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Serum IgG, IgM, and IgA levels in ankylosing spondylitis

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Using immunoelectrophoresis, Mackiewicz and Fenrych (1961) found broader and more intense IgM precipitation lines in sera from patients with ankylosing spondylitis (AS).

Kriegel, Burger, Kapp, and Alexopulos (1969) determined Ig levels in AS by single-radial immunodiffusion (Mancini, Vaerman, Carbonara, and Heremans, 1964) and reported a rise of the IgA level. Using the same technique, Langness, Banavsky, Alexopulos, Kriegel, and Burger (1971) found increased IgG and IgA serum levels in patients with AS. These authors did not consider the frequency distribution of the results nor the age distribution of the groups investigated.

We have determined the IgG, IgM, and IgA concentration in AS with the linear plate immunodiffusion technique (Wieme and Veys, 1970; Veys, 1971), and have compared the results with the Ig levels found in a normal population (Veys, Wieme, and Vuylsteek, in press) and in patients with rheumatoid arthritis (Veys, 1971). The patients with AS were then subdivided into groups to look for correlations between Ig levels and duration and activity of the disease.

Material and methods

Serum Ig levels were determined in 48 patients (42 men and 6 women) with ankylosing spondylitis. The diagnosis was made according to the criteria of Gofton (1968). The age distribution of these patients is given in Fig. 1. The controls comprised 297 normal healthy adults selected from members of the staff of the Post, Telegraph and Telephone Office in Ghent. A group of 100 patients with rheumatoid arthritis (RA) was also investigated. The difference in age distribution between the AS group and the control group (see Figs 1 and 2) necessitated comparisons between age classes.

The patients with AS were classified according to the following criteria:

(a) Presence or absence of peripheral involvement during the course of the disease and at the time of this investigation;

(b) Current activity of the disease. For this four parameters were used: erythrocyte sedimentation rate determined by Westergren's method; C-reactive protein activity; subjective complaints; strontium 87m scanning of sacroiliac joints and spine, as described by Van Laere, Veys, and Mielants (1972).

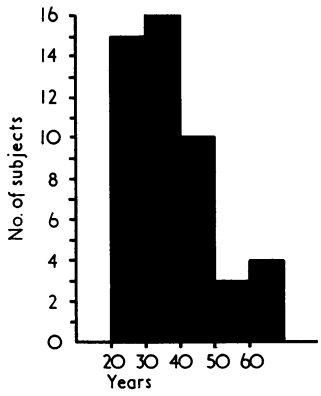

FIG. 1 *Age distribution of* 48 *patients with ankylosing spondylitis*

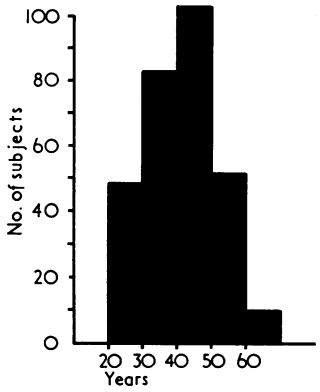

FIG. 2 *Age distribution of* 297 *control subjects*

Finally, Ig levels were compared with duration of disease.

The Ig levels were determined by the linear plate method (Wieme and Veys, 1970; Veys, 1971). In this technique antigen and antibody are incorporated in two separate agarose gels. Diffusion occurs between a square central piece of antibody-containing gel and two peripheral rectangular slabs containing antigen, *i.e.* the patient's serum. A precipitation line develops either in the antibody or in the antigen reservoir at a distance proportional to the logarithm of the antigen concentration. A calibration

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curve is plotted on lin/log paper, using samples of known concentration.

Results

The frequency distribution of the serum Ig levels in the 'AS' group is of the log normal type (Figs 3, 4, and 5). This finding corresponds with observations in a normal population (Veys and others, in press) and in cases of RA (Veys, 1971). Statistical calculations were therefore performed after log transformation of the serum Ig levels. Fig. 3 shows a very wide spread of IgG levels in AS with extreme values 1,024 and 4,640 mg./100 ml. The serum IgG levels observed in the women with AS are at the left of the frequency distribution curve. The IgM levels (Fig. 4) are also very widely spread, the extreme values being 50 and 512 mg./100 ml. The levels observed in females are in the middle part of the distribution. IgA levels also show a wide spread, with extreme values 112 and 880 gm./100 ml. The IgA levels observed in women spread over a large part of the distribution.

