

## SERUM IMMUNOGLOBULINS IN FIXED DRUG ERUPTION

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**Abstract.** The serum globulins IgG, IgA and IgM were studied in the serum of 47 patients with fixed drug eruption due to identified drugs. The diagnosis was established by using as a test the readministration of the responsible drug and the consequent appearance of the eruption. IgM was found in normal amounts in the acute phase and after the remission of the eruption, whereas IgG and IgA were found increased during the acute phase of the eruption though after the remission, levels returned to normal.

**Key words:** Immunodiffusion; Immune complexes; Fixed drug eruption

The term "fixed drug eruption" was coined by Brocq to describe a special type of cutaneous reaction to antipyrine (2).

The clinical characteristics of fixed drug eruption are: (a) sudden onset of well circumscribed inflammatory lesions. (b) reappearance in previously involved areas after readministration of the drug responsible.

It is well known that quite a few drugs can produce this disorder and some of them more often than others (9). Various chemical substances, not considered as drugs, such as dye additives and preservatives, are very often incriminated as causative agents (7).

Little is known of the nature of fixed drug eruption. Toxic and especially immunological mechanisms have been blamed for the abnormal response of the skin, but no convincing evidence has yet been provided (8).

The present paper reports elevated serum levels of IgA and IgG in patients with fixed drug eruption during the acute phase of the disorder.

### MATERIAL AND METHODS

Fifty-eight patients with fixed drug eruption due to identified drugs were studied. Of the above patients, 18

presented the eruption for the first time, 30 for a second time and 10 for the third (or more) times.

The diagnosis was established by clinical examination after taking a thorough history of the patient and by the test of readministering the responsible drug 20 days after the remission of the eruption. Fifty out of the 58 patients were willing to undergo the test of readministration of the incriminated drug, of whom 47 sustained the eruption again.

Five c.c. of blood was withdrawn from each patient (a) as soon as the disease was diagnosed (usually 48 hours after the appearance of the eruption, (b) 20 days after the remission of the eruption, (c) 48 hours after the reappearance of the eruption, giving the responsible drug, and (d) 20 days again after the new remission of the eruption. Finally, blood was taken from each patient four times, i.e. twice during active eruption, and twice, 20 days after remission.

The serum was separated from the blood and was kept in a deep freeze ( $-30^{\circ}\text{C}$ ) until tested. For the quantitative determination of IgG, IgA and IgM, the radial immunodiffusion technique (6) and Hyland immunoplates were used.

The results were compared with those taken from the serum of 32 normal adults with no previous history of drug reaction, who had been used as controls.

Statistical significance was assessed by probability value ( $P$ ) based on Student's  $t$ -test.

### RESULTS

The concentration of immunoglobulins in the sera of the patients in the acute phase of the eruption and in remission, as well as those values in the control group, are shown in Table I.

The value of IgM was found to be within normal limits, when estimated both at the time of active eruption and when the eruption had subsided ( $P < 0.5$ ). By contrast, IgG and IgA levels were highly elevated ( $P < 0.002$  and  $P < 0.001$ ) during active eruption, returning to normal levels when the eruption subsided ( $P > 0.5$ ).

The increased levels of IgG and IgA were found to be independent of the kind of drug responsible

Table 1. Indicates the mean value of IgG, IgA, IgM  $\pm$  S.D. in the serum of the patients in the various stages of the eruption, and in the control subjects

A1=appearance of the eruption, A2=remission of the eruption, B1=readministration of the drug responsible and appearance of the eruption, B2=remission of the eruption

		IgG	IgA	IgM
Patients (n=47)	A1	2 340 $\pm$ 228	552 $\pm$ 131	120 $\pm$ 14
	A2	1 320 $\pm$ 210	200 $\pm$ 50	115 $\pm$ 10
	B1	2 400 $\pm$ 200	580 $\pm$ 110	120 $\pm$ 10
	B2	1 250 $\pm$ 230	230 $\pm$ 48	105 $\pm$ 15
Controls (n=32)		1 280 $\pm$ 263	222 $\pm$ 40	111 $\pm$ 22

and the significance of the appearance of the eruption (whether it appeared for the first, second, third or more times).

### DISCUSSION

Several workers have investigated the possibility that immunological mechanisms underlie fixed drug eruption. Varying results of patch tests and autografts have been reported (1, 4, 5).

Wyatt et al. (10) found a thermolabile agent in the serum during the clinically active phase of a phenolphthalein-induced fixed drug eruption, and by intradermal injection of this agent into susceptible skin they produced a sustained inflammation.

In 1975 Gimenez-Gamarase et al. (3) found that when autologous serum, taken from patients with fixed drug eruption during the acute clinical reaction, was added to the lymphocyte culture, it produced lymphocyte blast transformation which increased when the drug responsible was added to the lymphocytes.

The above findings suggest that some disturbance of humoral immunity may exist in fixed drug eruption.

Our findings in the 47 patients with the disorder, where IgG and IgA serum levels were found to be highly elevated during the acute clinical phase but normal during the clinical remission of the eruption, support the above hypothesis.

The explanation of this phenomenon is difficult; perhaps toxic immune complexes are formed which could be responsible for the tissue damage.

Furthermore, it is difficult to explain if there is any relation between the lymphocyte-transforming factor, the humoral agent of Wyatt et al. (10) and the high levels of IgG and IgA found in the sera of our patients.

Future studies on fixed drug eruption may provide a better understanding of the immunological mechanisms involved and may explain the association of circulating humoral factors and the appearance of the eruption.

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