Section of Neurology

President Harvey Jackson FRCS

Meeting April 2 1964

The Nature and Management of Spasticity

Dr Geoffrey Rushworth
(Churchill Hospital, Oxford)

The Pathophysiology of Spasticity

Hughlings Jackson (1888) believed that the excitability of anterior horn cells was maintained by a balance of descending inhibitory and excitatory mechanisms and, consequently, spasticity would result from any pathological process which interrupted the inhibitory pathways. This classical view of spasticity has had to be modified in the light of modern physiological work derived from animal experiments, which has demonstrated the very great complexity of segmental spinal mechanisms, the inhomogeneity of anterior horn cells, and the importance of muscle spindles in motor mechanisms.

While much is known about the neurological mechanisms concerned with the active maintenance of spasticity, the nature of the passive shortening of muscle (muscle 'contracture'), which superimposes itself on to chronic spasticity, is, by contrast, poorly understood. It seems, however, to consist of two distinct phases: first, that of myostatic contracture (Ranson & Dixon 1928) and, later, by proliferation of fibroblasts and progressive shortening of their collagen fibres, a stage of fibrous contracture supervenes. Myostatic contracture can occur even in normal muscle if the muscle is forcibly shortened by approximating and fixing its bony attachments for several days (Moll 1886). It is as if the shortened muscle readapts its length to the new length that has been imposed on it. The onset of myostatic contracture can be prevented by destruction of some part of the local reflex arc, such as section of the dorsal roots (Fröhlich & Meyer 1920). It can be produced by tetanus toxin or tenotomy, and is not abolished by local or general anæsthesia.

The amount of contracture contributing to the abnormal limb posture in spastic patients may be overestimated by clinicians, for it can only be shown up when all the neurological mechanisms that maintain active muscular contraction are interrupted. A spastic arm with a fixed resistance at 45 degrees may extend to 170 or 175 degrees after local anæsthetic has been injected into the motor points of biceps and brachialis, and would show, in this case, how misleading one's initial impression could be and demonstrate the fact that contracture accounted for very little of the muscular shortening.

Spasticity is said to be present when a paretic limb involuntarily resists passive displacement, particularly in one direction of movement. Antigravity muscles are often affected, but spasticity is by no means restricted to these muscles. The resistance to passive displacement is compounded of passive and active forces; my remarks will refer only to the active forces.

The active resistance to limb displacement is the stretch reflex, and it has been shown that a sudden elongation of a muscle by as little as 10μ will excite the stretch reflex (Creed *et al.* 1932). When a muscle of a decerebrate cat is suddenly elongated and the new length maintained, it can be seen in the resulting isometric myogram that the active stretch reflex consists of two parts. The opening peak of tension is the phasic stretch reflex – identical to the tendon jerk – and is due to the initial high frequency and more or less synchronized discharge of stretch receptors. The steady plateau of tension results from the slower and more asynchronous discharge of the stretch receptors – and this is the tonic or static stretch reflex, the reflex that maintains posture.

Though recording from single muscle spindles has shown that the rate of sensory discharge to a sudden maintained stretch parallels roughly the tension curve of the phasic and tonic stretch reflexes, it seems probable that the two reflexes are distinct entities. For example, the phasic reflex, which has been shown to be a monosynaptic reflex, is very resistant to barbiturate anæsthesia, whereas the tonic stretch reflex is very rapidly abolished. This supports the contention

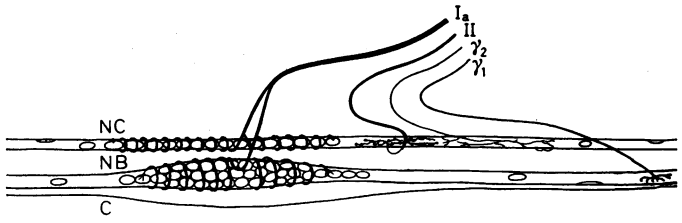

Fig 1 *Diagram of two representative intrafusal muscle fibres and their innervation. C, capsule of muscle spindle. NB, nuclear bag fibre. NC, nuclear chain fibre. The Group Ia afferent fibre originates from annulospiral (primary) endings on both the nuclear bag and nuclear chain fibres. The Group II afferent originates from secondary endings on nuclear chain fibres. The motor innervation of the nuclear chain fibre is through the fine γ_2 motor nerve fibre which terminates in a complex ramification on the myotube region. The γ_1 motor nerve fibre innervates the nuclear bag fibre in a discrete end plate in the polar region*

