Section of Neurology

President S P Meadows MD

Meeting October 7 1965

President's Address

Temporal or Giant Cell Arteritis[1] [*Abridged*]

by S P Meadows MD
(*London*)

The subject I have chosen is one of general medical interest, a disorder of the vascular tree, but it has considerable neurological and ophthalmic implications, and is also of particular interest to the geriatrician since symptoms rarely commence before the seventh decade. First described in 1932 in a short paper from the Mayo Clinic (Horton *et al.* 1932), it soon became evident that bilateral blindness was one of the striking complications (Jennings 1938). The term giant cell arteritis was introduced by Gilmour in 1941, emphasizing one of the prominent histological features.

There is now ample evidence for the view that giant cell arteritis is a widespread vascular disorder, and is not merely confined to the temporal and cranial arteries. The larger vessels are usually affected, and include the aorta and its large branches, and the pulmonary and coronary arteries. The renal arteries appear to be rarely affected, which is probably a factor in the usually favourable outcome of the disorder.

The histological features are now well recognized, and consist of a granulomatous arteritis. The striking changes are in the media, with disintegration of the internal elastic lamina, and cellular infiltration with mononuclear and plasma cells, giant cells and occasional eosinophils and polymorphs. The intima shows diffuse thickening, and the lumen may be reduced to a slit. Cellular infiltration may also be seen in the adventitia (Fig 1).

[1]To be published in full elsewhere

Clinical Features

The clinical features of giant cell arteritis are largely dependent upon gradual arterial occlusion. Involvement of the temporal, occipital and facial branches of the external carotid, and of the ophthalmic branch of the internal carotid, reigns supreme. But the clinical horizon has changed and expanded far beyond its original confines, and now includes the effects of occlusive arterial disease on the scalp, eye, brain, limbs, muscles, heart and abdominal viscera. Indeed, cases without local temporal artery symptoms have been described. The gradual nature of the

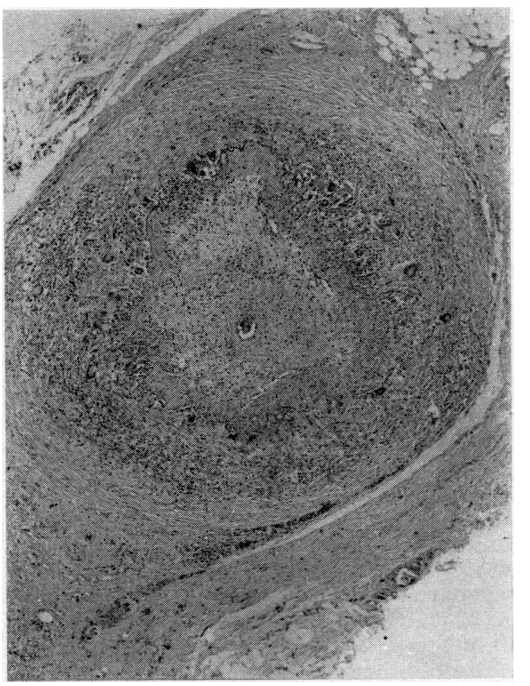

Fig 1 *Section of temporal artery showing granulomatous arteritis with giant cells. (Reproduced from Meadows, 1954, by kind permission)*

occlusive arteritis may allow time for collateral circulation to develop, and clinical symptoms may not appear unless the reduction in blood supply becomes critical. Further, recanalization of the obliterative arterial mass may occur.

Giant cell arteritis appears to be a self-limiting disorder tending to burn itself out over a period of some months to a year or more. It is not commonly fatal, though it often leaves blindness in its trail. The striking feature is the age incidence. It is rare below the age of 60 years, and almost 80% of my own cases were 70 years or older at the start of their illness.

In most of my own patients, the first symptom was headache and pain in the scalp. In only 2 out of 80 personal cases was there no pain, and in these sudden blindness was the first symptom; such cases are so rare as to warrant separate mention. The pain may radiate widely over the scalp, and into the face, jaws, tongue and neck on one or both sides, sometimes worse on chewing. The scalp is tender, and it is painful to rest the head on the pillow or brush the hair. The pain is constant, with sharp exacerbations, and often interferes with sleep. There is often an accompanying feeling of general ill health and exhaustion, with insomnia, loss of weight and appetite, and aching pains in the limbs. These latter symptoms may precede the onset of headaches by several weeks.

