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Communications

Posterior subcapsular cataracts and glaucoma associated with long-term oral corticosteroid therapy

In patients with rheumatoid arthritis and related conditions

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Centrally placed opacities lying under the capsule at the posterior part of the lens—posterior subcapsular cataracts (PSC)—have been reported in 12·5 to 60 per cent. (mean 36·7 per cent.) of patients receiving treatment with long-term oral corticosteroid therapy (Black, Oglesby, von Sallmann, and Bunim, 1960; Oglesby, Black, von Sallmann, and Bunim, 1961; Giles, Mason, Duff, and McLean, 1962; Crews, 1963; Spencer and Andelman, 1965; Furst, Smiley, and Ansell, 1966). No such cataracts were reported by these workers in patients who had never received oral corticosteroid therapy (Black and others, 1960; Oglesby and others, 1961; Giles and others, 1962; Crews, 1963; Furst and others, 1966) (Table I). Although Crews found five patients with PSC in non-steroid treated patients, he considered that he could distinguish these cataracts from corticosteroid-induced PSC. Other workers, however, have failed to note any definite relationship between long-term oral corticosteroid therapy and the development of PSC (Pfahl, Makley, Rothermich, and McCoy, 1961; Gordon, Kammerer, and Freyberg, 1961; Toogood, Dyson, Thompson, and Mularchyk, 1962; Leibold and Itkin, 1963; Irby, Toone, Wittkamp, and Wiesinger, 1964; Havre, 1965) (Table I, overleaf).

The first purpose of the present study was to determine the prevalence of PSC in patients with rheumatoid arthritis (RA) treated with long-term oral corticosteroid therapy and to determine which factors may be involved in the pathogenesis of these cataracts.

A pathological rise in the intraocular pressure (glaucoma) to above 20 mm. applanation tonometry has been described following topical steroid therapy. Indeed, genetic patterns of glaucoma can be determined by deliberately instilling steroid solutions (Becker and Shaffer, 1965).

Our second purpose was to determine the prevalence of glaucoma in the above group of patients and to determine its relationship to systemic steroid therapy.

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Table I *Prevalence of PSC in corticosteroid-treated and non-corticosteroid-treated subjects*

Authors	*Year*	*Number of patients with PSC Corticosteroid-treated subjects*	*Non-corticosteroid treated subjects*	*Comments*
Black, Oglesby, von Sallmann, and Bunim	1960	19 of 44 with rheumatoid arthritis (39 per cent.)	None of 19 with rheumatoid arthritis (0 per cent.)	
Oglesby, Black, von Sallmann, and Bunim	1961	28 of 72 with rheumatoid arthritis (42 per cent.)	None of 19 with rheumatoid arthritis (0 per cent.)	An extension of Black and others (1960) with the same non-steroid-treated patients
Giles, Mason, Duff, and MacLean	1962	15 of 38 with rheumatoid arthritis (37 per cent.) 2 of 12 with bronchial asthma (17 per cent.) None of 5 with systemic lupus erythematosus (0 per cent.)	None of 24 with rheumatoid arthritis (0 per cent.)	All RA patients examined had received systemic steroid therapy for 6 months or more
Pfahl, Makley, Rothermich, and McCoy	1961	2 of 40 with rheumatoid arthritis (5 per cent.)		
Gordon, Kammerer, and Freyberg	1961	4 of 45 with rheumatoid arthritis (9 per cent.) 20 of 206 with rheumatoid arthritis (9 per cent.) 7 of 105 without rheumatoid arthritis (7 per cent.)		Definition of PSC different from that used by Black and others (1960); commonest causes are listed as senility or pre-senility, uveitis, and retinitis pigmentosa
Toogood, Dyson, Thompson, and Mularchyk	1962	3 of 56: Bronchial asthma (53), Nephrotic syndrome (2), Bronchial asthma and arthropathy (1) (5·4 per cent.)		10 patients had gross steroid overdosage, but no PSC. 3 with PSC had no other evidence of steroid overdosage
Crews	1963	16 of 52 with rheumatoid arthritis (35 per cent.) 4 of 20 with nephrotic syndrome (20 per cent.) 2 of 7 with miscellaneous disorders (29 per cent.)	5 of 171 with rheumatoid arthritis (3 per cent.)	Most patients in cortico-steroid-treated group referred because of visual symptoms
Leibold and Itkin	1963	None of 72 with bronchial asthma (0 per cent.)		Most patients received inter-rupted courses of cortico-steroids in high dosage rather than continuous high-dosage therapy
Irby, Toone, Wittkamp, and Wiesinger	1964	15 of 76 with rheumatoid arthritis (20 per cent.)	7 of 159 ophthalmic outpatients (4·3 per cent.)	All RA patients examined had received systemic steroid therapy for at least one year No definite relationship between dose, duration of therapy, and incidence of cataract could be ascertained
Spencer and Andelman	1965	34 of 58 with rheumatoid arthritis (60 per cent.)		All patients examined had had at least 6 months' triamcinolone therapy and all had been treated with systemic corticosteroid therapy for some time before starting triamcinolone