that the tonic stretch reflex is a polysynaptic reflex, as synaptic transmission can be interfered with by barbiturates. Several years ago, Granit and his associates (Granit *et al.* 1956, Granit *et al.* 1957) found that ordinary α motoneurones could be divided into two types depending on how they responded to a long, brisk tetanus from spindle afferents. One type of α motoneurone responded with a very brief high frequency discharge to this prolonged stimulus, and it was therefore termed a 'phasic' motoneurone. The other type of motoneurone responded with a slower discharge, which, however, persisted and outlasted the stimulus. This was a 'tonic' α motoneurone, and it was inferred that the cell and its axon were of smaller diameter than the phasic α motoneurone. On repeated testing, it was further found that the tonic motoneurone became hyperexcitable following a tetanus of inflowing large sensory fibres – a state of post-tetanic potentiation. It seems likely that phasic α motoneurones would be fired in the phasic stretch reflex monosynaptically and that the tonic stretch reflex is maintained by tonic α motoneurones, bombarded first tetanically and later by asynchronous impulses.

The sensory organ responsible for the stretch reflex is the muscle spindle, and in recent years there have been some important discoveries about both its structure and its electrophysiology. Cooper & Daniel (1956) found two distinct types of intrafusal muscle fibres within human muscle spindles, and Boyd (1956) showed that the same was true for cat intrafusal muscle fibres. Some intrafusal muscle fibres were of relatively large diameter and carried in the equatorial region a collection of nuclei which distended the fibre into a 'nuclear bag'. Other intrafusal fibres were of relatively small diameter, and an arrangement of nuclei into chains was characteristic of the equatorial region (Fig 1). The innervation of these two types of fibres also had its own peculiarities (Boyd 1962, Cooper & Daniel 1963). Whereas both carry annulospiral or primary sensory endings in the equatorial region, the secondary sensory endings (or flower-spray endings in the cat) are principally carried on the myotube region of nuclear chain fibres. The motor innervation of the nuclear chain fibres is by a complex ramification of very fine motor nerve fibres (γ_2) in the myotube region, overlapping the secondary sensory ending. On the other hand, the nuclear bag fibres are supplied by thicker (γ_1) motor nerve fibres which terminate in localized end feet in the polar region.

When the discharge of de-efferented muscle spindles was studied during stretches of varying rates or at steady extensions, primary sensory endings were found to be particularly sensitive to the dynamic part of stretch (i.e., their discharge rate was a function of the rate of stretching) and, of course, they also discharged when the increased length was held constant (static stretch), and here the discharge rate was related to the actual extension (Harvey & Matthews 1961). Of particularly great interest, however, was the fact that the dynamic and static sensitivity of primary endings could be independently altered by γ motor activation (Jansen & Matthews 1962). On the other hand, secondary sensory endings responded poorly in the dynamic phase of stretch, and their sensitivity to static extension was greatly increased by γ motor activation. Jansen & Matthews (1962) and Matthews (1962) have suggested that the dynamic response originates in the primary ending lying on the relatively rigid nuclear bag, and its sensitivity is controlled by the central nervous system through γ_1 fibres. The primary ending lying on the nuclear chain fibres would be expected to be mainly responsive to static stretch like the secondary endings, and their sensitivities would be controlled from the central nervous system through the fine γ_2 fibres. Primary endings on both nuclear bag and nuclear chain fibres are terminals of branches of a single Group Ia afferent, so that information about the dynamic and static components of muscle stretch is channelled into the same nervous pathways. Presumably, however, impulses of high frequency