The superficial temporal arteries are usually swollen, nodular and tender, with diminution or loss of pulsation. The occipital and facial arteries may be similarly affected. Gangrene of the scalp or tongue is a rare complication.

Table 1
Neuro-ophthalmic complications (80 cases)

	No. of cases	
Blindness		
Unilateral	18	46 (57·5%)
Bilateral	28	
Ophthalmoplegia		
VI nerve palsy:		12 (15%)
Unilateral	4	
Bilateral	1	
III nerve palsy:		
Unilateral	3	
Bilateral	2	
Diplopia only	2	

3 patients with ophthalmoplegia later developed blindness

Of the 80 personal cases on which this communication is based, most were proved by temporal artery biopsy; over half (57·5%) became blind in one or both eyes, and 12 patients (15%) developed ophthalmoplegia or diplopia (Table 1). Three patients who developed ophthalmoplegia later became blind, so that the incidence of neuro-ophthalmic complications was as high as 68·75% or over two-thirds of the total cases. This high incidence may be attributed to undue selection, since many patients were first referred on account of blindness rather than headache.

The interval between the onset of headache and of blindness was between one and three months in most cases, with extremes of a few days to five months. It seems unlikely that blindness supervenes later than six months after the onset of headache.

Premonitory visual symptoms, consisting of temporary obscuration of vision of one or both eyes, occurred in a minority of patients over a period of one or two days before the onset of blindness, and presumably are indicative of vascular insufficiency of the optic nerve or retina. Visual hallucinations were described by 5 patients, occurring shortly before or soon after the onset of blindness, and consisted of coloured lights or stars, or more organized and complex pictures.

The onset of blindness has been abrupt in most cases, though in some it has been more gradual over a period of some hours, often starting in one segment of the visual field and spreading gradually across like a curtain. In cases of bilateral blindness, one eye is usually affected first, the remaining eye being involved within one to twelve days in most cases, though occasionally six weeks elapsed between involvement of the two eyes. Occasionally both eyes are affected simultaneously. A curious feature is that the appearance of blindness is sometimes accompanied by disappearance of the headache.

Although blindness is often total in one or both eyes, vision is sometimes retained in a small portion of one or both fields, usually in the periphery (Fig 2). In rare instances even central vision is preserved, due to preservation of the blood supply to the macula, which may receive an alternative blood supply.

The end-result of these cases with bilateral loss of vision has been unfortunate, in that in only a minority of cases has some useful vision been retained in one or both eyes.

A striking feature has been the ophthalmoscopic appearance in these cases of blindness. The loss of vision is almost certainly of ischæmic origin, yet in only 3 out of about 80 cases was the classical appearance of central retinal arterial occlusion seen. In the remainder there was ischæmic papillœdema, a rather pale swelling of the optic disc, with little or no narrowing of the retinal vessels, but with a few hæmorrhages and cotton-wool exudates near the disc. The papillœdema, rarely severe, subsides within a few weeks, being gradually replaced by optic atrophy. Thus in most cases the severity of the visual loss has been much greater than the visible changes in the optic fundus, a state of affairs which also exists in retrobulbar neuritis.

