Pharmacology References


Abstract: Tizanidine was evaluated in a prospective, double-blind, randomized, placebo-controlled trial in 187 patients with MS. Taken orally for 9 weeks and preceded by a titration phase for a period of 3 weeks starting at 2 mg daily, tizanidine produced a significant reduction in spastic muscle tone compared with placebo treatment. Within the effective dose range of 24 to 36 mg given daily in three doses, tizanidine achieved a 20% mean reduction in muscle tone. Approximately 75% of patients, with all degrees of spasticity, reported subjective improvement without an increase in muscle weakness, but there was no improvement in activities of daily living depending on movement. Tizanidine achieved its maximum effect on spasticity within 1 week of the start of treatment;
the benefit was maintained for at least 1 week after discontinuation of therapy. A variety of adverse events was recorded by patients taking tizanidine, but these were minor and reversible, and rarely limited treatment. Tizanidine is a well-tolerated and effective drug for symptomatic treatment of spasticity.


Abstract: Tizanidine hydrochloride (Zanaflex), an alpha 2-adrenoreceptor agonist, is the first new antispasticity agent to become available in the UK for more than 20 years. It provides effective reduction of spasticity without affecting muscle strength. The mechanisms of spasticity, its measurement and management, together with the place of tizanidine in its treatment, were discussed at a symposium held at the Royal College of Physicians on November 13 1997.


Abstract: Sensory rhizotomy in the treatment of spasticity has been evolving over the past century since its first use in 1888. This paper reviews its historical evolution, current physiologic basis, range in current surgical technique, and the outcome, along with complications seen over the past decade since its repopularization.

Abstract: Back spasm, or spasm of the back muscles, is the commonest adverse reaction encountered after chemonucleolysis. In order to overcome this troublesome complication, the authors present a new 'paradiscal injection technique'. After the injection of chymopapain into the affected disc, the needle is withdrawn to just outside the annulus. Bupivacaine is injected into the paradiscal 'space' which acts upon the paravertebral muscles. Eighty consecutive patients have been treated by chemonucleolysis with paradiscal injection for pain relief. All patients were discharged the same day or the following day and no immediate complications occurred. When reviewed 3 weeks later, only three (3.8%) patients complained of back pain (which was different in character to that present before the injection or was exacerbated by the injection). Pain persisted in the same patients until 6 months after the injection but was negligible. None of the remaining patients had developed back pain as a result of chymopapain. The
authors suggest that the addition of paradiscal injection of bupivicaine after
cymopapain injection can reduce the incidence of spasm of the back muscles.
This technique is a major contribution to increasing the efficacy of
chemonucleolysis for the treatment of herniated lumbar disc

Abstract: This study assessed the safety and efficacy of intrathecal baclofen in
the treatment of intractable spasticity caused by spinal cord injury or multiple
sclerosis. Twenty-three patients with severe chronic spasticity underwent bolus
test dosing with 50, 75, or 100 micrograms of intrathecal baclofen administered
by lumbar puncture. All patients were either refractory to oral baclofen at a dose
of 120 mg/d or side effects were unacceptable at a lower dose. There was a
significant decrease in tone and spasticity in all 23 patients. Nineteen patients
underwent implantation of a programmable pump and intrathecal catheter
designed to deliver baclofen directly to the spinal cord. Rigidity (tone) was
decreased from a mean prebolus Ashworth score of 3.8 to a mean postbolus
Ashworth score of 1.5 and spasms from a mean prebolus score of 3.5 to a mean
postbolus score of 1.2 for a minimum of 4 hours. Patients have been observed
for a mean of 16 months (range 2 to 34 months). Ashworth scores have
remained reduced to an acceptable level (< or = 2 with periodic adjustment in
dosage in all but three patients. There has been one pump malfunction and four
catheter malfunctions; few serious medication and postoperative complications
have occurred. There was one death caused by underlying disease, one patient
voluntarily withdrew, and three patients developed tolerance to the extent that
optimal control of spasticity tone could not be maintained. Although intrathecal
baclofen is safe and effective in the majority of patients, three patients required >
1,000 micrograms/d with increasingly higher doses over time and exhibited a
poor response

Abramson A.S. (1967) Modern concepts of management of the patient with


syndrome with symptoms resembling neuroleptic malignant syndrome]. Rinsho
Shinkeigaku 38, 637-640.
Abstract: Satoyoshi syndrome is a rare neurological disorder of unknown etiology
characterized by progressive muscle spasms, alopecia, diarrhea and skeletal
abnormalities. We here describe a 25-year-old man who developed symptoms
similar to neuroleptic malignant syndrome (NMS). He began to have the clinical
characteristics of Satoyoshi syndrome at the age of 12 years. He was admitted to
hospitals many times with painful muscle spasms and pyrexia in the early stage
of the disease. He received steroid pulse therapy and oral prednisone at the age
of 19, the extent and frequency of the spells being reduced thereafter. He was admitted to our hospital due to recurrence of his usual muscle spasms. He was treated with midazolam intravenously to relieve severe muscle ache, pain in the left shoulder, and insomnia. About 90 minutes later, he became comatose, with the following manifestations: hyperthermia, low blood pressure, tachycardia, profuse perspiration, acute respiratory failure, and ensuing cardiac arrest. He developed rhabdomyolysis, acute renal failure, hepatic damage, and diffuse intravascular coagulation. Serum creatine kinase level was elevated to 306,910 IU. He died of multiple organ failure 13 days after admission. His symptoms resembled NMS and malignant hyperthermia (MH). None of patients with Satoyoshi syndrome accompanied by NMS or MH have been reported. It remains to be clarified whether midazolam administration induces NMS in Satoyoshi syndrome. Nevertheless, careful attention should be paid when one administers midazolam to patients with this syndrome

Adamcho N.I., Bondar' V.P., and Rusavskii I.V. (1978) [Prevention and treatment of the complications of peridurography]. Vopr. Neirokhir. 43-47. Abstract: In lumbar peridurography conducted in 117 patients with discogenic radiculitis complications occurred both in the stage of peridural anesthesia and after introduction of the radiocontrast medium. During anesthesia the dura mater was punctured in 4 patients, in another 2 patients dicaine penetrated into the subarachnoid space and caused spinal anesthesia with a high upper level. Peridural anesthesia with paralysis of the respiratory musculature developed in 1 patient. After the injection of the radiocontrast medium, spasm in the lower extremities and trunk of the type of spinal epilepsy developed in 4 patients. The clinical picture, prevention, and treatment of these complications are discussed