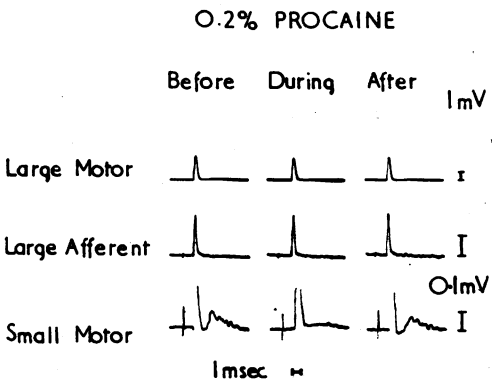

Fig 2 *The potentials recorded simultaneously from S.1 dorsal and ventral roots following a single maximal stimulus to the nerve to gastrocnemius. The size of the potential is related to the number of active fibres. The top record of each series is the α wave recorded from the ventral root, and the lowest record is the same recorded at very high amplification to demonstrate the γ wave. The middle record shows the Group I potential recorded from the dorsal root (Before)*
Application of 0·2% procaine to the muscle nerve resulted in abolition of the γ wave (small motor fibres), leaving the large motor and afferent fibres unaffected (During)
The γ fibres unblock when the procaine is washed off (After)
(Reproduced from Rushworth 1964 by kind permission)

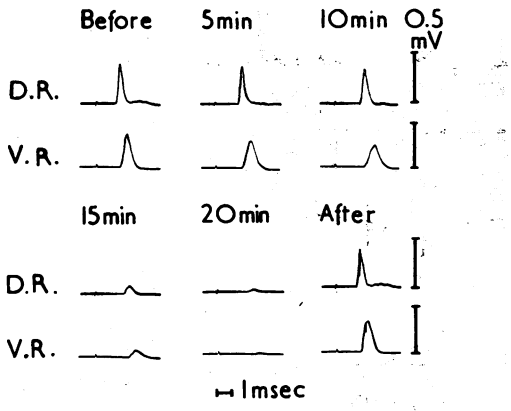

Fig 3 *The effect of 0·5% procaine on the dorsal (DR) and ventral (VR) root potentials in response to a maximal shock to the nerve to soleus. Note the progressive block with large motor fibres being slightly more susceptible than large sensory fibres*

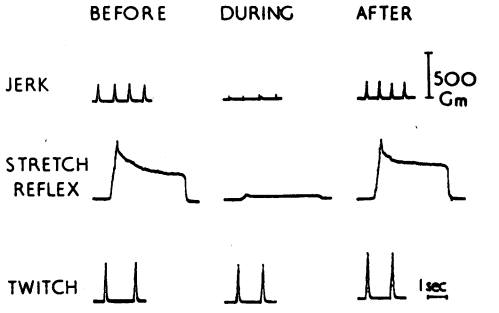

Fig 4 *Isometric myograms taken from the soleus muscle of a decerebrate cat. The tendon jerk, stretch reflex (to 12 mm extension) and maximal motor twitch (Before). Following application of 0·2% procaine to the muscular nerve distal to the stimulating electrodes, the stretch reflexes are abolished, but the maximal motor twitch is unaffected (During). By washing away the procaine with saline, the stretch reflexes are restored to their previous level (After). (Reproduced from Rushworth 1964, by kind permission)*

will have a greater chance of acting monosynaptically than will low frequency asynchronous impulses.

Another important discovery has been that of Eccles & Lundberg (1959) who have shown that spinal interneurones are themselves under descending control. An example of this was shown in the decerebrate cat, where those interneurones normally concerned with transmission of Golgi tendon organ inhibition, or of those afferents which given reflex flexion, are themselves held in inhibition.

Stretch reflexes, then, even at the segmental level, are very complexly organized, and if we think of muscular hypertonus as a release of these reflexes from descending inhibition we shall have to take into consideration many of the recent discoveries to try to account for the clinical varieties of muscle hypertonus.

The muscles of the classical decerebrate cat present features which are very similar to human spasticity.

