Multi-system Ocular Syndromes

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Uveitis

Inflammation of the uveal tract, which comprises the iris, ciliary body and choroid, is a significant cause of blindness particularly in the fourth decade of life. About 2,500 of the 100,000 registered blind people in this country were blinded by uveitis and its complications, and this is particularly so in young people in the 30 to 40 decade. It is traditional to subdivide uveitis into anterior uveitis (or iridocyclitis) and posterior uveitis (or choroiditis), but it is only convenient to retain this concept if it can contribute to a better understanding of the causes or mechanisms of the inflammatory process. It should nevertheless be remembered that it is an artificial distinction since the iris–ciliary body–choroid is a continuous structure, derived from the mesoderm surrounding the

Table 1. A classification of the patterns of uveitis

| A. Infections                  | B. Granulomatous disorders       |
|-------------------------------|----------------------------------|
| Fungi                         | Sarcodeiosis                     |
| Histoplasma                   | Crohn's regional enteritis       |
| Protozoa                      | Wegener's granulomatosis         |
| Toxoplasma                    |                                  |
| Metazoas                      |                                  |
| Toxocara                      |                                  |
| Oncho cercar                  |                                  |
| Spirochaetes                  |                                  |
| T. pallidum                   |                                  |
| Mycobacteria                  |                                  |
| M. tuberculosis               |                                  |
| M. leprae                     |                                  |
| Bacteria                      |                                  |
| Brucella                      |                                  |
| Virus                         |                                  |
| Epstein-Barr                  |                                  |
| Herpes simplex                |                                  |
| Herpes zoster                 |                                  |
| Mumps                         |                                  |
| Cytomegalovirus               |                                  |

| C. Muco-cutaneous syndromes   |                                  |
| Stevens-Johnson               |                                  |
| Behcet                        |                                  |
| Brodie-Reiter                 |                                  |
| Systemic lupus                |                                  |

| D. Rheumatic diseases         |                                  |
| Arthritis                     |                                  |
| Spondylitis                   |                                  |
| Polyarteritis nodosa          |                                  |
| Polychondritis                |                                  |

| E. Oculo-parotid syndromes    |                                  |
| Heerfordt's                   |                                  |
| Sjögren's                     |                                  |
| Mikulice's                    |                                  |

| F. = Miscellaneous           |                                  |
| Ulcerative colitis           |                                  |
| Vogt-Koyanagi-Harada         |                                  |
| syndrome                     |                                  |
| Phacoantigenic               |                                  |
Table 2. The infective causes of uveitis with distinguishing clinical features, investigations and treatment.

