Current Practice

PRACTICAL NEUROLOGY

Neurological Complications of Systemic Diseases—II

A. H. ROBERTS,* M.D., M.R.C.P., D.P.M.

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(Last week Dr. Roberts considered the neurological complications of diabetes and neoplastic disorders. His article is concluded this week.)

Collagen Diseases

Given some latitude in classification, it is possible to consider under this heading the group of inflammatory diseases of collagen tissue which include rheumatoid arthritis, giant cell arteritis and polymyalgia rheumatica, polyarteritis nodosa, disseminated lupus erythematosus, and the variants of polymyositis. The most prevalent of these, rheumatoid arthritis, which affects perhaps 3% of the population, is the least frequently complicated by involvement of neural structures, but even if fewer than the 1 in 300 of these patients seen in hospital practice develops a neuropathy due to an inflammatory vasculitis, the overall problem of neural complications in this disease in community terms is by no means negligible.

Carpal tunnel syndrome, due to thickening of the tissues compressed beneath the flexor retinaculum, may herald or complicate rheumatoid arthritis, and both the peroneal and ulnar nerves appear unusually vulnerable in this condition. A typical rheumatoid arthropathy may occur in patients with other collagen diseases in which arteritic lesions are invariable, but even where there is no overlap of this kind an acute necrotising arteritis may occur in rheumatoid arthritis, especially in patients whose disease is of long standing and who have been treated with steroids. Painful paraesthesiae with disturbances of sensory perception and focal muscle paralyses indicating a *mononeuritis* or a *mononeuritis multiplex*, often involving only digital nerves, are added to the patient's already distressing disabilities. Generalized atrophy of muscles related to joints affected by the rheumatoid process is common in advanced forms of this disease, but an inflammatory myositis causing a florid myopathic syndrome is unusual. An infrequent but important and easily overlooked complication of rheumatoid arthritis, especially in the early stages of its development in patients long used to pain and severe disability due to joint disease, is *atlanto-axial dislocation*. Degenerative changes in the ligament retaining the odontoid peg anteriorly within the upper cervical canal result in it becoming lax and allowing the head literally to fall forwards off the cervical spine. The upper cervical spinal cord and its blood supply are compressed, and a complete and permanent tetraplegia may result. The development of flexor spasms in the legs or a disturbance of bladder function, or a sudden deterioration in what use remains in the fingers, perhaps associated with a feeling of tightness and tingling in the hands, may be the first indications of this potentially treatable condition.

A surprisingly frequently encountered arteritis found in patients almost invariably over the age of 60 presents as the *cranial arteritis-polymyalgia rheumatica* complex. Though the arteritic process is almost certainly common to these two conditions and an overlap occurs clinically between them, it is characteristic only of cranial arteritis that the central nervous system is affected. Headache, with or without a tender nodular scalp, malaise, anorexia, and ischaemic pain in the jaws on chewing, together with vague aches in neck and shoulders, may be the only warning in a patient in this age group of a sudden and irreversible arterial occlusion causing blindness in one or both eyes, an oculomotor palsy, or a major stroke.

Polyarteritis nodosa and disseminated lupus erythematosus, though relatively rare diseases outside hospital practice, are frequently associated with lesions in the central nervous system. These commonly complicate the natural history of cases already diagnosed, but with great frequency they also provide the presenting symptoms. Polyarteritis nodosa causes ischaemic lesions of single or multiple peripheral nerves, and it is axiomatic that an unexplained peroneal, radial, or other single nerve palsy in a patient with asthma raises the question of this diagnosis. Rarely, larger neck and intracranial vessels are affected by the nodular inflammatory process, and major strokes and retinal arterial occlusions may cause profound hemipareses and blindness. In disseminated lupus erythematosus, by contrast almost confined to women, the vascular lesions causing occlusions are most frequently found intracranially associated with small areas of infarction in the cortex and presenting as focal or generalized epilepsy, paranoid confusional states, or a progressive dementia, and far less commonly with extensive focal cerebral deficits or peripheral neuropathy.

The multiple inflammatory foci which principally affect muscles in polymyositis are a cause of primary muscle disease second only in prevalence to the muscular dystrophies. Cramps and tenderness of the muscles are characteristically but not invariably a distinguishing feature of this predominantly proximal myopathy, and the weakness presents with the usual difficulties of rising from a bed or chair or climbing stairs, doing the hair or handling the washing on the line, often associated with a waddling lordotic walk. Vascular spasm of the fingers in cold weather, purple telangiectasia about the nose and cheeks and on the backs of the hands, together with hyperaemic nail beds, may herald the condition, which usually runs a fluctuating course associated with dysphagia and the development of contractures.

