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ACUTE AND CHRONIC URTICARIA

A Statistical Investigation on Clinical and Laboratory Data in 1,204 Patients and Matched Healthy Controls.

By

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The aim of this investigation was to study clinical and laboratory data in acute and chronic urticaria with statistical methods. To be able to evaluate the occurrence of certain signs and symptoms of urticaria it was necessary to study a group of healthy persons and compare them with the urticaria patients.

MATERIAL AND METHODS

The study is based upon 1,204 patients with urticaria, 591 men and 613 women, treated at the Department of Dermatology in Gothenburg, Sweden, during the period 1953-1962. Some of the patients were hospitalized but most of them received purely out-patient treatment. The data were collected from the hospital records and the out-patient registers. Most of the patients had extensive lesions. Only cases in which the diagnosis of urticaria was confident are included in the series.

945 of the patients with urticaria were acute and 259 chronic. Patients with chronic urticaria had suffered from their disease of more than 6 weeks.

The controls were selected so as to match the sex and age distribution of the patients with urticaria. They underwent laboratory tests concurrently with the urticaria patients.

The numerical comparisons made in this investigation were performed with the parametric Student's *t*-test and with the non-parametric, Chi-Square test, and the Sign test. Percentages of moving averages and seasonal index were computed. Level of significance: 0.05.

A. CLINICAL DATA

Incidence.

The incidence of urticaria at the Dermatologic Department of Gothenburg was 1.85 per cent. In series from the literature the incidence varies between 2.7 (*Hellerström*, 1962) and 3.9 (*Goodman*, 1928) per cent.

Sex Distribution.

The sex distribution of the total urticaria material i.e. both acute and chronic was 52 per cent women and 48 per cent men. The sex distribution for chronic urticaria was 64 per cent women and 35 per cent men. This predominance of women agrees with reports in literature (*Menagh*, 1928; *Fink & Gay*, 1934; *Stokes et al.*, 1935; *Urbach*, 1937; *Steinhardt*, 1954; *Rees*, 1957).

Age Distribution.

The age distribution for both acute and chronic urticaria together showed a rising incidence of onsets after 15 years of age, a maximum between 20-40 and then a decline. (*Fink & Gay*, 1934; *Stokes et al.*, 1935; *Sheldon et al.*, 1954; *Steinhardt*, 1954; *Mitchell et al.*, 1957). For women with chronic urticaria the tendency is the same but men with chronic urticaria seem on the average to acquire their disease in older ages with maximum between 30-40 years of age.

TABLE I
Occupational Groups.

	Rel. per cent of urticaria in occupational groups compared with the popula- tion of Gothenburg.	
	Males	Females
Agriculture, gardening, forestry, fishing	0.6	0
Industry and Crafts	0.4	0.5
Bank and Commerce	0.3	0.4
Transport	0.5	0.3
Public offices, Health services	0.7	0.7

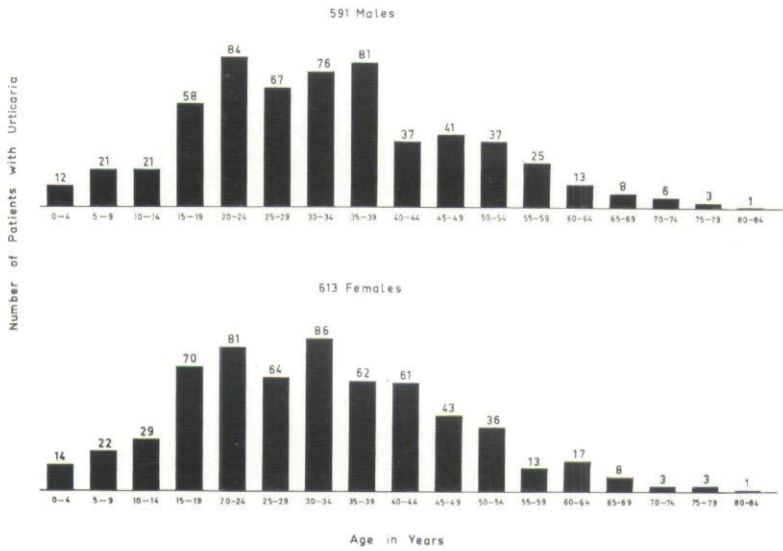


Fig. 1.