Authors	*Year*	*Number of patients with PSC* *Corticosteroid-treated subjects*	*Non-corticosteroid treated subjects*	*Comments*
Havre	1965	3 of 14 with miscellaneous childhood disorders (21 per cent.)		
Furst, Smiley, and Ansell	1966	7 of 56 with Still's disease (12·5 per cent.) 6 of 57 with rheumatoid arthritis (10·5 per cent.)	None of 48 with arthritis (0 per cent.)	All adult RA patients examined had received systemic steroid therapy for more than one year

Table II *Age and sex distribution in clinical groups studied*

Diagnosis	*Total no.*	*Corticosteroid-treated*				*Non-corticosteroid-treated*			
		No.	*Sex*		*Mean age ± S.D. (yrs) (Range)*	*No.*	*Sex*		*Mean age ± S.D. (yrs) (Range)*
			Female	*Male*			*Female*	*Male*	
Rheumatoid arthritis	307	148	134	14	52·5 ± 11·5 (18 – 80)	159	109	50	49·3 ± 15·0 (18 – 83)
Still's disease	4	1	1			3	1	2	
Reiter's syndrome	3					3		3	
Ankylosing spondylitis	3	2		2		1		1	
Gout	4	2		2		2		2	
Systemic lupus erythematosus	3	3	3						
Osteoarthritis	32	6*	4	2	62·6 ± 6·55 (53 – 71)	26	23	3	61·08 ± 7·81 (55 – 75)

* These patients had been prescribed oral corticosteroid therapy by their family doctors who had diagnosed the disorder as rheumatoid arthritis.

Patients studied

A series of 356 patients attending the Centre for Rheumatic Diseases in Glasgow was studied. The age and sex distribution and clinical diagnosis are shown in Table II. The 307 patients with RA had "definite" or "classical" disease by the 1958 criteria of the American Rheumatism Association (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959). The following clinical details were recorded in the patients with RA in addition to the age and sex of the patient: duration of arthritis, presence of subcutaneous nodules, articular score (Co-operating Clinics Committee of the American Rheumatism Association, 1965) and functional grade and *x*-ray stage (Steinbrocker, Traeger, and Batterman, 1949) (Table III). The following laboratory investigations were performed: haemoglobin concentration, erythrocyte sedimentation rate, serum albumin and globulin concentrations, sheep cell agglutination and latex fixation tests for rheumatoid factor, immunofluorescence tests for antinuclear factor (Beck, 1961), serum calcium and phosphorus concentrations, 90 min. post-prandial blood sugars, and in some patients serum cholesterol determinations and serological tests for syphilis (Table III, overleaf).

The duration, type and dosage of oral corticosteroid and other therapy, both past and present, were carefully recorded for each patient.

