

UVEITIS AND UROGENITAL DISEASE IN THE MALE*

BY

R. D. CATTERALL† AND E. S. PERKINS

Institute of Ophthalmology, University of London

IN the majority of patients with uveitis medical examination and routine investigations fail to elicit any notable systemic disease. Acute anterior uveitis—the most common clinical type of uveitis—frequently occurs in young, apparently healthy, adults with little evidence of any systemic disturbance. It is difficult to believe, however, that such a serious disease of the eye can be an isolated phenomenon unconnected with any other disease process in the body.

The urogenital system is not usually investigated in detail as part of a normal medical examination, but as it has been shown by Mason, Murray, Oates, and Young (1958) that chronic prostatitis is often associated with ankylosing spondylitis and Reiter's disease—two conditions in which uveal complications are known to occur—a series of patients with uveitis was investigated by one of us (R. D. C.) in conjunction with the Department of Venereology of The London Hospital. Preliminary reports and reviews of the relevant literature have been published previously (Catterall, 1958a, b).

Material and Methods

A consecutive series of male patients attending the Uveitis Clinic of the Institute of Ophthalmology was investigated regardless of the ophthalmological diagnosis. A detailed clinical history was taken and a thorough physical examination performed. Prostatic fluid was obtained by prostatic massage and five unstained specimens examined immediately. Stained smears were also examined and culture plates inoculated from the prostatic fluid and from the centrifuged deposits of urine. The prostatic fluid was considered to be abnormal if clumps of pus were found in the specimens or if more than ten leucocytes were present in several 1/12" microscopic fields. X rays of the chest, sacro-iliac joints, hands, feet, and ankles were taken in each case.

The incidence of chronic prostatitis in normal men has not been investigated in any large numbers, but of 36 men of a similar age group to those with uveitis, who were in-patients in the general surgical wards of The London Hospital, six (16.7 per cent.) were found to have chronic prostatitis. Moreover, some of the patients examined at the Uveitis Clinic did not in fact have uveitis, and provide a useful control series.

Results

Of the 226 cases examined and fully investigated, four cases were of non-inflammatory lesions such as degenerative choroidal disease and none of

* Received for publication August 12, 1960.

† Now at the General Infirmary, Leeds.

these had prostatitis. Eleven were diagnosed as cases of Eales's disease and only one of these had chronic prostatitis (9 per cent.). 211 cases of uveitis remained and of these 145 (68·7 per cent.) were found to have chronic prostatitis (Table I).

TABLE I
INCIDENCE OF PROSTATITIS IN WHOLE SERIES OF 226 CASES

Diagnosis	Total Cases	Cases with Prostatitis	
		No.	Per cent.
Non-uveitis	4	0	0
Eales's Disease	11	1	9
Uveitis	211	145	68·7

Table II shows the diagnostic categories of the 211 cases of uveitis, and it can be seen that acute uveitis accounts for more than half the total cases. It is the largest and most important group and the one in which the aetiology is particularly controversial.

TABLE II
DIAGNOSTIC CATEGORIES OF UVEITIS CASES

Uveitis Diagnosis	Acute		Chronic	
	No.	Per cent.	No.	Per cent.
Anterior	133	63·0	19	9·0
Posterior	25	11·8	5	2·4
Generalized	20	9·5	9	4·3

The incidence of chronic prostatitis in all cases of anterior uveitis is shown in Table III, and in the acute cases reaches an incidence of over 80 per cent. With such a large number of cases it is most unlikely that this can be a chance result. The difference in the incidence of prostatitis between the acute and chronic anterior cases is in fact statistically highly significant ($\chi^2 = 11·27$; $0·01 > P$). Additional evidence that this is not a chance association is provided by the fact that a high proportion of the acute anterior cases

TABLE III
INCIDENCE OF PROSTATITIS IN CASES OF ANTERIOR UVEITIS

Anterior Uveitis	Prostatitis			
	No Evidence		Present	
	No.	Per cent.	No.	Per cent.
Acute	26	19·5	107	80·5
Chronic	11	58·0	8	42·0

($\chi^2 = 11·27$; $0·01 > P$).

with prostatitis showed joint changes typical of Reiter's disease or ankylosing spondylitis, and smaller numbers had plantar fasciitis and atypical sacro-iliitis (Table IV).

TABLE IV
CASES OF ACUTE ANTERIOR UVEITIS WITH PROSTATITIS

Prostatitis	Uveitis	
	No.	Per cent.
Alone	36	33.6
With plantar fasciitis	2	1.9
With atypical sacro-iliitis	6	5.6
With Reiter's syndrome	38	35.5
With ankylosing spondylitis	25	23.4
Total	107	

Thus 38 (28.6 per cent.) out of 133 cases of acute anterior uveitis had Reiter's disease, while 25 (18.8 per cent.) had ankylosing spondylitis.

Of the eight cases of chronic anterior uveitis with prostatitis, two had Reiter's disease and one atypical sacro-iliitis (Table V). This group included twelve patients with heterochromic cyclitis; only three (25 per cent.) had chronic prostatitis and none showed any joint changes.