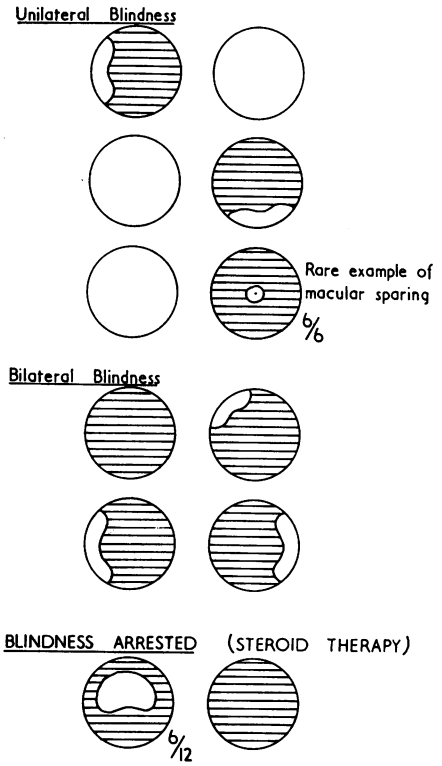

Fig 2 *Examples of visual field defects*

There is little doubt that the blindness is due to ischæmia of the retina or optic nerve, consequent on occlusive arteritis of the ophthalmic artery and its branches. Post-mortem studies in one of my own cases showed severe involvement and narrowing of the ophthalmic, ciliary and central retinal arteries outside the globe, with little or no arteritis in the eye (Crompton 1959). Location of the ischæmic damage to the papilla and optic nerve may be the cause of the ischæmic papillœdema.

There has been no significant improvement in vision in these 46 cases of giant cell arteritis with blindness, even on steroid therapy, except in 3, and even in these the improvement was not dramatic. Once vision has failed, recovery is extremely unlikely and our efforts are best directed to the prevention of blindness. A striking feature seen in some patients with bilateral blindness has been their acceptance of blindness in a surprisingly philosophic manner, which may be equated with the previous personality of the individual, or alternatively it may be due to the euphoric effects of cerebral ischæmia.

Ophthalmoplegia is a much less common complication, and occurred in 12 (15%) of the present 80 cases. It was followed by blindness in 3 instances, and hence is an added indication for urgent steroid therapy. In all cases there was a history of severe headache, usually for several weeks before the onset of diplopia, though in 2 cases the headache and ocular palsy seemed to appear simultaneously. An external rectus palsy occurred in 5 patients, and was bilateral in one (Fig 3). In 5 patients there was a partial III nerve palsy, bilateral in 2. The latter palsy was incomplete, with preservation of the pupil reflex. Two patients had diplopia without any gross ocular palsy. In some cases the diagnosis was not at first obvious, the history suggesting an intracranial aneurysm. On the whole, the ophthalmoplegia has a much better prognosis than blindness, and recovery occurred within a few months in most cases, sometimes even without steroid therapy.

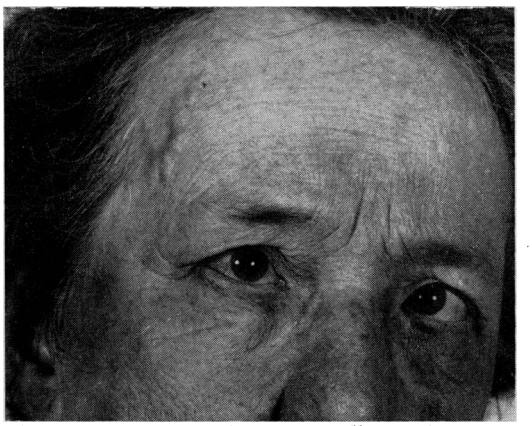

Fig 3 *External rectus palsy in giant cell arteritis*

These ocular palsies are reminiscent of those which are sometimes seen in elderly arteriopathic and hypertensive subjects, with an abrupt onset and a tendency to resolve after some weeks. Vascular lesions affecting the oculomotor nerves seem to be the most likely cause, though it is possible that some of these ocular palsies have their origin in the brain stem.

Cerebral Involvement

Involvement of the cerebral arteries, both carotid and vertebral, is now well recognized in giant cell arteritis. There is post-mortem, angiographic and clinical support for this, though it is only by post-mortem studies that certainty exists, since angiographic and clinical evidence might be open to the criticism that coincidental arteriosclerosis could be the cause of cerebral involvement. Histological evidence of arteritis of the carotid and vertebral arteries has been provided in numerous communications, as well as involvement of the intracranial and small meningeal vessels.

Involvement of the internal carotid artery was discussed by Cardell & Hanley in 1951, when they reviewed the previous cases in the literature in which a full post-mortem examination had been performed. Several of these patients had died of cerebral or cardiac infarction and had evidence of arteritis of the internal carotid artery.