Table III *Comparison of clinical and laboratory data in steroid and non-steroid treated rheumatoid arthritics*

Series			*Corticosteroid-treated*	*Non-corticosteroid treated*	*Significance*
No. of patients			148	159	
Age (yrs)		Mean Range	52·5 ± 11·5 (18–80)	49·3 ± 15·03 (18–83)	
Sex		Male Female	14 (10 per cent.) 134 (90 per cent.)	50 (30 per cent.) 109 (70 per cent.)	
Duration (yrs)		Mean Range	8·95 ± 6·35 (0·5–25)	6·55 ± 5·9 (0·5–20)	
Functional grade		I and II III and IV	51 of 94 (52 per cent.) 43 of 94 (48 per cent.)	101 of 140 (71 per cent.) 39 of 140 (29 per cent.)	
X-ray stage		I and II III and IV	45 of 129 (34 per cent.) 84 of 129 (60 per cent.)	74 of 137 (52 per cent.) 63 of 137 (48 per cent.)	
Articular index			28·06 ± 12·25	23·94 ± 11·56	"*t*" = 2·5972
Rheumatoid factor positive			136 (92 per cent.)	99 (63 per cent.)	
Erythrocyte sedimentation rate (mm. 1st hr)		Mean Range	47·1 ± 21·33 (16–150)	54·6 ± 22·07 (15–110)	
Serum Globulin (g./100 ml)		Mean Range	3·57 ± 0·36 (2·9 – 4·3)	3·48 ± 0·43 (2·7 – 4·8)	
Serum Calcium		Mean Range	4·82 ± 0·79 (4·2 – 5·3)	4·5 ± 1·2 (4·2 – 5·3)	"*t*" = 2·4877
90 min. post-prandial blood sugar		Mean Range	105·02 ± 19·96	105·17 ± 26·42	
Steroid therapy	Duration (yrs) in 117 patients		3·15 ± 2·45		
	Mean daily dose (mg. prednisolone)		10·89 ± 4·8		

Method

A detailed history of visual and other ocular symptoms was obtained from every patient. Each patient had a dilated ophthalmoscopic and slit-lamp examination, routine Schirmer I tear test (Schirmer, 1903) and staining of the external eye with the vital dyes, fluorescein 1 per cent. and rose bengal 0·5 per cent. In every patient in whom the Schirmer I test showed less than 15 mm. of wetting at 5 min., a Schirmer II test, using 10 per cent. ammonia, was carried out (Williamson, Cant, Mason, Greig, and Boyle, 1967). Each patient had at least two ophthalmological examinations and those who continued to take oral corticosteroid drugs have been examined at 3-monthly intervals for up to 2 years. Patients who had received oral corticosteroid therapy in the past, but were not receiving corticosteroid therapy at the time of their first attendance, were examined on two further occasions at 3-monthly intervals. Only four patients were not examined by the slit lamp because of the severity of their rheumatoid disease. The criteria for diagnosing and classifying PSC were those suggested by Crews (1963).

Grade 1 PSC occasional subcapsular opacities or vacuoles in the central region with or without polychromatic lustre and distortion of specular reflex.

Grade 2 PSC small clusters of opacities which remain discrete.

Grade 3 multiple clusters of opacities which have mainly coalesced.

Grade 4 extensive subcapsular opacities forming a plaque on the back of the lens and extending into the cortex. Figs 1 and 2 show examples of Grade 3 and 4 PSC.