Many years ago, Granit and his co-workers (Granit & Kaada 1952, Eldred *et al.* 1953) found evidence of release of γ motoneurones and overactivity of muscle spindle responses in the decerebrate preparation. Matthews & Rushworth (1957*a*, *b*) studied the problem differently. First, we showed that when very dilute procaine was applied to a muscular nerve, γ motor fibres were blocked before either large α motor or large afferent fibres were affected (Fig 2). These latter could, however, be blocked by much longer application of more concentrated procaine, and under these circumstances it was found that motor fibres were slightly more sensitive than were large sensory fibres (Fig 3).

When dilute procaine was applied to the nerve to soleus in a decerebrate cat, both tonic and phasic stretch reflexes were abolished long before the maximum motor twitch or tetanus was affected (Fig 4). From this it was inferred that large α motor fibres (i.e. phasic and tonic α fibres) were intact, and therefore it was probable that Group I sensory fibres were also intact. We concluded that γ motor fibres were essential for the

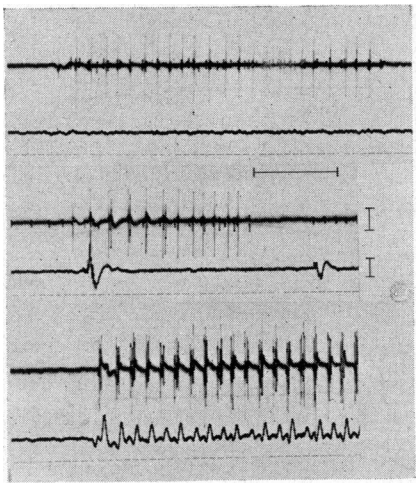

Fig 5 *Electromyographic recordings taken from the gastrocnemius muscle in a spastic patient, showing the effects of progressively faster stretches, from above downwards. Calibrations: 300 μV and 1 sec*

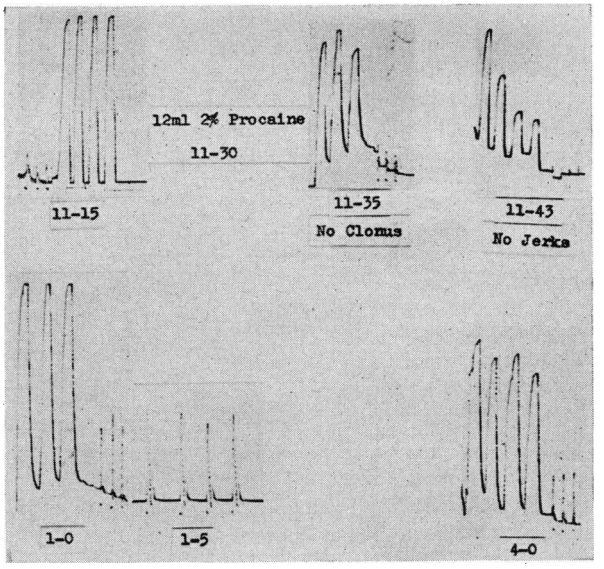

Fig 6 *Dynamometer records of voluntary plantar flexion and ankle jerks from a patient with intense spasticity. 11.15 record shows spontaneous clonus, three ankle jerks and four voluntary plantar flexions. Strong procaine was then infiltrated around the sciatic nerve. 11.35, and 11.45 shows the progressive blocking of jerks and some voluntary power. About one and a half hours later (1.0) voluntary plantar flexion had recovered and the jerks were now very large, though clonus and resistance to passive stretch were still absent. Four and a half hours later (4.0) the jerks were still longer than before the block. Clonus was still absent and there was now a little resistance to passive displacement. (Adapted from Rushworth 1960,* Journal of Neurology, Neurosurgery and Psychiatry, *by permission of the Editor and Publishers, BMA House, Tavistock Square, London, WC1)*

maintenance of decerebrate rigidity ('gamma rigidity'). Of course, small nerve fibres other than γ fibres were blocked by the procaine. Block of Group II and Group III afferents would remove an inhibitory influx on the soleus motoneurones, which would have an effect opposite to the one observed, and paralysis of sympathetic fibres has no effect on decerebrate rigidity (Cobb 1918, Phillips 1931).

