

in certain cases it can be dangerous or negligent. Dangerous because vertebral manipulation can result in spinal-cord or nerve-root damage or even death (for example, in patients with rheumatoid arthritis who have atlanto-axial subluxations, which can easily be missed on the X-ray by the untrained eye). Negligent because patients with seemingly innocuous complaints may have a carcinoma or other life-threatening disease, which obviously cannot be dealt with properly by purely symptomatic treatment. These are the reasons for the criticisms of chiropractors.

12012 Rochester Avenue,
Los Angeles,
California 90025,
U.S.A.

DENSON G. FUJIKAWA.

ACUTE ARTHRALGIA FOLLOWING HIGH-DOSE INTRAVENOUS METHYLPREDNISOLONE THERAPY

SIR,—Withdrawal symptoms following the cessation of long-term steroid therapy are well known. These include exacerbation of prior symptoms such as recurrence of arthritis and arthralgia in the rheumatoid patient, or fever, myalgia, hypotension, anorexia, nausea, lethargy, and desquamation of the skin. In severe cases, signs and symptoms of acute adrenal insufficiency may also occur.

Over the past two years we have observed a new group of severe withdrawal symptoms in kidney-transplant recipients. These occurred in patients who were already receiving maintenance doses of prednisone and, in addition, were being treated at the time for acute rejection episodes with large intravenous doses of methylprednisolone.

The four patients studied were aged 22–26 and were from 2 weeks to 2 years post-transplantation. All were on oral prednisone, 40–100 mg. daily. The patients were in hospital on account of acute rejection episodes and received "pulse therapy" courses of methylprednisolone, 1 g. daily for 3 days. All four patients developed severe bilateral knee-joint pain and tenderness 16 hours to 7 days after the pulse therapy. There was no evidence of joint effusion, erythema, or increased local heat. Chemical and serological determinations performed at that time, including antinuclear factor, A.S.O. titre, rheumatoid factor, febrile agglutinins, L.E. preparations, and serum-uric-acid were within normal limits in all but one case. The exception was a patient with a uric acid of 14.4 mg. per 100 ml. X-rays of the knee-joints were normal and all the patients improved within a few days, but required strong analgesic medication in the acute phase. A typical case-history is as follows:

A 24-year-old Negro woman with a diagnosis of chronic pyelonephritis had received a cadaver-kidney transplant and was doing well until several weeks before admission when she was treated for several acute rejections with 3 g. methylprednisolone pulse-therapy courses. At the time of her episode of acute arthralgia, she had completed such a course. 16 hours after the infusion she developed severe bilateral knee pain with tenderness, requiring meperidine (pethidine). There was no muscle pain or tenderness. There was no clinical evidence of adrenal insufficiency. Laboratory studies at that time, except for a serum-creatinine which had risen from less than 2 to 3.3 mg. per 100 ml., were essentially within normal limits. The severe arthralgia gradually resolved over the following 48 hours.

An additional forty-six patients similarly treated did not develop acute symptoms.

The clinical features described above cannot be ascribed to adrenal-cortical insufficiency since the patients were on prednisone doses ranging from 40 to 100 mg. a day. Amatruda et al.¹ have shown that patients experiencing symptoms of steroid withdrawal had normal urinary and

plasma levels of corticosteroids, and that there appeared to be no correlation between symptoms and various parameters of the hypothalamic/pituitary/adrenal axis. Good et al.² have shown that symptoms of myalgia and arthralgia tended to occur during the period in which the level of the plasma 17-hydroxycorticoids was decreasing rapidly, and usually at a time when the levels were still elevated or normal, suggesting that a rapid change in the plasma-cortisol level was of greater significance in the development of symptoms than the absolute concentration. Furthermore, the addition of stress, as in the acute rejection phenomenon, may require elevated steroid levels to maintain the patients' homeostasis. In man the serum half-life of methylprednisolone after intravenous administration has been shown to be 2½ hours, with the serum level falling rapidly to nearly baseline within 12 hours.³ Side-effects of intravenous methylprednisolone are remarkably slight. Weakness, flushing, malaise, and a metallic taste in the mouth may occur immediately after the intravenous injection.³ The acute arthralgias noted in the four patients were shortlived and had no permanent sequelae. In addition, these four patients were on daily steroids rather than our usual every-other-day steroid therapy because of frequent rejection with possible suppression of their own adrenal glands. We suggest that the rapid change in plasma levels of steroids in combination with the stress of rejection is probably responsible for the severe arthralgia affecting the knee-joints following intravenous methylprednisolone therapy.

Department of Nephrology,
Division of Medicine,
Mt. Sinai Hospital,
Cleveland, Ohio 44106.

KENNETH J. NEWMARK
SUMANTA MITRA
LEONARD B. BERMAN.