Advokat C., Mosser H., and Hutchinson K. (1997) Morphine and dextrorphan lose antinociceptive activity but exhibit an antispastic action in chronic spinal rats. Physiol Behav. 62, 799-804. Abstract: Within 3-4 weeks after spinal transection, morphine-induced antinociception, assessed with the tail flick reflex in rats, is profoundly reduced. The cause of this decrement is unknown. The present studies were conducted to determine whether this phenomenon reflects a general loss in opiate activity or a selective decline in opiate antinociception. This was accomplished by assessing the effect of morphine on two different responses, the tail flick reflex and the hindlimb spasticity that develops in chronic spinal rats. Because excitatory amino acid antagonists are also antinociceptive in acute spinal rats, the effect of one such drug, dextrorphan, on these two behaviors was also evaluated in chronic spinal animals. The antinociceptive and antispastic effect of subcutaneous (6 mg/kg) and intrathecal (5 micrograms) morphine injections were assessed in intact and chronic (21-28 days) spinal rats, whereas the effect of subcutaneous (25 and 40 mg/kg) and intrathecal (350 micrograms) dextrorphan was assessed in acute (1 day) and chronic spinal rats. The antinociceptive effect of both drugs was significantly reduced in chronic spinal animals, relative to saline controls. However, each drug treatment produced a significant antispastic effect in the
same animals, indicating a selective decline in opiate action. This outcome also suggests that excitatory amino acid antagonists may be useful as adjunct antispastic agents.


Abstract: OBJECTIVE: Baclofen is known for the alleviation of signs and symptoms of spasticity. Reports from our previous study have suggested that it may be at least as effective as clonidine in the management of physical symptoms of opiate withdrawal syndromes and superior to clonidine in the management of mental symptoms. We now report on a randomized double-blind comparison of baclofen vs. clonidine in view of side-effects profile. METHODS: A total of 62 opiate addicts were randomly assigned to treatment with baclofen or clonidine during a 14-day, double-blind clinical trial. All patients met the DSM IV criteria for opioid dependence. Maximum daily doses were 40 mg for baclofen and 0.8 mg for clonidine. This trial medication was given three times per day in divided doses. The severity of side-effects was measured in days 0, 1, 2, 3, 4, 7 and 14. RESULTS: There was no significant difference between two treatments in terms of retention in treatment (dropout) and overall side-effect. Nevertheless, significantly more problems relating to hypotension were encountered with subjects on clonidine. CONCLUSION: We conclude that the low incidence of hypotension with baclofen suggests that the drug may be suitable for outpatient ambulatory treatment of withdrawal from opiates.


Abstract: Twenty cases of acute neurological complications occurring within 7 days of pertussis immunization are reported. Convulsions were present in every case and status epilepticus was observed in five infants. In only 4 cases were neurological or epileptic sequelae lacking. The clustering of neurological complications in the 24 hours following immunization is not consistent with the hypothesis of a mere temporal coincidence. However, the mechanism and incidence of post-immunization encephalopathies remains obscure and epidemiological studies are in order.


Abstract: Baclofen is a centrally acting muscle relaxant used for treatment of spasticity. Some patients, to experience adequate symptomatic relief, require
dosages of baclofen that significantly exceed the conventional 80 mg daily maximum advocated by the 1992 Physicians’ Desk Reference. In this pilot study of baclofen kinetics and dynamics in eleven patients, the safety and efficacy of high dose baclofen was confirmed. The data suggest that the pharmacokinetics of high dose baclofen may vary from those described previously. Time-to-peak plasma levels and plasma half-lives were noted to be substantially longer than prior reports indicate. Baclofen blood levels were observed to rise gradually over time in some patients on a stable dosing regimen, probably a result of impaired renal clearance. These findings may indicate that a change in pattern of prescription is warranted and that a reliable and practical measurement of systemic baclofen levels has a useful role in clinical practice, particularly for the patient with neurogenic bladder and potential renal insufficiency.


Abstract: Baclofen, a centrally acting gamma-aminobutyric acid agonist is a commonly used pharmacotherapy for spasticity of spinal origin. It is primarily excreted by glomerular filtration with a clearance proportional to creatinine clearance. We describe a 39-year-old quadriplegic women who, over a 16-week period, developed clinical signs of baclofen toxicity confirmed by progressively rising serum baclofen levels while on a conventional stable dosing regimen. During this period blood urea nitrogen and creatinine concentrations were normal and stable (9mg/dL and 0.8mg/dL, respectively). However, creatinine clearance values were consistently low (55 to 60m/min), suggesting renal insufficiency as the underlying cause. After a decrease in baclofen dosage, evidence of baclofen toxicity resolved. Clinicians should be alert to signs of evolving baclofen toxicity even in patients on an apparently stable regimen. Baclofen dosage adjustments based on systemic baclofen level may play a role in optimizing the clinical management of spasticity.


Abstract: Concern over the development of tolerance in patients on continuous intrathecal baclofen therapy has arisen as this new form of treatment for spasticity has gained wider use. We have studied time-dose relationships in 18 spinal cord injured patients who have undergone intrathecal baclofen infusion pump implantation since February 1988 in our facility. Our data show that there was a significant increase in baclofen dosage needed to control spasticity during the first 12 months post implantation. After 12 months, however, no significant
changes in dosage requirement was detected. In addition, there was no significant difference between completely and incompletely spinal cord injured patients with regard to both the initial dose and the tolerance trend.

Abstract: A patient with a cervical spinal cord injury receiving intrathecal baclofen for spasticity control underwent a 7 week course of hyperbaric oxygen therapy to induce healing of an ischial decubitus ulcer. After completion of this treatment and during a routine baclofen infusion pump refill, the actual pump reservoir volume exceeded computer measurements obtained with telemetry. Examination of the physiology of hyperbaric oxygen therapy in relation to infusion pump function revealed that the intraspinal pressures attained during hyperbaric oxygen therapy produced retrograde leakage of cerebrospinal fluid into the infusion pump reservoir.

Abstract: The clinical, biochemical, pathological and neuroradiological findings of a 2-year-old Saudi boy with infantile G(M1) gangliosidosis are reported. The patient had a progressive neurologic deterioration, manifesting with developmental regression, sensorimotor and psychointellectual dysfunction and generalized spasticity that started at 4 months of age. Cherry-red macula, facial dysmorphia, hepatomegaly, exaggerated startle response to sounds, skeletal dysplasia, and vacuolated foamy lymphocytes that contain finely fibrillar material in addition to lamellar membranes and electron-dense rounded bodies were seen. MRI of the brain demonstrated mild diffuse brain atrophy and features of delayed dysmyelination and demyelination. Brain FDG PET scan revealed a mild decrease in the basal ganglia uptake, and moderate to severe decrease in thalamic and visual cortex uptake, and an area of increased glucose uptake in the left frontal lobe, probably representing an active seizure focus. The functional changes indicated by FDG PET scan and the structural abnormalities shown on MRI were found to be complementary in the imaging evaluation of infantile G(M1) gangliosidosis.