Frequency Distributions of Age at Onset in Urticaria

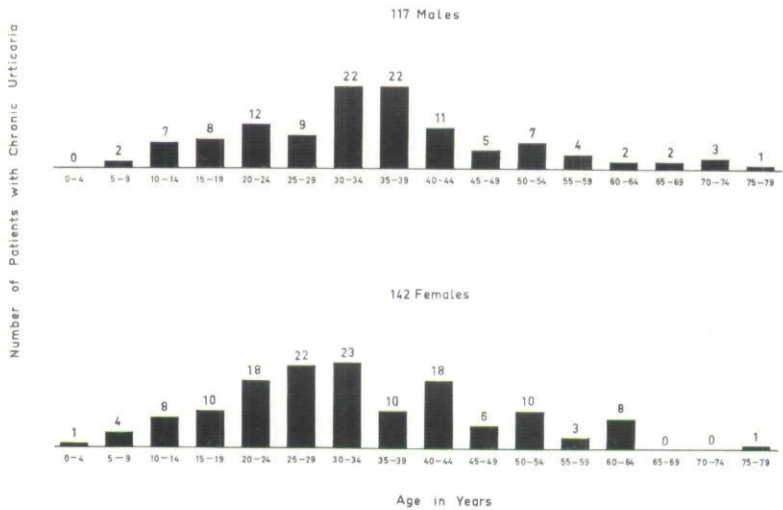


Fig. 2.

Frequency Distributions of the Age at Onset in Chronic Urticaria.

Occupational Distribution.

The occupational distribution of the patients with urticaria was compared with that of the total population of Gothenburg derived from the Swedish Statistical Yearbook, 1962. The urticaria patients is evenly distributed on the various occupational groups.

Seasonal Variations.

The number of cases of urticaria, acute and chronic, debuting each month of the year was registrated during the period 1953-1962 in order to ascertain the influence of seasons upon the onset of urticaria.

The percentages of centered twelve-month moving average for the patients with urticaria is shown in Fig. 3.

The number of urticaria debuting each month is expressed in per cent of the corresponding centered moving average. In calculating moving averages, each month is treated as the middle of its own particular, "year" or twelve-month period. The moving averages consume a number of observations at the beginning and end of the time series in this case 1953 and 1962. Thus these two years are not shown in Fig. 3.

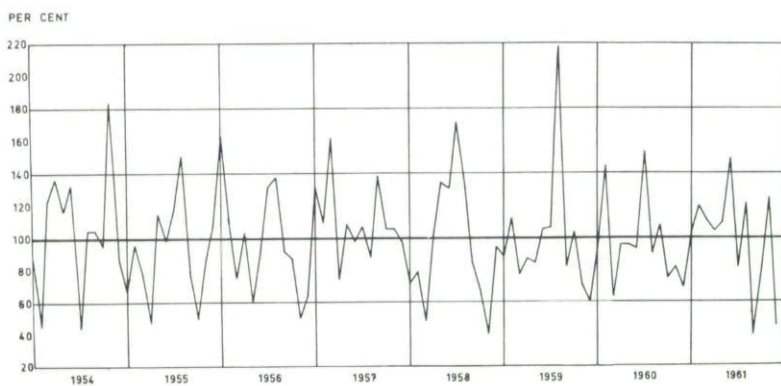


Fig. 3.

Percentage of Moving Average and Seasonal Index for Patients with Urticaria and for the Total Number of Patients with Skin Diseases at the Dermatological Department in Gothenburg 1953-1962.

As is shown in Fig. 3 there are variations in the incidence of urticaria during the year. The seasonal index was calculated for the patients with urticaria in order to better illustrate those variations.

