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Prevalence of *Helicobacter pylori*-Associated Gastritis in Chronic Urticaria

Abstract

Background: Chronic urticaria and concurrent angioedema are frustrating problems for both physicians and patients. **Methods:** 100 patients with chronic urticaria (mean duration 33.3±48.2 months) attending the urticaria consulting hour of our Department of Dermatology within 1 year were carefully analyzed for pathogenesis to avoid extensive unnecessary diagnostic approach in the future. **Results:** In 43 cases a potential infectious trigger could be identified, 35 were of idiopathic origin, and 15 demonstrated pseudoallergic reactions to acetylsalicylic acid or food additives, 5 had antibodies to thyroid gland, and 2 had malignant diseases. Of patients with foci, 26 had *Helicobacter pylori*-associated gastritis, 9 chronic tonsillitis or sinusitis, 4 infections with Epstein-Barr virus or cytomegalovirus, 2 dental focal infections and 2 suffered from Yersinia infection. High prevalence of *H. pylori* gastritis was found since 47% of patients showed elevated *H. pylori*-specific IgA and/or IgG antibodies. 27 patients underwent endoscopy and in all but 1 (96%) antral *H. pylori* infection was found. In contrast, a prevalence rate of 37% among asymptomatic adults has been published. Disappearance (67%) or improvement of urticaria (24%) occurred in most antimicrobially treated patients after 3–12 weeks. In contrast, only 50% of untreated *H. pylori*-seropositive patients with chronic urticaria showed spontaneous remission or improvement within 12 weeks. Prevalence of *H. pylori* infection may even be underestimated since only 27/100 patients underwent endoscopy. It is suggested that *H. pylori* infection may be present at least in all seropositive subjects (47%). Moreover, we found *H. pylori* infection in 2 seronegative subjects demonstrating gastric complaints. **Conclusions:** Thus, measurement of *H. pylori*-specific antibodies and/or gastroscopy should be included in the diagnostic management of chronic urticaria to identify patients who may profit from eradication treatment with disappearance of long-standing and annoying urticaria symptomatology.

Key Words

Helicobacter pylori
Chronic urticaria
Focal infection
Pseudoallergic reaction
Food additives

Introduction

Chronic urticaria is defined as a period of whealing lasting for at least 6 weeks often associated with concurrent angioedema. One-half of the patients demonstrate whealing

beyond 6 months but one-fifth of patients persist with considerable disability and reduction of quality of life beyond 10 years [1, 2]. Despite an exhaustive and expensive diagnostic approach, searches for etiologies of chronic urticaria have been mostly frustrating [3].

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Chronic urticaria has been described to be triggered by several disease states ranging from infectious disease to malignancy [4]. There is no increased incidence of atopy in patients with chronic idiopathic urticaria [5], but emerging data give evidence that some patients may have autoantibodies to thyroid, to the high-affinity IgE receptor (FcεRI) or to IgE [6–8]. Some patients demonstrate a peculiar susceptibility to develop pseudoallergic reactions to non-steroidal anti-inflammatory drugs, particularly acetylsalicylic acid (ASA), and/or food additives [9–13]. In contrast to genuine allergic reactions, pseudoallergic reactions are not mediated by specific sensitization. Thus, specific IgE antibodies are not found and skin tests cannot be employed for diagnostic purposes. Therefore, risky and time-consuming challenge tests are performed.

To achieve a rational pathophysiologic diagnostic approach to chronic urticaria in the future, we studied all patients with chronic urticaria attending the urticaria consulting hour of our Department of Dermatology during the course of 1 year with regard to pathogenesis. Particular attention was paid to potential gastric infection with *Helicobacter pylori* since recent reports related *H. pylori* infections with skin diseases like Schönlein-Henoch purpura and urticaria [14–17].