| Infective Causes of Uveitis | Clinical Accompaniments | Blood test | Investigations | Other | Treatment | Other |
|-----------------------------|-------------------------|------------|----------------|-------|-----------|-------|
| *Histoplasma capsulatum*    | Erythema nodosum        | Complement fixation (CFT) | Yes | Miliary lung infiltration | Amphotericin 5 Fluoro-cytosine |
|                            | Choroidoretinitis       |            |                |       |           |       |
| *Toxoplasma*               | Peripheral choroiditis  | Dye test CFT | Yes | Cerebral calcification | Pyrimethamine Sulphonamides |
|                            | Hydrocephalus            |            |                |       |           |       |
| *Toxocara*                 | Choroidoretinitis       | Eosinophilia | Yes | Miliary lung mottling | Thiaabendazole |
|                            | Hepatic granulomas      |            |                |       |           |       |
| *Onchocerca*               | General uveitis          | CFT        | Yes | Thin skin sections | Diethylcarbamazine Suramin |
|                            | Pruritic rash            | Eosinophilia |       |       |           |       |
|                            | Nodules                  |            |                |       |           |       |
| *T. pallidum*              | Congenital choroidoretinitis | Wassermann Anti-Treponemal | | Darkfield examination | No | Penicillin |
| *M. tuberculosis*          | Fever                    | Yes | Pulmonary infiltration | Isolate mycobacterium | Yes | Streptomycin Isoniazid Rifampicin |
|                            | Sweats                   |            |                |       |           |       |
|                            | Weight loss              |            |                |       |           |       |
| *M. leprae*                | Anaesthetic plaques     | Yes | Skin smears | Yes | Sulphones Rifampicin |
|                            | Thickened nerves         |            |                |       |           |       |
| *Brucella*                 | Fever                    | Agglutinins | Yes |             | Yes | Tetracycline |
|                            | Sweats                   |            |                |       |           |       |
|                            | Hepatic granulomas       |            |                |       |           |       |
| *Infectious mononucleosis* | Lymphadenopathy jaundice | Epstein-Barr antibodies Paul-Bunnell test | | Yes |           |       |
| *Herpes simplex*           | Keratitis                | Neutralising antibody | | Isolate virus | No | Iododeoxyuridine |
| *Herpes zoster*            | Skin vesicles at tip of nose | CFT | | Spinal fluid pleocytosis | Yes | Iododeoxyuridine |
| *Mumps*                    | Parotitis                | CFT        | Yes | Isolate virus | No |       |
| *Cytomegalovirus*          | Congenital choroidoretinitis | CFT | | Isolate virus | No |       |
optic cup, and this uveal tract is extremely vascular. It would indeed be surprising if inflammation of the anterior part did not affect the posterior part and vice versa. Uveitis may be secondary to penetrating wounds or other trauma, or follow chemicals that inflame any of the anterior layers of the eye. Uveitis may also follow surgical intervention or be secondary to some local intra-ocular cause. All these instances are usually obvious examples of exogenous or secondary uveitis. The ophthalmologist is not perplexed by the cause; and the management, whenever possible, is to remove the irritative source of the inflammation. The riddle of uveitis lies in the causes and course of endogenous uveitis.

Uveitis should not be regarded as a disease but rather as a symptom of some widespread multi-system disorder or infection involving many other tissues. In the investigation and management of uveitis, it is important to recognise it as one component of a pattern; there are several distinctive interwoven patterns (Table 1), some of them boldly designed, others confusing at the present time, but all of interest to the general physician.

Infections
Uveitis may be associated with a wide range of infections—fungal, protozoon, metazoon, treponemal, mycobacterial, bacterial and viral (Table 1). They are usually accompanied by distinctive clinical features and there are definitive investigations and treatments (Table 2).

Granulomatous Disorders
Uveitis is noteworthy in three granulomatous disorders—sarcoidosis, Crohn’s regional enteritis, and Wegener’s granulomatosis.

Sarcoidosis
Sarcoidosis is noted in about 4 per cent of patients with uveitis, but, conversely, uveitis is observed in about 25 per cent of patients with sarcoidosis. Uveitis is most commonly anterior (Table 3). The relative infrequency of posterior uveitis is artificial as it is difficult to recognise choroidoretinitis in the presence of acute inflammation of the anterior segment of the eye. Now that anterior uveitis is rapidly being brought under control by corticosteroids, it is possible to examine the fundus oculi at a much earlier stage when sarcoid lesions are still present. Consequently posterior uveitis is less likely to be overlooked in the future.

When confronted with the possibility of ocular sarcoidosis, the ophthalmologist should always carry out slit-lamp examination and bear in mind that it is
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### Table 3. Ocular manifestations in 147 patients with histologically-confirmed sarcoidosis

| Ocular Sarcoidosis       | No. of Patients | %  |
|--------------------------|-----------------|----|
| Anterior uveitis         | 107             | 73 |
| Acute                    | 44              |    |
| Chronic                  | 63              |    |
| Posterior uveitis        | 27              | 20 |
| Choroidal nodules        | 15              |    |
| Papilloedema             | 7               |    |
| Haemorrhages             | 5               |    |
| Conjunctiva              | 34              | 23 |
| Sicca                    | 11              |    |
| Non-specific             | 8               |    |
| Follicles                | 8               |    |
| Phlyctenular             | 7               |    |
| Scleral plaques          | 4               | 3  |
| Total                    | 147             | 100|

