when activity subsides (Bobek and Čepelák, 1958). This finding suggests that the increase in platelet adhesiveness observed here might be a consequence of endothelial disease or of continuing thrombosis rather than the cause of the recurrent thromboembolic episodes. However, whether cause or consequence, it seems reasonable to assume that an increase in platelet adhesiveness might contribute to the progression of the underlying thrombotic process and interfere with the re-establishment of normal venous patency.

The mechanism by which continuing or incompletely resolved venous thrombosis might increase platelet adhesiveness is not readily apparent. Murphy and Mustard (1962) reported increased platelet turnover in atherosclerosis and noted that in these patients there was an increase in platelet adhesiveness. It is possible that platelet turnover is also increased in chronic or recurrent venous disease and that the increase in platelet adhesiveness observed in our patients is a consequence of the presence of a relatively young platelet population.

The pathogenesis of idiopathic recurrent venous thrombosis is obscure. Treatment with oral anticoagulants does not appear to be as effective in reducing the number of thromboembolic episodes as in post-traumatic and post-operative venous thrombosis (Sevitt, 1962). In addition, the increase in platelet adhesiveness appears to persist between overt thrombotic or thromboembolic episodes. In keeping with previous observations (Hellem, 1960) platelet adhesiveness did not appear to be influenced by treatment with oral anticoagulants.

Other factors may be implicated in the pathogenesis of recurrent venous thrombosis. Spittel *et al.* (1960) reported accelerated thromboplastin generation in a proportion of patients with idiopathic recurrent venous thrombosis, and Nilsson *et al.* (1961) demonstrated a marked increase in fibrinolytic inhibitor activity in one patient with recurrent venous thrombosis. We were unable to find evidence of a significant increase in anti-urokinase or anti-plasmin activity in the patients studied. It is likely that the observed increase in platelet adhesiveness is but one of a number of factors which are impor-

tant in the pathogenesis of "idiopathic" recurrent venous thrombosis and thromboembolic pulmonary hypertension. The present findings are of particular interest because they would lead to a possible therapeutic approach to the problem. Investigations are currently in progress to explore the therapeutic possibilities of agents which have been reported to reduce platelet adhesiveness.

SUMMARY

Platelet adhesiveness was found to be increased in nine patients with either recurrent venous thrombosis or recurrent pulmonary embolism. The significance of these observations is discussed.

We are grateful to the consultant staff of Hammersmith Hospital for permitting us to study patients under their care. We wish to thank Professor J. V. Dacie for his helpful comments and Miss I. Leets for assistance with the preparation of the chart.

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REFERENCES

- Alkjaersig, N., Fletcher, A. P., and Sherry, S. (1959). *J. biol. Chem.*, **234**, 832.
 Bobek, K., and Čepelák, V. (1958). *Acta med. scand.*, **160**, 121.
 Brecher, G., and Cronkite, E. P. (1950). *J. appl. Physiol.*, **3**, 365.
 Hellem, A. J. (1960). *Scand. J. clin. Lab. Invest.*, **12**, Suppl. No. 51.
 Müllertz, S. (1952). *Acta physiol. scand.*, **26**, 174.
 Murphy, E. A., and Mustard, J. F. (1962). *Circulation*, **25**, 114.
 Nilsson, I. M., Krook, H., Sternby, N. H., Söderberg, E., and Söderström, N. (1961). *Acta med. scand.*, **169**, 323.
 O'Brien, J. R. (1964). *Blood*, **24**, 309.
 Sevitt, S. (1962). *Amer. J. Med.*, **33**, 703.
 Spittel, J. A., Pascuzzi, C. A., Thompson, J. H., and Owen, C. A. (1960). *Proc. Mayo Clin.*, **35**, 37.
 Wright, H. P. (1942). *J. Path. Bact.*, **54**, 461.