The seasonal index was calculated in the following manner: the mean value of the deviations between the individual monthly values and their respective means was calculated. This gave a new mean of the twelve modified mean values, one for each month. By dividing each modified mean value by the new mean and then multiplying by 100, a seasonal index was obtained as a measure of the months' mutual relationship as regards their incidence of urticaria.

A rise in the number of onsets of urticaria is noted in May, June, July, a maximum in August and a fall in September, October, November and December.

As the variations in the number of first attendances at the Department of Dermatology might be the reason for corres-

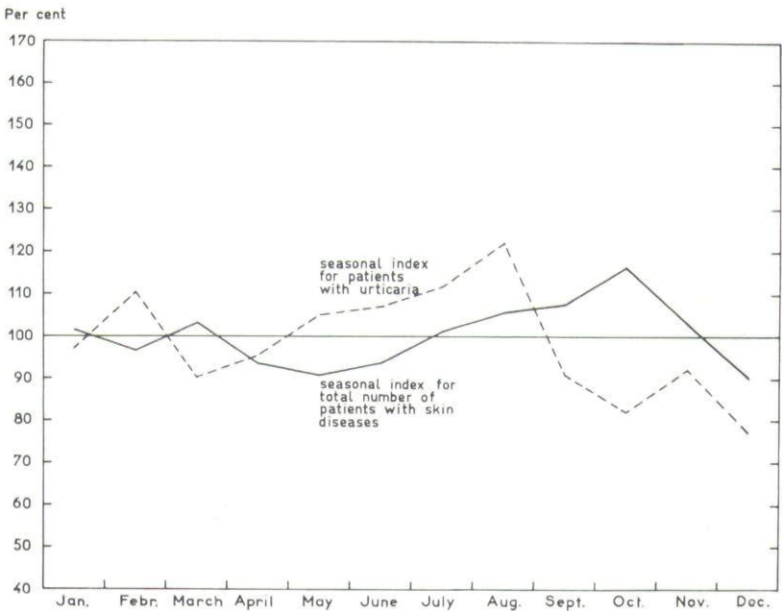


Fig. 4.

Percentages of Centered Twelve-Month Moving Average for Patients with Urticaria. Dermatologic Department, Gothenburg 1954-1961.

ponding changes in the recorded number of urticaria onsets each month a seasonal index was also calculated for first attendances at the hospital during this period. The variations in this index showed no seasonal variations corresponding to those in the urticaria series.

B. LABORATORY DATA

I. *Laboratory Blood Tests.*

In some 30 patients with acute urticaria, in some 30 patients with chronic urticaria and an equal number of healthy controls matched as to age, sex and time of examination comparisons were made as regards the red and white blood picture, sedimentation rate, total serum protein and the serum protein fractions.

Haemoglobin.

Acute urticaria. No significant difference was demonstrable between the mean values of patients with urticaria and matched healthy controls.

Ljungberg's colorimetric method of haemoglobin determinations was used. The arithmetic mean in 48 patients with acute urticaria was 85.7, variance 100.3, and in 48 controls 88.5, variance 94.4. Difference -2.8 $F = 1.0$. Student's test: not significant.

Chronic urticaria. No significant difference was demonstrable between the mean values of the patients with chronic urticaria and the matched healthy controls.

The arithmetic mean in 31 patients with chronic urticaria was 89.1, variance 82.7, and in 31 controls 92.8, variance 75.1. $F = 1.10$. Difference 6.4. Student's t -test: not significant. The Sign test: not significant (13 +, 15 -, 3 zeros).¹

¹ + sign mean higher values in the urticaria patient than in the control patient and - sign means lower values. Zero means no difference.

Red Blood Count.

Acute urticaria. No significant difference was demonstrable between the mean values in patients with acute urticaria and the matched healthy controls.

The Ellerman method was used. The arithmetic mean in 42 patients with acute urticaria was 4.4, variance 0.34 and in 42 controls 4.4, variance 0.30. F-test: not significant. The Student's t-test: not significant. The Sign test: not significant (22 +, 19 -, 1 zero).