### Table 4. Pattern of clinical and laboratory associations in 147 patients with ocular sarcoidosis

| Clinical Associations     | No. | %  |
|---------------------------|-----|----|
| Females                   | 100 | 68 |
| Aged 20 to 50             | 112 | 76 |
| Intrathoracic             | 111 | 75 |
| Reticulo-endothelial      | 65  | 44 |
| Skin plaques              | 53  | 36 |
| Erythema nodosum          | 38  | 26 |
| Nervous system            | 22  | 15 |
| Parotids                  | 14  | 12 |
| Lachrymals                | 10  | 8  |
| Bone cysts                | 12  | 8  |
| Positive Kveim-Siltzbach test | 105/132 | 80 |
| Negative tuberculin test  | 83/124 | 66 |
| Hypercalcaemia            | 20/99 | 20 |

Twice as common in women as in men (Table 4) and that three-quarters of patients with ocular sarcoidosis are aged 20 to 50 years old, only 3 per cent are under 20 years, and only 20 per cent over 50 years. He should adopt the following diagnostic routine—

1. Full general medical examination to determine whether it is acute-onset or insidious-onset sarcoidosis (Table 5). The natural history varies with the pattern of onset.
2. Biopsy of any enlarged lachrymal glands or obvious conjunctival follicles. Blind biopsy of the conjunctiva in which there are no obvious follicles is fruitless.
Table 5. Differences between acute and chronic iridocyclitis due to sarcoidosis in a series of 107 patients with anterior uveitis

| Anterior Uveitis (107) | Acute | Chronic |
|------------------------|-------|---------|
| Number of patients     | 44    | 63      |
| Onset                  | Abrupt| Insidious|
| Decade of onset        | 20–30 | 40–50   |
| Course                 | Transient| Persistent|
| Signs                  | Ciliary congestion| Fatty nodules|
|                        | Turbid aqueous| Synechiae|
|                        | Keratic precipitates| |
| Sequelae               | Rare| Lens opacities|
|                        | | Glaucoma|
|                        | | Cataract|
|                        | | Blindness|
| Associations           | Hilar adenopathy| Pulmonary fibrosis|
|                        | Erythema nodosum| Lupus pernio|
|                        | | Bone cysts|
| Response to corticosteroids | Good | Poor |
| Alternative treatment  | Oxyphenbutazone| Chloroquine|
|                        | Indomethacin| |

3. Chest radiography, since this is abnormal in three-quarters of patients with ocular sarcoidosis (Table 4).

4. Kveim-Siltzbach and Mantoux skin tests, for these frequently provide helpful information (Table 4).

5. Serum or urine calcium levels, preferably both.

In the treatment of ocular sarcoidosis, topical corticosteroids may be sufficient for anterior uveitis, in the form of eye-drops applied frequently during the day, reinforced with a corticosteroid ointment at night. If there is no substantial and continuing improvement within ten days, local subconjunctival inoculation of cortisone may be employed to increase its concentration in the anterior segment of the eye. Oral corticosteroids are indicated if local treatment does not lead to a rapid response or if ophthalmoscopy reveals posterior uveitis. In addition, the inflamed iris is rested by local atropine medication.

