fascinating topic of steroid glaucoma has been dealt with by Professor Perkins. Mydriasis has also been noted in the normal eye; possible mechanisms demonstrated elsewhere in the body would be the potentiation of the adrenergic effect or a direct action on smooth muscle.

I have left the question of cataracts until last because I have little to add to what I have already published (Crews 1963). Although the typical posterior subcapsular lens opacities have been mainly noted in patients on long-term systemic therapy they have more recently been reported following local medication (Streiff 1964, Becker 1964). They were originally described by Black *et al.* (1960) in 17 out of 44 patients with rheumatoid arthritis and later the series was expanded to 30 out of 72 including those with other diseases. The opacities could be differentiated from those due to other causes except for radiation and toxic. A relationship was found between incidence and dosage though later reports indicated considerable variation in the incidence. My own series substantially agreed with the original report from the National Institutes of Health: of 79 patients on long-term therapy for a variety of conditions 25 had typical opacities, chiefly affecting those on a moderate or high dose for more than two years. There was also a relationship between the dosage and degree of opacity. Vision remained good in half of the eyes, but in 7 it was greatly impaired. Several patients have had cataract extraction which they withstood very well. Most of the patients showed other marked steroid side-effects. The series has now increased to 39 of whom 7 (with nephrotic syndrome) are under 22 years old.

It has not proved possible to produce these opacities in animals. Probably the best indication that steroids are involved is the demonstration that in a few very early cases, after treatment has ceased, clear lens fibres are laid down outside the opacities; with local therapy, lens changes develop only in the eye receiving medication.

With regard to the management, patients on a moderate or high dose (i.e. over 10 mg prednisone or equivalent) for more than two years should be examined at intervals by an ophthalmologist. If typical opacities are found there should be a joint revaluation of the necessity for steroids: a reduction to minimal suppressing dose may ensure that opacities remain stationary. If large doses are essential then it can be advised that extraction of cataracts seems free from added risk.

With all these adverse reactions there is the difficulty of establishing whether they are caused by the therapy. Often it is suspected that the steroids act on a background of disease, impaired nutrition, or genetic predisposition, which explains the considerable delay in the recognition of these complications. There may be less risk of reactions in the presence of an active inflammatory process, because of increased local utilization of corticosteroids, and potential danger if the dosage is not reduced after the inflammation quietens, or where excess drug acts on adjacent tissues. If, for example, a powerful local preparation is instilled into the eye for a mild superficial affection (e.g. allergic conjunctivitis) a high intraocular level may lead to complications which would not have occurred had the inflammation affected deeper structures. The development of preparations with surface action but low intraocular penetration is an obvious solution.

I would re-emphasize the need for recognizing the more serious complications and for joint consultation with physicians to review steroid requirements. Further study of the mechanism of reactions may aid our basic knowledge of ocular disease and enable therapeutic products to be developed which do not have these disadvantages.

Corticosteroids have enormous value in ophthalmology. Nothing I have said detracts from their use in properly selected conditions.

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Arterial Fluorescein Studies in Diabetic Retinopathy

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The retinal circulation has been investigated by following the passage of fluorescein injected intravenously. Serial photographs, taken with the aid of selective filters in the illuminating and receiving light paths, record only the fluorescent light (Dollery *et al.* 1962). Preliminary studies in diabetic retinopathy revealed a number of