Abstract: OBJECTIVE: To present and discuss treatment of severe spasms related to spinal cord injury with botulinum toxin type A. DESIGN: A 2-year follow-up study of an incomplete T12 paraplegic patient, who was reluctant to undergo intrathecal baclofen therapy, presenting severe painful spasms in his lower limbs treated with intramuscular injections of botulinum toxin type A.
SETTING: Department of Physical Medicine and Rehabilitation, Hopital de Gravelone, Sion, Switzerland. SUBJECT: Single patient case report. MAIN OUTCOME MEASURE: Spasticity, spasms and pain measured with the modified Ashworth scale, spasm frequency score and visual analogue scale. RESULTS: Treatment of spasticity with selective intramuscular injections of botulinum toxin type A resulted in subjective and objective improvement. CONCLUSION: Botulinum toxin type A has its place in the treatment of spasticity in spinal cord injury patients. This treatment is expensive and its effect is reversible. It can complement intrathecal baclofen in treating upper limb spasticity in tetraplegic patients. Tolerance does occur to the toxin. Although high doses of the product are well tolerated, the quantity should be tailored to the patient's need. The minimal amount necessary to reach clinical effects should be adhered to and booster doses at short period intervals should be avoided

Abstract: A 24-yr-old, completely (T8) paraplegic male patient presenting with severe spasticity had a drug administration device implanted in April 1991 for continuous intrathecal administration of baclofen. After a period of remarkable improvement in both the spasticity level and his quality of life, the patient experienced several short-lasting episodes of increased spasticity, with severe spasms. Among the possible causes of these deleterious episodes were microcrystalluria, obstipation, a decubitus ulcer, a foreign body in the buttocks, drug tolerance to baclofen, electromagnetic interference, and erroneous filling and programming of the pump. The catheter was the most common source of intrathecal baclofen withdrawal symptoms and had to be changed four times in 5 yr. Intrathecal baclofen administered through an implantable drug administration device is a highly effective but complex and expensive procedure that requires careful patient selection and close monitoring by highly qualified and well-trained health professional. Withdrawal symptoms may be related to noncompliance on the part of the patient, erroneous filling or programming of the pump, depletion of the battery, random component failure, concomitant illness, drug tolerance, or advancement of the disease itself. When failure of the device is suspected, substitution with oral baclofen is recommended until a full work-up is performed to determine the defect

Abstract: Physical and occupational therapists play important roles in the evaluation and management of patients receiving botulinum toxin injections for spasticity. Baseline evaluation includes areas beyond the muscles being injected, since local spasticity reduction may lead to more widespread functional changes. Because the evaluation itself influences tone, a consistent order of muscle evaluation is recommended. The range of preinjection assessments includes
evaluation of tone, mobility, strength, balance, endurance, assistive devices, and
others. After injection, therapeutic interventions have multiple aims, including
strengthening and facilitation, increasing range of motion, retraining of
ambulation and gait, improving the fit and tolerance of orthoses, and improved
functioning in ADLs

in cerebral palsy. JAMA 265, 1418-1422.
Abstract: Seventeen patients with congenital spastic cerebral palsy and six
patients with other forms of spasticity were injected intrathecally with doses of
placebo or baclofen, 25 micrograms, 50 micrograms, or 100 micrograms, in a
randomized, double-blind manner. Muscle tone in the upper and lower
extremities was assessed by Ashworth scores both before the injections and
every 2 hours afterward for 8 hours. Function of the upper extremities was
evaluated before the injections and 4 hours afterward. Muscle tone in the lower
extremities was significantly decreased within 2 hours after baclofen injection and
remained lower than baseline 8 hours afterward. Upper extremity tone and
function were not significantly affected by these single doses. Confusion and
drowsiness occurred in two of the youngest children in the study after the 50-
micrograms dose, but cleared within 2 hours. Our findings indicate that
intrathecal baclofen reduces spasticity in children with cerebral palsy, as it does
in adults with spasticity of spinal origin

Abstract: The pathophysiology of spasticity and the history of posterior
rhizotomies are reviewed. The rationale for selective posterior rhizotomies is that
electrical stimulation identifies afferent posterior rootlets that terminate on
relatively uninhibited alpha motoneurons; if these uninhibited rootlets are divided,
spasticity can be alleviated without loss of other posterior root functions.
Indications, technique, and results of selective posterior rhizotomies are
presented. The use of continuous intrathecal baclofen (CITB) is summarized.
CITB at doses of approximately 300 micrograms/day consistently reduces lower
extremity spasticity and diminishes or alleviates muscle spasms in adults with
spasticity of spinal origin. Single doses of intrathecal baclofen significantly
decrease lower extremity muscle tone in children with cerebral palsy, and the
effects can be maintained in these patients by CITB infusions which diminish
muscle tone not only in the lower extremities, but in the upper extremities as well.
CITB is best accomplished via an externally programmable pump that allows
titration of the daily dose to attain the desired reduction in spasticity. Factors
influencing the decision for rhizotomy or CITB are presented

Continuous intrathecal baclofen infusion for spasticity of cerebral origin. JAMA
270, 2475-2477.
Abstract: OBJECTIVE--To determine if continuous intrathecal baclofen infusion
(CIBI) would provide continuous relief of spasticity in patients with spasticity of cerebral origin, especially children with cerebral palsy. DESIGN--Prospective, unblinded trial, before and after CIBI. SETTING--Children's Hospital of Pittsburgh (Pa). PATIENTS--Thirty-seven patients, 5 to 27 years of age, with spasticity of cerebral origin. INTERVENTION--Continuous intrathecal baclofen infusion for 3 to 48 months. MAIN OUTCOME MEASURES--Muscle tone, range of motion, upper extremity timed tasks, activities of daily living (ADLs). RESULTS--Six and 12 months after CIBI, muscle tone was significantly decreased in the upper (P = .04) and lower (P = .001) extremities. There was a significant relationship between baclofen dosage and muscle tone in the upper (P = .02) and lower (P = .001) extremities. Hamstring motion, upper extremity function, and ADLs were significantly improved in 25 patients who were capable of self-care. CONCLUSION--Spasticity of cerebral origin can be effectively treated with CIBI. Because baclofen dosages can be titrated for the desired clinical response, CIBI is particularly useful for patients who need some spasticity to stand and ambulate.