**Crohn’s Regional Enteritis**

A more precise incidence of the ophthalmic manifestations of Crohn’s disease will be evident only when routine slit-lamp examination of the eye has been
| Mucocutaneous syndrome | Sex and age | Ulceration of mucous membranes | Skin Lesions | Conjunctivitis | Eye | Polyarthrits ± effusions | Other Tests | Treatment |
|------------------------|-------------|--------------------------------|--------------|---------------|-----|------------------------|------------|----------|
| Stevens–Johnson        | M.2:1       | Yes                            | Erythema multiforme and nodosum | +             | +   | Corneal ulceration     | Cold agglutinin | Tetracycline |
|                        | 15–50       |                                |              |               |     | Swollen eyelids | Pneumonia          | Steroids   |
| Behçet                 | M.2:1       | Yes                            | Erythema nodosum | +             | +   | Retinal vasculitis    | Migraine Encephalitis | Steroids   |
|                        | 20–40       |                                |              |               |     | Scleritis Panophthalmitis | Deep vein thrombosis | with azathioprine |
|                        |             |                                |              |               |     |                        | Cranial nerve palsy |           |
| Brodie–Reiter–Harkness | M.20:1      | Yes                            | Keratodermia blennorrhagica | +             | +   | Episcleritis Keratitis Retinitis | Auto-antibodies | Steroids   |
|                        | 20–40       |                                |              |               |     |                        | fetal oral mucosal | Phenylbutazone |
| Systemic lupus erythematosus | F.9:1 | Yes                            | Discrete facial lupus Purpura | Urticaria | Vasculitis | Retinal vasculitis | Nephrotic syndrome | Steroids with |
|                        | 20–40       |                                |              |               |     |                        | Anti-nuclear factor | azathioprine or |
|                        |             |                                |              |               |     |                        | Pericarditis Pleurisy | cyclophosphamide |
undertaken in a large series of patients with this chronic granulomatous disorder. It is likely that iritis is more frequent than in a control population and there are also reports of associated episcleritis and keratitis.

Wegener's Granulomatosis
Granulomatous angiitis involves arteries and veins throughout the respiratory tract and kidneys, causing severe necrosis, ulceration and gangrene of tissue. The ophthalmic manifestations include orbital lid oedema, nasolachrymal duct obstruction, conjunctival chemosis, sclero-keratitis, anterior uveitis, and a retinal vasculitis with cotton wool exudates. Corticosteroids should be given in combination with azathioprine or cyclophosphamide. Antilymphocytic globulin has not yet been given a trial.

Mucocutaneous Syndromes
There are four syndromes in which ocular inflammation is associated with mucocutaneous ulceration, skin lesions and polyarthralgia, sometimes with joint effusions (Table 6).

Stevens–Johnson Syndrome
This is somewhat commoner in men in young adult life. It may be triggered off by various drugs, vaccination, *Mycoplasma pneumoniae* and other agents capable of inciting a widespread hypersensitivity reaction.

Behçet’s Syndrome
It is most frequently seen in Turkish or Japanese men aged 20 to 40 years. Associated with the ocular disease and aphthous stomatitis, there may be polyarthritis, deep vein thromboses, encephalitis, or cranial nerve palsies. The serum contains aggressive autoantibodies against fetal oral mucosa, suggesting that this is an autoimmune disorder (Lehner, 1972).

Reiter’s Syndrome
Sir Benjamin Brodie described this syndrome clearly in 1817, that is precisely one hundred years before Reiter’s single case presentation. Harkness added to both descriptions as a result of his lifelong experience at the Lock Hospital, Soho. It is most commonly seen in young adult men, in whom the triad usually comprises arthritis, urethritis, conjunctivitis.

Systemic Lupus Erythematosus
Oral ulceration occurs sufficiently often to include it as a multi-system mucocutaneous syndrome. It is the only one of the four syndromes that predominates in women (Table 6). It is also the only one of the four syndromes in
Table 7. Rheumatic disorders and the eye

| Disorder                          | Conjunctivitis | Keratitis | Scleritis | Scleralacia | Keratoconjunctivitis sicca | Anterior uveitis | Retinal vasculitis |
|-----------------------------------|----------------|-----------|-----------|-------------|-----------------------------|-----------------|-------------------|
| Rheumatoid arthritis              |                |           |           |             |                             |                 |                   |
| Adult                             |                |           |           |             |                             |                 |                   |
| Juvenile                          |                |           |           |             |                             |                 |                   |
| Ankylosing spondylitis            |                |           |           |             |                             |                 | +                 |
| Systemic lupus erythematosus      | +              |           |           |             |                             | +               |                   |
| Sjögren’s syndrome                |                |           |           |             |                             |                 | +                 |
| Behçet’s syndrome                 |                |           |           |             |                             | +               | +                 |
| Reiter’s syndrome                 |                |           | +         |             |                             | +               | +                 |
| Erythema nodosum                  |                |           |           |             |                             |                 | +                 |
| Progressive systemic sclerosis (scleroderma) |                |           |           |             |                             |                 | +                 |
| Wegener’s granulomatosis          |                |           |           |             |                             | +               | +                 |
| Polyarteritis nodosa              |                |           |           |             |                             | +               | +                 |
| Dermatomyositis                   |                |           |           |             |                             |                 | +                 |
| Relapsing polychondritis          | +              |           |           |             |                             |                 | +                 |
which iritis is inconspicuous. There may be conjunctivitis or subconjunctival haemorrhages but the most significant and sinister ocular disturbance is the retinal vasculitis with widespread cotton wool exudates and haemorrhages.

