

Serum immunoglobulin levels in acute and chronic urticaria

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Although the pathogenesis of acute urticaria may frequently involve an allergic mechanism, the etiology of chronic urticaria is a diagnostic dilemma in most patients. A recent study described 9 children with immunoglobulin deficiencies in a group of 16 children with chronic urticaria and recurrent upper respiratory tract infections. The purpose of this investigation was to quantitate the three major serum immunoglobulins, γ G-, γ A-, and γ M-globulins, in adult patients with acute or chronic urticaria. None of these patients was subject to repeated upper respiratory tract or other infection. No deficiency of serum γ G-, γ A-, or γ M-globulins was demonstrated in the 10 adult patients with acute urticaria or the 24 adult patients with chronic urticaria. In fact, when compared with normal adults, the patients with chronic urticaria had statistically significant increased serum γ G-globulin concentrations. The clinical significance of this increased γ G-globulin synthesis in adult patients with chronic urticaria has not been elucidated.

Acute urticaria is frequently the result of an allergic reaction.¹ However, in chronic urticaria a recognizable immunologic basis can seldom be identified. Green and associates² studied 236 patients with chronic urticaria, and in only 8 per cent of the patients could they relate the urticaria to physical or allergic factors. Buckley and Dees³ recently studied 16 children with chronic urticaria and recurrent upper respiratory infections. They reported that 9 of the 16 children had either a single or multiple γ A-, γ G-, or γ M-globulin deficiency.

The purpose of this investigation was to quantitate the three major serum immunoglobulins, γ G-, γ A-, and γ M-globulins, in adult patients with acute and

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chronic urticaria and compare these concentrations with those measured in a normal adult population. Any significant variation in serum immunoglobulins might be a reflection of differences in etiologic mechanisms. The results of this study showed statistically significant increases in γ G-globulin and γ A-globulin concentrations in the sera of chronic urticaria patients as compared with γ G- and γ A-globulin levels in the sera of normal subjects and an increase in γ A-globulin concentrations in the sera of acute urticaria patients as compared with that of the normal adults.

MATERIAL AND METHODS

Patients

Adults with urticaria were seen in the allergy clinic of the Presbyterian University Hospital or in the private practice of one of us (M. I. L.). Patients had been investigated with complete history and physical examinations and appropriate laboratory and intradermal skin testing where indicated.

For purposes of this study, the diagnosis of acute urticaria (10 patients) was based on the presence of urticarial skin lesions and/or angioedema of less than 4 weeks' duration. In many cases, the cutaneous lesions were manifest for one to several days. Of the 10 cases of acute urticaria, 7 were due to penicillin hypersensitivity, one was possibly due to a food hypersensitivity, and 2 were unexplained. On the other hand, the diagnosis of chronic urticaria was made in those persons (24 patients) who had hives and/or angioedema for longer than 4 weeks. Throughout this paper the term "urticaria" will mean urticaria and/or angioedema.

Sera

The blood from these patients was obtained over an 11 year period. The separated sera were stored at -18° C. until the immunoglobulin determinations were performed. Normal sera were obtained from healthy medical center personnel. Each normal donor denied a past history of urticaria, angioedema, or allergic disease.

Immunochemical quantitation of γ G-, γ A-, and γ M-globulins

Serum immunoglobulins were quantitated by a modification of the radial diffusion-plate method of Mancini.⁴ Monospecific goat antihuman γ G-, γ A-, and γ M-globulin antisera were obtained from Hyland Laboratories. Double-gel diffusion and immunoelectrophoretic techniques verified the monospecificity of each antiserum. The reference standards were dilutions of a pooled normal human standard serum obtained from Hoechst Pharmaceuticals. The radial diffusion plates were incubated in a humidity chamber at approximately 24° C. The precipitin rings which developed were recorded at 16 and 20 hours for γ G-globulin, 24 and 48 hours for γ A-globulin, and 48 hours for γ M-globulin. From photographic enlargements the precipitin rings were measured to the nearest millimeter. The logarithms of the concentrations of the specific proteins measured were proportional to the precipitin ring diameters as previously pointed out by Mancini and associates.

