

# CHRONIC URTICARIA AND ANGIONEUROTIC EDEMA

## *Statistical Analysis of 159 Cases*

J. R. EVANS, M.D.\* and C. R. K. JOHNSTON, M.D.

Department of Allergy

ONE hundred and fifty-nine cases of chronic urticaria and angioneurotic edema have been observed at the Cleveland Clinic during the 2 year period 1947 to 1948.

Seventy-eight cases were treated in 1947 and 81 during the following year. The over-all incidence of these syndromes as compared to all new admissions to the Clinic was 0.25 per cent.

Urticaria and angioneurotic edema are generally considered as part of the same process occurring in different sites in the skin. This view is supported by the evidence presented in Table 1 which shows that more than half of our patients had both hives and angioneurotic edema.

As shown in Table 2, sex was not a significant factor in the incidence of urticaria. However, angioneurotic edema alone occurred much more frequently in men.

In 102 of the cases in this series the approximate date of onset of the original symptoms was known but we were unable to demonstrate any significant seasonal incidence. This conclusion is not consistent with certain other opinions expressed in the current literature.

Many possible causes have been proposed, and as shown in Table 3, most of our cases have more than one probable etiologic factor. A tabulation of the incidence of the various responsible factors in this series is presented in Table 4.

Of the 26 per cent showing evidence of some focus of infection, 11 patients had tonsillitis, 8 prostatitis, 5 epidermophytosis, 4 sinusitis, 4 evidence of gall-bladder abnormality, 14 dental caries, 2 intestinal parasites, and 2 bronchiectasis.

External contactants responsible in 3.2 per cent of the cases studied were shampoo, cosmetics, wool, and shaving cream. In 15.6 per cent of the patients physical agents constituted an etiologic factor. There were 14 instances of pressure, 3 of exercise, 10 of heat, and 2 of cold.

Even though 29.7 per cent of the patients were found to have had a history of constipation, in practically none did the duration of the constipation coincide with that of the urticaria. However, there was suggestive evidence that some correlation existed between the taking of laxatives for the constipation and the urticarial lesions.

\*Former Fellow. Now practicing in Salt Lake City, Utah.

Table 1

	Cases	Per Cent
Hives and angioneurotic edema (ANE)	92	57.8
Hives only	48	30.4
ANE only	19	12.0

Table 2

	Men	Per Cent	Women	Per Cent
Total cases	77	48.4	82	51.6
ANE only	14	....	5	....
Urticaria only	21	....	27	....

Table 3

	Cases	Per Cent
No etiologic factors	15	9.6
One etiologic factor	50	32.2
More than 1 etiologic factor (2 to 6)	90	58.1

Table 4

Etiologic Factors	Per Cent
Focus of infection	26
Suspected food factors	14.4
Possible drug factors	28.8
Possible inhalation factors	7.3
External contactant factors	3.2
Physical agent factors	15.6
History of constipation	29.7
Psychogenic factors	63.5
Endocrine factors	7.1

Table 5

**Abnormal Laboratory Tests**

Test	No. Cases		Per Cent
	Tested	Abnormal	
Hematologic			
a. anemic	156	6	3.8
b. eosinophiles	92	11	12.0
c. leukocytosis	156	15	9.6
Urinalysis	148	14	9.5
Blood sugar	150	3	2.0
Serology	152	1	0.6
Stool examination	52	4	....
Gastric analysis	31	6 (low gastric acid)	
Basal metabolic rates	16	7 (5 above—2 below)	
			normal

The abnormal laboratory observations are tabulated in Table 5. No known laboratory tests are consistently positive in this condition; even the incidence of eosinophilia is remarkably low. Thus in only 11 out of 92 cases was there any increase (over 4 per cent), these cases varying from 5 to 12 per cent with an average of 7.2 per cent. Besides those tabulated in Table 5, other laboratory tests were made and roentgenograms taken as follows:

Roentgenograms: 57 chests, 24 gallbladder dye, 25 kidney, ureter and bladder, 17 plain gallbladder, 19 upper gastrointestinal, 14 colon, 16 sinuses, 4 skull, 4 urograms, 2 lumbar spine, and 1 each of the cervical spine, shoulder, dorsal spine, knees, and left ankle. There were 6 electrocardiograms, 3 bromsulphalein tests, 3 blood uric acid determinations, 3 blood urea nitrogen determinations, 3 serum calcium determinations, 3 spinal fluid examinations, and 1 urobilinogen determination.