Chronic urticaria. No significant difference was demonstrable between the mean values in the patients with chronic urticaria and the matched healthy controls.

The arithmetic mean in 27 patients with chronic urticaria was 4.5, variance 0.33, and in 27 controls 4.5, variance 0.38. F-test: not significant. The Student's t-test: not significant. The Sign test: not significant (14 +, 10 -, 3 zeros).

Erythrocyte Sedimentation Rate.

Acute urticaria. No significant difference was demonstrable between the mean values in patients with acute urticaria and the matched healthy controls.

Westergren's method of determination was used. The arithmetic mean in 50 patients with acute urticaria was 15.9, variance 253.0 and 50 controls 14.0, variance 317.0. Difference 1.9. F-test: not significant. Student's t-test: not significant. The Sign test: not significant (23 +, 22 -, 4 zeros).

Chronic urticaria. No significant difference was demonstrable between the mean values in the patients with chronic urticaria and the matched healthy controls.

The arithmetic mean in 34 patients with chronic urticaria was 6.9, variance 53.6 and in 34 controls 8.3, variance 67.9. Difference - 1.4. $F = 1.27$. Student's t-test: not significant. The Sign test: not significant (15 +, 16 -, 3 zeros).

White Blood Count.

Acute urticaria. No significant difference was demonstrable between the mean values in patients with acute urticaria and the matched healthy controls.

Ellerman's method was used. The arithmetic mean in 37 patients with acute urticaria was 7091.9, variance 6693484.4 and in 37 controls 6762.2, variance 3360487.8. Difference 329.7. F-test: not significant. The Student's t-test: not significant. The Sign test: not significant.

Chronic urticaria. No significant difference was demonstrable between the mean values in the patients with chronic urticaria and the matched healthy controls.

The arithmetic mean in 29 patients with chronic urticaria was 6896.6, variance 3622857.2 and in 29 controls 7296.6, variance 5703551.4. Difference 400.0. $F = 1.57$. Student's t-test: not significant. The Sign test: not significant (13 +, 15 -, 1 zero).

Neutrophilic Leucocytes—(Juvenile and Adult).

Acute urticaria. No significant difference was demonstrable between the mean values in patients with acute urticaria and the matched healthy controls.

The arithmetic mean in 34 patients with acute urticaria was 4501.0, variance 5086732 and in 34 controls 3556.9, variance 1369872. Difference + 944.1. F-test: not significant. Student's t-test: not significant. The Sign test: not significant (18 +, 16 -).

Chronic urticaria. No significant difference was demonstrable between the mean values in the patients with chronic urticaria and the matched healthy controls.

The arithmetic mean in 28 patients with chronic urticaria was 3901.7, variance 3896431 and in 28 controls 3955.3, variance 2985438. Difference - 53.6. F-test: not significant. Student's t-test: not significant. The Sign test: not significant (14 +, 14 -).

Eosinophilic Leucocytes.

Acute urticaria. No significant difference was demonstrable between the mean values in patients with acute urticaria and the matched healthy controls. This agrees with reports in the literature (Fink & Gay, 1934; Mitchell *et al.*, 1957).

The arithmetic mean in 27 patients with acute urticaria was 285.5, variance 63757 and in 27 controls 310.1, variance 86089. Difference - 24.6. F-test: not significant. Student's t-test: not significant. The Sign test: not significant.

Chronic urticaria. No significant difference was demonstrable between the mean values in the patients with chronic urticaria and the matched healthy controls.

The arithmetic mean in 26 patients with chronic urticaria was 275.4, variance 46545 and in 26 controls 309.3, variance 71227. Difference - 33.9. F-test: not significant. Student's t-test: not significant. The Sign test: not significant (11 +, 14 -, 1 zero).

Monocytes.

Acute urticaria. No significant difference was demonstrable between the mean values in patients with acute urticaria and the matched healthy controls.

