Current Practice

PRACTICAL NEUROLOGY

Myopathy

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A previous article in this series has considered the diagnosis and management of the muscular dystrophies.¹ This article will therefore be restricted to non-dystrophic muscle disorders, and will be limited to outlining the clinical features of the major diseases of this type, the main investigative procedures employed in their diagnosis, and the general principles employed in treatment.

A wide variety of disease processes may affect muscles and for convenience these will be grouped, somewhat arbitrarily into inflammatory, metabolic and endocrine, toxic, and miscellaneous myopathies. References to original articles will not be given, as more extensive reviews on muscle disease have recently been published.^{2,3}

Inflammatory Myopathy

Polymyositis and Dermatomyositis.—There has been much discussion as to the precise definition and classification of these disorders. In general terms, polymyositis gives rise to limb girdle and proximal limb weakness which may develop either acutely or insidiously and at almost any age. The neck and bulbar muscles and also the distal limb muscles are sometimes affected. Particularly when the onset is acute, the muscles may be painful and tender, but this is not a constant feature. Histologically, the muscles show evidence of necrosis of muscle fibres and infiltration with inflammatory cells. Spontaneous improvement can occur, and the disease sometimes displays a fluctuating course. In about half of the cases there are associated cutaneous manifestations, this combination being designated dermatomyositis. The cutaneous changes consist of a mottled erythematous or violaceous rash over the face, neck, upper trunk, and the extensor aspects of the forearms and hands. There may be considerable oedema of the skin in acute cases. In chronic cases atrophic changes with vitiligo or telangiectasia are seen.

In many instances features such as a mild arthropathy of rheumatoid type or sclerodermatous changes are observed, indicating affinities with the collagen disorders. Raynaud's phenomenon is also a frequent accompaniment. Conversely, a polymyositic syndrome may accompany systemic lupus erythematosus, scleroderma, rheumatoid arthritis, or Sjögren's syndrome. Many cases, however, show no other evidence of collagen disorder, even after prolonged observation, but probably have a similar basis to those associated with one of the collagen diseases, the changes being confined to the muscles.

Most cases of polymyositis should be treated with steroids, the dosage being adjusted by the clinical response and the

serum enzyme levels, creatine kinase being the most useful. Though patients with an acute onset of symptoms tend to show the most dramatic response, chronic cases may at times exhibit a gratifying improvement. In some otherwise typical cases inflammatory changes are not found in muscle biopsies, but a response to steroid treatment is nonetheless obtained. A possible explanation is that the muscle may be affected in a patchy manner so that sampling difficulties arise in the taking of biopsies.

Carcinomatous Myopathy.—A proximal myopathy or dermatomyositis may be observed in association with malignant disease, most commonly of the bronchus, gastrointestinal tract, breast, or ovary, but at times with the malignant reticulosos. When a myopathic syndrome occurs together with one of the non-metastatic neurological complications of carcinoma, such as a peripheral neuropathy or cerebellar degeneration, the term carcinomatous neuromyopathy is sometimes employed. The appearance of myopathy may antedate the detection of the underlying tumour, occasionally by as much as three years.

Sarcoid Myopathy.—A rare cause of inflammatory myopathy is sarcoidosis, which can give rise to a syndrome resembling polymyositis with proximal muscular weakness and wasting, and without evidence of sarcoidosis elsewhere. The muscles are infiltrated with sarcoid tissue. Treatment with steroids has been found to be of little benefit.

Polymyalgia Rheumatica.—This condition presents in elderly patients, more commonly women, who complain of muscle pain and stiffness, without weakness, especially around the shoulders and hips. There may be associated malaise and pyrexia, and the erythrocyte sedimentation rate is characteristically considerably elevated. The disorder may be associated with temporal arteritis or other manifestations of giant cell arteritis, but the precise disturbance within the muscles is not understood. It may be a disorder of the intramuscular connective tissue, there being no indication of a true myopathic process. There is a dramatic response to steroid treatment, usually in quite moderate dosage.