TABLE V
CASES OF CHRONIC ANTERIOR UVEITIS WITH PROSTATITIS

Prostatitis	Uveitis	
	No.	Per cent.
Alone	5	62.5
With atypical sacro-iliitis	1	12.5
With Reiter's syndrome	2	25.0
With ankylosing spondylitis	0	0.0
Total	8	

The patients with posterior uveitis showed a much lower incidence of prostatitis than those with anterior uveitis (Table VI).

TABLE VI
INCIDENCE OF PROSTATITIS IN CASES OF POSTERIOR UVEITIS

Posterior Uveitis	Prostatitis			
	No Evidence		Present	
	No.	Per cent.	No.	Per cent.
Acute	16	64	9	36
Chronic	1	20	4	80

The majority of the cases of acute posterior uveitis were considered to be due to toxoplasmosis, but the chronic cases were not typical of this disease. The cases of acute anterior and posterior uveitis are compared in Table VII, and there is a significant difference in the incidence of prostatitis between the two groups. None of those with acute posterior uveitis had Reiter's disease or ankylosing spondylitis, but one had prostatitis and atypical sacro-iliitis. One case of Reiter's disease occurred in association with a chronic posterior uveitis.

TABLE VII
COMPARISON OF INCIDENCE OF CHRONIC PROSTATITIS IN CASES OF ACUTE ANTERIOR AND POSTERIOR UVEITIS

Acute Uveitis	Prostatitis			
	No Evidence		Present	
	No.	Per cent.	No.	Per cent.
Anterior	26	19.5	107	80.5
Posterior	16	64.0	9	36.0

($\chi^2 = 8.75$; $0.01 > P$).

The high incidence of prostatitis and joint involvement in anterior uveitis is significant and differs markedly from that in posterior uveitis, in which toxoplasmosis appears to be the chief cause.

The cases which we have classified as generalized uveitis comprise patients in whom a marked anterior uveitis was found in conjunction with evidence of choroidal involvement. In many cases the lesions in the posterior segment were probably secondary to the iridocyclitis and certainly the incidence of prostatitis was higher in this group than in the cases of focal choroiditis (Table VIII).

TABLE VIII
INCIDENCE OF PROSTATITIS IN CASES OF GENERALIZED UVEITIS

Generalized Uveitis	Prostatitis			
	No Evidence		Present	
	No.	Per cent.	No.	Per cent.
Acute	9	45.0	11	55.0
Chronic	3	33.3	6	66.6

Comparison with anterior and posterior uveitis shows that the generalized group occupies a middle position with regard to the incidence of prostatitis (Table IX, opposite).

TABLE IX
INCIDENCE OF PROSTATITIS IN CASES OF UVEITIS

Uveitis	Total Cases	Cases with Prostatitis	
		No.	Per cent.
Anterior	152	115	75.6
Posterior	30	13	43.3
Generalized	29	17	58.6

There were four cases of Reiter's disease and one case of ankylosing spondylitis in the generalized uveitis group. The incidence of Reiter's disease and ankylosing spondylitis in the whole series is shown in Table X.

TABLE X
INCIDENCE OF REITER'S SYNDROME AND ANKYLOSING SPONDYLITIS

Diagnosis	Total	Reiter's Syndrome		Ankylosing Spondylitis	
		No.	Per cent.	No.	Per cent.
Anterior Uveitis	152	40	26.3	25	16.4
Posterior Uveitis	30	1	3.3	0	0.0
Generalized Uveitis	29	4	13.8	1	3.4
Eales's Disease and Other Non-uveitis Cases	15	0	0.0	0	0.0

It may help to clarify the overall picture to consider that uveal inflammation, chronic prostatitis, and joint changes, including Reiter's disease, ankylosing spondylitis, and sacro-iliitis, constitute a triple syndrome. Uveitis may occur alone, in combination with prostatitis, or with prostatitis and joint changes (Table XI).

TABLE XI
INCIDENCE OF UVEITIS ALONE AND COMBINED WITH CHRONIC PROSTATITIS AND CHANGES IN THE JOINTS

Diagnosis	Uveitis Alone	Uveitis + Prostatitis	Uveitis + Prostatitis + Joint Changes
Anterior Uveitis	37	43	72
Posterior Uveitis	17	10	3
Generalized Uveitis	12	10	7
Eales's Disease and Other Non-uveitis Cases	15	1	0

It is clear from these figures that it is in the cases of anterior uveitis that this triad is most frequently found, and the figures suggest that in a large proportion of these cases there is a common aetiology. In particular the results support the view that the uveitis is part of a systemic disease and

not a purely local ocular condition. Further support for this contention is provided by the erythrocyte sedimentation rates, the cases of anterior uveitis showing the highest incidence of a raised erythrocyte sedimentation rate (Table XII).