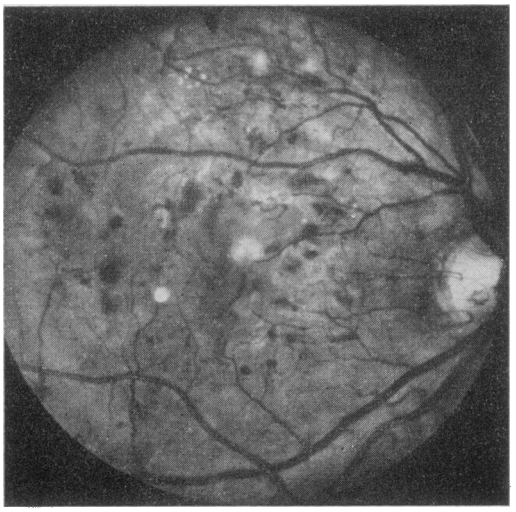

Fig 1 *Reproduction of a colour transparency of the right macular region of a male diabetic patient aged 28 years. Diabetes diagnosed at the age of 10 years. Visual symptoms of recent onset, acuity 6/6. The retina shows advanced changes, irregularity of the small veins, abnormal vessels, many hæmorrhages punctate and blot, microaneurysms, scattered small hard exudates, two soft exudates above and early connective tissue proliferation around the macula. The central bright spot and that in the lower left quadrant are artifacts. This figure should be compared carefully with Figs 2 and 3. The scale is different as the fluorescein photographs are slightly more magnified*

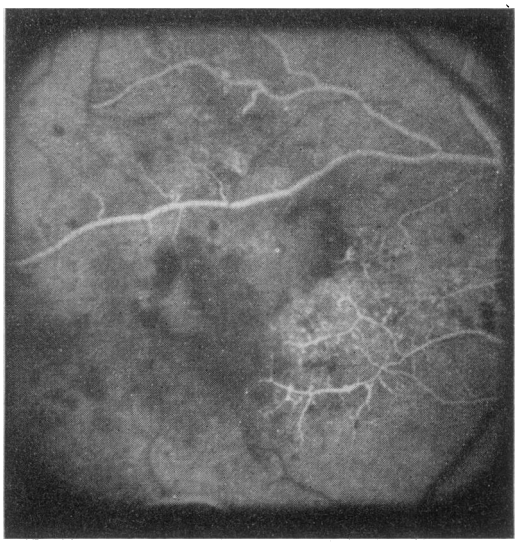

Fig 2 *Fluorescein photograph of the macular area of the retina shown in Fig 1. The fluorescein appears white and the unfilled vessels dark against the background. The passage of dye is in the early arterial phase except near the disc, where some small venules have already filled. The smaller arterioles show some irregular dilated segments, and microaneurysms in close relationship. Background fluorescence, due at this stage to the choroidal circulation, is masked at many points by hæmorrhages*

interesting features; multiplicity of microaneurysms which far exceeded those visible with the ophthalmoscope, new vessels with abnormal blood flow, and regions of leakage both from retinitis proliferans and microaneurysms were described by Scott *et al.* (1964).

A technique for fluorescence retinal photography of the right eye by arterial injection has been developed by one of the authors (C T D), and yields photographs of enhanced definition from a much smaller injection of fluorescein. A catheter is passed retrogradely from the brachial into the innominate artery, so that the injection passes directly into the right carotid arteries. Several patients with severe diabetic retinopathy have been examined by this technique (Fig 1), and some interesting facts emerge from the photographs.

Under favourable circumstances the capillary network can be seen; where healthy it shows a reticular pattern, but elsewhere abnormalities and areas of closure of the capillary bed are evident (Fig 3). A few irregular vessels cross the areas of closure; microaneurysms are seen on these vessels and, more profusely, in the areas bordering the closure. The whole pattern is similar to that revealed by injected histological specimens of diabetic retinopathy (Ashton 1950, 1953).

Examination of the serial photographs taken during the passage of fluorescein through the retina reveal that vascular abnormalities, tortuosity, calibre changes and microaneurysms, occur on both the arteriolar and venous sides of the capillary network (Fig 2). Furthermore there is occasional evidence of local delay in the arteriolar circulation. In areas where the capillary circulation is abnormal, some precapillary arterioles are seen to fill later than their neighbours, and the feeding branch arteriole is slow to empty. Delay can also be detected in filling the collecting venules.