Arithmetic mean for 29 patients with acute urticaria was 353.9, variance 83434, and for 29 controls 333.9, variance 56313. Difference + 20.0. F-test: not significant. Student's t-test: not significant. The Sign test: not significant.

Chronic urticaria. No significant difference was demonstrable between the mean values in the patients with chronic urticaria and the matched healthy controls.

Arithmetic mean for 26 patients with chronic urticaria was 338.5, variance 48538 and for 26 controls 329.5, variance 90541. Difference + 9.0. F-test: not significant. Student's t-test: not significant. The Sign test: not significant (13 +, 12 -, 1 zero).

Lymphocytes.

Acute urticaria. No significant difference was demonstrable between the mean values in patients with acute urticaria and the matched healthy controls.

Arithmetic mean for 31 patients with acute urticaria was 2226.1, variance 397947 and for 31 controls 2639.6, variance 133069. Difference - 413.5. Student's t-test: not significant. The Sign test: not significant.

Chronic urticaria. The mean values for the lymphocytes in the patients with chronic urticaria was significantly lower than in the controls.

The arithmetic mean for 28 patients with chronic urticaria was 2374.4, variance 1114969 and for 28 controls 2775.8, variance 1003969. Variances homogen-

ous. Difference = 401.4. Student's t-test: significant. The Sign test: significant (7 +, 20 -, 1 zero).

Serum Protein.

Reports on serum proteins in urticaria with matched healthy controls seem not to be available in the literature. A comparison of serum proteins in chronic urticaria and controls is here accounted for.

Total Serum Protein.

No significant difference was demonstrable between the mean values in the patients with chronic urticaria and the matched healthy controls.

The arithmetic mean in 29 patients with chronic urticaria was 6.9, variance 0.44 and in 29 controls 6.9, variance 0.09. Difference 0. Student's t-test: not significant. The Sign test: not significant (13 +, 12 -, 4 zeros).

Serum Protein Fractions.

The determinations were made with paper electrophoresis method.

Albumin. The mean value for albumin in patients with chronic urticaria did not differ from that of the controls.

The arithmetic mean in 29 patients with chronic urticaria was 3.9, variance 0.27 and in 29 controls 3.9, variance 0.02. Student's t-test: not significant. The Sign test: not significant (15 +, 4 -, 3 zeros).

Alpha₁ Globulin. The mean value for alpha₁ globulin in patients with chronic urticaria did not significantly differ from that of the controls.

The arithmetic mean for 29 patients with chronic urticaria was 0.36, variance 0.02, and in 29 controls 0.38, variance 0.01. Difference = 0.02. Student's t-test: not significant. The Sign test: not significant (15 +, 10 -, 4 zeros).

Alpha₂ Globulin. The mean value for alpha₂ globulin in patients with chronic urticaria did not significantly differ from that of the controls.

The arithmetic mean for 29 patients with chronic urticaria was 0.61, variance 0.04 and in 29 controls 0.53, variance 0.01. Difference + 0.08. Student's t-test: not significant. The Sign test: not significant (12 +, 10 -, 7 zeros).

Beta Globulin. The mean value for beta globulin in patients with chronic urticaria did not significantly differ from that of the controls.

The arithmetic mean for 29 patients with chronic urticaria was 0.78, variance 0.04 and in 29 controls 0.78, variance 0.01. Difference 0. Student's t-test: not significant. The Sign test: not significant (12 +, 13 -, 4 zeros).

Gamma Globulin. The mean value for gamma globulin in patients with chronic urticaria did not significantly differ from that of the controls.

The arithmetic mean in 29 patients with chronic urticaria was 1.29, variance 0.08 and in 29 controls 1.26, variance 0.02. Difference 0.03. The Student's t-test: not significant. The Sign test: not significant (12 +, 13 -, 4 zeros).

Antistreptolysin Titre (ASL).

In present series the antistreptolysin titre was determined in patients with acute and chronic urticaria and in healthy controls. Normal values for the ASL-titre are stated to be 250 and below.