TABLE XII
PERCENTAGE INCIDENCE OF RAISED ERYTHROCYTE SEDIMENTATION RATE

Uveitis	Prostatitis		
	No Evidence	Alone	+ Reiter's Disease or Ankylosing Spondylitis
Acute Anterior	23.1	29.6	52.4
All Other Cases	17.5	10.0	11.1

Bacteriological examination of the prostatic fluid from these cases has shown no particular organism to be predominant. Streptococci, staphylococci, and diphtheroids were grown in most cases and *E. coli* in a few, but these organisms are usually regarded as contaminants of the male urogenital tract. Pleuropneumonia-like organisms have recently been suggested as the aetiological agent in cases of uveitis, but careful search for these organisms in the prostatic fluid and centrifuged deposit from urine gave positive results in only approximately 10 per cent. of patients. This incidence is higher than that found by Klieneberger-Nobel (1959) in a group of male patients attending the general medical out-patients' of The London Hospital, but lower than that found in patients attending a V.D. clinic. A complement-fixation test for pleuropneumonia-like organisms was positive in approximately 20 per cent., but no correlation could be found between the occurrence of a positive test and any of the categories of arthritis or fasciitis, or any of the types of uveitis.

Discussion

It must be emphasized that the results of this work should not be interpreted as meaning that acute anterior uveitis is necessarily caused by chronic prostatitis. It has only been shown that there is a strong association between the two conditions, and in the present state of knowledge care must be taken to avoid the temptation to ascribe causal relationships to such an association. Instead, factors in common between the uveal tract, the prostate, and the joints involved in Reiter's disease and ankylosing spondylitis should be sought, as it may be that these three tissues share a common pathological process rather than that disease in one causes disease in the others.

All the evidence suggests that acute non-specific urethritis is an infection of venereal origin which may initiate classical acute Reiter's disease; spread of this infection *via* connecting lymphatics has been suggested to account for subsequent disease of the sacro-iliac joints. The causal organism is

unknown, but if this were a virus, its spread could be responsible for the changes in the uveal tract. It is possible, however, that the initial acute infection is the trigger mechanism for secondary changes in the prostate and joints which are self-perpetuating.

It should be remembered that the uveal tract, the joints, and the prostate have a common embryological origin from the mesoderm. The retina is developed from neural ectoderm, but the uvea—apart from the neural epithelium of the iris—is mesodermal in origin. So are the skeletal elements of the body and part of the prostate gland, and it is possible that mesodermal tissues in general may be susceptible to different types of pathological process from those affecting ectodermal and endodermal tissues.

The auto-immune reaction as a cause of disease is an attractive hypothesis and provides a possible explanation in many diseases of obscure aetiology. For example, in our present problem of the association between uveitis, prostatitis, and joint disease, it can be postulated that the tissues concerned all have a common antigenic component. Following an acute infective episode—acute non-specific or even gonococcal urethritis and prostatitis—this antigen in the prostate stimulates the formation of antibodies. These antibodies will react with the antigen wherever it is found, *i.e.* in the joints and the uveal tract.

However attractive such an hypothesis is, it remains idle speculation until we have some solid facts to support it. Perhaps it will nevertheless provide a starting point for some useful investigations.

One important aspect of this work from the ophthalmological point of view is that it deals only with males. Acute anterior uveitis is not confined to males, although it is in fact more common in males than in females. The sex incidence is approximately equal in posterior uveitis and in the chronic types of anterior and generalized uveitis, but there is a definite preponderance of male cases of acute anterior uveitis (Table XIII), so that it is fair to say that the problem is more important in males. It may be significant that this sex incidence is paralleled by the sex incidence of ankylosing spondylitis and Reiter's disease. Oates (1959) suggests that only 20 per cent. of ankylosing spondylitis and 10 per cent. of Reiter's disease occurs in women. At

TABLE XIII
SEX INCIDENCE OF ACUTE ANTERIOR UVEITIS

Sex	Total Cases	Acute Anterior Uveitis	
		No.	Per cent.
Male	243	147	60
Female	181	76	42

the moment we have no information concerning the relationship between uveitis, chronic genital infection, and joint changes in women, but a series of cases is under investigation.

Summary and Conclusions

This investigation has shown that a high proportion of male patients with acute anterior uveitis have chronic urogenital infection, and that many of them show changes in the sacro-iliac joints, spine, and lower limbs typical of ankylosing spondylitis or Reiter's disease. No causal relationship between the chronic prostatic infection and the uveitis has been established, and in most cases the organism responsible for the chronic genital infection is unknown. It is clear however that acute anterior uveitis in the male cannot be considered as an isolated disease entity but is closely linked with disorders of other mesodermal constituents of the body.

This investigation was undertaken whilst one of us (R.D.C.) was working under the aegis of the Medical Research Council Working Party on Non-Specific Urethritis with the aid of a grant from the U.S. Department of Public Health.

REFERENCES

- CATTERALL, R. D. (1958a). *Trans. ophthal. Soc. U.K.*, **78**, 523.
——— (1958b). *Brit. J. vener. Dis.*, **34**, 254.
KLIENEBERGER-NOBEL, E. (1959). *Ibid.*, **35**, 20.
MASON, R. M., MURRAY, R. S., OATES, J. K., and YOUNG, A. C. (1958). *Brit. med. J.*, **1**, 748.
OATES, J. K. (1959). *Brit. J. vener. Dis.*, **35**, 81.