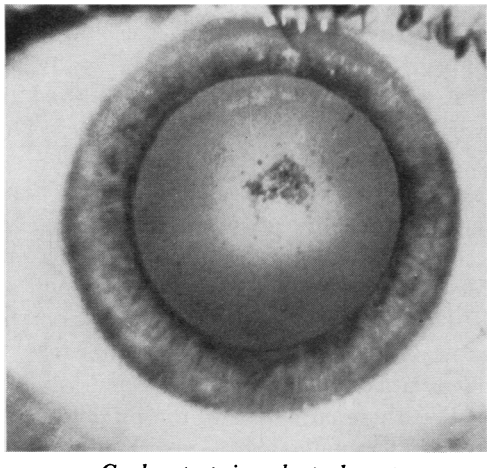

FIG. 1 *Grade 3 posterior subcapsular cataract*

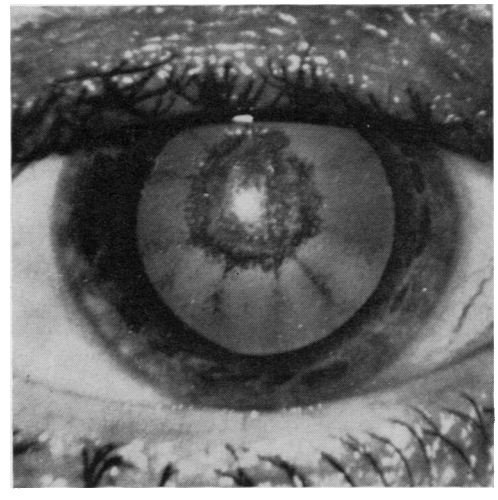

FIG. 2 *Grade 4 posterior subcapsular cataract*

Measurements of the intraocular pressure were made by applanation tonometry on all of the corticosteroid-treated patients and on 100 of the non-corticosteroid-treated patients (62·5 per cent.).

Whenever the intraocular pressure was found to be greater than 20 mm. applanation tonometry, the patient was admitted to hospital and the following tests were carried out: 24-hour intraocular pressure measurements at 4-hourly intervals, water-drinking tests, mydriatic tests, visual field examinations, and gonioscopy to determine the state of the angle of the anterior chamber. If glaucoma was still suspected then tonography was subsequently arranged.

Results

Rheumatoid arthritis group

The results in the 307 patients are summarized in Table IV. The diagnosis of PSC was made in seventeen patients who had received oral corticosteroids and in one patient who had never at any time received oral corticosteroids or corticotrophin therapy (Table IV).

Table IV *Patients with PSC and raised intraocular pressure*

Diagnosis	*Corticosteroid-treated*	*Non-corticosteroid-treated*
Rheumatoid arthritis	148 (17*) 6†	159 (1) 3†
Still's disease	1	3
Reiter's syndrome		3
Ankylosing spondylitis	2	1
Gout	2	1
Systemic lupus erythematosus	3	
Osteoarthritis	6 (2)	26 3†

Figures in parenthesis indicate number with PSC

*Six had uveitis and one had high myopia

†Number with raised intraocular pressure on at least one occasion

In all but one patient the PSCs were bilateral. Six of the patients with PSC had evidence of uveitis in one or both eyes and one patient with PSC had high myopia. Since uveitis and high myopia may by themselves be associated with PSC, these patients have been excluded from the analysis. When these seven patients are excluded, ten of the 148 (6 per cent.) who had received oral corticosteroid drugs had PSC, whereas only one of the 159 patients (0·6 per cent.) who had never received oral corticosteroid therapy had PSC. The difference between the two groups of patients is significant ($\chi^2 = 8{\cdot}33$; $P < 0{\cdot}001$). The non-corticosteroid-treated patient was a 55-year-old female who had suffered from erosive, non-nodular, sero-positive rheumatoid arthritis for 8 years. There was no history suggestive of ocular disease in either the patient or her relatives. The pupils reacted briskly to light and to the accommodation convergence reflex. Schirmer I tear tests were normal and slit-lamp examination under mydriasis revealed no abnormalities of the corneae, irides, or anterior chambers of the eyes. Applanation tonometry was normal and the angles of the anterior chambers were open as seen through a gonioscope. The PSCs were classified as Grade II (Crews, 1963). Ophthalmoscopic examination revealed no abnormalities of the fundi. The patient was not myopic.