DIAGNOSIS OF SUPERIOR-VENA-CAVA OBSTRUCTION

SIR,—Superior-vena-cava obstruction is an unusual and often misdiagnosed syndrome, often confused with constrictive pericarditis.^{4,5} Recently we faced the problem of differentiating superior-vena-cava obstruction from cardiac tamponade.

A 67-year-old man had three months' history of hæmoptysis and progressive weight loss. Physical examination on admission revealed hypotension (blood-pressure 90/50 mm. Hg), jugular venous distension at 90°, cyanosis of the face, distant heart-sounds, right upper extremity œdema, and bilateral ankle œdema. Initial chest film showed right apical density, right pleural effusion, and borderline cardiomegaly. Shortly after admission he became profoundly hypotensive without change in physical signs.

Although the preliminary diagnosis was superior-vena-cava obstruction, we felt the hypotension might be due to cardiac tamponade. The usual signs of tamponade (i.e., Kussmaul's signs, or pulsus paradoxus) were not evident. To confirm our diagnosis we placed intravenous catheters in the superior vena cava (via the right internal jugular) and the inferior vena cava (via the right femoral vein). The position of the catheters was confirmed radiologically. Simultaneously venous pressures were then measured with the patient supine. There was a 20 cm. H₂O difference between the two measurements. This finding clearly pointed to local superior-vena-cava obstruction, whereas with cardiac tamponade we would have expected equal pressures. Subsequent echocardiography failed to reveal a pericardial effusion.

This simple bedside technique carries a very slight risk

1. Amatruda, T., Hurst, M. M., D'Esopo, N. *J. clin. Endocr. Metab.* 1965, 25, 1207.

2. Good, T. A., Benton, J. W., Kelley, V. C. *Arthritis Rheum.* 1959, 2, 299.
3. Woods, J. E., Anderson, C. F., DeWeerd, J. H., Johnson, W. J., Donadio, J. V., Jr., Learey, F. J., Frohnert, P. P. *J. Am. med. Ass.* 1973, 223, 896.
4. Spencer, F. C. in *Principles of Surgery* (edited by S. I. Schwartz); p. 715. New York, 1969.
5. Effler, D. B., Groves, L. K. *J. thorac. cardiovasc. Surg.* 1962, 43, 574.

and allowed rapid diagnosis of superior-vena-cava syndrome.

Department of Medicine,
Department of Surgery,
University of Michigan,
Ann Arbor, Michigan.

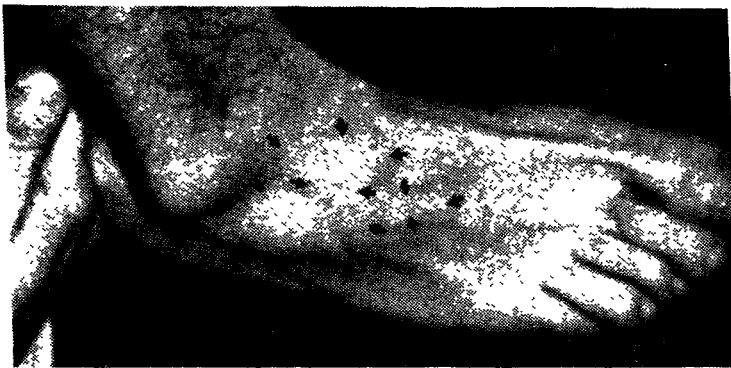
JEFFREY P. CALLEN.

BRUCE L. GEWERTZ.

HYPERTROPHY OF EXTENSOR DIGITORUM BREVIS IN LIMB-GIRDLE MUSCULAR DYSTROPHY

SIR,—We wish to report clinical and electrophysiological findings in the extensor digitorum brevis (E.D.B.) muscle of 8 patients with limb-girdle muscular dystrophy, 3 patients with facioscapulohumeral muscular dystrophy, and 10 patients with chronic spinal muscular atrophy. The illness was longer in dystrophic patients.

In all patients with the muscular dystrophies the E.D.B. was hypertrophic (see accompanying figure), despite the



Hypertrophy of extensor digitorum brevis in a 28-year-old patient with limb-girdle muscular dystrophy.

severe atrophy of proximal muscles. Conversely, the E.D.B. was usually atrophic (7 patients) or relatively normal (3 patients) in chronic spinal muscular atrophy. Hypertrophy of the E.D.B. was also indicated by the common electrophysiological finding of high amplitude M-responses in the E.D.B. of muscular dystrophies, while small amplitude M-responses were recorded in patients with chronic spinal muscular atrophy.

Since misdiagnosis is common in patients with progressive proximal muscular atrophy, hypertrophy of the E.D.B. may be a useful clinical point in differential diagnosis.