Methods

Patients

After having given informed consent, 100 outpatients (47 men and 53 women), mean age 44.4 ± 15.4 years (range 17–82), subjected within 1 year to the urticaria consulting hour of the Department of Dermatology with the diagnosis chronic urticaria (duration >6 weeks), were screened. Mean duration of disease was 33.3 ± 48.2 months (range 2–190). 23 patients (25%) had concurrent angioedema. In all patients, physical urticaria was excluded by history and/or diagnostic skin tests.

Routine Diagnostic Approach

At least the following parameters were determined: complete blood count with a differential analysis, erythrocyte sedimentation rate, C-reactive protein, basal TSH (thyroid-stimulating hormone), thyroid microsomal and thyroglobulin antibodies. Bacterial and/or viral focal infections were excluded by serological assessment for staphylococci and streptococci, Epstein-Barr virus (EBV) cytomegalovirus (CMV), Yersinia, stool examination for ova and parasites, and analysis of urine. Moreover, dental or ear-nose-throat focal infections were excluded by consultation. To define an atopic diathesis, total IgE (CAP IgE FEIA; Pharmacia-Biotech, Freiburg, Germany) and Sx1 Phadiatop = RAST atopy screening test for seven frequent allergens (CAP IgE-FEIA; Pharmacia-Biotech) were analyzed. Depending on positive history, additional skin tests for IgE-mediated reactions to foods, seasonal, and perennial allergens were carried out.

Assessment of *H. pylori* Infection

Antibodies to *H. pylori* were measured separately for IgG and IgA by an enzyme immunoassay method (Pyloriset-EIA; Orion Diagnostica, Finland). In a multi-laboratory comparison of eight commercially available *H. pylori* serology kits, the Pyloriset-EIA used in this study was regarded to be a good all-round performed. Its sensitivity and specificity were determined to be 95.8 and 95.5%, respectively [18]. Due to their limited diagnostic value, IgM antibodies were not assessed [19]. Sera were diluted 1:201 and analyzed according to the instructions of the manufacturer. Titers are expressed as reciprocals. Lower limits of raised titers were defined as 500 for both IgA and IgG. Seropositive patients and seronegative patients with gastric complaints (reflux, epigastric discomfort, nausea) were asked to undergo endoscopy. 27 patients gave informed consent. Mucosal samples from antrum and corpus were taken for *H. pylori* screening and histopathological examination as described previously [20]. Gastritis was classified according to the Sydney system using hematoxylin and eosin stains. Grade and activity of gastritis (mild, moderate, severe) were determined depending on the extent of infiltrate with lymphocytes and plasma cells or polymorphonuclear leukocytes, respectively. Presence of *H. pylori* was assessed in Giemsa stains and by a rapid urease test.

Treatment and Follow-Up of *H. pylori* Infection

Patients who were shown by histology to be infected with *H. pylori* were given triple antimicrobial treatment consisting of omeprazole (2×20 mg daily), amoxicillin (2×1 g daily) and clarithromycin (2×250 mg daily) for 7 days (= OAC). Two patients were treated with metronidazole (3×400 mg daily) instead of amoxicillin due to allergy to penicillin. Four to maximal 6 weeks after treatment, eradication was assessed by biopsy samples for histology and serum samples for circulating *H. pylori* antibodies were controlled. If eradication (defined by negative histology 4–6 weeks after completion of therapy) was not achieved with OAC a second treatment course consisting of metronidazole, bismuth and tetracycline was given. The effect of the second treatment was controlled within a third endoscopy. Six months after the first treatment course, *H. pylori* antibodies were controlled, if ever possible.

In all patients irrespective of the triggering factor of their chronic urticaria, concomitant treatment with the nonsedating antihistamines cetirizine or loratadine was allowed. Patients in whom no trigger factor could be identified received treatment with cetirizine or loratadine alone. Improvement of urticaria was determined by patients' assessment including symptoms like itch, number and frequency of urticarial eruptions and/or angioedema. Improvement of urticaria in an individual patient was accepted when urticarial symptoms declined and when treatment with antihistamines could be significantly reduced or stopped. Healing was accepted when disappearance of urticarial eruptions and/or angioedema occurred for at least 6 weeks without antihistamine treatment.