Medical Memoranda

Pure Neural Tuberculoid Leprosy

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In the literature on leprosy there is scant reference to leprosy of a pure neural type (nerve involvement without skin lesions), and there are probably several reasons for this. First, patients in the tropics tend to ignore early symptoms of peripheral nerve damage; secondly, it is not generally appreciated by the medical profession that leprosy is primarily a neurological disease, hence pure neuritic leprosy is likely to be overlooked or misdiagnosed; and, thirdly, even when primary neural leprosy is suspected, nerve biopsy is usually impracticable. One of us (Jopling, 1956) has reported a case of borderline (dimorphous) leprosy which remained purely neural for eight years and in which nerve biopsy showed a typical borderline histology, but in our search of the literature we have not been able to find a report in which a pure neural form of tuberculoid leprosy has been proved. Hargrave and Marion (1964) reported a case of leprotic involvement of multiple peripheral nerves in the absence of skin lesions, and, judging by the number of nerves involved and

the microscopical appearances on nerve biopsy, this was another example of pure neuritic borderline leprosy. A lepromin test was not carried out on this patient. On the subject of pure neural tuberculoid leprosy Cochrane and Davey (1964) state that this type of leprosy is theoretically possible and that primary neuritic cases are occasionally encountered in which the lepromin test is strongly positive. But they admit that no case has been proved by nerve biopsy, and add: "So far any nerves which have shown a tuberculoid histology have come from cases in which there have also been visible cutaneous manifestations." We consider it important that the existence of this form of tuberculoid leprosy should be established beyond doubt, not only to satisfy leprologists who may have doubted its validity but also to draw the attention of neurologists to this clinical entity. This necessitates a nerve biopsy. The lepromin test is not enough, for it is a non-specific test, and though it is always positive in tuberculoid leprosy it may equally be positive in healthy persons.

CASE REPORT

An Anglo-Indian man, aged 38, was born in Hyderabad and came to England in October 1961. He worked as a van driver, and

was admitted to the National Hospital under the care of Professor Gilliatt in February 1964, his hospital number being A 14874.

He fractured his right forearm in childhood, and in 1953 while working as a bus driver in India he developed weakness of his right hand which recovered after three months. In October 1963 he first noticed a dull aching pain behind the right elbow which radiated down the medial aspect of the forearm into the ring and little fingers. It was aggravated by exercise and was eased by resting the arm. A week later he developed weakness of his right hand together with tingling and numbness at the tip of the little finger. After five weeks the pain subsided, but the weakness slowly progressed and was followed by wasting of the muscles of the hand.

On examination the positive findings were confined to the right hand and arm, and indicated a lesion of the ulnar nerve at the elbow. The ring and little fingers were slightly flexed at the interphalangeal joints, and there was moderate weakness and wasting of the ulnar-innervated muscles of the hand. There was also slight weakness of flexion of the terminal phalanges of the ring and little fingers, but flexor carpi ulnaris was spared. Appreciation of pain, light touch, and temperature was impaired over the medial aspect of the hand, the little finger, and the ulnar side of the ring finger; two-point discrimination was defective at the tip of the little finger. Palpation of peripheral nerves revealed marked thickening of the right ulnar nerve just above the medial epicondyle, and of the right radial nerve at the wrist. The deep tendon reflexes were preserved, and general examination was entirely negative. Careful examination of the skin over the face, trunk, and limbs revealed no abnormality.

The results of investigations were as follows:—blood: haemoglobin 13.5 g./100 ml., white blood cells 11,900 per c.mm. (72% polymorphs, 26% lymphocytes, 2% eosinophils); erythrocyte sedimentation rate 7 mm. in 1 hour (Westergren); cerebrospinal fluid: cells, nil; protein, 30 mg./100 ml.; Lange, no change; W.R., negative; skin smears: six skin smears from random sites were negative for acid-fast bacilli; lepromin test: using Mitsuda antigen, the late reading at four weeks showed an erythematous papule, 12 mm. $\times$ 10 mm., with central ulceration—result: strongly positive (+++); electromyographic studies: sampling of the ulnar-supplied muscles in the right hand revealed evidence of partial denervation.

Conduction velocity in the right ulnar nerve was then studied. Supramaximal shocks were delivered to the nerve just above the wrist and elbow, and in the axilla, the muscle action potentials being recorded from abductor digiti minimi through surface electrodes. Though the muscle response showed some dispersion, conduction velocity in the fastest fibres was 41 metres per second (m./sec.), which is only slightly below the normal range of 46–74 m./sec. (Gilliatt and Thomas, 1960). However, exploration of the hand muscles with a coaxial needle electrode, combined with nerve stimulation, made it possible to demonstrate markedly reduced conduction velocities in single motor-nerve fibres, since their individual motor-unit action potentials were easily identifiable in the dispersed muscle response.