We have also found that the number of motor units was normal in patients with muscular dystrophy and significantly small in chronic spinal muscular atrophy. These findings, as well as those previously reported for Duchenne muscular dystrophy,^{1,2} do not support the neurogenic hypothesis³ of muscular dystrophies.

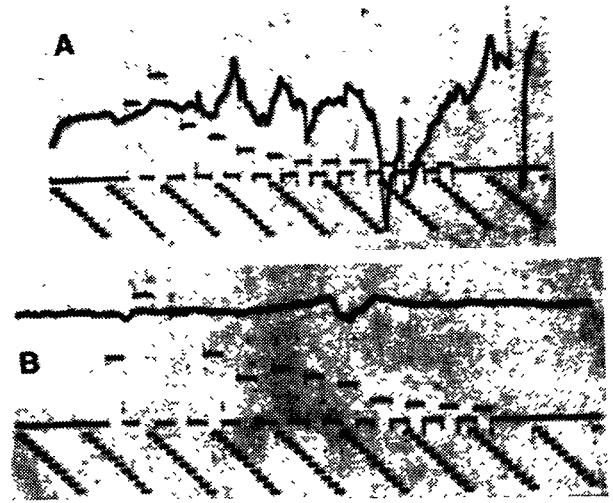
Department of Neurology,
University of Athens,
74 Vas. Sophias Avenue,
Athens.

C. P. PANAYIOTOPOULOS
S. SCARPALEZOS.

STIMULATION OF THE SPINAL CORD IN MOTOR-NEURONE DISEASE

SIR,—In a previous note⁴ I indicated the possibility of validating, by our experiences with electrical stimulation of the spinal cord in man, the hypothesis of Illis⁵ regarding restoration of function in the nervous system. This, it was believed, was related to the disconnected part

1. Scarpalezos, S., Panayiotopoulos, C. P. *Lancet*, 1973, ii, 458.
2. Panayiotopoulos, C. P., et al. *J. neurol. Sci.* (in the press).
3. McComas, A. J., Sica, R. E. P., Campbell, M. J. *Lancet*, 1971, i, 321.
4. Cook, A. W. *Lancet*, 1973, i, 1442.
5. Illis, L. S. *ibid.* p. 1035.



Electromyogram of left anterior fibial muscle in patient with motor-neurone disease.

- A. During spinal-cord stimulation (200 microvolts, 10 msec.).
- B. Without stimulation.

of the nervous system, the synaptic zone. Illis⁶ had also demonstrated in cats that chronic dorsal-root stimulation enlarged the segmental synaptic zone.

In another but related area—namely, neurone-muscle disease—McComas et al.⁷ offered a hypothesis regarding healthy, sick, and dead motor neurones. It was stated that the healthy neurone could carry out its natural function, including trophic influences on muscle fibres of the motor unit. It could grow axonal branches which establish synaptic connections with previously denervated muscle fibres. A sick motor neurone had difficulty in maintaining satisfactory synaptic connection with muscle fibres, as evidenced by defective neuromuscular transmission and its inability to acquire previously denervated muscle fibres. Dead motor neurones had no excitability or trophic effect on muscle. These concepts of Illis and McComas have assumed particular significance as our experience with spinal-cord stimulation in man has been extended from patients with multiple sclerosis to motor-neurone disease.⁸

In three patients with verified motor-neurone disease (clinical, muscle biopsy, electromyography), stimulation of the spinal cord has produced significant improvement in voluntary motor performance. This is not limited to isolated muscles but encompasses total synergistic activity. Speech, upper and lower limbs, and trunk all participate in the improved motor function. The electromyogram is modified (see fig. 1) by stimulation. Withdrawal of stimulation, as in patients with multiple sclerosis, results in abolition of the improvement. The fact that patients with motor-neurone disease have the potential for restoration of synergy of voluntary movement in gait, posture, and performance of individual appendages emphasises the importance of hypotheses of Illis and McComas. Certainly the renewed function in these patients cycled with spinal-cord stimulation must be the result of engagements of systems of motor neurones, interneurones, and their connections previously unresponsive to the will. Presumably only healthy, or perhaps sick, motor neurones can participate in such renewed activity. With chronic stimulation more and more functional restoration is seen, including a decrease in visible muscle fasciculation. This suggests increasing recruitment of motor neurones for greater areas of activity and influence. The degree to which this can occur depends upon the number of healthy cells.

Our experience is small and brief (6 months). The long-

6. Illis, L. S. *Nature*, 1968, 223, 76.
7. McComas, A. J., Sica, R. E. P., Campbell, M. J. *Lancet*, 1971, i, 321.
8. Cook, A. W., Weinstein, S. *N.Y. State J. Med.* 1973, 73, 2868.