (13.6 %)	12 (14.8 %)	-	-	-	-	-
Patients without reaction n = 121 (89 %)	19 (86.4 %)	69 (85.2 %)	11 (100 %)	5 (100 %)	2 (100 %)	9 (100 %)	6 (100 %)
Patients examined / tested n = 136 (40.1 %)	22 (57.9 %)	81 (46.3 %)	11 (27.5 %)	5 (23.8 %)	2 (12.5 %)	9 (37.5 %)	6 (24 %)
Patients without further specifications n = 203 (59.9 %)	16 (42.1 %)	94 (53.7 %)	29 (72.5 %)	16 (76.2 %)	14 (87.5 %)	15 (62.5 %)	19 (76 %)

that 50–65 % of all patients with chronic urticaria had chronic tooth or gingival infections. In only 4–35 % of such affected patients did cure of the infections lead to improvement of urticaria [25], which is in agreement with the results of Henz and Zuberbier [17].

Physical urticaria

Table 4 shows the relative frequencies of cholinergic and physical urticaria in comparison with similar results in the literature. In the present study, the frequency of pressure urticaria was 2 % (4 patients) and in the literature is estimated at between 2 and 35 % [26, 27]. Cold urticaria was diagnosed in 5 % of all patients (30 % of patients with physical urticaria), corresponding to reports in the literature of about 1–3 % [28, 29]. Further causes of cold urticaria, especially cryoproteins in association with acute infections or systemic lupus erythematosus, was not detected among these patients, as was the case in previous investigations [30].

Food intolerance

The frequency of food intolerance in urticaria is reported with high variability.

Food additives, such as ASA, are assumed to induce whealing in 5 % [29] to up to 45 % [31] of patients with chronic urticaria. In our study, oral provocation testing demonstrated an intolerance of a food dye or additive in 15 (11 %) of patients. In 20 % intolerance was towards indomethacin, in 13 % towards ASA and in only 2 % of tested patients (3 of 123) towards sodium bisulfite. In a study

by Paul encompassing 237 patients, 45 % reacted in oral provocation testing towards ASA and about 25 % towards indomethacin [31]. Juhlin could demonstrate ASA intolerance in about half of all patients with chronic urticaria [32]. Before possible inpatient testing, a three-week pseudoallergen-free diet should be adhered to in order to make the relationship with food additives likely [1].

Table 4: Relation of cholinergic or physical urticaria, urticaria factitia (dermographism) and cold urticaria in the group of chronic urticaria. Reports in the literature and own results.

	Buss, Garrelfs, Sticherling (present study)	Humphreys and Hunter 1998 [3]	Paul and Greilich 1991 [4]	Häcki-Hermann 1978 [5]
Total collective of all urticaria patients [n]	339	390	281	316
Cholinergic or physical urticaria [n]	53	59	72	48
Urticaria factitia (dermographism) [n]	21	37	30	25
Cold urticaria [n]	16	8	12	7

Conclusions

Despite exhaustive tests in our study, the cause of urticaria remained unknown in 80 % of cases. After inpatient work-up the patients were followed by general practitioners and dermatologists in private practice, so that it was impossible to assess the effects of treating possible underlying conditions. Exhaustive work-ups with extensive laboratory or technical diagnostics and provocation testing should be reserved for individual cases following detailed history. An individual management of patients in a center specialized in urticaria, where history, diagnosis, treatment and follow-up are stressed, appears more economic and logical on medical grounds, in order to concentrate diagnostic and therapeutic measures and perform them in a sequential manner. <<<

Conflict of interest

None.

