Postgraduate Medical Journal (August 1970) **46**, 501–504.

Ocular sarcoidosis

H. JACKSON

*Central Middlesex Hospital, London, N.W.*10

Summary

In 5529 new patients attending eye clinics 0·8% of patients were found to have endogenous uveitis. None had radiographic evidence of sarcoidosis. Of thirty-four who had a Mantoux test 56% were negative. A Kveim test done on twenty-four of the cases revealed that 12·5% were positive, and in two of these histological evidence of sarcoidosis was found.

Eighty-two patients with multisystem sarcoidosis were similarly investigated and in addition their lachrymal secretion was measured. Of these twelve (14·6%) had an ocular lesion, six having bilateral uveitis, two unilateral uveitis and four lachrymal gland enlargement. 58% of these cases were found to have reduced lachrymal secretion. In addition fifty-seven of these patients without ocular abnormality had their lachrymal secretion measured and 49% of these were found to have reduced lachrymal secretion.

In the period September 1966 to March 1969 a total of 5529 new attendances were recorded in the out-patient departments of the Central Middlesex Hospital Group and the Mount Vernon Hospital. From this total a diagnosis of endogenous uveitis was made in forty-four patients (0·8%).

The age and sex distribution of these patients on diagnosis is shown in Table 1. Of the total of forty-four patients, twenty-six were female and eighteen male. There was a female predominance, particularly among patients over 45 years of age.

TABLE 1. Endogenous uveitis

	Age on diagnosis					
Years:	10–19	20–29	30–39	45–49	50+	Total
Female	3	2	3	5	13	26
Male	0	3	6	2	7	18
Total	3	5	9	7	20	44

All forty-four patients had a PA chest radiograph; none showed any abnormality suggestive of sarcoidosis. A Mantoux test was done in thirty-four patients; fifteen (44%) were positive and nineteen (56%) negative (10 i.u, PPD). In the remaining ten patients the Mantoux test was either not done or not completed. A Kveim test was done in twenty-four of these patients, the results of which are shown in Table 2. Of the fifteen female and nine male patients tested, three (12·5%), two female, aged 34 and 41 years respectively, and one male, aged 29 years, had microscopically positive Kveim tests. These three Kveim positive patients were further investigated by biopsy of a mediastinal lymph node; in two this showed the presence of non-caseating epithelioid and giant cell granulomas, compatible with a diagnosis of sarcoidosis.

TABLE 2. Microscopic reading of Kveim tests

Patients	Positive	Equivocal	Negative	Total
Female	2	0	13	15
Male	1	0	8	9
Total	3	0	21	24

During the same period (September 1966 to March 1969) a further eighty-two patients, in whom a diagnosis of sarcoidosis had already been confirmed either by Kveim test or mediastinal lymph-node biopsy or by both, were similarly investigated for the presence of ocular abnormality. In particular, the lachrymal secretion in each eye was estimated by the colorimetric method of Norn. The essential details of this method are as follows:

0·01 ml of a solution containing 1% of Rose Bengal and 1% of fluorescein in normal saline is instilled into the lower fornix of each conjunctival sac from a needle 0·5 × 16 ml (No. 12). The patient is allowed to blink but not to screw his eyes up. After 5 min the dilution of the dye in the lachrymal fluid at the upper margin of the lower lid is observed with a slit-lamp microscope and compared with a colour scale consisting of six capillary tubes each containing a dilution which is 1 in 4 of that in the preceding tube, so that the dilutions extend from 1 in 4, which signifies no lachrymal secretion, to a dilution of 1 in 4096, indicating a dilution of the dye to 1 in 1024, and a secretion of 0·02 ml/min or

TABLE 3. Ocular abnormality and measurement of lachrymal secretion in forty-two of eighty-two patients with multisystem sarcoidosis

	Bilateral anterior uveitis		Unilateral uveitis		Lachrymal gland enlargement		
% of normal secretion*	Male	Female	Male	Female	Male	Female	Total
100		1					1
80	1	2				1	4
60					1	1	2
40		1		1	1		3
20							
Nil							
Schirmer Test (Reduced secretion)		1	1				2
Total	1	5	1	1	2	2	12

* Lachrymal secretion was measured in each eye. Results are related to the eye in which the lower estimation was recorded.

28·8 ml/24 hr, corresponding to 100% on our scale. For the purpose of this investigation, and taking into consideration the age groups of the patients in this study, dilutions of 1 in 256 and above were regarded as normal.

An ocular lesion was found in twelve (14·6%) of the eighty-two patients in whom a diagnosis of sarcoidosis had previously been confirmed (Table 3). Six (7·3%) had bilateral anterior uveitis; of these three showed reduction of lachrymal secretion in one or both eyes, in the remaining three the lachrymal secretion was normal. Unilateral uveitis was found in two (2·4%) patients; in one of these the lachrymal secretion was reduced in both eyes and in the other no measurement was made. Lachrymal gland enlargement without evidence of other ocular abnormality was found in four patients (4·8%); three of these patients had reduced lachrymal secretion in both eyes.