Trichinosis.—Trichinosis, caused by eating uncooked or undercooked pork infested with the nematode *Trichinella spiralis*, is rare in Britain, but occasional cases are encountered. Because of the rarity of the condition examples may be mistaken for acute polymyositis. Diarrhoea is sometimes the initial manifestation, usually occurring on the day following ingestion, and is related to the development of the adult worms in the intestinal mucosa. Symptoms related to the migration of the larvae into the muscles begin about a week later and may persist for several weeks. The muscles become painful and tender, but weakness is not prominent. The illness often includes fever, oedema of the eyelids, and chemosis, and there is usually an eosinophilia.

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Epidemic Myalgia (Bornholm Disease).—In this condition a febrile illness lasting a few days with malaise and other constitutional upset is accompanied by intense pain over the lower chest wall and upper abdomen. This is associated with local tenderness and cutaneous hyperaesthesia. The pain is aggravated by breathing or other movement of the affected muscles, and a pleural friction rub may be heard. It is now established that the disease is caused by viruses of the Coxsackie group, and additional manifestations of Coxsackie infection such as a lymphocytic meningitis may occur simultaneously. The myalgia is probably the result of direct involvement of the muscles of the chest wall.

Metabolic and Endocrine Myopathy

Hypokalaemic and Hyperkalaemic Paralysis.—The muscle membrane potential depends upon the ionic distribution across the membrane, there being a high intracellular and a low extracellular potassium concentration. If the extracellular potassium level is elevated or reduced beyond certain limits the muscle membrane becomes inexcitable, and flaccid paralysis ensues. This may be accompanied by muscle pain and tenderness. Hypokalaemic paralysis can result from a wide variety of circumstances, including excessive urinary loss of potassium because of the administration of steroids or diuretics, because of the presence of an aldosterone-secreting adrenal tumour, or from gastrointestinal potassium loss. Hyperkalaemic paralysis is most usually encountered in patients with renal failure and oliguria.

Familial Periodic Paralysis.—This rare inherited disorder is characterized by attacks of muscular weakness, usually lasting a matter of hours. Three different types exist, the most common being the hypokalaemic variety, in which the plasma potassium level is reduced in the attacks. These tend to occur during rest after exercise, or after a heavy carbohydrate meal. Persistent muscle wasting may slowly develop. Potassium administration will relieve the paralysis in an attack, and small frequent meals, or the administration of the aldosterone antagonist spironolactone, which reduces urinary potassium loss, are helpful in prophylaxis.

In the second or hyperkalaemic variety, the plasma potassium level is elevated in the attacks, which tend to occur in the fasting state. Myotonia, particularly myotonic lid-lag, is sometimes a feature. The paralysis can be improved by carbohydrate administration, and diuretics, such as hydrochlorothiazide, which lead to increased urinary potassium loss, can be useful in prophylaxis. In a third and much rarer variety the plasma potassium level is normal in the attacks, which respond to sodium administration. These three disorders display an autosomal dominant pattern of inheritance.

Hereditary Absence of Myophosphorylase (McArdle's disease).—Skeletal muscle may be affected in a number of the glycogenoses (glycogen storage diseases), but McArdle's disease merits particular attention. In this disorder there is a failure of breakdown of muscle glycogen on exercise, so that the normal elevation of blood lactate and pyruvate does not take place. The patients experience painful cramps on exercise. Dissolution of muscle fibres may occur, leading to attacks of myoglobinuria on exercise, and the slow development of persistent muscle wasting. The disorder displays an autosomal recessive pattern of inheritance, usually with an onset of symptoms during childhood. A clinically similar disorder has recently been demonstrated to be due to hereditary phosphofructokinase deficiency.

Metabolic Bone Disease.—Proximal weakness and wasting in the limbs, at times accompanied by muscle pain, is not infrequently met in cases of osteomalacia. The cause of the myopathy is not understood, but there is no close relationship with the serum calcium level. A similar syndrome may be encountered,

but less commonly, in association with hyperparathyroidism. The myopathy of osteomalacia responds to the administration of vitamin D; that accompanying hyperparathyroidism from a parathyroid adenoma recovers after surgical removal of the tumour.