Six of the 148 steroid-treated rheumatoid arthritis patients had raised intraocular pressures on at least one occasion. All of these patients and the three in the non-steroid-treated group (Table IV) were screened for glaucoma as described above. Only one patient had both PSCs and bilateral raised pressures and he was the only patient judged to have glaucoma induced by systemic steroid therapy. The patient was a 45-year-old male rheumatoid arthritic who had received eight tablets of Medrone per day for 8 years. He had no family history of ocular disorders and had no siblings. His pressures were 40 mm. Hg applanation in both eyes and he had Grade II PSCs. Both discs were grossly cupped and atrophic, his fields being reduced within the 10° isopter to 10 mm. white targets at one metre from the Bjerrum screen. The angles of the anterior chambers were open and no abnormalities in the trabecular meshwork were detected. The outflow of aqueous humour from the anterior chamber was markedly reduced. When the systemic steroids were reduced his intraocular pressures fell. However, the withdrawal of steroids had to be reversed and his intraocular pressures rose once again. In all, three attempts were made to reduce the steroid intake and on each occasion the intraocular pressure fell only to rise again with increased steroid dosage. In between each attempt the intraocular pressures were controlled with miotics. Finally he was weaned off steroids and the intraocular pressure has remained normal on miotics three times a day for 1 year. When miotics are withdrawn his intraocular pressures rise to 26 to 28 mm. Hg but never to the previous levels of 40 mm. Hg recorded while on systemic steroids. The other five steroid-treated patients proved to be within normal limits. One of the three non-steroid- treated patients had chronic simple glaucoma; the other two were judged to be normal.

Table III shows that both groups of patients were well matched in respect of age, sex, duration of disease, functional grade, *x*-ray stage, articular index, and the presence or absence of subcutaneous nodules. In terms of the laboratory data, that is, rheumatoid factor, haemoglobin concentration, erythrocyte sedimentation rate, serum albumin and globulin concentrations, and 90 min. post-prandial blood sugars (Table III), the groups compared favourably. The serum calcium was higher in the steroid-treated than in the non-steroid-treated group of patients.

22 of the 148 steroid-treated (13·6 per cent.) and 23 of the 159 non-steroid-treated patients (13·7 per cent.) had keratoconjunctivitis sicca (38 females and 7 males).

RHEUMATOID ARTHRITIS AND UVEITIS

Seven of the 307 patients with RA were also suffering from uveitis (2·3 per cent.). One of the seven also had scleritis. Five of the seven patients had received long-term oral corticosteroid therapy, and in each of them PSC had developed in the eye or eyes showing evidence of uveitis. No PSC was present in either of the two remaining patients who had never received systemic steroid therapy (Table V).

Table V *PSC in seven cases of rheumatoid arthritis associated with uveitis (relationship to steroid therapy)*

Case no.	*Age (yrs)*	*Sex*	*X-ray stage of arthritis*	*Duration (yrs)*	*Eye involvement*	*Systemic steroids given (+)*	*PSC present*
1	63	F	III	6	Bilateral anterior uveitis	+	Bilateral
2	58	F	III	6	Bilateral anterior uveitis	+	Bilateral
3	66	F	III	2	Bilateral uveitis and scleritis	+	Bilateral
4	61	F	III	10	Unilateral anterior uveitis	+	Unilateral
5	44	M	III	3	Bilateral anterior uveitis	+	Unilateral (early)
6	66	M	III	2	Bilateral anterior uveitis	−	Nil
7	51	F	III	15	Unilateral anterior uveitis	−	Nil

Osteoarthritis group

32 patients with osteoarthritis were included in the survey (Table II), of whom six had been treated with oral corticosteroid therapy by their family doctors in the belief that they were suffering from RA. Two of the corticosteroid-treated patients developed PSC, but none of the 26 patients who had never received oral corticosteroids (Table IV). Of the three osteoarthritic patients who had raised intraocular pressures on one occasion (Table IV), one had chronic simple glaucoma and the others were normal.

Four of the female patients with osteoarthritis (all aged 62 years) also had kerato-conjunctivitis sicca; none of them had received systemic steroids.

Miscellaneous group

Sixteen patients presented with five other disorders (Table IV). None of them was found to have PSC. One patient with Still's disease had kerato-conjunctivitis sicca and she had never received systemic corticosteroid therapy.