Latencies and conduction velocities for four separate motor-unit action potentials are shown in the Table, and it can be seen that, in the case of motor units A and B, nerve conduction was much faster in the upper arm than in the elbow segment and below it, whereas for motor units C and D conduction velocity was reduced to a similar extent above and below the elbow. Thus some of the motor fibres in the right ulnar nerve showed evidence of local

damage at the level of the elbow, while others were more uniformly affected throughout their length.

Other electrical studies included examination of sensory conduction in the digital fibres of the median and ulnar nerves on both sides. No ascending action potential could be recorded from the right ulnar nerve at the wrist when the fifth finger was stimulated, whereas results for both median nerves and the left ulnar nerve were normal. Values for maximal conduction velocity in the right median nerve in the forearm and the right lateral popliteal nerve in the leg were also normal.

A biopsy was taken of the thickened radial nerve at the wrist, and Dr. W. G. P. Mair reported as follows: "Transverse and longitudinal sections from the portion of the right radial nerve examined show extensive destruction of the nerve bundles. The destroyed regions are replaced by varying-sized granulomatous lesions, the centres of which are formed of endothelial (epithelioid) cells and multi-nucleated giant cells. Around these collections there is usually a zone of small round-cell reaction. The giant cells are mainly of the Langhans type, but foreign-body multi-nucleated giant cells also occur. In some of these giant cells there occur clear vacuoles in the haematoxylin and eosin preparations. In the connective tissue between the nerve bundles and in the connective tissue surrounding the nerve similar endothelial and giant-cell reaction is also seen. Van Gieson preparations show that strands of collagen permeate among the endothelial cells and giant cells in the centre of the granulomata. In sections stained by the Ziehl-Neelsen method for tubercle bacilli and by a modification of this technique for *M. leprae* alcohol-fast and acid-fast micro-organisms were not seen."

CONCLUSIONS

A case of pure neural tuberculoid leprosy is described in which peripheral nerve thickening was localized to the right ulnar and radial nerves, with intrinsic muscle wasting and sensory disturbance in the right hand. Conduction velocity was markedly reduced in some of the affected motor fibres of the right ulnar nerve. This case illustrates the importance in neurological practice of examining for thickened peripheral nerves, particularly the terminal portion of the radial nerve as it travels over the lower end of the radius on the lateral side of the wrist. Not only is the nerve easily palpable but it is suitable for biopsy in cases of doubt, as it is purely sensory in this part of its course. Though nerve thickening should always suggest leprosy, there are two rare neurological diseases in which it may occur—namely, familial progressive hypertrophic interstitial neuritis (Déjerine and Sottas, 1893) and primary amyloidosis affecting the peripheral nervous system (Andrade, 1952).

We would like to thank Dr. R. G. Willison for his help with the electromyographic studies and Professor R. W. Gilliatt for his permission to publish the case. We also wish to thank Dr. W. G. P. Mair for his histological report.

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REFERENCES

- Andrade, C. (1952). *Brain*, 75, 408.
Cochrane, R. G., and Davey, T. F. (1964). *Leprosy in Theory and Practice*, 2nd ed., p. 277. John Wright & Sons, Bristol.
Déjerine, J., and Sottas, J. (1893). *C.R. Soc. Biol. (Paris)* 45 (9me sér., 5, pt. 2), 63.
Gilliatt, R. W., and Thomas, P. K. (1960). *J. Neurol. Neurosurg. Psychiat.*, 23, 312.
Hargrave, J. C., and Marion, M. (1964). *Leprosy Rev.*, 35, 78.
Jopling, W. H. (1956). *Trans. roy. Soc. trop. Med. Hyg.*, 50, 478.

Conduction Velocity in Single Motor Fibres of Right Ulnar Nerve

Motor Unit	Muscle	Latency (Milliseconds)			Conduction Velocity (Metres per Second)	
		Wrist-muscle	Elbow-muscle	Axilla-muscle	Elbow-wrist	Axilla-elbow
A	Abductor digiti minimi	21.0	32.0	35.0	25.0	43.0
B	First dorsal interosseous	7.0	23.0	26.7	20.0	40.5
C	Abductor digiti minimi	35.0	64.0	97.0	11.0	3.9
D	First dorsal interosseous	7.0	18.0	25.1	25.0	18.5

Normal range for maximal motor-conduction velocity in the ulnar nerve: 46–74 m./sec. (Gilliatt and Thomas, 1960).