The statistical evaluation of the Ig levels in AS compared with the normal population and with a group of patients with RA is given in Table I. A highly significant increase of the IgG, IgM, and IgA levels in AS is seen by comparison with the normal population. There was no statistically significant difference in IgM and IgA level between RA and AS. It is noticeable that the IgG level in AS (mean 1,785 mg./100 ml.) is significantly higher than the IgG level in RA (mean 1,514 mg./100 ml.). Since the age distribution of the normal population and of the group of patients with AS was different, results obtained in corresponding age classes of the two populations were compared statistically. The number of AS cases in the older age classes was too small for statistical evaluation, but below the age of 50 there was a significant increase in IgG, IgM, and IgA levels in AS in each age group compared, with P values $<0{\cdot}001$ for the 20 to 29-year, 30 to 39-year, and 40 to 49-year age groups.

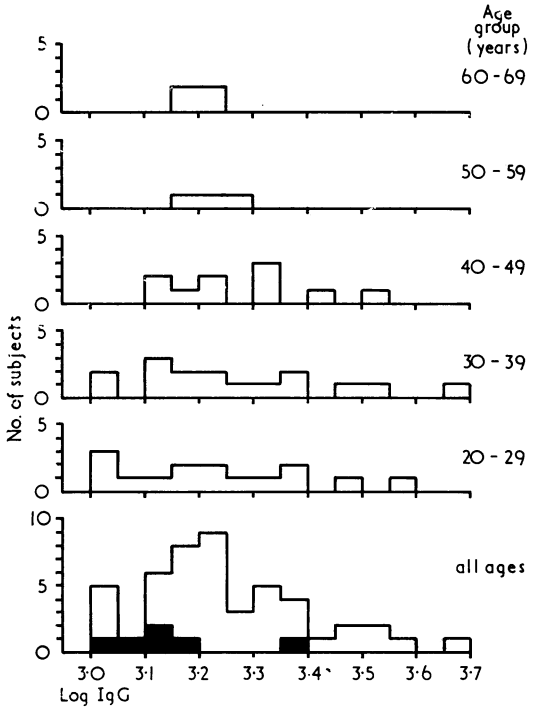

FIG. 3 *Frequency distribution of serum IgG levels in AS by age group. The levels observed in female patients are darkened on the diagram.*

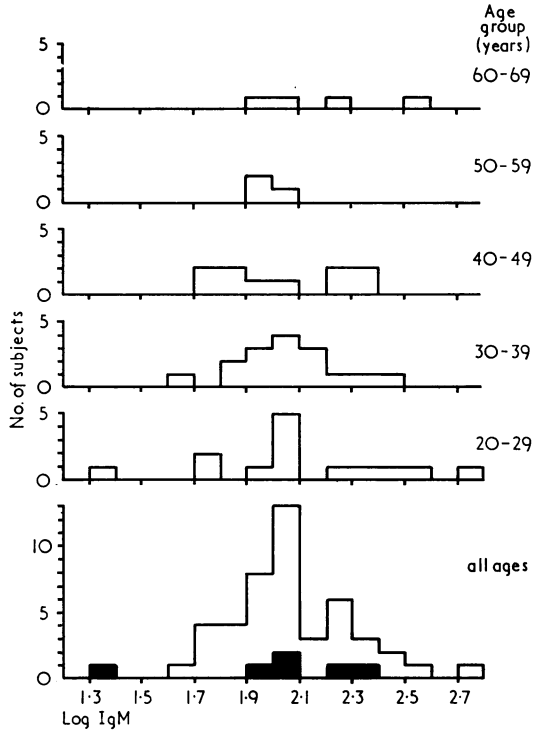

FIG. 4 *Frequency distribution of serum IgM levels in AS.*

We found no significant difference in Ig levels between patients with peripheral involvement and patients without. Furthermore, no correlations were found between any of the four criteria of disease activity and Ig levels, except that, when the erythrocyte sedimentation rate was above 20 mm. 1st hr, IgA and IgM (but not IgG) levels were significantly raised.

Finally, we investigated the relationship between the duration of disease and the Ig levels. There was no effect on IgM and IgA levels, but IgG levels were increased in patients in whom the duration of disease was between 10 and 15 years (Table II).