Analysis of Possible Pseudoallergic Reactions in Remaining Subjects with Urticaria Not Triggered by Infections

Patients in whom no infectious trigger could be found dieted with avoidance of food additives for at least 6 weeks as has been previously described [10]. Under diet no concomitant treatment with antihistamines was allowed. When symptoms improved under diet, subjects were provoked in the clinic under single-blinded placebo-controlled conditions with increasing doses of food additives in gelatin capsules. Only one group of additives was exposed per day. The following maximal doses of pseudoallergens were used: sodium benzoate 500 mg;

potassium metabisulfite 300 mg; tartrazine 50 mg; p-hydroxybenzoate 500 mg; colorings I: quinoline yellow (E104, FD&C yellow No. 10), sunset yellow (E110, FD&C yellow No. 6), Ponceau 4 R (E124), azorubine (E122), amaranth (E123), 5 mg each; colorings II: erythrocyte (E127, DF&C red No. 3), patent blue V (E131), idigotine (E132, FD&C blue No. 2), brilliant black BN (E151), iron (III) oxide red (E172), 5 mg each; aspartame 250 mg; tyramine 100 mg; sodium nitrite 50 mg; sodium salicylate 1,000 mg; sorbic acid 500 mg, and 1,000 mg. Provocation tests were considered positive when symptoms like urticarial eruptions, bronchial asthma, angioedema, or anaphylactoid reactions occurred. Positive reactions were confirmed by repeated testing on a later day, except for ASA.

Statistics
Statistical significance of the data was assessed by Mann-Whitney-Rank-Sum test or χ^2 test with $\alpha = 0.05$ using a statistical software package (SigmaStat for Windows, Jantel Scientific, Erkrath, Germany).

Results

Triggering Factors of Chronic Urticaria
Table 1 summarizes the possible triggering factors of chronic urticaria. A strikingly high prevalence of potential focal infections (43%) was found. 15% of subjects demonstrated pseudoallergic reactions to ASA or food additives in oral provocation tests. 5% showed antibodies to thyroid, but no manifest autoimmune thyroiditis was found by additional diagnostic procedures. In 2 subjects (2%) underlying malignant diseases were found, namely acute myeloid leukemia and breast cancer. Taken together, a triggering factor, either focal infection, pseudoallergic reaction or underlying disease, could be found in 65% of subjects. However, in 35% of cases no pathogenesis could be identified and those cases were classified as idiopathic. No patient demonstrated allergic reactions to food.

Among focal infections there was a strikingly high prevalence of *H. pylori* gastritis (60%). In contrast, other focal infections were less frequent in chronic urticaria (table 2): ear-nose-throat focus in 9 patients (21%), infection with EBV or CMV in 5 patients (9%), dental foci or yersiniosis in 2 patients each (5%).

High Prevalence of *H. pylori* Infection
In 47/100 patients (47%), elevated *H. pylori* IgA and/or IgG antibodies were found (table 3). 57% of them had raised titers of IgA antibodies (mean reciprocal titer 1,731.0, range 520–15,000, median 1,050) and 83% of IgG antibodies (mean reciprocal positive titers were 2,117.1, range 550–8,000, median 1,515). There was a relative higher prevalence of *H. pylori* seropositivity in younger patients