Abstract: This study was performed to compare the effects of continuous intrathecal baclofen infusion (CIBI) and selective posterior rhizotomy (SPR) on upper extremity (UE) spasticity and range of motion in children with cerebral palsy. Spasticity was assessed with the Ashworth scale of muscle tone and range of motion was evaluated. Thirty-eight patients who had been treated with CIBI for at least 6 months were paired, according to pretreatment UE muscle tone and functional status, with 38 patients who had undergone SPR. The CIBI dosage had been titrated to reduce over lower extremity spasticity and improve lower extremity function, rather than to improve UE tone. The pretreatment muscle tone in the two groups was virtually identical. The UE tone of children treated with CIBI decreased from 2.07 prior to treatment to 1.66 after 1 year (p < 0.01). The tone of children treated with SPR decreased from 2.03 to 1.70 after 1 year (p = 0.005). In that group, the likelihood of a clinically significant reduction in muscle tone (one point or greater) was greater in children with a higher pretreatment UE muscle tone. There was no correlation between the percentage of posterior lumbar roots divided in SPR and the subsequent reduction in UE tone. There were no significant changes in the range of motion in any UE joint, at either 6 or 12 months, after either CIBI or SPR. We conclude that both CIBI and SPR significantly reduce UE spasticity, in addition to the previously documented reduction in lower extremity spasticity.

Abstract: Intrathecal baclofen reduces spasticity in individuals with cerebral palsy. Intrathecal doses are far lower than oral doses and the effects are considerably greater, and the side effects are fewer. Response to intrathecal baclofen must be confirmed by a screening trial before implantation of a pump for chronic infusion. Intrathecal baclofen reduces spasticity in the upper and lower extremities and is often associated with improved gait and upper extremity function. Quality of life improves for patients and caregivers. The Medtronic pump has been exceedingly reliable and typically functions for 4 or 5 years. The currently available intrathecal catheter is associated with far fewer complications than the initial catheter. Baclofen overdoses are unusual and are usually caused by pump programming errors rather than pump malfunction. Preliminary studies suggest that continuous intrathecal baclofen infusion reduces generalized dystonia in cerebral palsy. Screening to determine response of dystonia to intrathecal baclofen is by continuous infusion. The doses required to reduce dystonia are higher than those for cerebral spasticity. Additional investigations are underway to quantify the effects of continuous intrathecal baclofen infusion on communication, disability, and dystonia.


Abstract: Baclofen, a gamma-aminobutyric acid agonist, acts at the spinal cord level to impede the release of excitatory neurotransmitters that cause spasticity. Oral baclofen improves cerebral spasticity mildly, but its activity is limited because of its poor lipid solubility. Cerebrospinal fluid baclofen levels after intrathecal administration are many times higher than those achieved after oral administration. Continuous intrathecal baclofen infusion has been used to treat cerebral spasticity in two patient groups: in older ambulatory children with inadequate underlying leg strength, and in patients with severe spasticity in both the upper and lower extremities. Responsiveness to intrathecal baclofen is confirmed by test injections before insertion of a programmable subcutaneous pump. Continuous intrathecal baclofen infusion dosages vary from 27 to 800 micrograms/day. Continuous intrathecal baclofen infusion reduces spasticity in the upper and lower extremities, and improves upper extremity function and activities of daily living but has no effect on athetosis in the dosages used to treat spasticity. Complications related to the intrathecal catheter occur in approximately 20% of patients, and infection requiring pump removal occurs in approximately 5%. Preliminary studies indicate that continuous intrathecal baclofen infusion alleviates some forms of generalized dystonia associated with cerebral palsy.


Abstract: To determine the plasma baclofen concentrations of children undergoing continuous intrathecal baclofen infusion for treatment of cerebral spasticity, we assayed plasma samples from six children, 8 to 18 years of age, who were receiving intrathecal baclofen at constant rates of 77 to 400
micrograms/day. Plasma levels were at or below the limit of quantification (10 ng/mL) in all patients.


Abstract: Pharmacological interest in the tripeptide thyrotropin-releasing hormone (TRH) is due to the multiple effects it produces. In fact, apart from taking part in regulating the activity of the hypothalamo-pituitary-thyroid axis, TRH produces various neuropharmacological effects which indicate a biological role that is probably more important than that of a releasing hormone. Trials performed in animals have shown, for example, the dose-dependent capacity of TRH to induce analgesia, probably by interacting with the opioid peptide system. Motor activity is affected by TRH. In fact this tripeptide elicits an increase in spontaneous motor and explorative activities by interacting with the dopaminergic neurotransmitter system at the nucleus accumbens level. The neuropharmacological activities of TRH include an interesting arousal effect and an analeptic action on generalized depression of the CNS whether this depression is of natural origin, such as hibernation, or induced pharmacologically (barbiturates, ethanol) or of a traumatic origin (coma). This analeptic action is attributable to stimulation of cholinergic neurons in the septo-hippocampal area and to the presence of terminals containing TRH in the lateral septum and TRH receptors concentrated especially in the medial septum and diagonal band of Broca. It has also been suggested that TRH localized in the pineal gland has a part in activating the neuronal mechanisms of arousal. Associated with the arousal effect and especially evident in variously originated shock conditions are the activating effects of TRH on vegetative functions (body temperature, circulation, the gastrointestinal tract). These stimulatory activities on the CNS were the rationale for therapeutic use of TRH in the initial treatment of coma due to brain trauma and for the treatment of endogenous depression. A most interesting property of TRH is that of counteracting the neurological deficit due to experimental lesion of the spinal cord particularly with regard to spasticity and ataxia. Electrophysiological trials have shown that TRH depolarizes the motoneurons in frog spinal cord thereby increasing the monosynaptic reflex. Furthermore, TRH has recently been shown to have a trophic effect on cultures of rat fetus spinal cord. On this basis TRH has been used successfully for the treatment of amyotrophic lateral sclerosis (Charcot’s syndrome) and spinocerebellar degeneration. Further support for this therapeutic strategy is given by the demonstration that deafferentiation of rat spinal cord produces an increased density of TRH spinal receptors. Recent studies have also given encouraging results on the possible therapeutic use of TRH for the treatment of Alzheimer's disease. (ABSTRACT TRUNCATED AT 400 WORDS)

Abstract: We examined the 123I-iodoamphetamine SPECT for 3 patients with ALS, who were clinically diagnosed. Patient 1 was a 31-years-old man, who had bilateral muscle weakness of his upper extremities, and spasticity in lower extremities. Patient 2 was a 51-years-old woman, who had marked weakness of her upper extremities and bulbar sign. Patient 3 was a 68- years-old man, who had severe degree of marked weakness of his upper extremities and mild bulbar signs. Cerebral cognitive function were all normal in three patients. Computed tomographic and magnetic resonance imagings showed moderate degree of cortical atrophy in patient 1, but no abnormalities in patients 2 and 3. In 123I-IMP SPECT, however, hypoperfusion were recognized on the bilateral fronto-parietal border zone areas in these three patients with ALS. It was suggested that patients with ALS showed varying degrees of impaired perfusion in the fronto-parietal border zone areas in spite of normal cognitive functions.


