

Despite immunosuppressive therapy, liver function also remained stable until this time. During the following year chronic rejection occurred, leading to complete loss of graft function, even though steroid treatment was intensified. This was associated with rapid deterioration of liver function and development of significant portal hypertension. This simultaneous failure of two vital organs carried a hopeless prognosis, at least for conventional therapy. He was referred here for combined liver and renal transplantation.

On Dec 28, 1983, the patient was given an orthotopic liver graft and a kidney from the same donor. Hyperimmunoglobulin against hepatitis B was administered during the anhepatic phase followed by active vaccination of the recipient. Notwithstanding a cold ischaemia time of almost 8 h, the transplanted liver showed excellent initial function. This was also true of the kidney grafted immediately afterwards. Immunosuppression was started with azathioprine and prednisolone.

On day 8 post-transplantation, a biopsy-proven acute cellular rejection of the kidney set in. Concurrently, however, the liver lacked both biochemical and morphological evidence of rejection. Unfortunately, at the same time bronchopneumonia of the right lower lobe developed. This serious infectious complication prompted us to switch from conventional immunosuppression to cyclosporin instead of high-dose methylprednisone for treatment of rejection. Intravenous cyclosporin reversed the rejection but induced long-standing cholestatic jaundice with bilirubin levels of up to 40 mg/dl as well as transient nephrotoxicity. Both these complications resolved on reduction of the cyclosporin dose on the basis of blood levels. This illustrates the difficulty of postoperative management of patients with transplants of both the organs that are crucially involved in drug excretion and/or metabolism. The subsequent course was uneventful, and the patient was discharged on day 68. Renal function (creatinine 1.2 mg/dl) and serum bilirubin levels were normal. Demonstration of HB_s and HB_e antigens and slightly increased aminotransferase levels suggested minimally active graft infection. 1 month later, the patient had completely recovered and had resumed normal activity.

In countries like Austria, where HB_sAg positive patients are not excluded from haemodialysis or from transplantation programmes, patients with both chronic active hepatitis and end-stage renal disease are frequently encountered. Combined transplantation should be further evaluated before this double organ failure is declared intractable.

Department of Surgery J,
University Hospital,
A-6020 Innsbruck, Austria

Department of Internal Medicine,
Allgemeine Krankenhaus, Linz

Department of Surgery J,
University Hospital, Innsbruck

RAIMUND MARGREITER

REINHARD KRAMAR

CHRISTOPH HUBER

EKKEHARD STEINER

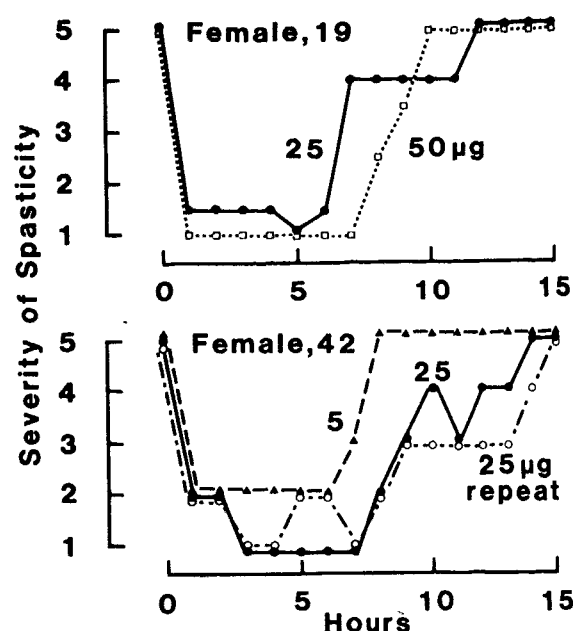
DIETGER NIEDERWIESER

GERD JUDMAIER

WOLFGANG VOGEL

INTRATHECAL BACLOFEN ALLEVIATES SPINAL CORD SPASTICITY

SIR,—Baclofen, a γ -aminobutyric acid (GABA) analogue, is useful in the treatment of spasticity of spinal cord origin.¹ However, severe spasticity is not adequately alleviated with oral baclofen. Following systemic administration, very little of the drug enters the central nervous system.² Increasing the oral dose produces drowsiness. Direct infusion into the spinal subarachnoid space could allow higher spinal cord drug levels to be attained, while minimising brain dysfunction. We have found that microgram doses of baclofen given in this manner can produce normal muscle tone and eliminate flexor-extensor spasms even in patients with severe spasticity.



Change in lower limb spasticity following intrathecal baclofen.

Ordinate is Ashworth scale (5 = rigid, 1 = no increase in tone; half numbers occur when two limbs differ by 1).

Two patients with midthoracic spinal cord injuries, one due to a spontaneous epidural haematoma and the other due to scoliosis surgery, were evaluated in their response to intrathecal baclofen, in preparation for chronic treatment via an implantable pump system. Both patients had frequent flexor and extensor spasms and severe hypertonia in the lower limbs, with minimal voluntary control. One patient could not tolerate oral baclofen because it caused mental confusion and the other had not responded adequately to doses of up to 80 mg a day.

A 4F 'Silastic' catheter was percutaneously inserted through a Tuohy needle into the lumbar subarachnoid space at L3-4 and the tip manoeuvred to L1. The catheter was attached to a subcutaneous reservoir. Test doses of baclofen were injected via a needle through the skin into the reservoir and then by barbotage into the subarachnoid space. The Ashworth scale was used to grade muscle tone and the frequency of spasms was monitored.¹

The figure shows the marked decrease in tone that occurred within 1 h and which, depending on dose, lasted 5-8 h. No spasms occurred in either patient when the muscle tone was in the normal or slightly increased range (1-2); nor could spasms be elicited by vigorous sensory stimulation to the lower extremities during that period. No adverse effects on vital signs were seen, nor mental confusion or lethargy. The patients' strength in the upper extremities did not change and they could sit and manoeuvre more comfortably in their wheelchairs. The limited voluntary control was unchanged.

This is the first time baclofen has been injected into the lumbar subarachnoid space in man, and the effects were as dramatic as in our animal studies.³ Only 5-25 μ g was necessary to reduce the increased tone to level 4 or 5 on the Ashworth scale and to eliminate spasm. In contrast, oral doses over 1000 times higher are necessary to produce moderate clinical effects (1-2 on the Ashworth scale) and these are often accompanied by lethargy or other central side effects.¹ These two patients seem to be good candidates for a programmable implantable pump for long-term baclofen delivery, similar to the pump used for morphine delivery to the spinal cord.⁴

Drug received courtesy of Ciba-Geigy Corporation, Summit, New Jersey.

Department of Neurosurgery,
Rush Medical College,
Chicago, Illinois 60612, USA

RICHARD D. PENN
JEFFREY S. KROIN

- Hattab JR. Review of European clinical trials with baclofen. In: Feldman RG, Young RR, Koella WP, eds. *Spasticity: Disordered motor control*. Miami: Symposia Specialists, 1980: 71-85.
- Knutsson E, Lindblom U, Martensson A. Plasma and cerebrospinal fluid levels of baclofen (lioresal) at optimal therapeutic responses in spastic paresis. *J Neurol Sci* 1974; **23**: 473-84.

- Kroin JS, Penn RD, Beissinger RL, Arzbaecher RC. Reduced spinal reflexes following intrathecal baclofen in the rabbit. *Exp Brain Res* 1984; **54**: 191-94.
- Penn RD, Paice JA, Gottschalk W, Ivankovich AD. Cane pain relief using chronic morphine infusion: Early experience with a programmable implanted drug pump. *J Neurosurg* (in press).