No significant abnormal observations resulted from these tests except for 2 cases of polyps in the paranasal sinuses, 2 cases of sinusitis, and 2 cases of diverticulosis.

Sixty-eight different diseases were diagnosed in this series. However none appeared to be associated with urticaria or angioneurotic edema in significant numbers with the exceptions of chronic allergic rhinitis, psychoneurosis, perennial bronchial asthma, and possibly obesity (table 6).

In no one type of employment did urticaria occur more frequently than in any other.

Of the 55 patients skin-tested for allergies, there were 54 instances of significant reactions to various allergens. (The high incidence of positive skin tests may be explained by the fact that only those patients suspected of having definite allergic conditions are tested. In the absence of symptomatic clues such as cases in which focal infection, drug sensitivity and obvious nervous factors have been excluded, such tests are indicated.) Fifty-two manifested definite reactions to foods; 12 out of 50 showed positive reactions to pollens, and in 54 out of 55 there were pronounced reactions to inhalants, epidermals, molds or bacteria. In addition to those tested in the Clinic, there were 14 other patients who had had previous skin tests elsewhere, 10 of whom showed positive reactions.

We were able to follow 99 of these cases for at least  $12\frac{1}{2}$  months. Our longest follow-up was  $38\frac{3}{4}$  months, with an average of slightly more than 23 months. Forty-one patients obtained relief and have remained symptom-free; 27 were improved; 31 were not benefited or have experienced return of the symptoms after original relief (table 7). It must be remembered in evaluating the success of therapy that practically all of the patients in this series had been referred to the Clinic after one or more unsuccessful attempts at treatment elsewhere.

Of the 41 "cures" (table 8), 5 responded and remained improved after the use of antihistaminics alone. Three obtained relief after the use of antihistaminics and other therapy. Out of the 99 cases, 84 had used one or more antihistaminics and 65 of these (77.4 per cent) had experienced at least temporary relief as a result. Therapeutically it is important to note that even

Table 6

	Cases
Chronic allergic rhinitis . . . . .	41
Various psychoneuroses . . . . .	33
Perennial bronchial asthma . . . . .	24
Obesity . . . . .	14

Table 7

	No. Cases	Per Cent
Cured . . . . .	41	41.4
Improved . . . . .	27	27.3
Not helped or relapsed . . . . .	31	31.3

Table 8

“Cures”

	Only Therapy	Other Associated Therapy
Antihistaminics . . . . .	5	3
Stock bacteria vaccine . . . . .	5	4
Other allergenic vaccines . . . . .	3	3
Avoidance of drugs . . . . .	5	..
Elimination diets . . . . .	4	5
Reassurance or removal of neurogenic factors . . . . .	5	..

though one type of antihistaminic does not work, the administration of others often produces relief. It is essential to realize that failure to respond to these drugs may be due to insufficient dosage. These concepts have been demonstrated in our studies.

A nonspecific therapy commonly used in the Clinic consists of a stock bacterial vaccine containing *B. coli*, *Streptococcus faecalis*, *B. proteus*, *Salmonella paratyphi*, and *S. schottmulleri*. In the 99 patients adequately followed, this vaccine was prescribed for 29. Of these 9 were cured, and another showed improvement amounting practically to a cure. The latter patient had 2 minor episodes of angioneurotic edema after taking the vaccine.

In all 5 cases “cured” by avoidance of drugs, the offending agent was either a coal tar derivative or a compound containing phenolphthalein. In 5 other cases the patients were aware that various drugs caused hives but had experienced urticaria from other factors as well.

In 1 patient the symptoms persisted until a noninfected cyst was removed from the root of an incisor tooth. One case was “cured” by a cholecystectomy for chronic cholecystitis and 1 by removal of hemorrhoids in which no signs of infection had been evident. In 6 patients treated with oral hydrochloric acid no improvement was noted. Calcium was given to 7 patients either orally or intravenously; in 1 the hives disappeared after 4 months of this therapy. One patient treated with calcium reported some cessation of itching. Of 11

other patients who had had previous calcium therapy, 5 experienced partial temporary relief.

### **Summary and Conclusions**

1. A series of 159 cases of chronic urticaria and angioneurotic edema is reviewed and the observations presented.

2. Chronic urticaria and angioneurotic edema are symptom complexes in which multiple etiologic factors have been thought responsible but no common etiologic denominator demonstrated.

3. While numerous therapeutic agents have proved successful in urticaria and angioneurotic edema, no single therapy has been found beneficial in all cases.