Abstract: Satoyoshi syndrome is a very rare disease of unknown etiology, characterized by intermittent painful muscle spasms, alopecia, multiple epiphyseal changes, diarrhea and endocrine disorders. We administered intravenous gammaglobulin to a 7-year-old girl with Satoyoshi syndrome. Frequency of muscle spasms and the titers of antinuclear antibody and anti-DNA antibody decreased. This is the first report of gammaglobulin therapy of Satoyoshi syndrome. We suggest that this illness could be related to an autoimmune mechanism.


Abstract: Management of severe spasticity in children is often a difficult problem. Orally administered medications generally offer limited benefits. This study examines the value of intrathecally administered baclofen in the treatment of 19 children with severe spasticity of cerebral origin: eight of whom sustained brain injury associated with trauma, near drowning, or cardiac arrest; 10 with cerebral palsy (spastic quadriplegia); and one child with Leigh’s disease. At the time of entry into the study, patients ranged from 4 to 19 years of age, and all were completely dependent on caretakers for activities of daily living. Children who responded positively to a trial dose of intrathecal baclofen underwent insertion of
a drug delivery system for continuous infusion. This was followed by a double-blind trial of baclofen or placebo and follow-up review at 3 and 6 months, and yearly thereafter. Seven children did not undergo pump implantation because of excess sedation or poor response. The 12 remaining children have been followed for a period of 1 to 5 years. Favorable responses were present in all 12 children as determined by the Ashworth Scale, with the greatest benefit being reduction of lower limb tone. Except in the case of one child who had reduction in lower limb tone that resulted in difficulty with transfers, the caretakers all reported significant benefits from intrathecal baclofen, with improvement in muscle tone, behavior, sitting, and general ease of care being most commonly noted. Central side effects were seen in some children who received continuous intrathecal baclofen infusion and included hypotension (two patients), bradycardia (two), apnea or respiratory depression (two), and sedation (one). During a total of 568 months of pump operation there were 10 mechanical complications, including two related to pump or side port failure and eight related to catheter kinks, extrusions, or dislodgment. Pump pocket effusion occurred in five children and a cerebrospinal fluid fistula was seen in one child. Local infection occurred in three children and meningitis in two children. The results demonstrate the potential value of continuous intrathecal baclofen infusion for treatment of severe spasticity of cerebral origin. However, this treatment can result in significant complications and more experience is required before the long-term benefits can be determined.


Abstract: As mentioned previously, both MS and PML are demyelinating conditions of the CNS and pose diagnostic difficulties in their differentiation because of similarities in their clinical findings. However, certain features unique to each of these diseases are helpful in clinical diagnosis. MS, unlike PML, is a disease of unknown cause. Polygenetic influences in combination with exposure to an environmental agent and immune-mediated factors may be operative in the pathogenesis of MS. Age of onset peaks in the third to fourth decades with a predominance in women, as contrasted with PML, which peaks in the fifth to sixth decades in most non-AIDS-associated cases with a slight predominance in men. MS is more prevalent in areas farther from the equator: North America, Europe, Australia, and New Zealand. Common initial symptoms seen in MS include bilateral limb weakness (with the legs being affected twice as often as the arms), hyperreflexia, spasticity, optic neuritis, diplopia, incoordination, and paresthesias. (Paresthesias are typically found in the lower limbs in a symmetric pattern, but
may follow no obvious anatomic distribution and often do not correspond to the
distribution of sensory symptoms. Vibration and position sense are more
frequently disturbed than pain and temperature.) Intellectual impairment and
mental deterioration are uncommon early in MS, whereas they are a more
frequent initial presentation in PML. In addition, the presence of speech
impairment and monoparesis or hemiparesis with homonymous hemianopsia is
more suggestive of PML. Brain stem involvement is infrequent.


Baclofen suppresses bursting activity induced in hippocampal slices by differ-
Abstract: Epileptiform activity was induced in area CA3 of hippocampal slices by
superfusion of medium containing 50 microM bicuculline and 3.5 mM K, 50
microM bicuculline and 5 mM K, 50 nM kainic acid and 3.5 mM K, or 7 mM K.
Burst potentials were recorded at rates between 5 and 44/min, depending on the
convulsant treatment. Baclofen reduced the frequency of burst firing in all slices
tested in a dose-dependent manner, with little change in the morphology of
individual bursts. Thus baclofen primarily affected the initiation of epileptiform
discharges. IC50 values varied between 27 and 500 nM and were positively
correlated with the rate of bursting. These experiments indicate that baclofen, at
concentrations present in the CSF of patients treated for spasticity, has an
anticonvulsant-like effect in the hippocampal formation and suggest that its mode
of action is to reduce the excitability of pyramidal cells.

Botulinum toxin injection as an adjunct when planning hand surgery in children
with spastic hemiplegia. Neuropediatrics 31, 4-8.
Abstract: The usefulness of botulinum toxin A treatment when planning hand
surgery in eight children with spastic hemiplegia was evaluated. The hand
function of the children was assessed before and after treatment using a test
battery consisting of quantitative and qualitative functional assessment. The
results of preoperative botulinum treatment supported surgical intervention in four
children and serial botulinum treatment in three children. In one child, the
preoperative botulinum treatment provided no additional information. We
conclude that preoperative botulinum A treatment in most children with spastic
hemiplegia, for whom hand surgery is being considered, identifies the patients
who would not benefit from the planned surgery or for whom the functional
benefit would probably not outweigh the burden of surgical procedure and
postoperative rehabilitation.