This arterial technique provides a dynamic record of the abnormalities previously demonstrated in static histological preparations. The extent to which arteriolar changes occur is interesting. Ashton (1963) comments on the possibility of gradual arteriolar obliteration, and mentions that much of the capillary closure occurs on the arteriolar side of the network. The abnormalities described in this paper affect the residual patent vessels. Despite their dilated appearance the flow rate of fluorescein does not

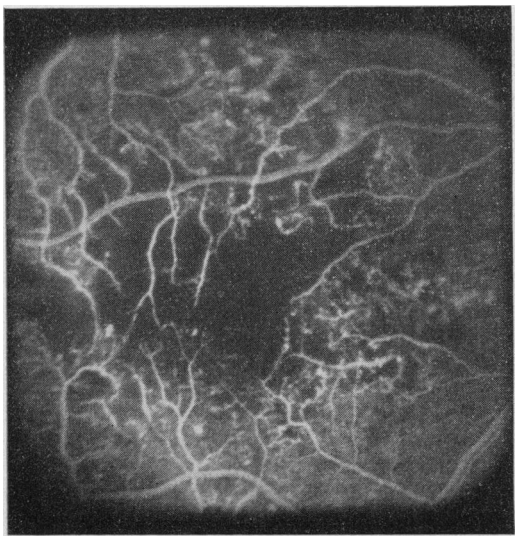

Fig 3 *Further fluorescein photograph taken a few seconds after Fig 2. The passage of dye has reached the late arterial and mid-venous stage. The image of the large arterioles is beginning to fade, particularly axially, and the branch arteriole seen at the top of Fig 2 has emptied. The large vein in the lower right corner of the photograph shows laminar flow, the fluorescein from the proximal venules remaining close to the walls of the vessel. The capillary bed just outside the macula is well filled and in some areas the normal reticular pattern can be seen. Many of the arterioles and venules are abnormal in size and shape, and there are many micro-aneurysms of differing sizes, related to both arterioles and veins. There are a number of diffuse spots where fluorescein has leaked extravascularly. Centred on the macula is a large irregular dark area of capillary closure; it is devoid of vessels save for a few, irregular and grossly abnormal, which cross it. The size of the area far exceeds the physiological avascular zone at the fovea*

seem increased, but occasionally slowed, suggesting that the vessels do not act in any way as shunts, but are the survivors of an obliterative process.

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The Neuro-ophthalmological Complications of Diabetes

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The neuro-ophthalmological complications of diabetes include ocular palsies, pupillary abnormalities, visual field defects, 'optic neuritis' and optic atrophy.

Ocular Palsies

Ocular palsies occur in 0·5% of diabetics and the majority of cases present with diplopia in undiagnosed diabetes and either glycosuria or a mildly diabetic glucose tolerance curve is found. The patients usually belong to the maturity onset group and the III nerve is as likely to be affected as the VI; both nerves together are not infrequent but an isolated IV nerve palsy is exceedingly rare. One of the characteristic features of the III nerve palsy seen in diabetes is that the pupil is usually not dilated and this is in marked contrast to III nerve palsy seen with pressure, e.g. in an aneurysm, when involvement of the pupil is an early and almost invariable sign of oculomotor paralysis. This is an important point not only in diagnosis but also in considering pathogenesis. The sudden onset, together with localized headache, would suggest a hæmorrhage into the brain stem involving the III nerve nucleus, but since the deficit in III nerve function is only partial, it is difficult to visualize a hæmorrhage so localized. A more likely explanation is an occlusive lesion of the vasa nervorum (Dreyfus *et al.* 1957) which affects predominantly the central fibres of the nerve and spares the peripheral pupilloconstrictor fibres (Kerr & Hollowell 1964); the usual recovery within a few weeks is also more in favour of a thrombotic than a hæmorrhagic lesion.

Pupillary Abnormalities

Sluggish responses are said to be due to glycogen deposition in the iris, but this does not explain the differential response to light and convergence seen in the Argyll Robertson pupil where the site of the lesion is in the mid-brain. Argyll Robertson pupils in diabetes are uncommon but their association with absent knee and ankle reflexes due to a peripheral neuropathy produces the syndrome of diabetic 'pseudo-tabes'; the distinction from tabes should not prove difficult since in a peripheral neuropathy the sensory loss has a glove-and-stocking distribution; furthermore, the Charcot's joints seen in diabetes usually occur in the foot. Horner's syndrome (ptosis and miosis) is due to involvement of the carotid sympathetic plexus in carotid occlusion; this is not specific to