Discussion

PSCs were found in twenty and glaucoma was detected in three of the 356 patients attending the Centre for Rheumatic Diseases in Glasgow. In all but one case of PSC the patients had received long-term oral corticosteroid therapy. Only one case of glaucoma was attributed to systemic steroid therapy.

Rheumatoid arthritis group

Ten of 148 (6 per cent.) corticosteroid-treated rheumatoid arthritic patients and one of 159 (0·6 per cent.) non-corticosteroid-treated patients had developed PSC. The difference is statistically significant ($\chi^2 = 8{\cdot}33$; $P < 0{\cdot}001$). PSC was found more frequently in the series of patients on long-term steroid therapy examined by Black and others (1960) (39 per cent.), Giles and others (1962) (37 per cent.), Crews (1963) (35 per cent.), Spencer and Andelman (1965) (60 per cent.), and Furst and others (1966) (10·5 per cent.). In all these reports and in the present study, the incidence of cataract rose with higher dosage and longer duration of systemic corticosteroid therapy. There was no evidence of steroid overdosage in any of the patients who had developed PSC as judged by excessive increase in weight, moon facies, pitting oedema, low serum potassium, or excessive osteoporosis. However, the mean serum calcium level in the steroid-treated patients was $4{\cdot}82 \pm 0{\cdot}9$ mEq./litre, and in the non-steroid-treated patients it was $4{\cdot}53 \pm 1{\cdot}2$ mEq./litre ("t" $= 8{\cdot}92$; $P < 0{\cdot}001$). The steroid-treated patients had serum calcium levels significantly higher than the non-steroid-treated patients. The serum calcium levels of the steroid-treated patients with PSC did not, however, differ significantly from those in the steroid-treated patients as a whole.

Two clinical problems confronted the ophthalmologists in this study. First the detection of the posteriorly-placed lens opacities, and secondly their differentiation into steroid-induced and other types. Iridescent changes in the posterior subcapsular region with no other corroborative evidence of lens pathology were ignored because their detection was very much a matter of opinion. Iridescent changes were recorded by Black and others (1960) but were only mentioned by Crews (1963) to be discarded as too subjective. The workers in this present study agree with the latter opinion. The diagnosis of steroid-induced PSC depends on the exclusion of all other possible causes of posteriorly-placed lens opacities*. There is considerable overlap in the use of the terms posterior subcapsular cataract and posterior cortical cataracts and this may account in part for the conflicting reports mentioned above. Gordon and others (1961) list as the commonest causes of PSC senility or pre-senility, uveitis, and retinitis pigmentosa. Most other workers would describe the senile lens changes as posterior cortical cataract in the first instance. Thus in this study all causes of PSC or posterior cortical cataract were considered before the diagnosis of steroid PSC was made. Seven patients who had PSC had evidence of uveitis and one other patient with PSC was a high myope. One patient had retinitis pigmentosa and another diabetes mellitus, but neither had cataract. Since most of the patients had been referred to the Centre for Rheumatic Diseases from many sources, it was not possible to estimate the *x*-ray dosage to which they had been subjected. No correlation between the incidence of PSC and exposure to *x* rays has been found to date (Black and others, 1960; Toogood and others, 1962), but it must be recorded that radiation and steroid cataracts are clinically identical. In this series of patients, the incidence of PSC was highest in those steroid-treated patients who had had rheumatoid arthritis for more than 9 years, and who could be expected to have had frequent *x*-ray examinations. Radiation cataract is caused by the direct effect of *x* rays on the subcapsular epithelium resulting in deranged mitotic activity. There is a latent period of 2 to 12 years before lens opacities appear. Not infrequently patients with RA require *x*-ray examinations of the cervical region, and scatter of *x* rays to the orbits is conceivable. The pathology of two lenses with steroid-induced cataract has been described (Black and others, 1960; Crews, 1963) and in both cases the epithelium near the equator and the nuclear bow

*These include uveitis, senility or pre-senility, myopia, retinitis pigmentosa, radiation, hypoparathyroidism, diabetes mellitus, atopic dermatitis, myotonia congenita, and ingestion of other toxic substances.