Abstract: The mechanism of nonhemorrhagic neurological deterioration from spinal arteriovenous malformation (AVM) and the role of acute surgical intervention in this setting are not well understood. The case is described of a 65-year-old man who presented with a 2-year history of mild gait spasticity and vague sensory complaints affecting both lower extremities. Following a diagnostic lumbar puncture, these symptoms progressed painlessly over a 4-day period to total motor paraplegia, urinary retention, and hypesthesia in all modalities with a midthoracic sensory level. Magnetic resonance imaging showed a probable spinal AVM but no evidence of hemorrhage or cord compression. Spinal angiography confirmed the diagnosis of spinal AVM fed by radicular branches of left T-7 and T-8 segmental intercostal arteries. Drainage was via long dorsal veins caudally. Emergency laminectomy with intradural exploration was performed. There was no evidence of prior hemorrhage or focal mass effect, although the cerebrospinal fluid pressure was elevated. The dural component of the spinal AVM was excised, and its communications with the spinal cord were disconnected intradurally. Neurological function started improving within 6 hours of the patient awakening from anesthesia. He had achieved antigravity strength in every muscle group of the lower extremities by the time of discharge to a rehabilitation center 10 days after surgery. Three months postoperatively, he was ambulating with a walker and was continent of urine and stool. Possible pathophysiological mechanisms are discussed in light of the favorable response to timely surgical intervention

Abstract: Intrathecal baclofen is a very powerful antispastic agent. Its mechanism of action on the monosynaptic H-reflex in spinal patients was investigated. It could inhibit rapidly and profoundly monosynaptic reflexes in lower limbs, but did not modify Ia vibratory inhibition of the soleus H-reflex. To assess more precisely its effect on Ia afferents, an experimental paradigm using Ia heteronymous facilitation of the soleus H-reflex was used. Intrathecal baclofen did not modify the amount of monosynaptic facilitation of the soleus H-reflex brought about by stimulation of the femoral nerve. This demonstrates that the main part of the inhibitory effect of baclofen on the H-reflex in spinal patients is not due to a presynaptic effect, suggesting a postsynaptic site of action

Azouvi P., Mane M., Thiebaut J.B., Denys P., Remy-Neris O., and Bussel B. (1996) Intrathecal baclofen administration for control of severe spinal spasticity:

Abstract: OBJECTIVES: To assess long-term efficacy and functional benefits of intrathecal baclofen for severe spinal spasticity. DESIGN: A prospective before-after trial. SETTING: A neurological rehabilitation department of a university hospital. Pump implantation was realized in neurosurgery; follow-up was carried out mostly on an outpatient basis. PATIENTS: Eighteen patients with severe and disabling spinal spasticity received intrathecal baclofen by an implantable pump; average follow-up was 37.4 months (range, 9 to 72). MAIN OUTCOME MEASURES: Spasticity (Ashworth and spasms frequency scores); disability (Functional Independence Measure [FIM]). RESULTS: A significant decrease in tone and spasms was observed in all patients. Tolerance appeared during the first 6 to 9 months. Later on, efficacy remained stable, except in cases of mechanical problems of the pump or catheter. Functional assessment found a highly significant (p < .001) increase of FIM score (particularly for bathing, dressing lower body, transfers, and in some cases, locomotion). This was particularly marked in patients with thoracic spinal cord lesion. In cases of severe upper limb dysfunction, FIM was only improved for wheelchair displacements, due to a better sitting position, but nursing became easier and life comfort was enhanced. Severe side effects (overdose) were observed in two cases.

CONCLUSION: Efficacy remained stable after 6 to 9 months. Marked improvement of functional independence was observed in paraplegic patients. Improvement was less spectacular in patients with severe upper limb dysfunction, but nevertheless appreciable in terms of life comfort and use of attendants.


Abstract: Cold induced arterial vasospasm was studied in ten patients with single digit replantation, by measuring finger systolic pressure at different finger temperatures. Each patient was examined three times; within 2 weeks of surgery, after 1 year and after 3 years. The replantations were performed using long arterial and venous grafts. Cold-related vasospasm is established during the first year after trauma, and thereafter seems to be persistent. It is concluded that the subjective cold tolerance, which affects all patients after digital amputation regardless of whether replantation is performed or not, is partly due to vasospasm. It is less pronounced in patients without pathological vasospasm in the replanted digit. Cold intolerance is likely to decrease during the first 2 years after replantation, but not to disappear completely.

Abstract: A yin-yang hypothesis is presented linking noradrenergic activity, thromboxane, melatonin, left hemisphere functioning, and cyclic AMP on the one hand, and dopamine, beta-endorphin, calcium, right hemisphere functioning, and cyclic GMP on the other. It is further suggested that there is a yoking of NA, TXA2, serotonin and melatonin in the left hemisphere, and a similar yoking of DA, BE, calcium and cGMP in the right. Evidence is presented to support the hypothesis that each element (NA, TXA2, etc.) on one side can modulate or balance a corresponding element (DA, BE, etc.) on the other. It is suggested that thromboxane is the key element in noradrenergic overactivity and that not taking this into consideration has confounded much prior research. This theory takes into account information processing models as well as pharmacological data and neurochemical theory on coupling of adenylate cyclase to its hormone receptors. Inhibiting noradrenergic overactivity can be obtained by inhibiting thromboxane and concomitantly activating opiate receptors. This protocol may have clinical utility in treating a wide range of disorders such as: anxiety, depression, schizophrenia, sleeplessness, withdrawal states, enuresis, Gilles de la Tourette syndrome, Parkinsonism, Alzheimers, dementia, anorexia, infant ruminations, essential tremor, spasticity of spinal cord injury, diarrhoea, ulcerative colitis, extrapyramidal symptoms, akathisia, neuroleptic malignant syndrome, attention deficit disorder, hyperhidrosis, and possibly AIDS.


Abstract: Prolonged immobilization, such as occurs after the spinal cord injury (SCI), results in several physiological problems. It has been demonstrated that the standing posture can ameliorate many of these problems. Standing exercise can be efficiently performed by the help of functional electrical stimulation (FES). The first application of FES to a paraplegic patient was reported by Kantrowitz in 1963. It was later shown by our group that standing for therapeutic purposes can be achieved by a minimum of two channels of FES delivered to both knee extensors. The properties of the stimulated knee extensors (maximal isometric joint torque, fatiguing, and spasticity) were not found as sufficient conditions for efficient standing exercise. According to our studies, the ankle joint torque during standing is the only parameter which is well correlated to the duration of FES assisted standing. For good standing low values of the ankle joint torque are required. To minimize the ankle joint torque the lever belonging to the vertical reaction force must be decreased. Adequate alignment of the posture appears to be the prerequisite for efficient FES assisted and arm supported standing exercise. Some patients are able to assume such posture by themselves, while many must be aided by additional measures. At present, surface stimulation of
knee extensors combined with some appropriately "compliant shoes" looks to be adequate choice