RHEUMATIC DISORDERS
Inflammation of various coats of the eye is commonly associated with a large spectrum of rheumatic disorders, creating overlapping patterns and syndromes. The type of ocular disease is a reflection of the rheumatic disorder, so common links can be recognised between the eye and the locomotor system (Table 7).

When assessing the ocular component, it is important to try to recognise which of the four basic patterns of disease is responsible. This may be difficult because of confusing overtones of involvement of adjacent coats of the eye. The three basic patterns are—

(a) Involvement of the sclera, the outer collagenous coat of the eye. Nodular scleritis, episcleritis and scleromalacia perforans are similar to the subcutaneous rheumatic nodules of rheumatoid arthritis, and they are also associated with rheumatic pericarditis, pleurisy and cardiac valvulitis. This is the ocular component of adult rheumatoid arthritis, particularly in its extra-articular systemic facets.

(b) Iritis or iridocyclitis is associated with juvenile rheumatoid arthritis (Still’s disease), particularly when there is pauciarticular or monarticular joint disease and minimal systemic involvement. Iritis is also a feature of a circulating immune complex as in erythema nodosum and sarcoidosis.

(c) Vasculitis involves retinal vessels as it does the skin, kidneys, muscles and respiratory tract in such conditions as systemic lupus erythematosus, Wegener’s granulomatosis, polyarteritis nodosa, dermatomyositis and erythema nodosum.

(d) The Sicca syndrome of dry eyes and dry mouth is not specific. It is the classical feature of Sjögren’s syndrome but it is also commonly seen in chronic liver disease and following drugs.

OCULO-PAROTID SYNDROMES
There are certain syndromes in which iritis or other ocular disorders are associated with generalised disease (Table 8).

Heerfordt’s Syndrome
Heerfordt (1909), a Copenhagen ophthalmologist, described ‘Febris uveoparotidea and enlargement of the parotid glands, running a chronic and
Table 8. Oculo-parotid syndromes

| Oculo-parotid syndromes | Sex | Ocular Features | Other Features | X-rays | Histology | Tests | Treatment |
|-------------------------|-----|----------------|---------------|--------|-----------|-------|-----------|
| Heerfordt (Denmark)     | Women more frequently | Iritis | Enlarged lachrymals | Hilar adenopathy | Sarcoid tissue | Positive Kveim-Siltzbach | Steroids |
|                         |     |                | Fever | Pulmonary infiltration |               |       |           |
|                         |     |                | Facial palsy |               |           |       |           |
|                         |     |                |        |                |           |       |           |
| Sjögren (Sweden)        | Menopausal women | Dry eyes | Like systemic lupus | Pulmonary infiltration | Sarcoid tissue | Positive Kveim-Siltzbach | Artificial tears |
|                         |     | Corneal ulcers | Enlarged lachrymals | Rheumatoid arthritis |               |       |           |
|                         |     |                | Dry mouth |               |           |       |           |
|                         |     |                | Dry bronchi |               |           |       |           |
|                         |     |                | Dry joints |               |           |       |           |
|                         |     |                | Dry vagina |               |           |       |           |
|                         |     |                |        |                |           |       |           |
| Mikulicz (Vienna)       | Either |                |                | Pulmonary infiltration | LE cell | Low serum complement | Oestrogens |
|                         |     |                |                |                |           |       | Chloroquine |
|                         |     |                |                |                |           |       | Steroids |
|                         |     |                |                |                |           |       | Azathioprine |
|                         |     |                |                |                |           |       | Steroids |
|                         |     |                |                |                |           |       | Steroids |
|                         |     |                |                |                |           |       | Steroids |