appeared to be normal. In radiation cataract mitosis disappears in the epithelium near the equator, aberrant cells develop, and the nuclear bow is deranged. Radiation could excite an initial lesion and steroids could potentiate the effect of that radiation on the subcapsular epithelium. Thus a smaller than usual cataractogenic dose of *x* rays could start off a PSC leaving the nuclear bow apparently normal. In this context we note that two attempts to produce PSC in rats by feeding them with the equivalent of a large dose of prednisolone (von Sallmann, Caravaggio, Collins, and Weaver, 1960; Spencer and Andelman, 1965) have failed. It may be possible to produce "steroid" PSCs in animals previously or simultaneously exposed to subcataractogenic doses of *x* rays. Bettman, Fung, Webster, Noyes, and Vincent (1968) were unable to demonstrate that corticosteroids increased the cataractogenic effect of dinitrophenol, xylose, triparanol, or radiation. However, four of fifty corticosteroid-treated rabbits developed lens opacities in the non-irradiated eye, whereas none of 25 non-corticosteroid-treated rabbits developed cataract in the non-irradiated eye. These authors felt that this difference was of questionable significance. A striking acceleration in the formation of galactose cataract was demonstrated by these workers in corticosteroid-treated rats.

Posterior subcapsular cataracts were most often demonstrated in the steroid-treated patients who had suffered from rheumatoid arthritis for more than 9 years and whose disease had reached an advanced stage radiologically (Table VI). Both stage and duration of the disease were accurately known in 129 of the 148 steroid-treated patients (Table III). Five of the 61 steroid-treated patients (9·3 per cent.) who had had RA for more than 9 years had PSC, whereas only two of the 69 patients who had had RA for less than 9 years (2·9 per cent.) had steroid cataracts.

These findings could mean either that corticosteroid drugs produce PSC in some patients or that severe RA may cause the condition. The available data suggest that the first of these probabilities is correct, for there was a very significant relationship between

Table VI *Relationship of occurrence of PSC to stage and duration of rheumatoid arthritis (PSC in brackets)*

Series	*Duration of disease (yrs)*	*Stage of rheumatoid arthritis*					*Total*
		0	I	II	III	IV	
Corticosteroid-treated	0–1	5	1	0	6	0	12
	2–3	8 (1)	4	1	4	0	17 (1)
	4–6	3	1	4	18 (1)	0	26 (1)
	7–9	2	2	2	7	0	13
	10–12	3	0	4 (2)	12 (2)	0	19 (4)
	13 plus	2	0	3 (1)	30	7	42 (1)
	Total	23 (1)	8	24 (3)	77 (3)	7	
Non-corticosteroid-treated	0–1	24	3	1	7	0	35
	2–3	18	1	0	14	0	33
	4–6	9	1	0	16	1	27
	7–9	5	1	0	4 (1)	0	9 (1)
	10–12	4	0	0	4	1	9
	13 plus	6	0	1	12	3	
	Total	66	6	2	57 (1)	5	

Five of 61 over 9 years (9·3 per cent.)
Two of 68 under 9 years (2·9 per cent.)

the estimated mean daily dose of corticosteroids and the occurrence of PSC; moreover, the estimated total dose of corticosteroid also correlated well with the presence of PSC. The duration and mean daily dose of steroids were accurately known in 117 of the 148 steroid-treated patients. Six of the seven patients with PSC had received over 15 mg. prednisolone or its equivalent per day for over 2 years, and one had been treated with 10 mg. prednisolone equivalent for 3½ years (Table VII).