Steroid Myopathy.—A limb girdle myopathy related to steroid administration is well recognized. This usually affects the pelvic girdle muscles more severely than the upper limbs, giving rise to a waddling gait. Steroids possessing a fluorine atom at the 9 α position, such as triamcinolone, seem most likely to produce this complication, but it may occur with all types of steroid. In general, the occurrence of myopathy is related to the dosage and duration of treatment. Recovery takes place on withdrawal of the drug. The condition is probably analogous to the proximal myopathy occasionally seen in Cushing's syndrome.

Thyroid Disorders.—The majority of patients with thyrotoxicosis have some associated myopathy, and in some it can be the presenting complaint. In chronic thyrotoxic myopathy the muscular weakness and wasting are proximal in distribution, particularly affecting the shoulder girdle muscles. Recovery occurs with treatment of the thyrotoxicosis. In rare instances myasthenia gravis and hypokalaemic periodic paralysis may be associated with thyrotoxicosis.

In hypothyroidism the tendon reflexes are often sluggish and of increased duration. This is the result of an alteration in the contractile mechanism itself and not to any neural abnormality. The muscles may be abnormally bulky and firm. The patients complain of muscle stiffness and of muscle pain after use, and these symptoms can be the presenting feature of myxoedema. They resolve with treatment. Rarely, proximal weakness and wasting may occur.

Though exophthalmic ophthalmoplegia (endocrine exophthalmos) may occur in association with thyrotoxicosis, it also develops in euthyroid or even hypothyroid individuals, sometimes after treatment of previous thyrotoxicosis. The salient features are unilateral or bilateral proptosis and diplopia. The proptosis can be gross with much associated chemosis and can threaten vision. The proptosis is the result of an increase in the volume of the orbital contents. The external ocular muscles become swollen and infiltrated with lymphocytes and may later become fibrotic. The cause of the disorder is not yet established. It is not due to the action of thyroxine or thyroid stimulating hormone, and probably not to long acting thyroid stimulator, but possibly due to a separate exophthalmos producing factor. Medical treatment is not usually rewarding, though the use of steroids has been suggested. Thyroxine is perhaps helpful in those cases associated with hypothyroidism. Surgical decompression of the orbit may be required if vision is threatened. Most cases ultimately subside spontaneously.

Toxic Myopathy

Alcoholic Myopathy.—Muscle weakness in alcoholism is usually the result of a peripheral neuropathy. At times an acute myopathy follows prolonged drinking in which weakness and swelling of the muscles is accompanied by severe muscle aching and tenderness. Necrosis of muscle fibres occurs and may lead to myoglobinuria. It is of interest that it has been suggested that muscle glycogenolysis may be impaired in a manner similar to that existing in McArdle's disease. In other patients with chronic alcoholism proximal muscle weakness and wasting develop insidiously. In both types improvement occurs with cessation of drinking.

Chloroquine Myopathy.—Chloroquine, used in treating lupus erythematosus and certain other collagen disorders, occasionally gives rise to a proximal myopathy. "Red" muscle fibres tend to be selectively affected and display a vacuolar change. The myopathy is reversible on withdrawal of the drug.

Miscellaneous Disorders

Ischaemic Myopathy.—Infarction of muscle may take place as a result of arterial embolism or thrombosis. It also may occur as a consequence of arterial damage related to closed fractures of a limb, usually supracondylar fractures of the humerus or fractures at the upper end of the femur. Fibrotic shortening of the muscle may ensue, as for instance in Volkmann's ischaemic contracture of the forearm muscles seen following damage to the brachial artery with fractures in the region of the elbow. Muscle infarction also occurs in polyarteritis nodosa and can contribute to the muscle weakness and wasting that may develop in this disease, in addition to that caused by vascular lesions of the peripheral nerve trunks.

The anterior tibial syndrome consists of severe pain in the muscles of the anterolateral compartment of the lower leg after vigorous or unaccustomed exercise. It is considered to be the result of muscle swelling and consequent ischaemia as the muscles are contained within an inelastic fibro-osseous space. Infarction of muscle may take place, leading to persistent weakness, but is possibly preventable by surgical decompression of the compartment.