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References

- Zuberbier T, Bindslev-Jensen C, Canonica W, Grattan CEH, Greaves MW, Henz BM, Kapp A, Kozel MMA, Maurer M, Merk HF, Schäfer T, Simon D, Vena GA, Wedi B. EAACI/GA²LEN/EDF guideline: definition, classification and diagnosis of urticaria. *Allergy* 2006; 61 (3): 316–320.
- Henz BM. Das Spektrum der Urtikaria. In: Henz BM, Zuberbier T, Grabbe J (Hrsg.) *Urtikaria - Klinik, Diagnostik, Therapie*. Berlin: Springer-Verlag, 1996: 1–17.
- Humphreys F, Hunter JAA. The characteristics of urticaria in 390 patients. *Br J Derm* 1998; 138: 635–638.
- Paul E, Greilich KD. Zur Epidemiologie der Urtikariaerkrankungen. *Hautarzt* 1991; 42: 366–375.
- Häcki-Hermann D. Urtikaria. Eine retrospektive Studie anhand von 316 konsekutiven Fällen der Jahre 1974–1976 der Dermatologischen Klinik der Universität Zürich. Med. Inauguraldissertation, Zürich, 1978.
- Juhlin L. Recurrent urticaria: clinical investigation of 330 patients. *Br J Derm* 1981; 104: 369–381.
- Nizami RM, Baboo MT. Office management of patients with urticaria: an analysis of 215 patients. *Ann Allergy* 1974; 33: 78–85.
- Lennig P. Lumbalpunktion und „Angioneurotisches Zirkumskriptes Oedem“, zum 150. Geburtstag des Klinikers Heinrich Quincke (1842–1922). *Z ärztl Fortbild* 1992; 86: 1127–1132.
- Cooper KD. Urticaria and angioedema: diagnosis and evaluation. *J Am Acad Dermatol* 1991; 25 (Suppl.): 166–176.
- Rajka G. *Essential aspects of atopic dermatitis*. Springer Verlag, Berlin, 1989.
- Grattan CEH, Wallington TB, Warin RP, Kennedy CTC, Bradfield JW. A serological mediator in chronic idiopathic urticaria – a clinical, immunological and histological evaluation. *Br J Derm* 1986; 114: 583–590.
- Wüthrich B. Immunglobuline (IgG, IgA, IgM und IgE) und Komplementfaktoren (C3, C4 und C1-Inhibitor) bei Urtikaria chronica. *Dermatol Monatsschr* 1979; 165: 191–197.
- Lipsky, PE. Rheumatoide Arthritis. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL (Hrsg.) *Harrisons Innere Medizin* 2, 13. Auflage. Berlin: Blackwell Wissenschafts-Verlag, 1995: 1921–1930.
- Zuberbier T, Henz BM. Diagnostik der Urtikaria. In: Henz BM, Zuberbier T, Grabbe J (Hrsg.) *Urtikaria - Klinik, Diagnostik, Therapie*. Berlin: Springer-Verlag, 1996: 137–156.
- Grattan C, Powell S, Humphreys F. Management and diagnostic guidelines for urticaria and angio-oedema. *Br J Derm* 2001; 144: 708–714.
- Doutre M. Chronic urticaria and thyroid auto-immunity. *Clin Rev All Immunol* 2006; 30: 31–37.
- Henz BM, Zuberbier T (1996) Ursachen der Urtikaria. In: Henz BM, Zuberbier T, Grabbe J (Hrsg.) *Urtikaria - Klinik, Diagnostik, Therapie*. Springer-Verlag, Berlin: 19–35.
- Hartmann H. Extrahepatische Manifestationen der HBV- und der HCV-Infektion. *Praxis* 1997; 86: 1163–1166.
- Chantraine-Hess S, Czarnetzki BM. Chronische Urtikaria und Hepatitis A. *Hautarzt* 1995; 46: 874.
- Carvalho P. Dans quelles circonstances la mise en évidence d'une étiologie atelle une incidence sur le traitement de l'urticaire chronique et sur son évolution? *Ann Dermatol Venerol* 2003; 130: 1S121–128.
- McGuigan JE. Peptisches Ulcus und Gastritis. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL (Hrsg.) *Harrisons Innere Medizin* 1, 13. Auflage. Berlin: Blackwell Wissenschafts-Verlag, 1995: 1599–1622.
- Wedi B, Kapp A. Helicobacter pylori infections in skin diseases: a critical appraisal. *Am J Clin Dermatol* 2002; 3 (4): 273–282.
- Cribier B, Noacco G. Urticaire chronique et infections. *Ann Dermatol Venerol* 2003; 130: 1S43–52.
- Möller A, Zuberbier T, Chantraine-Hess S, Henz BM. Bedeutung der Fokussuche für die Urtikaria-Diagnostik. *Allergologie* 1995; 11: 547–552.
- Tanphaichitr K. Chronic urticaria associated with bacterial infection – a case of dental infection. *Cutis* 1981; 27: 653–656.
- Krüger-Krasagakes S. Verzögerte Druckurtikaria. In: Henz BM, Zuberbier T, Grabbe J (Hrsg.) *Urtikaria - Klinik, Diagnostik, Therapie*. Berlin: Springer-Verlag, 1996: 62–67.
- Barlow RJ, Warburton F, Watson K, Black AK, Greaves MW. Diagnosis and incidence of delayed pressure urticaria in patients with chronic urticaria. *J Am Acad Dermatol* 1993; 29 (6): 954–958.
- Casale TB, Sampson HA, Hanifin J, Kaplan AP, Kulczycki A, Lawrence ID, Lemanske RF, Levine MI, Lillie MA. Guide to physical urticarias. *J Allergy Clin Immunol* 1998; 82: 758–763.
- Nettis E, Pannofino A, D'Aprile C, Ferrannini A, Tursi A. Clinical and aetiological aspects in urticaria and angio-oedema. *Br J Derm* 2003; 148: 501–506.
- Buss Y, Sticherling M. Cold Urticaria. Disease course and outcome – an investigation of 85 patients before and after therapy. *Br J Derm* 2005; 153: 440–441.
- Paul E. Urtikaria: Standards in Diagnostik und Therapie. *Derm* 1998; (4): 124–129.
- Juhlin M. Incidence of intolerance to food additives. *Int J Dermatol* 1980; 19: 548–551.