**Table 8. Oculo-parotid syndromes**
usually febrile course, and frequently complicated by cranial nerve palsies especially of the seventh cranial nerve with pleocytosis of the cerebrospinal fluid'. Heerfordt described three cases and referred to other examples he had found in the literature. Greenberg et al. (1964) observed enlargement of the parotid gland in 23 of 388 (6 per cent) patients with sarcoidosis; the most frequent clinical accompaniments were enlargement of spleen and lymph nodes, uveitis and abnormal chest radiographs.

Sjögren's Syndrome.
If a women in her forties complains of dry, smarting, burning or itching eyes and a dry mouth, then the possibility of Sjögren’s syndrome (Sjögren, 1933) should be considered. The other common component of the syndrome is rheumatoid arthritis, but this may be replaced or overshadowed by parotid or lachrymal gland enlargement, purpura, Raynaud’s phenomenon, subcutaneous nodules, dry skin, scleroderma, splenomegaly or peripheral lymphadenopathy. Thus, the patient may be seen in either the ophthalmic or the rheumatology clinic, thereby determining which set of investigations will be undertaken. The ophthalmologist will insert Schirmer filter paper inside the lower eyelid near the external canthus to demonstrate deficiency of lachrymal secretion; a drop of rose-bengal dye to demonstrate obvious staining of the bulbar conjunctiva and cornea; and he may find, by slit-lamp examination, punctate corneal staining with fluorescein. By these means the presence of keratoconjunctivitis sicca may be confirmed. The rheumatologist, on the other hand, will seek clinical confirmation by radiology and serology (Table 8).

Sjögren’s syndrome is an insidious disorder of menopausal women, many of whom are also suffering from endogenous or reactive depression. It may co-exist with primary biliary cirrhosis which is also common in women in their forties. Under these circumstances, depression and primary biliary cirrhosis may prove dominant and mask concomitant Sjögren’s disease unless the serological abnormalities of the latter are specifically sought.

It remains a distressing affliction since treatment is so unsatisfactory. Local treatment of the eyes for relief of symptoms due to the dryness includes 1 per cent methylcellulose in saline (artificial tears) or sulphacetamide eye drops. The latter are bland and alkaline and minimise bacterial complications. The danger of corneal ulceration is always present so that corticosteroid drops should incorporate an antibiotic. Sealing of the puncta by cautery helps to conserve what little moisture is present. Because of its similarities to rheumatoid arthritis, systemic corticosteroids and azathioprine provide considerable symptomatic relief of the distressing eye and joint symptoms, some re-watering
of the mouth and amelioration of the pulmonary picture, but this improvement may be at a price. Immunosuppression may lead to infection and corneal ulceration, so immunosuppression is only indicated for limited periods to overcome acute episodes of the disorder.

*Mikulicz’s Syndrome*
Mikulicz (1892), a Breslau professor of surgery, described a 42-year-old man with xerostomia and bilateral enlargement of lachrymal, submaxillary and parotid glands. Histology revealed lymphocytic infiltration of the glands. The cause was unknown—and still is. This syndrome is now regarded as a ragbag for those idiopathic disorders that cannot be categorised.

**MISCELLANEOUS (Table 1)**

*Ulcerative Colitis*
Iritis may be associated with ulcerative colitis, arthritis, sacro-iliitis, aphthous stomatitis and chronic active hepatitis in an overlapping series of patterns of disease.

*Vogt–Koyanagi–Harada Syndrome*
Like so many syndromes, it was described first by Hutchinson (1892) as a case of blanched eyelashes. The bilateral uveitis is associated with encephalitis, alopecia, vitiligo, dysacousia and exudative retinal detachment.