Myoglobinuria.—Release of myoglobin because of acute destruction of muscle fibres may cause myoglobinuria, which can lead to acute renal failure. Myoglobinuria is seen from a wide variety of causes, including extensive crush injury or infarction of muscle, acute polymyositis, hypokalaemic paralysis, and acute alcoholic myopathy. The occurrence of myoglobinuria on exercise in McArdle's disease has already been mentioned. Exercise may be a provocative factor in acute idiopathic myoglobinuria, in which the nature of the metabolic disturbance has not yet been defined.

Myasthenic Myopathy.—Though disturbances of neuromuscular transmission fall outside the scope of this article, it is worthy of note that myopathic weakness and wasting may supervene in patients with myasthenia gravis. Collections of lymphocytes (lymphorrhages), together with occasional necrosis or atrophy of muscle fibres, are a not uncommon histological finding in the muscles of patients with myasthenia gravis who clinically do not show frank muscle wasting. When persistent weakness and wasting develop they most commonly affect the external ocular, tongue, and proximal limb muscles. This generally appears only after the disorder has been present for many years, but it sometimes develops quite early. It represents one reason for muscle weakness in myasthenia becoming refractory to treatment with anticholinesterase drugs.

Diagnosis of Primary Muscle Disease

Not infrequently it is difficult to decide on clinical grounds whether muscular weakness and wasting are due to primary muscle disease or whether they are secondary to denervation. The three investigative procedures that are most helpful in making this distinction are electromyography, serum enzyme estimations, and muscle biopsy.

In myopathic disorders electromyography reveals short duration, polyphasic motor unit potentials of low amplitude. These changes result from the diffuse loss of muscle fibres throughout the muscle, so that the number of muscle fibres per motor unit is diminished. In patients with polymyositis increased mechanical irritability of the muscle fibres and spontaneous fibrillation may also be observed—findings that are normally associated with denervation. It has been suggested that this is the consequence of the involvement of the intramuscular nerve fibres by the inflammatory process. It is more likely, however, that they are the result of the segmental necrosis of muscle fibres so that portions become separated from their end-plates and therefore display the same changes as in denervation.

Though a number of muscle enzymes are released when muscle fibres are damaged, the serum creatine kinase level is the most sensitive indicator of primary muscle disease. It is particularly likely to be elevated in acute or rapidly progressive disorders and less likely to be abnormal in chronic, slowly progressive myopathies. It is normal or only slightly elevated in cases of denervation atrophy.

Muscle biopsy, in addition to assisting in deciding between primary muscle disease and denervation atrophy in cases in which this is in doubt, may provide information as to the precise nature of the muscle disorder. This is especially true of inflammatory myopathy. In the endocrine myopathies muscle biopsy is less likely to be diagnostic and the associated clinical features are more helpful. In certain of the metabolic myopathies, such as the glycogenoses, detailed chemical and histochemical studies on muscle biopsies may be required in order to establish the diagnosis.

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TODAY'S DRUGS

Bronchodilators

With the help of expert contributors we print in this section notes on drugs in current use.

Bronchodilator drugs are used to reverse or diminish generalized peripheral airway obstruction. This occurs in bronchial asthma and in chronic non-specific obstructive lung disease. The latter includes patients with what is sometimes called the emphysema-bronchitis syndrome, in which one component, in Britain most commonly the bronchitic one, predominates. The way in which airway obstruction is produced differs in these conditions, and this has an important bearing on the extent to which this can be relieved by drugs. In bronchial asthma narrowing of the airways is due to contraction of the

smooth muscle in the bronchi, oedema of their walls, and the retention of viscid bronchial secretion. In chronic non-specific obstructive lung disease distortion and narrowing of the smaller peripheral bronchial airways occurs from repeated episodes of bronchial infection, added to which there is marked hypertrophy of mucus-producing glands, both in the bronchial walls and in the epithelium lining the bronchi, and excess bronchial secretion. When destructive emphysema is present in addition, whether of the centrilobular or panacinar variety, loss of elastic tissue support of the peripheral airways at bronchiolar level leads to collapse and severe narrowing of these airways during expiration.

Objective Tests

It follows, therefore, that the greatest relief of airway obstruction from bronchodilator drugs can be expected in bron-