Arteritis of the vertebral artery is well documented in post-mortem cases. In one of my own patients, who died of coronary occlusion due to giant cell arteritis, gross occlusive arteritis of the vertebral arteries was present, with parenchymatous changes in the brain stem, cerebellum and vermis but without clinical counterpart (Crompton 1959). Clinical evidence of brain-stem infarction occurred in a recent case of my own about nine weeks after the onset of symptoms of temporal arteritis, proved by biopsy (A R, NH No. A24280). The clinical features were dramatic in onset, and consisted of severe dysarthria and dysphagia, with palatal, vocal cord and facial palsy, nystagmus, and evidence of bilateral cerebellar signs, right hemiparesis and left-sided spinothalamic sensory loss. Nasal intubation and adequate airway were instituted, as well as high dosage steroid therapy, and gradual improvement occurred. Some weeks later bulbar symptoms had subsided, and he was ambulant, though mildly ataxic, and was able to lead a life of restricted activity. A similar case of brain stem and cerebellar infarction, under the care of Dr Ronald Henson, occurred two months after the onset of symptoms of temporal arteritis, with a fatal outcome. Post-mortem examination by Dr H Urich showed bilateral vertebral artery occlusion due to giant cell arteritis.

Bilateral cortical blindness due to infarction of both occipital lobes and associated with vertebral arteritis has been described by Heptinstall *et al.* (1954), and by Symonds & Mackenzie (1957).

There is thus adequate pathological, angiographic and clinical evidence for the view that affection of the vertebral, internal carotid and cerebral arteries is as much a part of the spectrum of giant cell arteritis as is involvement of the temporal and ophthalmic vessels, though clinical expression is less common. Considerable stenosis of both vertebral and internal carotid arteries may well occur without clinical symptoms, as is well recognized in arteriosclerosis, provided the collateral circulation is adequate. Cerebral symptoms appear only when the vascular supply to the brain stem or cerebral hemisphere reaches a critical level, due to gross occlusive arteritis of the appropriate vessels, and perhaps to insufficiency of the circle of Willis and coincidental arteriosclerosis.

Affection of the *peripheral nerves and nerve roots* is not usually regarded as an integral part of the clinical picture. In the present series, involvement of the lateral popliteal nerve, with consequent foot-drop, occurred in one patient, and in another case bilateral weakness of the shoulder girdle muscles appeared two months after the onset of symptoms of temporal arteritis, with weakness localized to the muscles innervated by the V cervical root on both sides. These rare clinical manifestations are reminiscent of those which may occur in polyarteritis nodosa.

Arteritis of the main *limb vessels*, including the subclavian, femoral and radial arteries, has been recorded *post mortem* though clinical evidence of limb ischæmia is rare. Involvement of muscles has been recorded, and it seems likely that giant cell arteritis may be the cause of at least some of the cases of polymyalgia rheumatica. The latter syndrome occurs in elderly patients, in whom muscular pain and stiffness, with general symptoms consisting of loss of weight and appetite, and depression, are the presenting feature, and the ESR is almost invariably raised. Biopsy of the temporal artery and of muscle has shown evidence of giant cell arteritis in some cases, and angiographic evidence of stenosis of the limb arteries has been reported (Russell 1962, Alestig & Barr 1963, Hamrin *et al.* 1965).

Involvement of the *aorta*, a diffuse granulomatous aortitis, is well recognized, although clinical symptoms are uncommon, apart from those due to coronary occlusion, which is one of the causes of death in the acute stage. Dissecting aneurysm of the aorta and aortic dilatation have been recorded at a later stage. Involvement of the cœliac and mesenteric arteries is authenticated, with melæna due to mesenteric thrombosis as a rare complication.

Clinical Course and Treatment

Giant cell arteritis is a self-limiting disorder, tending to run a course of several months or more, and it seems likely that almost half the patients will emerge relatively unscathed without treatment other than the symptomatic relief of pain. It is not commonly fatal, but frequently causes permanent disablement, and especially blindness. Death in the acute phase is relatively uncommon, and usually a result of cardiac or cerebral infarction. Unfortunately many patients present themselves for medical advice only after they have lost the sight of one or both eyes, and

once this has occurred therapy can have little effect except to improve the general symptoms and headache, and perhaps prevent blindness in the remaining eye. We cannot treat blindness with any hope of improvement, but there seems little doubt from the study of the literature, and from personal experience, that the early institution of adequate steroid therapy reduces the incidence of blindness.