Table VII *Relationship of occurrence of PSC in 117 rheumatoid arthritics to dosage and duration of steroid therapy (PSC in brackets)*

Duration of steroid therapy (yrs)	*Daily dosage of steroids (mg.) (Prednisolone equivalent)*			*Total*
	Less than 10	10–15	*Over 15*	
0·5–1	25	12	2	39
1–2	9	13	4	26
2–4	4	11 (1)	11 (2)	26 (3)
4–8	2	9	13 (3)	24 (3)
8 plus	1	0	1 (1)	2 (1)
Total	41	45 (1)	31 (6)	

PSCs were not found in any of the 65 patients who had been treated with corticosteroid drugs for less than 2 years; of the 52 patients who had received corticosteroids for more than two years, seven had PSC. This difference is statistically significant. ($\chi^2 = 9{\cdot}3068$; $P < 0{\cdot}01$).

Glaucoma was detected in one of the 148 patients on systemic steroid therapy. This patient also had PSC and had been taking the equivalent of 40 mg. prednisolone a day for 8 years. Glaucoma induced by systemic steroid therapy was diagnosed only after it was demonstrated that a fall in the intraocular pressure accompanied a reduction in steroid intake and a rise in intraocular pressure followed increased steroid intake. The most tragic feature of this patient's case was the complete absence of visual symptoms until 4 months before his first ocular examination, yet the deeply cupped optic discs and gross visual field loss represented pathology of several years' duration. The rise in intraocular pressure was caused by a fall in the facility of outflow of aqueous from the anterior chamber of the eye. The angle of the anterior chamber appeared to be normal. In this respect the patient had eyes like those of a patient suffering from chronic simple glaucoma where no adhesions of peripheral iris have occurred. However, we do not know the relationship between systemic steroid therapy and any rise in the intraocular pressure in patients known to have or to be predisposed to chronic simple glaucoma. It may be that this patient would have developed chronic simple glaucoma in time without the help of systemic steroids. The patient had no siblings or close relatives and so it was not possible to determine any hereditary predisposition to glaucoma. On the other hand, his intraocular pressures returned to almost normal levels on withdrawal of the systemic steroids suggesting that the Medrone was playing a major part in the reduction of aqueous outflow. Further, he had developed steroid-induced PSCs indicating that the systemic steroids had adversely affected the functioning of his eyes at least as far as the maintenance of lens clarity was concerned.

RHEUMATOID ARTHRITIS AND UVEITIS

Systemic steroids may be prescribed for patients with arthritis who also develop anterior uveitis. Seven patients in this series were found to have uveitis and five of these were receiving long-term oral corticosteroids. These five patients developed PSC and in one case the cataract progressed rapidly to complete maturity in the presence of continued uveal inflammation. There was no evidence in this small group that systemic steroids had inhibited the course of the intraocular inflammation. Each of the patients with uveitis and PSC had been given oral steroids for 2 to 10 years; each had severe rheumatoid arthritis and had received large doses of prednisolone or its equivalent. The remaining two patients with uveitis and without PSC had equally severe arthritis but had not been given oral steroids. There was no significant difference in age between the two groups: mean 58·5 years (Table V). Although the group of patients is small we may conclude that caution should be observed in prescribing systemic steroids as a specific measure in patients with rheumatoid arthritis and uveitis. None of these patients had glaucoma.

Osteoarthritis

Two of the six patients with osteoarthritis who had received long-term corticosteroid therapy developed PSC. This would substantiate the findings of Crews (1963), of "steroid-induced" cataracts in diseases other than rheumatoid arthritis and further suggests that oral steroid therapy is a major factor in the aetiology of the lens opacities. One patient, not treated with steroids, had chronic simple glaucoma.

Miscellaneous conditions

Neither cataracts or glaucoma were found in any of these patients. No conclusions can be drawn as the number of patients was small.

Summary

356 patients attending the Centre for Rheumatic Diseases, Glasgow, were examined for posterior subcapsular cataracts and glaucoma. Approximately one half of them had been treated with long-term systemic corticosteroids and a definite relationship was found between the dose and duration of systemic steroid therapy and the incidence of cataract. Only one case of glaucoma induced by systemic steroids could be demonstrated with certainty, and this occurred in a patient who had had the equivalent of 40 mg. prednisolone a day for 8 years.

A possible relationship between exposure to *x* rays, systemic steroid therapy, and posterior subcapsular cataracts is discussed.

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