*Phacoantigenic Uveitis*
Lens-induced iridocyclitis occurs up to 14 days after leakage of the lens either as a result of long-standing uveitis or following trauma or extracapsular lens extraction. It may be associated with sympathetic ophthalmia.

*Senile Giant Cell Arteritis*
The old term temporal or cranial arteritis should be abandoned for it is too restrictive in describing this multi-system giant cell arteritis which occurs in the over-sixties of both sexes. The necrotic granulomatous reaction is most evident in the media, although it also involves the intima, leading to thickening, narrowing of the lumen and thrombus formation. It is recognised most frequently in a branch of the carotid artery, for the dramatic clinical manifestations may include blindness, but the process may also involve the subclavian, coronary, pulmonary, mesenteric and renal arteries.

This condition should always be kept in mind when the elderly complain of headache with hyperalgesia of the scalp, anorexia and weight loss, polymyalgia rheumatica, temple or jaw pain on chewing, neck stiffness, blurring of vision...
or confusion. The quickest confirmatory investigations are the ESR and temporal artery biopsy. The ESR is almost always over 50 mm/hour. This finding is sufficient evidence to start parenteral and oral corticosteroids, for immediate treatment may be sight-saving, and any delay may lead to irreversible blindness. Indeed, this is probably about the only indication for treating the ESR in human disease. Within hours of initiating treatment, there is a striking amelioration of symptoms.

The ESR almost always returns to normal within one month. Thereafter, treatment should be tailored to keep the patient symptom-free and with a normal ESR. We (Turner et al., 1974) have recently analysed a series of 47 patients admitted to our Medical Ophthalmology Unit with visual symptoms and a constitutional upset. The majority were over 70 years of age and women were affected three times more frequently than men. The ocular signs were of ischaemic papillopathy (in 80 per cent), which was unilateral in two-fifths, or central retinal artery occlusion in 13 per cent of patients. The ESR was always elevated above 40 mm, and in one-third it was above 100 mm. The main ophthalmic differential diagnosis was to determine whether it was arteritic or atherosclerotic ischaemic papillopathy in this age group; principal differences are outlined in Table 9. Following corticosteroid therapy, vision improved in

Table 9. Differences between arteritic and atherosclerotic papillopathy

| Differential Features | Ischaemic Papillopathy due to |
|----------------------|--------------------------------|
|                      | Arteritis | Atherosclerosis |
| History of           |          |                |
| Polymyalgia rheumatica | +        | –               |
| Intermittent claudication | –     | +               |
| Angina of effort      | ±         | +               |
| Signs of             |          |                |
| Generalised atherosclerosis | ±      | + +             |
| Absent pulses         | –         | +               |
| Attenuated retinal vessels | ±     | +               |
| Wide pulse pressure   | ±         | + +             |
| ECG                  | Usually normal | Frequently ischaemic |
| ESR                  | Elevated | Normal          |
| Immunoglobulins      | Abnormal | Normal          |
| Histology            | Vasculitis | Atherosclerosis |
| Response to Steroids | Dramatic | Nil             |
| Immunosuppressives   | Good     | Nil             |
one-quarter, remained unchanged in two-fifths, and deteriorated in one-eighth of patients. Visual deterioration predominated in elderly women who received steroids late in the course of the disorder. Early steroid therapy is particularly recommended in elderly patients with visual symptoms and significantly raised ESRs.

**Retinal Vasculitis**

Primary retinal vasculitis affects young adults, usually men, causing considerable deterioration of vision and even blindness. Henry Eales, a Birmingham ophthalmologist, described it in 1880 in men, aged 19 to 29 years, with recurrent peripheral retinal haemorrhages. He felt that these haemorrhages were due to raised pressure as a result of the strain of defaecation in these constipated young men. He seems to have been shrewd and accurate for Hart et al. (1971) demonstrated grossly elevated venous pressures by ophthalmodynamometry; and fluorescein angiography showed marked leakage of dye from large veins and at the disc. The diagnosis of retinal vasculitis depends on the exclusion of certain diseases which produce a confusingly similar picture, namely diabetes mellitus, hyperviscosity states, chronic renal disease, sickle cell disease, and local arteriovenous malformations. When vasculitis secondary to such disorders has been excluded, primary retinal vasculitis is described as a disorder of peripheral retinal haemorrhages, usually in young men, frequently unilateral, and in particular involving veins by patchy perivascular and intramural infiltration by lymphocytes. The presenting symptom of blurred vision is associated with signs of venous congestion and sheathing of veins, disc swelling and scattered haemorrhages. There are no demonstrable

