

Immunoglobulins in endogenous uveitis

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Plasma electrophoresis gives information on the albumin and globulins in the blood. Globulin is divisible into α_1 , α_2 , β_1 , β_2 , and γ globulin. Gamma globulin is immunoglobulin, which again is divisible into immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin M (IgM).

Goodner (1968) found that the gamma globulin level was often raised in anterior uveitis, but that it was often lowered in posterior uveitis.

Aronson (1968) showed that IgM levels could be raised in uveitis. Among 37 patients with acute unilateral iridocyclitis he found that 34 had raised levels of IgM and 17 lowered levels of IgG. The method used, however, was simple qualitative serum electrophoresis.

Raised IgM represents a genetically-determined tendency towards rheumatic reaction (Aronson, Elliott, Moore, and O'Day, 1970). Aronson even suggested that some individuals (those who had had raised levels of IgM since birth) were liable to get endogenous uveitis, but not herpes, while those with lowered levels of IgA might become affected with herpes, but not uveitis.

Vasina (1971) likewise found that the gamma globulin level was raised in uveitis, while the albumin level was found to be lowered, but significant values were found only in acute iritis.

Koliopoulos, Perkins, and Seitanides (1970) found levels of IgM were raised in four cases of uveitis, but not in 13 cases of retinal vasculitis without uveitis. The method employed was that of radial immunodiffusion.

Ghose, Quigley, Landigan, and Asif (1974), on the other hand, likewise using the radial immunodiffusion technique, found normal immunoglobulin values in serum from five patients with uveitis.

The object of the present study was to estimate the immunoglobulin values in different forms of uveitis by the most accurate quantitative method.

Material and method

The clinical series comprised all patients with endogenous uveitis (a total of 300) referred to the Ophthalmic

Outpatient Department, Kommunehospitalet, during the period 1968 to 1974.

The age incidence is shown in the Figure. The average age was 46.8 years, and 58 per cent of the patients were men. The types of uveitis are shown in Table I.

Blood examinations were carried out routinely on the first visit. The proteins were estimated quantitatively by immunochemical plasma-electrophoresis using the 'rocket method' (Laurell, 1966).

The principle of the method is that the antigen (for example, IgM) is subjected to electrophoresis in a gel containing the specific antibody concerned. The distance from application hole to peak of the rocket is measured and compared with the peak height of a corresponding antigen standard.

Neither age nor sex variations were shown for any of the three immunoglobulin categories in 99 normal subjects (Weeke, 1968).

The following normal values were employed in the present report:

Albumin: 36-51 g/l, IgG: 5.8-14.3 g/l, IgA: 0.6-3.4 g/l, IgM: 0.3-1.5 g/l.

These figures represent a 95 per cent range using our own method developed on blood donors.

Result

Abnormal immunoglobulin levels were found in some patients with endogenous uveitis. Levels of IgM were raised in 10 per cent, IgA in 17 per cent,

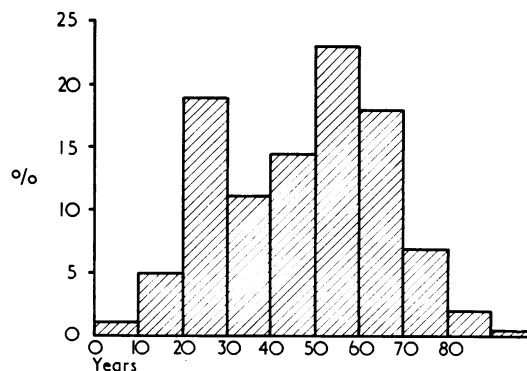


FIGURE Age incidence in 300 patients with endogenous uveitis

and IgG in 24 per cent. In 39 per cent of patients one or more of these immunoglobulins showed pathologically raised levels.

The uveitis series under review did not therefore confirm Aronson's observation of a particularly high incidence of raised IgM. In this series levels of IgA, and especially IgG, were more often raised than levels of IgM.

Lowered levels were found for IgM in 7 per cent, IgA in 1 per cent, and IgG in 0.3 per cent of the 300 patients examined.

UVEITIS TYPE

The immunoglobulin level was more often raised in relation to anterior uveitis than to the posterior form (Table I). In the group of patients with anterior uveitis 44 per cent showed an increase in one immunoglobulin or more, compared with 24 per cent of the group with posterior uveitis (Student's *t* test, $P < 0.01$).

The results in fibrinous iritis were the same as in the other anterior uveitis cases. This was unlike the erythrocyte sedimentation rate (ESR) which was found to be raised, particularly in cases of fibrinous iritis (70 per cent compared with 48 per cent in cases of non-granulomatous iritis, $P < 0.01$).

The difference between anterior and posterior uveitis was particularly marked for IgA (21 per cent raised in anterior uveitis compared with 5 per cent in posterior) and for IgG (27 compared with 14 per cent), but not for IgM (11 compared with 9 per cent), raised levels of which were evenly distributed within the individual diagnostic groups.

Elevated immunoglobulin levels were found more frequently in cases in which the uveitis was associated with a general disease than in cases in which uveitis alone was present.