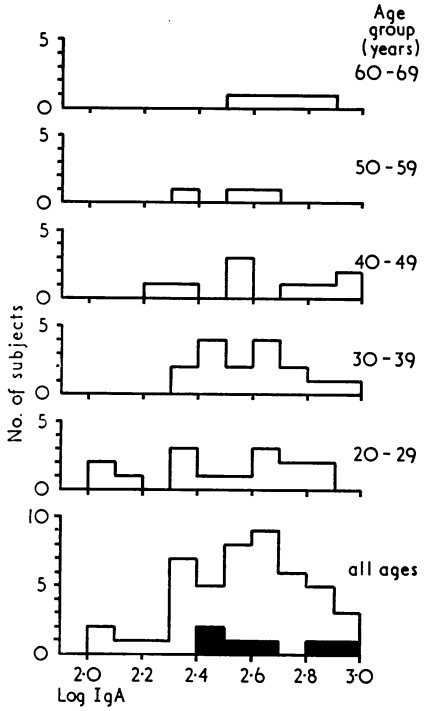

FIG. 5 *Frequency distribution of serum IgA levels in AS*

Discussion

From the wide spread of Ig values in Figs 3, 4, and 5, it may be concluded that serum Ig determination in ankylosing spondylitis is of no diagnostic value. Nevertheless, analysis by age of Ig levels in AS as compared with normal subjects showed significant differences at all ages.

In view of the increased IgG, IgM, and IgA levels in AS, we may conclude that the B-immune system is stimulated in this disease. Although some authors (Amor, Coste, and Delbarre, 1965) accept an infectious aetiology in AS, others have doubts (Kinsella, Norton, and Ziff, 1968). The only conclusion which can be drawn from our observations is that in AS there exists an inflammatory process in which the immune mechanism is involved. The nature of the stimulus to the immune system remains unknown; exogenous antigens or an autoimmune process could possibly be the basis for it. If there is antigenic stimulation, exogenous or endogenous, we could postulate that it occurs repeatedly because of the increase in the IgM level. On the other hand, the possible role of genetically determined or random somatic mutations of lymphoid stemcells in the aetiology of ankylosing spondylitis cannot be overlooked and we think that the stochastic approach to the disease may give more information on this point.

Summary

Serum IgG, IgM, and IgA levels were determined in 48 patients with ankylosing spondylitis. The results were compared with the serum Ig levels in 297 normal subjects and in a group of 100 patients with rheumatoid arthritis. The serum Ig levels were determined by the linear plate immunodiffusion technique.

The frequency distribution of the serum Ig levels was found to be of the log normal type in the three groups. An increase in IgG, IgM, and IgA levels was found in the cases of ankylosing spondylitis compared to the normal subjects. No difference was found between IgM and IgA levels in patients with AS and with RA, but IgG levels were significantly increased in AS by comparison with RA.

No statistically significant difference in Ig levels were found between patients with and without peripheral involvement, nor were differences related to disease activity.

Table I *IgG, IgM, and IgA serum levels*

Immunoglobulim	*Diagnosis*	*No. of cases*	*Mean serum level (mg./100 ml.)*	*Mean of log*	*Standard deviation of log*	*Standard error of mean log*	*t and P*
IgG	Normal	297	1,275	3·1056	0·1024	0·0059	t = 8·5371 P < 0·001
	AS	48	1,785	3·2517	0·1532	0·0221	
	RA	100	1,514	3·1801	0·1220	0·0122	t = 3·9461 P < 0·001
IgM	Normal	296	77	1·8879	0·2066	0·0120	t = 5·2923 P < 0·001
	AS	47	116	2·0655	0·2565	0·0374	
	RA	100	109	2·0405	0·2455	0·0245	t = 0·5769 0·50 < P < 0·90
IgA	Normal	297	224	2·3502	0·2260	0·0131	t = 6·5172 P < 0·001
	AS	47	380	2·5796	0·2147	0·0313	
	RA	100	304	2·4836	0·2821	0·0282	t = 2·1046 0·02 < P < 0·05

Table II *IgG related to duration of disease in* 48 *cases of ankylosing spondylitis*

Duration of disease (yrs)	*No. of cases*	*m log*	*s log*	*sm log*	*t and P*
0–5	15	3·1990	0·1496	0·0386	t = 0·9049 0·30 < P < 0·50
6–10	14	3·2505	0·1449	0·0418	
11–15	7	3·4192	0·1802	0·0681	t = 2·2491 0·02 < P < 0·05
>15	12	3·2305	0·1104	0·0332	t = 2·7815 0·01 < P < 0·02

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