TABLE 4. Measurement of lachrymal secretion (Norn's method) in fifty-seven patients with sarcoidosis who showed no evidence of ocular abnormality

% of normal secretion* (i.e. of 28·8 ml/24 hr)	Male	Female	Total
100	6	7	13
80 (Dilt. 1:256)	6	10	16
60	7	12	19
40	2	6	8
20	0	1	1
Nil	0	0	0
Total	21	36	57

* Lachrymal secretion was measured in each eye. Results are related to the eye in which the lower estimation was recorded.

Using the colorimetric method described above, lachrymal secretion was measured in each eye in fifty-seven (twenty-one male and thirty-six female) of the remaining seventy patients with sarcoidosis who showed no evidence of lachrymal gland enlargement nor other ocular abnormality (Table 4). Of these, twenty-nine (51%) had normal secretion and twenty-eight (49%) showed a reduced secretion having less than 80% of the normal lachrymal secretion in one or both eyes.

Discussion

Only a small proportion of patients presenting with uveitis are found to have sarcoidosis. Perkins (1958) found evidence of sarcoidosis in only 2·1% of 653 such patients. In this study, in which twenty-four patients presented with endogenous uveitis in which there was no clinical, radiological or biochemical evidence suggestive of sarcoidosis in other organs, positive Kveim tests were found in only three (12·5%) of the twenty-four patients tested. Smellie & Hoyle (1960) have drawn attention to the liability for uveitis to persist or recur after enlarged hilar lymph nodes have regressed or after infiltration in the lungs has become quiescent or has cleared radiographically. None of the twenty-four patients gave a history suggestive of previous sarcoidosis or a prior episode of uveitis. Nonetheless, the histology of a subsequent mediastinal lymph-node biopsy was compatible with a diagnosis of sarcoidosis in two of the three Kveim-positive patients All twenty-four patients who were Kveim-tested had recent acute uveitis and, since the Kveim test was positive in only three cases, it is probable that in a high proportion of the remaining cases the uveitis was caused by some condition other than sarcoidosis.

Conversely, seven of the twelve (58%) patients with definite clinical sarcoidosis, who were found to have a concurrent ocular abnormality, had positive Kveim tests; a frequency similar to that found in all types of sarcoidosis. Similarly, Ainslie & James (1956) found positive Kveim tests in fifteen (79%) of nineteen patients with ocular sarcoidosis; in ten of the fifteen Kveim-positive cases corroborative histological evidence of sarcoidosis was found by biopsy of other organs.

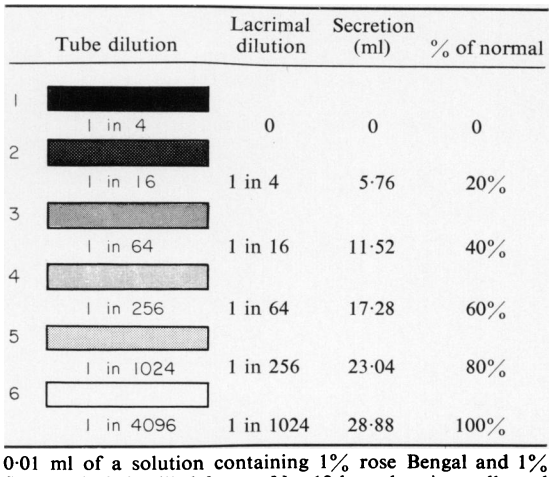
Among patients presenting with lesions other than uveitis and in whom a diagnosis of sarcoidosis had previously been confirmed, either by the Kveim test or by mediastinal lymph-node biopsy, evidence of ocular abnormality was found in twelve (14·6%) of the eighty-two patients referred for examination. Of these eight (9·8%) had unilateral or bilateral anterior uveitis. Since all these lesions were considered to be potentially serious and to require treatment with mydriatics and topical steroids, they have not been further sub-divided into the customary acute and chronic varieties. Four patients, two male and two female, were found to have bilateral lachrymal gland enlargement without evidence of other ocular abnormality. The overall incidence of eye changes in this study was thus similar to that reported by many other authors. Thus, James (1959) found iridocyclitis in fifty (25%) of 200 patients with sarcoidosis. Later, James *et al.* (1964) reported finding iridocyclitis in eighty-eight (20%) of 442 patients. Crick, Hoyle & Smellie (1961) found uveitis in sixty-one (33%) of 185 patients. Longcope & Freiman (1952) found ocular sarcoidosis in forty-six (64%) of a series of seventy-two patients which included many Negroes. Ricker & Clark (1949) also reported the relatively high frequency of eye lesions among Negro patients with sarcoidosis. Conversely, Sones & Israel (1960) found ocular lesions in only 17·6% of 211 patients, of whom 184 were Negroes. Scadding (1967) found that the proportion of female patients with uveitis was slightly higher than for his series as a whole; of thirty-nine patients fourteen (36%) were men and twenty-five (64%) were women. Of the twelve patients with sarcoidosis who were found to have an ocular abnormality in this study, seven were female aged 30–40 years and four were male aged 25–30 years. There was no special racial predominance.