Thus, raised levels were measured for one

Table I *Raised values for immunoglobulin A, G, or M in relation to different uveitis types (percentages)*

<i>Uveitis</i>	<i>Immuno-globulin*</i>	<i>IgG</i>	<i>IgA</i>	<i>IgM</i>	<i>Patients (no.)</i>
Acute fibrinous iritis	40	24	18	12	68
Non-granulomatous subacute iritis	51	30	25	11	83
Granulomatous iritis	52	38	19	5	21
Glaucomatous iritis	53	37	27	11	19
Hypopyon, panophthalmia	24	15	15	12	33
Choroiditis centralis	24	13	7	7	45
Choroiditis juxtapapillaris	15	0	0	12	8
Peripheral choroiditis	30	22	4	13	23
Total	39	24	17	10	300

*One or more immunoglobulins raised

immunoglobulin or more in 60 per cent of 45 patients having general diseases (chronic rheumatoid arthritis, spondylarthritis ankylopoietica, tuberculosis, syphilis, or gonorrhoea) compared with only 35 per cent of the remaining 255 cases ($P < 0.01$).

Neither dilated retinal veins nor optic disc oedema was found to be associated with raised immunoglobulin levels. As only 4 per cent of the total cases of uveitis had been treated with systemic steroids, such treatment would have had little influence on the results.

PROGNOSIS

Immunoglobulin levels were looked at in all patients of the series after they had been classified on the basis of the poorest visual acuity recorded during the course of the uveitis. Of patients with a visual acuity of 6/18 or less 43 per cent had raised levels of one or more immunoglobulins, compared with 35 per cent of patients who had better vision. The difference was not significant.

No correlation was noticed between number of attacks of uveitis and immunoglobulin levels.

Bilateral attacks were more often associated with elevation of one or more immunoglobulins (bilateral in 47 per cent, unilateral in 35 per cent, $P < 0.05$). The correlation with bilateral attacks seemed to involve IgM and IgG, but not IgA.

AGE INCIDENCE

The series was classified in 10-year age groups (Table II). All the immunoglobulins and the ESR showed a tendency to rise with increasing age. The difference was significant for IgA (20 per cent of those aged under 40 years had raised levels compared with 28 per cent aged over 40 years, $P < 0.05$), for one or more immunoglobulins and for ESR (31 compared with 46 per cent).

This correlation seemed to be independent of observation period, number of uveitis attacks, and type of uveitis.

Table II *Dependence of immunoglobulins on age at first uveitis attack. Figures indicate percentage of patients with raised Ig in 300 patients*

<i>Age (years)</i>	<i>Immuno-globulin*</i>	<i>IgG</i>	<i>IgA</i>	<i>IgM</i>	<i>ESR</i>	<i>Patients (no.)</i>
< 20	31	17	7	7	33	29
20	30	19	16	6	23	67
30	33	23	6	10	54	48
40	40	24	14	14	50	42
50	44	20	28	16	42	50
60	44	35	14	7	56	43
≥ 70	67	38	43	14	86	21

*One or more immunoglobulins raised

OTHER FINDINGS

Table III shows the other findings in the proteinogram. No relationship was demonstrable between lowered immunoglobulin or altered albumin, alpha or beta globulin, and type of uveitis or prognosis.

The relationship of ESR with immunoglobulins is shown in Table IV. There was a positive correlation between raised ESR and raised levels of IgG ($P < 0.001$), IgA ($P < 0.01$), and an increase in one or more immunoglobulins ($P < 0.001$), whereas no significant correlation was seen with IgM.

Discussion

The present study of unselected cases of endogenous uveitis material did not confirm the hypothesis of Aronson (1968) that IgM played a central role in uveitis. The examinations showed that all immunoglobulins might show raised levels, al-

though IgM did so more rarely than IgG and IgA.

The investigation showed a certain relationship between raised immunoglobulin and type of uveitis (more often raised in anterior uveitis). However, any prognostic conclusions from the proteinogram would be unjustified, except that there was a greater risk of bilaterality.

The simple ESR is, perhaps, more reliably correlated with uveitis type (especially fibrinous iritis) and uveitis prognosis than immunoglobulins (Norn, 1969). A positive correlation was detected between raised ESR and immunoglobulins. Changes in immunoglobulins did not seem to be a factor related to uveitis type and prognosis.

The simple, cheap laboratory ESR test is possibly of greater practical importance in endogenous uveitis than electrophoresis as performed in the present study. On the other hand, it is worth pointing out that in some cases a raised fraction might suggest a general disease underlying the diagnosed uveitis attack.

Summary

Examination of 300 patients suffering from endogenous uveitis revealed raised levels of IgG in 24 per cent, IgA in 17 per cent, and IgM in 10 per cent.

A raised level of one or more immunoglobulins was found more frequently in anterior uveitis than in the posterior form (44 compared with 24 per cent), in bilateral cases (47 compared with 35 per cent), and in relation to certain general diseases.

No differences were demonstrated within the individual types of uveitis (fibrinous, nodular, etc.), nor was there any difference in prognosis (recurrence rate, visual impairment). Immunoglobulin levels were raised most often in elderly patients.

I wish to thank Miss Elly Norup Sørensen for practical aid.

Table III Proteinogram in endogenous uveitis (percentage of 300 patients)

Levels	Total protein	Albumin	α_1	α_2	β_1	β_2	IgG	IgA	IgM
Raised	20	3	6	8	3	13	24	17	10
Lowered	0	8	1	1	0	0	0.3	1	7

Table IV Relationship between raised ESR (female > 15, male > 10 mm/h) and raised immunoglobulin (percentage of patients)

ESR	IgG	IgA	IgM	Immuno-globulin*	Patients (no.)
Raised	35	27	13	53	135
Normal	15	9	8	28	165

*One or more immunoglobulins raised

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