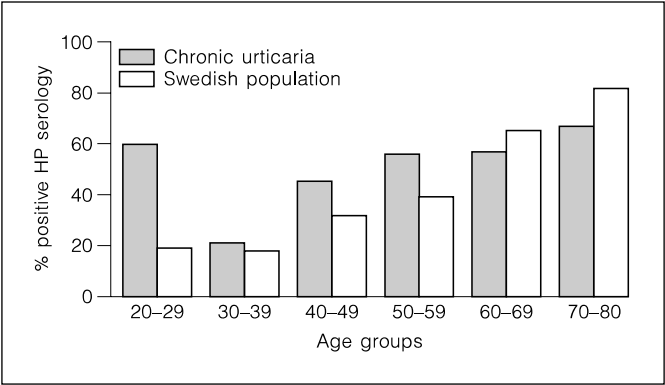


Fig. 1. Comparison of data obtained from a representative sample of a Swedish municipality (n = 150; 50 asymptotic controls, 50 with dyspepsia and 50 with irritable bowel syndrome) published by Agr  us et al. [21] with present data from chronic urticaria patiens (n = 100). The proportion of positive *H. pylori* (HP) serology in different age groups. Age distribution of all studied patients were similar in both studies (not shown). HP serology in the Swedish population was determined using HM-CAP immunoassay (Enteric Products Inc., Westbury, N.Y., USA; sensitivity >98%, specificity of 100%) whereas HP serology in urticaria patients was determined by Pyloriset-EIA (Orion Diagnostica, Finland; sensitivity 95.8%, specificity 95.5%).

Table 1. Possible eliciting factors of chronic urticaria based on patient’s history and extensive diagnostic approach (n = 100)

Focal infection	43%
Pseudoallergic reactions	15%
Antibodies to thyroid	5%
Malignant disease	2%
Idiopathic origin	35%
Total	100%

Table 2. Focal infections in detail (n = 43)

<i>H. pylori</i> gastritis	60%
Ear-nose-throat focal infection	21%
Infection with EBV or CMV	9%
Dental focal infection	5%
Yersiniosis	5%
Total	100%

with chronic urticaria compared with previously published results from a resrepresentative sample of a Swedish municipality (fig. 1) whereas the age distribution of studied individuals did not differ significantly (fig. 1) [21].

Table 3. Characterization of patients with chronic urticaria

	n	Male, %	Age years	Duration of cU months	total IgE ¹	Positive Sx1 (%)	Elevated CRP (%)	WBC ×10 ³ /mm ³
<i>H. pylori</i> -seronegative	53	69	42.7±14.8	35.3±57.1	244.4±338.6	18 (34)	6 (12)	7.4±1.6
<i>H. pylori</i> -seropositive	47	45	46.4±16.1	31.3±38.0	188.3±245.5	16 (34)	14 (29)	8.0±2.6
<i>H. pylori</i> gastritis ²	26	46	47.1±15.3	30.2±38.1	195.9±249.1	7 (27)	5 (19)	8.6±3.8
Total	100	47	44.4±15.4	33.3±48.2	219.7±300.4	33 (33)	19 (19)	8.5±3.3

Data are given as mean ± SD.

cU = Chronic urticaria; Sx1 = atopy screening test (see Methods); CRP = C-reactive protein in serum; WBC = white blood count. Statistically there was no significant difference or correlation between the groups (χ^2 test, Mann-Whitney-Rank-Sum test).

¹ Geometric mean ± SD in kU/l.

² Patients with endoscopically verified *H. pylori* gastritis, 24 of them were seropositive and 2 seronegative.

Twenty-five of 47 seropositive subjects underwent endoscopy with biopsies. Gastritis of antrum (100%) and/or corpus (46%) was confirmed histologically in all of these patients. Moreover, in all but 1 patient (96%), *H. pylori* infection was detected in biopsy specimens. The 'negative' patient had only mild gastritis and titers were 1/2,300 for IgA and 1/180 for IgG. Furthermore, 2 patients with negative *H. pylori* serology underwent endoscopy due to gastric complaints and were found to have *H. pylori* colonization. Thus, *H. pylori*-associated gastritis was diagnosed by histopathologic examination in 26/100 (26%) patients with chronic urticaria, although only 27 patients underwent endoscopic gastric examination. 9/26 (35%) *H. pylori* infections of antral mucosa were mild, 13/26 (50%) moderate and 4/26 (15%) severe. According to the age distribution of seropositive subjects, prevalence of *H. pylori* gastritis seemed to be higher in younger individuals with chronic urticaria (fig. 1).