The ASL-titre was more often elevated in patients with acute urticaria than in healthy controls.

Titres	Acute Urticaria	Controls	Chi-Square test
Normal	13	18	Significant
≥ 400	8	1	
	21	19	

The ASL-titre was not more frequently elevated in patients with chronic urticaria than in healthy controls.

Titres	Chronic Urticaria	Controls	Chi-Square test
Normal	40	18	Not significant
≥ 400	12	1	
	52	19	

II. Roentgenographic Examinations.

Focal infections have been considered to be an etiologic factor in urticaria. The percentages of focal infections in urticaria have been reported to be 4 (Urbach, 1937), 10 (Siegel *et al.*, 1954), 12 (Eisenberg, 1959), 14 (Rees, 1957; Steinhardt, 1954), 24 (Eichenlaub, 1925), 30 (Fink & Gay, 1934; Castelain, 1959; Göbel, 1961), 43 (Stokes *et al.*, 1935), 50 (Resch & Evans, 1958). The number of patients with urticaria cured by focal clearing has been reported to be 45 from 69 (Göbel, 1961), 18 from 55 (Lindemayer, 1961), 6 from 17 (Resch *et al.*, 1958).

In about 60 patients with chronic urticaria in present series X-ray of the accessory nasal sinuses, teeth and pulmonaries was performed as a routine in the search for possible etiologic foci. As psoriasis is considered often to be associated with infections (Hellgren, 1964) it was interesting to compare the patients with chronic urticaria with an equal number of psoriatics of the same age and sex regarding the roentgenologic pulmonary, sinus and teeth findings.

1. Accessory Nasal Sinuses.

In 59 patients with chronic urticaria a roentgenologic suspect inflammation in the accessory nasal sinuses was demonstrable in 32 percentages. An equal number of psoriatics showed positiv findings in 12 per cent. The difference was statistically significant.

2. Teeth.

In 45 patients with chronic urticaria abscesses at the roots and advanced paradental disease were found in 29 percentages. An equal number of matched psoriatics showed these findings in 27 percentages.

3. Pulmonaries.

In 61 patients with chronic urticaria parenchymatous and pleural findings were demonstrable in 18 percentages. In

psoriatics matched as to number, age and sex to the patients with chronic urticaria parenchymatous and pleural findings were also shown to be 18 percentages.

SUMMARY

1,204 patients with urticaria, 945 acute and 259 chronic, treated at the Department of Dermatology in Gothenburg during the period 1953-1962 were studied and compared with apparently healthy controls matched as to number, age and sex.

1. *Incidence*: 1.85 percentages.
2. *Sex distribution*: 52 percentages women, 48 percentages men.
3. *Age distribution*: a maximum of onsets between 20-40 years of age.
4. *Occupational distribution*: no definite differences between various occupational groups.
5. *Seasonal variations*: a maximum in the number of onsets of urticaria was demonstrable in August, a minimum in December.
6. *Laboratory tests*. No differences was demonstrable between about 35 patients with acute urticaria and matched controls or between patients with chronic urticaria and matched controls as regards *haemoglobin, red blood counts, erythrocyte sedimentation rate, white blood count, neutrophilic leucocytes, eosinophilic leucocytes, monocytes, total serum protein, albumin, alfa₁ globulin, alfa₂ globulin, beta globulin, gamma globulin*.

There was a statistically significant:

1. Reduction in lymphocytes in chronic urticaria but *not* in acute urticaria.
2. Higher number of elevated ASL titres in patients with acute urticaria than among the controls. No differences were demonstrable between patients with chronic urticaria and controls.

7. *Roentgenographic examinations.* In patients with chronic urticaria signs of accessory sinus inflammation was found in 32 percentages (19/59), dental abscesses and paradental diseases in 29 percentages (13/45) and pulmonary parenchymatous and pleural changes in 18 percentages (11/61). Matched groups of psoriatics showed similar frequency of pulmonary- and teeth foci but only in 12 percentages signs of accessory sinus inflammations.

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