In human spasticity the electromyogram can be used to record the activity of muscles. During slow stretch the rate of motoneurone firing is remarkably constant but, as stretch proceeds, more and more motoneurones may be recruited. If excessive tensions are reached, inhibition of motoneurones may supervene and resistance collapses. (This is the clasp-knife reaction.)

In spasticity, the resistance to passive stretch is very much dependent on the rate of stretching being greater for faster stretches. With fast stretches, however, the initial near synchronous discharge of the spindles may be sufficient to fire off a large number of motoneurones, causing a phasic muscle contraction which would unload the spindles. There would thus be the alternation of activity and silent period which we know as clonus (Fig 5).

Though tendon jerks are usually very brisk in spasticity, occasionally, with intense spasticity, they may be occluded by the very great tonic stretch reflex.

Many years ago, Walshe (1924) showed that 1% procaine injected intramuscularly abolished the exaggerated stretch reflexes of hemiplegic spasticity, and in 1960 I published experiments which confirmed this observation and extended the findings (Rushworth 1960). In 19 out of 20 adult patients with spastic limbs (of varying ætiology) the injection of dilute procaine around the major nerve trunk resulted in a regional abolition of the hyperactive stretch reflexes without affecting motor power – a result identical to that found in the decerebrate cat by Matthews & Rushworth (1957*a*).

In some patients with intense spasticity with small tendon jerks, very large tendon jerks appeared at some stage of the differential nerve block – an observation which suggests either occlusion of the tendon jerk (phasic stretch reflex) by a large tonic stretch reflex, or a greater susceptibility of γ_2 fibres (rather than γ_1 fibres) to procaine (Fig 6).

The findings show, however, that the exaggerated stretch reflexes of spasticity, as in the classical decerebrate cat, require, for their maintenance, the integrity of γ motor fibres. If we continue the similarity further, human spasticity would depend

on the release of γ motoneurones from descending inhibition. I agree with Jansen (1962) who has postulated that, in mild spasticity, the small motoneurones innervating nuclear bag endings through γ_1 fibres are particularly hyperactive for antigravity muscles. This would well account for the increased phasic stretch reflexes in this state and for the resistance to passive displacement being so dependent on the rate of stretching. In intense spasticity, however, one would have to postulate a hyperactivity of the γ_2 system in addition, again affecting, principally, antigravity muscles (unlike parkinsonian rigidity, which affects flexor muscles particularly).

It also appears probable that those spinal interneurones responsible for transmitting Golgi tendon organ inhibition and secondary ending activity are themselves inhibited, as Eccles & Lundberg (1959) showed for the decerebrate cat (again unlike parkinsonism, where it would appear that these mechanisms are facilitated).

Only very occasionally has a spastic patient been encountered in whom the muscular responses to stretch and the effects of procaine on the stretch reflexes and on voluntary movement have been quite different from those described above. They resemble those seen in the anæmically decerebrate cat (i.e. lacking anterior lobe of cerebellum as well as forebrain), in which the muscular rigidity is not abolished even by dorsal root section and is therefore independent of muscle spindles (alpha rigidity) (Pollock & Davis 1930, 1931, Granit 1955). Electromyography reveals that motoneurones are firing even when the muscles are apparently at rest and supported. Passive stretch may contribute very little to this already high firing rate, and tendon jerks may be absent. The injection of dilute procaine around major nerves has no effect on the rigidity, and with more concentrated procaine solutions the rigidity is reduced only as voluntary power is diminished by progressive block of α motor fibres (Rushworth *et al.* 1961).

There thus appear to be in patients, as in the cat, two types of spasticity – the commoner type being maintained by muscle spindles through the hyperactivity of γ motoneurones; the rarer type through hyperactivity of α motoneurones alone. One would expect some overlap of these two types, but I have never found any clear evidence of this.