Early diagnosis and treatment with steroids in these latter complications offer the best chance of preventing serious and irreversible neurological damage. Treatment with substantial doses of oral steroids in the presence of an erythrocyte sedimentation rate of 50 mm. per hour but a not altogether typical

* Senior Registrar, Department of Neurology, The London Hospital.

story is justified while temporal artery biopsy is being arranged and the diagnosis of cranial arteritis still in doubt. The risks of this treatment are minor compared with those of arterial occlusion, and the sudden relief of headache within 24 hours may be confirmatory evidence of the diagnosis. In the case of polymyositis rest during periods of exacerbations should be combined with instructions to the relatives and the patient. Daily gentle passive stretching of weak muscles may result in the prevention, or at least a delay in the development, of disabling contractures.

Thyrotoxicosis and Myxoedema

Though considerably rarer than diabetes mellitus, other forms of disturbed endocrine function provide a rich source of neurological complications and diagnostic confusion. Of these thyroid hypo- or hyper function presents with some frequency in practice. In one survey in general practice the prevalence rate was slightly in excess of 1 in 1,000 of the population at risk in the case of thyrotoxicosis, and even more frequent in the case of myxoedema, especially among older women.

Both thyrotoxicosis and myxoedema are often manifested early in a disturbance of mood or intellectual function. Anxiety and agitation may precede the other overt clinical signs of hyperthyroidism, and appear to respond initially to currently fashionable forms of sedation sufficiently to delay for some time the correct diagnosis and confuse interpretation of estimations of the serum protein-bound iodine. An involutional depressive illness responding poorly to antidepressive drugs may herald the onset of myxoedema, which has been cited as "one of the most important, one of the least known, and one of the most frequently missed causes of organic psychoses". Florid paranoid confusional states may in fact complicate either condition, but seldom in the case of thyrotoxicosis when the diagnosis is not otherwise evident. Rarely, coma with hypothermia may develop rapidly and unexpectedly in an elderly woman, considered by her relatives in some way mildly out of sorts, who has spent a few days in bed uncomplaining with the bedclothes pulled up to her nose against the cold. A mild extrapyramidal tremor, unnoticed until the development of otherwise occult thyroid hyperfunction in an elderly patient, may become sufficiently florid a feature of the condition to suggest that paralysis agitans, a common enough accompaniment of ageing, is the only diagnosis to be considered.

A proximal myopathy may complicate either condition, and in a minor form is probably present in a large proportion of cases of thyrotoxicosis. The usual difficulties experienced, indicating weakness of limb girdle musculature and already described above, gradually increase over the course of several weeks or months and may come to dominate the clinical picture. Often nonspecific complaints of tiredness may be shown to be intimately related to weakness of the limb girdles and trunk by asking the patient to get down on the floor and then noting the remarkable difficulty she has getting up unaided. Very occasionally, but with more than the frequency of chance association, a marked and rapid fatiguability of these muscles suggests a myasthenic component; and, rarely in Britain, a florid episodic paralysis of all the muscles below the neck, usually experienced on attempting to rise in the mornings, may present a syndrome indistinguishable from familial periodic paralysis.

Eyelid retraction due at least partly to sympathetic overactivity is a banal accompaniment of thyroid hyperfunction, and is often associated with some degree of limitation of elevation or abduction of the eyes, causing mild and inconstant double vision. The syndrome of progressive exophthalmic ophthalmoplegia, though rare, poses considerable problems in treatment and may worsen despite adequate treatment of the thyrotoxicosis, or occur without clinical or more than marginal

biochemical evidence of thyroid dysfunction. The syndrome may present with or without lid retraction and proptosis as double vision, and may not infrequently affect only one eye, suggesting any but the correct diagnosis of endocrine disturbance.

Progressive deafness in a middle-aged woman, and the development of a *carpal tunnel syndrome*, pain in the arms, and paraesthesiae in the hands waking the patient in the early hours of the morning, may not seem a sufficiently unusual association for the diagnosis of myxoedema to be considered. A brief examination of biceps or ankle tendon reflexes may demonstrate the slow myotonic relaxation of the jerk characteristic of hypothyroidism. Rarely, paraesthesiae and disturbed sensory perception may be associated with depressed tendon reflexes in all the limbs, indicating a polyneuropathy due to deposits of mucoid material within the nerves. Myxoedema also appears established as an uncommon but treatable cause of a *cerebellar syndrome* with dysarthria and unsteadiness of gait and limbs masking the primary disturbance of endocrine function.

Treatment is of the underlying disorder, replacement therapy in the case of myxoedema relieving the neurological syndromes simultaneously with the other systemic manifestations of the disease. In the case of the more severe forms of dys-thyroid ophthalmopathy the need to preserve the cornea and sight may necessitate more complex management with steroids, tarsorrhaphy, and occasionally decompression by unroofing the orbit. Treatment of selected patients with thyroxine seems often sufficient to limit the progression of the milder ophthalmic complications of these endocrine disturbances in which diplopia occurs; and reassurance is considered as effective a form of therapy by some. A patch covering one eye or a spectacle lens will deal symptomatically with the double vision.