Bakay B., Nissinen E., Sweetman L., Francke U., and Nyhan W.L. (1979) Utilization of purines by an HPRT variant in an intelligent, nonmutilative patient with features of the Lesch-Nyhan syndrome. Pediatr. Res. 13, 1365-1370. Abstract: The patient, H.Chr.B., was among the first reported with hyperuricemia and central nervous system symptoms. He has been found to have a variant of hypoxanthine guanine phosphoribosyl transferase (HPRT; E.C.2.4.2.8) distinct from the enzyme present in patients with the Lesch-Nyhan syndrome. The patient had choreoathetosis, spasticity, dysarthric speech, and hyperuricemia. However, his intelligence was normal and he had no evidence of self-mutilation. There was no activity of HPRT in the lysates of erythrocytes and cultured fibroblasts when analyzed in the usual manner. Using a newly developed method for the study of purine metabolism in intact cultured cells, this patient was found to metabolize some 9% of 8-14C-hypoxanthine, and 90% of the isotope utilized was converted to adenine and guanine nucleotides. In contrast, cells from patients with the Lesch-Nyhan syndrome were virtually completely unable to convert hypoxanthine to nucleotides. The patient's fibroblasts were even more efficient in the metabolism of 8-14C-guanine, which was utilized to the extent of 27%, over 80% of which was converted to guanine and adenine nucleotides. The growth of the cultured fibroblasts of this patient was intermediate in media containing hypoxanthine aminopterin thymidine (HAT), whereas the growth of Lesch-Nyhan cells was inhibited and normal cells grew normally. Similarly in 8-azaguanine, 6-thioguanine, and 8-azahypoxanthine, the growth of the patient's cells was intermediate between normal and Lesch-Nyhan cells. These observations provide further evidence for genetic heterogeneity among patients with disorders in purine metabolism involving the HPRT gene. They document that this famous patient did not have the Lesch-Nyhan syndrome

Baker D., Pryce G., Croxford J.L., Brown P., Pertwee R.G., Huffman J.W., and Layward L. (2000) Cannabinoids control spasticity and tremor in a multiple sclerosis model. Nature 404, 84-87. Abstract: Chronic relapsing experimental allergic encephalomyelitis (CREAE) is an autoimmune model of multiple sclerosis. Although both these diseases are typified by relapsing-remitting paralytic episodes, after CREAE induction by sensitization to myelin antigens Biozzi ABH mice also develop spasticity and tremor. These symptoms also occur during multiple sclerosis and are difficult to control. This has prompted some patients to find alternative medicines, and to perceive benefit from cannabis use. Although this benefit has been backed up by small clinical studies, mainly with non-quantifiable outcomes, the value of cannabis use in multiple sclerosis remains anecdotal. Here we show that cannabinoid (CB) receptor agonism using R(+)-WIN 55,212, delta9-tetrahydrocannabinol, methanandamide and JWH-133 (ref. 8) quantitatively ameliorated both tremor and spasticity in diseased mice. The exacerbation of these signs after antagonism of the CB1 and CB2 receptors, notably the CB1
receptor, using SR141716A and SR144528 (ref. 8) indicate that the endogenous cannabinoid system may be tonically active in the control of tremor and spasticity. This provides a rationale for patients' indications of the therapeutic potential of cannabis in the control of the symptoms of multiple sclerosis, and provides a means of evaluating more selective cannabinoids in the future.


Abstract: Spasticity is a complicating sign in multiple sclerosis that also develops in a model of chronic relapsing experimental autoimmune encephalomyelitis (CREAE) in mice. In areas associated with nerve damage, increased levels of the endocannabinoids, anandamide (arachidonylethanolamide, AEA) and 2-arachidonoyl glycerol (2-AG), and of the AEA congener, palmitoylethanolamide (PEA), were detected here, whereas comparable levels of these compounds were found in normal and non-spastic CREAE mice. While exogenously administered endocannabinoids and PEA ameliorate spasticity, selective inhibitors of endocannabinoid re-uptake and hydrolysis—probably through the enhancement of endogenous levels of AEA, and, possibly, 2-arachidonoyl glycerol—significantly ameliorated spasticity to an extent comparable with that observed previously with potent cannabinoid receptor agonists. These studies provide definitive evidence for the tonic control of spasticity by the endocannabinoid system and open new horizons to therapy of multiple sclerosis, and other neuromuscular diseases, based on agents modulating endocannabinoid levels and action, which exhibit little psychotropic activity.


Abstract: BACKGROUND AND PURPOSE: We sought to define an effective and safe dose of botulinum toxin type A (Dysport) for the treatment of upper limb muscle spasticity due to stroke. METHODS: This was a prospective, randomized, double-blind, placebo-controlled, dose-ranging study. Patients received either a placebo or 1 of 3 doses of Dysport (500, 1000, 1500 U) into 5 muscles of the affected arm. Efficacy was assessed periodically by the Modified Ashworth Scale and a battery of functional outcome measures. RESULTS: Eighty-three patients were recruited, and 82 completed the study. The 4 study groups were comparable at baseline with respect to their demographic characteristics and severity of spasticity. All doses of Dysport studied showed a significant reduction.
from baseline of muscle tone compared with placebo. However, the effect on functional disability was not statistically significant and was best at a dose of 1000 U. There were no statistically significant differences between the groups in the incidence of adverse events. CONCLUSIONS: The present study suggests that treatment with Dysport reduces muscle tone in patients with poststroke upper limb spasticity. Treatment was effective at doses of Dysport of 500, 1000, and 1500 U. The optimal dose for treatment of patients with residual voluntary movements in the upper limb appears to be 1000 U. Dysport is safe in the doses used in this study

Abstract: Botulinum toxin A (BTX-A) is widely used in the management of muscle spasticity in children. However, at present the dose of BTX-A for a given patient is selected empirically. The aim of this study is to provide dosage guidelines that are based on risk/benefit assessment. This was a multicentre retrospective study of the safety profile and efficacy of BTX-A in children with chronic muscle spasticity. Data in 758 patients who received a total of 1594 treatments were analysed (mean age 7.2 years; 429 males, 329 females). Spastic cerebral palsy (CP) was the most common diagnosis (94% of the study sample). Of all treatments 7% resulted in adverse events; incidence was related to the total dose rather than the dose calculated on the basis of body weight. The highest incidence of adverse events was observed in patients who received >1000 IU of BTX-A per treatment session. The odds of an adverse event was 5.1 times greater for this group of patients than for those who had 250 IU or less (p<0.001). A good overall response to treatment was reported in 82% and treatment goals were fully or partially achieved in 3% and 94% of participants respectively. More patients in the highest dose group reported functional deterioration. Interestingly, multilevel treatments resulted in a better response than single-level treatments (odds ratio 1.7, 95% CI 1.3 to 2.2,p=0.001)