The separation into α or γ type is important from the therapeutic point of view. The γ system is a functional unit within the central nervous system, and it is likely that drugs will be developed to damp down its excessive activity. Its peripheral outflow through γ motor fibres to muscle spindles is, however, accessible, either in the ventral root or peripheral nerve, to blocking agents which attack small nerve fibres selectively, such as the cocaine group of local anæsthetics and alcohol (Tardieu *et al.* 1963, Tardieu *et al.* 1964, Tardieu & Hariga 1964). With a selective block of γ fibres neither voluntary power nor the large muscle afferents should be further affected. Intrathecal phenol, which has been used extensively, destroys also large motor and sensory nerve fibres (Nathan & Sears 1960) so that there is reduction of voluntary power as well as interruption of the stretch reflex arc.

The therapeutic problem often concerns the local reduction of spasticity such as that in the adductors of the thighs, and it is here that a peripheral approach is likely to be of more value than a central approach with drugs which, if they work at all, will tend to render the whole body musculature flaccid.

The α motoneurone maintained spasticity is much more difficult to deal with. One will have to look for drugs which damp motoneurone excitability or that of sensory organs (such as the labyrinth) which are powerful facilitators of lower motoneurone discharge.

The physiological work on experimental rigidities in the cat provides a working hypothesis to account for spasticity in patients, and experimental testing has so far confirmed the correlation. Such a hypothesis provides a definite rationale of treatment which is a challenge to pharmacologists and all those concerned with the therapy and rehabilitation of patients crippled by disease of the central nervous system.

REFERENCES

Boyd I A
(1956) *J. Physiol.* **133**, 35P
(1962) *Phil. Trans.* **B 245**, 81
Cobb S (1918) *Amer. J. Physiol.* **46**, 478
Cooper S & Daniel P M
(1956) *J. Physiol.* **133**, 1P
(1963) *Brain* **86**, 563
Creed R S, Denny-Brown D, Eccles J C, Liddell E G T & Sherrington C S (1932) Reflex Activity of the Spinal Cord. London
Eccles R M & Lundberg A (1959) *J. Physiol.* **147**, 565
Eldred E, Granit R & Merton P A
(1953) *J. Physiol.* **122**, 498
Fröhlich A & Meyer H H
(1920) *Arch. exp. Path. Pharmakol.* **87**, 173
Granit R (1955) Receptors and Sensory Perception. New Haven
Granit R, Henatsch H-D & Steg G
(1956) *Acta physiol. scand.* **37**, 114
Granit R & Kaada B R
(1952) *Acta physiol. scand.* **27**, 130
Granit R, Phillips C G, Skoglund C R & Steg G
(1957) *J. Neurophysiol.* **20**, 470
Harvey R J & Matthews P B C
(1961) *J. Physiol.* **157**, 370
Jackson J H (1888) *Brain* **10**, 312
Jansen J K S (1962) *Acta neurol. scand.* **38**, Suppl. 3, 41
Jansen J K S & Matthews P B C (1962) *J. Physiol.* **161**, 357
Matthews P B C (1962) *Quart. J. exp. Physiol.* **47**, 324
Matthews P B C & Rushworth G
(1957*a*) *J. Physiol.* **135**, 245
(1957*b*) *J. Physiol.* **135**, 263
Moll A (1886) *Virchows Arch.* **105**, 466
Nathan P W & Sears T A (1960) *J. Physiol.* **150**, 565
Phillips G (1931) *Brain* **54**, 320

Pollock L J & Davis L
(1930) *J. comp. Neurol.* **50**, 377
(1931) *Amer. J. Physiol.* **98**, 47
Ranson S W & Dixon H H (1928) *Amer. J. Physiol.* **86**, 312
Rushworth G (1960) *J. Neurol. Neurosurg. Psychiat.* **23**, 99
Rushworth G (1964) The Role of the Gamma System in Movement and Posture. Association for the Aid of Crippled Children, New York
Rushworth G, Lishman W A, Hughes J T & Oppenheimer D R (1961) *J. Neurol. Neurosurg. Psychiat.* **24**, 132
Tardieu C, Tardieu G, Hariga J, Gagnard L & Velin J (1964) *Arch. franç. Pédiat.* **21**, 5
Tardieu G & Hariga J (1964) *Arch. franç. Pédiat.* **21**, 25
Tardieu G, Tardieu C, Monfraix C, Gagnard L & Velin J (1963) *Rev. neurol.* **108**, 87
Walshe F M R (1924) *Brain* **47**, 159