General Considerations

Limiting this review to a description of the neurological complications of these four groups of systemic diseases has done little more than scratch the surface of the topic, but at least a substantial amount of neurological morbidity secondary to common systemic disease prevalent in the community has been touched on. No mention has been made of the degenerative cardio-vascular diseases, particularly common in diabetics, which undoubtedly contribute a major part of the neurological lesions encountered in practice, since the subject has been covered in other articles in this series. Chronic respiratory disorders, though no doubt providing a substantial number of the metabolic confusional states seen in general practice, seldom present with or develop neurological complications which obscure the underlying diagnosis; and though sarcoid frequently affects the nervous system, papilloedema due to uveitis and facial palsies being common manifestations, it is probably best discussed in the more general context of tuberculosis, which, with other infectious diseases, has not been considered in this article. Hepatic encephalopathy, presenting with a confusional illness and the characteristic flapping tremor of the hands or, occasionally, with a progressive dementia, parkinsonism, or cerebellar ataxia, is uncommon in Britain, where cost limits a greater prevalence of alcoholism and cirrhosis. Apart from the occasional case of hypertensive encephalopathy complicating acute glomerulonephritis and presenting with epilepsy, confusion, and papilloedema, the neurological complications of renal disease were, until the recent development of chronic dialysis, a terminal event. Peripheral neuropathies and myopathy are now seen in an appreciable proportion of these patients, whose management is already under close supervision in highly specialized units.

Disturbed neurological function not infrequently provides the presenting symptomatology of the rarer genetically deter-

mined metabolic anomalies and endocrine disorders, but even a brief discussion of these syndromes would extend the scope of this review beyond its limited objectives toward the daunting prospect of an examination of the entire field of medicine.

FURTHER READING

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CURRENT TOPIC

Influenza and Respiratory Failure

J. C. STODDART,* M.D., F.F.A. R.C.S.

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At this time of the year, and particularly in association with epidemics of respiratory tract infection such as the prevalent influenza, a number of patients will die from respiratory failure unless their need for first-aid is recognized. On the other hand, if recognition is prompt the condition may be self-limiting or of short duration, with subsequent full recovery of pulmonary function. In the belief that respiratory failure is less well recognized than is, for example, cardiac failure, a guide to its recognition and treatment is offered.

Recognition

Respiratory failure is one of the conditions for which the aphorism, "If you consider it you recognize it," holds good. Respiratory failure means respiratory inadequacy and not respiratory arrest. It implies that there is a progressive inability of the lungs to oxygenate and remove carbon dioxide from venous blood.

Predisposing Factors

Predisposing factors are: (1) Extremes of age. Although respiratory failure may occur at any age it is commoner in the very young and those over 60. (2) Pre-existing chronic respiratory disease, particularly bronchitis, emphysema, and asthma. (3) Ill-health or self-neglect.

Although the above conditions commonly are associated with respiratory failure, an overwhelming infection may lead to failure in any patient with no apparent predisposition.

Clinical Picture

Any patient with respiratory disease which is not responding to conventional treatment should be considered to be in impending respiratory failure. The diagnosis should be made before the patient is moribund. If more than two of the following signs co-exist the patient is ill, and if more than four he is in extremis: exhaustion; irritability, anxiety, or stupor; rapid or slow shallow breathing, pallor and/or cyanosis; cold, moist skin; rapid, feeble pulse.

The cardiovascular signs are variable, and respiratory failure can coexist with apparent cardiovascular stability for some time in the absence of heart disease.

Biochemical Investigation

Biochemical confirmation of the diagnosis is not necessary before beginning treatment, but is a useful guide to its adequacy. In asthma the blood gases may not be grossly abnormal, but the decision to begin treatment is based on dyspnoea and exhaustion. In other cases respiratory acidosis with hypoxemia will give confirmatory evidence and will provide a baseline for comparison with subsequent measurements.

Treatment

If the patient is not already in hospital admission is essential. He must be accompanied in the ambulance by a medical attendant who can recognize the need for, and is able to give, artificial ventilation. If artificial ventilation has to be given, ideally these patients should be intubated and ventilated with oxygen-enriched air. Alternatively expired-air resuscitation or bag-and-mask ventilation is acceptable. Unless the attendant is very skilled in its application, automatic rescue breathing apparatus should probably not be used. Assisted ventilation should be given early rather than late, and should not be delayed until respiratory arrest has occurred. Oxygen should not be given to patients who are breathing spontaneously unless they are under continuous expert supervision.

After admission to hospital definitive treatment is begun. This need not concern us here except in outline. It will include intermittent positive-pressure ventilation and tracheobronchial lavage, together with the use of antibiotic and bronchodilator drugs. Sedative, respiratory depressant, or muscle-paralysing agents may also be used. These patients are always actually or functionally hypovolaemic and require large volumes of plasma expanders and electrolyte solutions intravenously.

Although almost any patient in respiratory failure may be temporarily improved by treatment his ultimate prognosis is markedly influenced by the speed with which the condition is recognized and definitive treatment instituted.

* Consultant Anaesthetist, Royal Victoria Infirmary, Newcastle upon Tyne.