Interestingly, gastric complaints were reported by only 7 of 26 (27%) patients with *H. pylori* gastritis. Occurrence of gastric symptoms did not coincide with a more severe grade of gastritis. There was no significant relation of seropositivity or gastritis with duration of chronic urticaria (table 3). Further analysis of laboratory parameters did not reveal any association of raised titers for *H. pylori* or gastritis with total IgE, Sx1, C-reactive protein or white blood count. Moreover, there was no correlation with age or sex (table 3). Anamnestic angioedema did not correlate with seropositivity and/or gastritis or any of the laboratory parameters.

Due to losses (removal), only 24/26 patients with *H. pylori* gastritis received antimicrobial therapy. Four patients needed a second course of treatment until bacteria were absent. There was no association of treatment failure with severity of gastritis (2 mild, 1 moderate, 1 severe). Except

in 1 case (occurrence of diarrhea), treatment was well tolerated. One patient missed the follow-up appointments and 2 patients were not willing to undergo further control endoscopy. Thus, in 21 patients, eradication was confirmed histologically. In 14 of them (67%) urticaria and/or angioedema discontinued 3–12 weeks after treatment and complete remission was observed (follow-up 6–9 months, no antihistamines). Mean duration of urticaria in these patients before treatment was 29.0 months (range 5–190). Additionally, 5 patients (24%) were significantly improved (mean duration of urticaria 28.0 months, range 9–68; no or significantly reduced use of antihistamines). Eradication was not beneficial in 2 patients (9%), both with mild gastritis (5 and 8 months' duration of urticaria, respectively). One of the 2 patients not willing to undergo re-gastroscopy after therapy showed remission, the other had a significant improvement of urticaria. Taken together, almost all (91%) of antimicrobially treated subjects showed disappearance or improvement of chronic urticaria. In contrast, among the seropositive patients with chronic urticaria (n = 18) only 28% showed significant improvement (significant reduction of urticarial symptoms and/or use of antihistamines) and 22% spontaneous remission (no further use of cetirizine or loratadine) within 12 weeks.

Pseudoallergic Reactions

Patients in whom no infectious trigger could be found (n = 50) received a diet free of artificial additives and known naturally occurring pseudoallergens for at least 6 weeks. Urticaria improved in 29 of them (58%). Thus, oral challenge tests were performed. 12% of provoked subjects showed pseudoallergic reactions to ASA. Most of them had ingested low-dose ASA daily or 500–1,000 mg weekly, thereby provoking whealing. Interestingly, subjects with

pseudoallergic reactions to ASA were of younger age (median 29.5 years, $n = 12$) when compared to the remaining subjects with chronic urticaria (median 44.0 years, $n = 88$), $p < 0.05$. However, only 3% of patients who benefitted from the diet reacted to food additives (2 to potassium metabisulfite 300 mg, and 1 to sodium nitrite 50 mg).

Course in H. pylori Seronegative Subjects

Among seronegative subjects ($n = 53$), 17 showed a focal infection (dental, ear-nose-throat, yersiniosis). Of these 17 subjects, 12 showed healing after treatment of the focal infection. The other 5 showed no improvement of urticaria. With 2 exceptions, subjects with pseudoallergic reactions to ASA or food additives ($n = 15$) showed improvement or healing after discontinuation of ASA and/or individual additive-free diet. From the 5 subjects with thyroid antibodies, only 2 improved spontaneously. The 2 patients with malignant diseases showed an unchanged disease course and were not improved by antihistamines. Among the remaining 14 subjects with idiopathic urticaria, only 6 showed improvement or healing within 3–6 months. Taken together, in *H. pylori*-seronegative subjects, 33 (62%) were improved or healed versus 20 (38%) patients further requiring regular treatment with antihistamines.