| Table 10. The differential diagnosis of retinal vasculitis and central retinal vein occlusion |
|--------------------------------------------|-----------------|-----------------|
| **Feature**                              | **Retinal Vasculitis** | **Central Retinal Vein Occlusion** |
| Age at onset (years)                      | Under 40        | Over 40         |
| Sex                                       | Male > Female   | Either          |
| **Clinical Associations**                 |                 |                 |
| Hypertension                              | -               | +               |
| Atherosclerosis                           | -               | +               |
| Hyperviscosity states                     | -               | +               |
| Malignancy                                | -               | +               |
| Chronic simple glaucoma                   | -               | +               |
| Macular haemorrhage                       | Insignificant   | Yes             |
| Depression of central vision              | No              | Yes             |
manifestations of systemic disease apart from elevated serum IgM levels (Chilman, 1974). The course is variable, for there may be only one attack, or it may progress insidiously with recurrent haemorrhages in the same or the other eye. Progression is characterised by bilaterality, arterial involvement and failure of vision. When it presents in an older age group there is considerable difficulty in distinguishing it from central retinal vein occlusion, since the differential points are sparse (Table 10).

Oral steroids may be of temporary benefit in suppressing retinal vasculitis, but we find that the early use of azathioprine with steroids may be sight-saving. The addition of azathioprine exerts added immunosuppression, and

| Table 11. Adverse ocular reactions to drugs |
|-------------------------------------------|
| **Drug** | **Cornea** | **Neuritis/Atrophy** | **Retina** | **Other** |
|-----------|------------|----------------------|------------|----------|
| Sulphonamide | Stevens-Johnson syndrome | Amblyopia | | Ocular palsy |
| Streptomycin | | | | |
| Isoniazid | | | + | Vertigo |
| Ethambutol | | | + | Peripheral neuritis |
| Indomethacin | Deposits | | | |
| Allopurinol | Deposits | | | |
| Chloroquine | Deposits | | | |
| Chlorpromazine | Opacities | | | |
| Contraceptives | Contact lens difficulty | Papilloedema | | |
| Chloramphenicol | | | + | |
| Clomiphene | | | | |
| Chlorpropamide | Stevens-Johnson syndrome | | | |
| Anticonvulsants | Stevens-Johnson syndrome | | | |
| Calciferol | Bands | | | |
| Disulfiram (Antabuse) | | | + | |
| Sodium aurothiomalate | Deposits | | | |
| P.A.S. | | | + | |
| Nalidixic acid | | Papilloedema | | |
| Tetracycline | | | | |
| Corticosteroids systemic | | | Papilloedema | Posterior polar lens opacities |
| Eye drops | | | | Glaucoma |
permits the use of smaller doses of systemic steroids. Coagulation of leaking areas, demonstrated by fluorescein angiography, is also essential.

**Adverse Ocular Reactions to Drugs**

It is essential to remain alert to possible toxic ocular effects of drugs, for they may be insidious in their development and far-reaching in their consequences (Table 11). The following routine is recommended—

1. Intra-ocular pressure should be measured in everybody receiving corticosteroid eye drops.
2. Slit-lamp examination should be done periodically for all patients receiving long-term oral chloroquine (for evidence of corneal deposition) and oral steroids (for evidence of posterior cortical lens opacities).
3. Ask patients (particularly those taking chloroquine) to report any phenomena such as haloes around lights.
4. Electrophysiological tests of retinal function on all patients receiving long-term administration of drugs for tuberculosis and rheumatic disorders.

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