Among the eighty-two cases of sarcoidosis referred for ocular examination in the present study, the peak of incidence was in the 30–34 years age-group for females, whereas that for the males was in the 20–24 years age-group. The age at onset for both male and female patients found to have uveitis was thus similar to that of other patients in this series who showed no ocular abnormality. This is similar to the findings of Scadding (1967) but it is of interest that James (1959) reported that his patients with eye changes were older at the onset of their symptoms than those without, and in this respect resembled those with skin changes.

Lachrymal gland enlargement only was found in four (4·8%) of patients with sarcoidosis; this is perhaps an unusually high proportion. Scadding (1967) reported lachrymal gland enlargement in only two of his 275 cases and in both the enlargement was transitory. James (1959) reported palpable lachrymal enlargement in one case out of 200; similarly, Crick *et al.* (1961) found one such example among 185 cases of sarcoidosis. Conversely, Longcope & Freiman (1952) reported lachrymal gland enlargement in five of ninety patients in Baltimore, the series including a high proportion of Negroes, and Maycock *et al.* (1963) found lachrymal gland involvement in two (1·3%) of 145 cases. Nin-Avelleyra (1963) found eight (13·5%) patients with lachrymal gland enlargement among fifty-nine cases of sarcoidosis.

It is of interest that the lachrymal secretion was reduced in three of four patients with lachrymal gland enlargement in this study. Moreover, of the fifty-seven patients, twenty-one male and thirty-six female, with sarcoidosis in this study who showed no evidence of ocular abnormality, lachrymal secretion was reduced in no less than twenty-eight (49%) as measured by the colorimetric method of Norn. Norn (1965; 1966) measured the secretion in 183 healthy eyes in ninety-three patients. His results were remarkably consistent between the sexes, although there was some variability with age, the greater secretion being found in the age-group 10–20 years (Fig. 1). Of the twenty-eight patients in

FIG. 1. Norn's lacrimal secretion test



0·01 ml of a solution containing 1% rose Bengal and 1% fluorescein is instilled from a No. 12 hypodermic needle and the lacrimal streak dilution is compared with the colour in the tubes.

whom lachrymal secretion was diminished in the present study, nine were male and nineteen female. This is a remarkable finding and is presumably due to occult infiltration of the lachrymal glands by sarcoidosis. Crick *et al.* (1961) estimated the lachrymal secretion in a group of thirty patients using Schirmer's test; they found that the findings correlated with the percentage showing corneal staining following the instillation of 1% Rose Bengal solution which stains degenerate cells. No such correlation was attempted in the present study.

References

AINSLIE, D. & JAMES, D.G. (1956) Ocular sarcoidosis. *British Medical Journal*, **1**, 954.

CRICK, P.R., HOYLE, C. & SMELLIE, H. (1961) The eyes in sarcoidosis. *British Journal of Ophthalmology*, **45**, 461–81.

JAMES, D.G. (1959) Ocular sarcoidosis. *American Journal of Medicine*, **26**, 331.

JAMES, D.G., ANDERSON, R., LANGLEY, D. & AINSLIE, D. (1964) Ocular sarcoidosis. *British Journal of Ophthalmology*, **48**, 461.

LONGCOPE, W.T. & FREIMAN, D.G. (1952) A study of sarcoidosis. *Medicine*, **31**, 1.

MAYCOCK, R.L., BERTRAND, P., MORRISON, C.E. & SCOTT, J.H. (1963) Manifestations of sarcoidosis. *American Journal of Medicine*, **35**, 67–89.

NIN-AVELLEYRA, C. (1963) Lesiones oculares en 59 casos de sarcoidosis. *El Torax*, Vol. XII, nos 3y4, 115–25.

NORN, M.S. (1965) Tear secretion in normal eyes. *Acta Ophthalmologica*, **43**, 567–73.

NORN, M.S. (1966) Tear secretion in normal and diseased eyes estimated by a new method. *Proceedings of the Tenth International Congress of Ophthalmology*, Munich 1966. Excerpta Medica International Congress Series 1164–6, no. 146.

PERKINS, E.S. (1958) The aetiology and treatment of uveitis. *Transactions of the Ophthalmic Society of the United Kingdom*, **78**, 511.

RICKER, W. & CLARK, M. (1959) Sarcoidosis: A clinicopathological review of 300 cases. *American Journal of Clinical Pathology*, **19**, 725.

SCADDING, J.G. (1967) *Sarcoidosis*. Eyre & Spottiswoode, London.

SMELLIE, H. & HOYLE, C. (1960) The natural history of pulmonary sarcoidosis. *Quarterly Journal of Medicine*, **116**, 539.

SONES, M. & ISRAEL, H.L. (1960) Course and prognosis of sarcoidosis. *American Journal of Medicine*, **29**, 84.