Discussion

The present study provides new data regarding eliciting factors of chronic urticaria. 43% of subjects presented important focal infections, 15% demonstrated pseudoallergic reactions by oral challenging, 5% showed antibodies to thyroid but without manifest autoimmune thyroiditis, and 2% had underlying malignant diseases. Taken together, we identified a relevant etiology of chronic urticaria in 65% of cases, only 35% of subjects were considered to suffer from chronic idiopathic urticaria. In contrast, Quaranta et al. [22] suggested that an etiology is determined in much less than 10% of patients with chronic urticaria.

In this study, focal infections – in particular *H. pylori*-associated gastritis – represented the most frequent eliciting factor of chronic urticaria pointing to a specific skin pathogenesis of *H. pylori*. *H. pylori* infection was found in 96% of endoscoped subjects with chronic urticaria and may be present at least in all seropositive subjects (47%). Moreover, in 91% of subjects, urticaria disappeared or improved after eradication treatment whereas only 50% of untreated *H. pylori*-seropositive subjects improved spontaneously. In contrast, other focal infections were less frequent in chronic urticaria: ear-nose-throat focal infection 21%, infection

with EBV or CMV 9%, dental focal infection 5% or yersiniosis 5%. Infection with EBV or CMV was found exclusively in young adults. Thus this diagnostic serology might be restricted to children and young adults in the future. Subjects with yersiniosis always presented with diarrhea and/or arthritis. Subjects with ear-nose-throat or dental focal infection could be identified by careful history. Regarding the fact that incidence of dental focal infection was very low, this diagnostic approach may be neglected in the future. Confirming previous data demonstrating less than 2% allergic reactions to foods in adults with chronic urticaria [2], we did not find allergic reactions to foods. In acute urticaria a strikingly high prevalence (39.5%) of associated upper respiratory tract infections (common cold) was observed [23]. This could not be confirmed for chronic urticaria.

Reports on *H. pylori* gastritis associated with dermatologic diseases have been scarce but have indicated a possible relation with chronic urticaria. Rebora et al. [16] found seropositivity in 4/7 patients with chronic urticaria. In 3 of them, urticaria disappeared after *H. pylori*-specific treatment (not specified). Tebbe et al. [15] diagnosed *H. pylori* infection in 17/25 unselected patients with chronic urticaria by positive ^{13}C -urea breath test and circulating specific IgG antibodies. In all patients who underwent gastroscopy with biopsies (only 12), *H. pylori* infection was confirmed by histologic examination. 14/17 patients showed clinical remission or partial remission after *H. pylori* eradication whereas disease remained unchanged in untreated chronic urticaria patients without evidence for *H. pylori* infection.

In the present study, elevated *H. pylori* IgG and/or IgA antibodies were found in 47% of chronic urticaria. Similar prevalence rates of *H. pylori*-positive tests (with similar sensitivity and specificity like the Pyloriset-EIA used in this study) have been reported in symptomless individuals [21, 24]. Among 150 randomly selected Swedish adults (50 symptomless, 50 with dyspepsia, 50 with irritable bowel syndrome) there was a significant increase in the prevalence of seropositivity with age [21]. However, in this study, age distribution was different. Individuals with chronic urticaria aged 20–30 years showed relative high rates of seropositivity and *H. pylori* gastritis compared with results of population-based epidemiological data (fig. 1). The number of individuals in each age group (from 20 to 80 years) was comparable in both studies. In contrast, in patients with psoriasis who were younger than 50 years of age, only 4% showed antibodies directed against *H. pylori* [25]. In addition, we assessed *H. pylori* seropositivity in our laboratory staff (mean age 30.0 ± 5.7 years) and found seropositivity in only 11% of subjects ($n = 28$, not shown) whereas 60% of similar aged subjects with chronic urticaria showed