Dr R M Maher
(Pain Relief Centre, Manchester)

The Medical Treatment of Spasticity

In the medical treatment of spasticity one is more often limited to treating symptoms and preventing sequelæ than able to attempt a cure. Apart from administration of vitamin B_{12} for spasticity arising from deficiency, early antispecific therapy for neurosyphilis causing spasticity or surgical intervention for tumours &c., therapeutic measures largely consist in prevention and treatment of the effects of the disease.

Otherwise the principal cause of spasticity is cord injury from trauma. Disseminated sclerosis is still perhaps the commonest cause of spastic paraplegia with its own peculiar problems. Less common causes are amyotrophic lateral sclerosis and the late effects of disc lesions and the sequelæ of surgery.

Spinal injury has been treated with considerable success mainly owing to the excellent routine adopted at various special centres. Particular mention must be made of the pioneer work of Dr Ludwig Guttmann (1961). His regime includes 'first aid and early treatment' with five assistants to move the patient 'in one piece' soon after injury. He is opposed to hasty laminectomies and favours postural reduction of the spinal deformity. Whenever the patient is turned, the same care is employed. In cases of quadriplegia, early extension of the arms is carried out. The avoidance of bedsores by prone positioning is now established; this treatment may be prolonged and tedious for the patient, but results fully justify the regime. Guttmann's principles of treatment for traumatic cases can also be applied to other types of spasticity.

The commonest cause of spastic paraplegia is disseminated sclerosis. Such patients may show anything from slight disability to severe paraplegia in flexion with varying degrees of urinary dysfunction. The medical regime given by Miller (1964) is to be recommended. The psychological effect of the diagnosis of disseminated sclerosis tends to augment the spastic state. In many patients the disability may be slight, and can wax and wane, the patient remaining content over a long period, without the label of disseminated sclerosis.

Exercise should be gentle, for spastic muscles are easily fatigued. On the other hand, confinement to bed brings about increased difficulty later. Infection, pregnancy and trauma appear to aggravate the spastic state. Bedsores and urinary infection may also increase the paraplegia. Physiotherapy should be minimal during the acute phases of the disease. Regular passive movements of joints should be directed towards keeping them supple. Some patients show fixed deformities of the feet, requiring appropriate support to prevent foot-drop.

Drugs

Muscle-tone relaxants are used, many being derivatives of mephenesin, which is given in doses of 2–4 tablets daily. We have chiefly employed tigloidine, 1,000–2,000 mg in divided doses, and it has undoubtedly lessened muscular spasms. Being a drug without anticholinergic activity, it acts by fatigue of repeated stimuli. Mephenesin carbamate, given as two tablets four-hourly, is another preparation with similar effect. Blood transfusion is said to bring about remissions. Pyrexial therapy, malaria or *Esch. coli* were at one time claimed to do so. Corticotrophin gel 20–40 units daily for long-term cases has also been advocated. Treatment by direct application intrathecally to the nerve roots of absolute alcohol in doses of 0·5 ml was introduced by Dogliotti (1931) for pain.

Treatment by Subarachnoid Phenol

In 1955 I first introduced subarachnoid phenol contained in glycerin or Myodil for relief of pain in incurable cancer. Later (Maher 1957) it was applied to non-malignant conditions, and among this series was included the first case of spasticity to have this treatment (1 ml 5% phenol in glycerin). The patient suffered from extreme flexor spasms from spinal hemiplegia due to embolism from coronary disease. The function of the limb was restored for walking and the spasms have never returned. At an earlier date in 1956 (Maher 1960) it had been noted that subarachnoid injections of heavy cinchocaine, 0·5–0·75 ml, temporarily relieved spasticity in a patient with disseminated sclerosis. Cinchocaine has occasionally been used as an index to the value of phenol