Steroid therapy in high dosage (40 to 60 mg prednisolone daily) is best instituted immediately the clinical diagnosis has been confirmed by the presence of a raised ESR, and continued for six months, with gradual reduction in dosage after the first month or so. Biopsy of the temporal artery is advisable in all cases, but can wait for a day or so. It is the only means of absolute proof of the diagnosis. Occasionally cessation of therapy is followed by recurrence of headache and a rise in the ESR even after six months of treatment, and steroid therapy in moderate dosage may be needed for a year or more.

There has been a complete change in the prognosis of giant cell arteritis since the introduction of steroid therapy. Blindness may be prevented, and the patient converted from a state of misery, with severe headache and general feeling of ill-health, into one of comparative well-being. In view of the high incidence of blindness, one is forced to the conclusion that giant cell arteritis should be regarded as a medical emergency. Once the painful stage has subsided, the patient often appears to take on a new lease of life, even though blind, and may live a life of restricted activity for some years.

Four patients in the present series developed failure of vision while actually on steroid therapy. In every case this occurred within 11 days of the commencement of treatment, and it seems likely that the arterial supply to the optic nerve and retina was at that time at a critical level, and that therapy was instituted too late to prevent ischæmic blindness: a case of *post hoc* rather than *propter hoc*. One of these cases is perhaps worthy of individual mention, a man of 74 years (NH No. A3599), in whom prednisolone therapy was instituted two weeks after the onset of unilateral blindness. Seven days after the commencement of treatment vision began to fail in the remaining eye, but the loss was limited to the inferior portion of the visual field and did not reach fixation. Such an arrest is most unusual during the natural course of this disorder, and must, I believe, be attributed to steroid therapy. There has been no further deterioration in vision three years after the onset.

Anti-coagulation therapy had a vogue some years ago, but as the pathology is that of a granulomatous arterial occlusion it seems unlikely that this form of treatment offers any advantage, and of course poses iatrogenic problems. It may possibly be helpful in those rare cases with brain-stem ischæmia due to vertebral occlusion, in addition to steroid therapy.

I would like to finish on a historical note. That engaging and superb clinical observer, Jonathan Hutchinson, described a case of arteritis of the temporal vessels as long ago as 1890, probably the first case on record, when he was President of the Royal College of Surgeons and Consultant Surgeon to the London Hospital (Hutchinson 1890). In an article on 'Diseases of the Arteries', in the first volume of the *Archives of Surgery*, to which incidentally he seems to have been virtually the sole contributor, he described the case of an old man named Rumbold, the father of a former beadle at the London Hospital College. He had been a gentleman's servant, had lived in the family of a peer of the realm, and had suffered from gout. He was upwards of 80 years of age, a tall, fine-looking man, rather thin and quite bald, and almost in his dotage. Hutchinson saw him on account of 'red streaks on his head', which prevented him from wearing his hat. These turned out to be inflamed and swollen temporal arteries. Pulsation was present at first, but finally ceased, and the vessels were left as impervious cords. Rumbold senior lived for several years after this without any other manifestations of arterial disease. There have been various attempts at nomenclature of this disorder, including temporal arteritis, cranial arteritis, arteritis of the aged and giant cell arteritis, but in 1890 it was certainly Rumbold's disease.

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Meeting November 4 1965
at the National Hospital for
Nervous Diseases, London

The following cases were shown:

Metachromatic Leucodystrophy Presenting as Dementia in a Young Adult
Dr R S Kocen (for Dr R T C Pratt)

'Benign Intracranial Hypertension' and Cervical Root Lesions Following Meningococcal Meningitis
Dr J F Hallpike (for Dr S P Meadows)

Spontaneous Cerebrospinal-fluid Rhinorrhœa with a Persistent Craniopharyngeal Canal
Dr S H Wray (for Dr J N Blau)

Hypotension after Exercise
Dr D B Calne (for Dr C J Earl)

Temporal Arteritis with Intracranial Complications in a Man Aged 66
Dr J C Brown
(for Dr S P Meadows)

Malignant Thymoma with Polyneuritis
Dr A B Herring
(for Dr R A Henson)

'Jakob-Creutzfeldt Disease'
Dr E H Jellinek
(for Dr S Nevin)

Basilar Artery Insufficiency Showing Palatal and Laryngeal Myoclonus
Dr J D Carroll
(for Dr S Nevin and Dr M S Kataria)