antibodies specific for *H. pylori*. Whereas only 37% of asymptomatic adults were shown to have an *H. pylori*-associated gastritis [26], we confirmed *H. pylori* infection in 96% of subjects with chronic urticaria who underwent endoscopy. The reported association between *H. pylori* and urticaria is consistent with an etiologic role of *H. pylori* but does not prove it. However, the disappearance or improvement of urticaria in almost all subjects (91%) after *H. pylori* eradication provides strong evidence for a causal relation between *H. pylori* gastritis and urticaria. One could speculate that triple therapy also treated another unidentified focus triggering the urticaria, but 4 patients needed a second treatment course to reach eradication. Healing or improvement of urticaria in these patients only followed eradication, whereas an unidentified focus likely would have been treated successfully by the first antimicrobial course. However, for unknown reasons in 2 patients, eradication did not change urticaria symptomatology.

The resolution of chronic inflammation in *H. pylori* gastritis was demonstrated to be a rather slow process and healing was regarded to take several months [27] which fits for the fact that healing or improvement of chronic urticaria occurred within 3–12 weeks after successful eradication treatment. To date, none of the remitted or improved patients showed recurrence or aggravation of chronic urticaria (follow-up 6–12 months). Several studies demonstrated a low *H. pylori* reinfection rate (<5%/year) [28, 29]. Thus, future long-time follow-ups not included in the present study will have to address this point.

The cutaneous pathology of *H. pylori* remains an enigma. It is tempting to speculate that structural components (flagella, adhesins) or products of *H. pylori* (urease, protease, phospholipase, cytotoxin) are involved in the development of urticarial eruptions. Several relationships between *H. pylori* colonization and mucosal inflammation have been described implicating modulation of immunologic processes which may also involve the skin [30–35]. Recently a modulatory action of *H. pylori* on histamine release from mast cells and basophils was demonstrated in vitro [36]. The immunomodulatory role of *H. pylori* might be mediated by its membrane lipopolysaccharide [37].

In the past, encouraging results have repeatedly reported improvement of chronic urticaria on an additive-free diet [10, 12]. In our study, 58% of those subjects in whom no infectious trigger could be found demonstrated benefit from a pseudoallergen-free diet (i.e. 29% of all subjects studied). However, only in 3% an individual additive was found to provoke urticaria symptomatology. In contrast, Zuberbier et al. [10] found that in 73% of patients with chronic urticaria, symptoms ceased or were greatly reduced within 2 weeks

on additive-free diet, and 19% of them responded to individual pseudoallergens on provocation tests. With regard to the estimated number of additives used in food processing (range between 2,000 and 20,000) [38] and drugs [39] it is tempting to speculate that patients with improved urticaria under diet may have reacted to individual pseudoallergens which were hitherto not used for testing. However, we found 12 patients reacting to ASA confirming previous results demonstrating a certain susceptibility of subjects with chronic urticaria to develop pseudoallergic reactions particularly to ASA. Most of these patients took ASA daily or once weekly, thereby triggering their urticaria. In conclusion, the most important steps to best approach the symptom complex chronic urticaria are a careful medical history and the specific search for focal infections, particularly *H. pylori* gastritis, which may play a main pathogenic role in chronic urticaria. Measurement of *H. pylori* IgA and IgG, ¹³C-urea breath test and/or gastroscopy with biopsies [40] may be included in the diagnostic management of chronic urticaria to identify patients who may profit from eradication treatment with disappearance of annoying long-standing urticaria symptomatology. However, further studies including control groups, e.g. patients with physical urticaria, where there are sound grounds for believing pathogenesis is quite distinct, will have to be made to confirm the growing evidence for a cutaneous pathology of *H. pylori*. Those patients in whom no treatable focal infection can be found may profit from a simple diet avoiding food additives and ingestion of ASA. For the remaining so-called idiopathic cases (here 35%), the mainstay of treatment may be non-sedating antihistamines of the newest generation [41].

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