Table I. *Serum immunoglobulin concentrations in acute and chronic urticaria*

<i>Patients</i>	<i>γG-globulin (mg.%)</i>		
	<i>Arithmetic mean</i>	<i>Standard deviation</i>	<i>Range</i>
Normal (50)	977	178	730-1,500
Acute urticaria (10)	997	215	760-1,570
Chronic urticaria (24)	1,281	374	770-2,650

RESULTS**Normal adults**

The mean concentrations of the three major immunoglobulins in 50 normal adult subjects were: γ G-globulin, 977 milligrams per cent; γ A-globulin, 111 milligrams per cent; and γ M-globulin, 194 milligrams per cent. The arithmetic means, standard deviation, and ranges are shown in Table I. The value for γ G-globulin is in agreement with that reported by other authors.⁵⁻⁷ In contrast, the mean serum concentration of γ A-globulin was lower and that of γ M-globulin was somewhat higher than that reported by other investigators.⁵⁻⁷

Urticaria patients

Serum γ G-, γ A-, and γ M-globulins were quantitated in 10 patients with acute urticaria and in 24 patients with chronic urticaria. The mean, standard deviation, and ranges for each of the serum immunoglobulins for each of the patient groups are shown in Table I. None of the urticaria patients was deficient in any of the three immunoglobulins measured. When these data were subjected to logarithmic transformation, it was found that these data closely adhered to a normal distribution. Since these data were approximately normally distributed, statistical analyses with the use of Student's *t* test were performed. It was found that statistically significant increases existed ($P < 0.05$) for serum γ G- and γ A-globulin in the chronic urticaria patients as compared with the acute urticaria patients and normal subjects and for serum γ A-globulin in the acute urticaria patients as compared with the normal adults.

DISCUSSION

With the exception of hereditary angioneurotic edema, a familial and rare disease in which patients lack an inhibitor of the first component of serum complement⁸ and serum inhibitor to plasma kallikrein,⁹ there were no reported immunoglobulin defects or biochemical abnormalities in patients with recurrent urticaria or angioedema until the study by Buckley and Dees.³ These investigators reported that in a group of 16 children with chronic urticaria and recurrent upper respiratory infections, 9 children had deficiencies of either one or more immunoglobulins, γ G-, γ A-, or γ M-globulin. In the present study, none of our adult patients with urticaria had any unusual frequency of upper respiratory infection or other infectious process. Furthermore, none demonstrated any deficiency of the three major serum immunoglobulins. The fact that Buckley and Dees studied a pediatric population may account for the differences in the two studies.

patients and normal adults

γA -globulin (mg.%)			γM -globulin (mg.%)		
<i>Arithmetic mean</i>	<i>Standard deviation</i>	<i>Range</i>	<i>Arithmetic mean</i>	<i>Standard deviation</i>	<i>Range</i>
111	50	60-202	194	112	90-470
191	92	103-394	201	120	80-355
184	102	62-450	174	82	70-400

Statistically significant increases in the level of serum γG - and γA -globulins were found when our chronic urticaria patients were compared with the normal adult group. Similarly, a significant increase in the level of serum γA -globulin was demonstrated in the acute urticaria group. The significance of the observed increases in γA -globulin in the urticaria patients cannot be stated with certainty. It has been reported previously⁵ that differences in methodology, antisera, and primary reference standards can result in considerable variation in the reported concentrations of the three major immunoglobulins. Therefore, it is necessary to point out that the mean serum concentration of γA -globulin in our normal adult population is somewhat lower than that reported by other investigators.⁵⁻⁷ When the mean serum γA -globulin concentration in our acute and chronic urticaria patients was compared with the normal serum γA -globulin concentrations reported by others, there were no statistically significant differences noted.

It has been shown that γ -globulin levels are somewhat higher in the Negro.¹⁰ Two Negroes were included in the chronic urticaria patients studied, while one Negro was in the acute urticaria group. Since the number of Negro patients was too small to produce a sizeable change in our data, the patients were not separated on the basis of race.

The observed increase in γG -globulin in the chronic urticaria patients as compared with our normal adult population may be meaningful in that the increase in γG -globulin concentration is also statistically significant ($P < 0.05$) when compared with the normal γG -globulin concentrations reported by others. The possibility that the increase in serum γG -globulin observed in the chronic urticaria patients represents a stimulation of the lymphoid system must be entertained. Documentation of hypersensitivity to drugs, foods, or environmental allergens could not be elicited in the 24 patients with chronic urticaria. In addition, these patients had no history, physical findings, or laboratory evidence to suggest chronic infectious diseases or collagen-vascular disease. The clinical significance of the elevated γG -globulin concentrations in patients with chronic urticaria cannot be ascertained at this time.

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