Abstract: 16 subjects with severe spasms secondary to traumatic and nontraumatic myelopathy underwent epidural spinal cord stimulation. 4 patients had a complete motor and sensory spinal cord lesion. 6 of the subjects with an incomplete spinal cord lesion were ambulatory. All patients had previously undergone extensive trials with medications and physical therapy. All 14 subjects in whom a satisfactory placement of the electrode could be obtained had a reduction in the severity of the spasms. In 6 patients, the spasms were almost abolished. Extremity, trunkal and abdominal spasms were affected. Clonus in the
upper extremities was consistently reduced. Marked improvement in bladder and bowel function was observed in each of 2 subjects. In over 1-year follow-up, 5 subjects show persistence of the results, with less stimulation required to maintain the therapeutic effects. No neurological deterioration occurred following the procedure or after long-term spinal stimulation. 1 patient showed after several months of continuous stimulation increased voluntary motor control present only when spinal cord stimulation was activated. Complications included 1 system infection, 1 electrode migration, 1 wire breakage and skin breakdown at a connector site, development of high impedance in 1 electrode and 1 skin breakdown over the lead.

Abstract: Spasms and spasticity constitute a significant problem in spinal cord injured individuals. Surgical intervention may be indicated when spasms and spasticity cannot be satisfactorily controlled by medications and physical therapy. Surgical procedures carried out on the nervous system include neurotomy, rhizotomy, myelotomy, cordectomy and spinal cord stimulation. The various procedures and their indications will be discussed.

Abstract: This article summarizes the experience gained with implantation of 509 plate electrodes performed by a single neurosurgeon. 350 patients were subjected to implantation of plate electrodes in the dorsal epidural space. 227 patients were implanted for chronic pain management (reflex sympathetic dystrophy, failed back syndrome/arachnoiditis, pain following spinal cord injury, nerve injury pain and other miscellaneous pain conditions), 105 patients for motor disorders (spasms/spasticity following spinal cord or head injury, cerebral palsy, multiple sclerosis, spasmodic torticollis and other miscellaneous conditions) and 18 patients for both. A total of 509 electrodes were implanted in the dorsal epidural space. The electrodes types were: 442 Medtronic Resume, 39 Medtronic Resume-TL and 25 Neuromed Lamitrode. 378 electrodes were implanted for chronic pain management, 106 for motor disorders and 25 in patients presenting with both pain and motor disorders. 192 electrodes were implanted in the cervical area and 317 in the thoracic area. 3.7% of the implanted electrodes became infected and had to be surgically removed. Electrode migration occurred in 1.1% of the patients and electrode breakage in 4 patients. 288 (70%) of the implanted electrodes are still being used. Technical factors relevant to the surgical implantation of plate electrodes at various levels in the spine are presented and discussed.

Abstract: Forty-eight spinal cord injury victims were implanted with an epidural
spinal cord stimulation system to treat spasms that had not satisfactorily responded to medical therapy. All the patients were at least 6 months after the injury. The protocol included assessment by independent examiners preoperatively and at 3, 6, 12 and 24 months after the implant. Pre- and postoperative data collection included the frequency and severity of the spasms. Combining the frequency and intensity scores into a 'severity' score provided a more accurate clinical picture. No patient observed neurological deterioration following the surgical procedure or the neurostimulation treatment. A statistically significant reduction in the severity of the spasms was observed in the follow-up evaluations, with results that progressively increased in time. It is appears that spinal cord stimulation is an effective and safe alternative in the management of spasms in spinal cord injury victims. Its exact role in relation to intrathecal baclofen infusion and ablative procedures remains to be defined.


Abstract: Femoral fractures during the physical therapy in two patients with spinal cord injury and consequent osteoporosis in the paralyzed limbs are reported. The fractures were caused by a minor trauma and the spasticity was considered to be an additional factor in the accident. During the physical therapy the patients were seated with hip abduction and flexion of the knee. It is important that the patients participate in a program of physiotherapy. This, however, should be performed under strict control.


Abstract: From the data discussed in this review it appears that GABA receptor agonists exhibit a variety of actions in the central nervous system, some of which are therapeutically useful (Table V). GABA receptor agonists, by changing the firing rate of the corresponding neurons accelerate noradrenaline turnover without changes in postsynaptic receptor density and diminish serotonin liberation with an up-regulation of 5HT2 receptors. These effects differ from those of tricyclic antidepressants which primarily block monoamine re-uptake and cause down-regulation of beta-adrenergic and 5HT2 receptors. The GABA receptor agonist progabide has been shown to exert an antidepressant action which is indistinguishable from that of imipramine in patients with major affective disorders. The fact that: (a) GABA receptor agonists and tricyclic antidepressants affect noradrenergic and serotonergic transmission differently; and (b) tricyclic antidepressants alter GABA-related parameters challenges the classical monoamine hypothesis of depression and suggests that GABA-mediated mechanisms play a role in mood disorders. Decreases in cellular excitability produced by GABAAergic stimulation leads to control of seizures in practically all animal models of epilepsy. GABA receptor agonists have a wide spectrum as they antagonize not only seizures which are dependent on decreased GABA synaptic activity but also convulsant states which are apparently independent of
alterations in GABA-mediated events. These results in animals are confirmed in a wide range of human epileptic syndromes. GABA receptor agonists decrease dopamine turnover in the basal ganglia and antagonize neuroleptic-induced increase in dopamine release. On repeated treatment, progabide prevents or reverses the neuroleptic-induced up-regulation of dopamine receptors in the rat striatum and antagonizes the concomitant supersensitivity to dopaminomimetics. Behaviorally, GABA receptor agonists diminish the stereotypies induced by apomorphine or L-DOPA suggesting that GABAergic stimulation results also in an antidopaminergic action which is exerted beyond the dopamine synapse. These effects of GABA receptor agonists may represent the basis of the antidyskinetic action of these compounds which, however, remains to be fully confirmed. GABA receptor agonists reduce striatal acetylcholine turnover, an effect which occurs at doses much lower than those which affect dopamine neurons. Since hyperactivity of cholinergic neurons plays a determinant role in the pathogenesis of some parkinsonian symptoms, it is conceivable that GABAergic stimulation is effective in ameliorating Parkinson’s disease. (ABSTRACT TRUNCATED AT 400 WORDS)


Abstract: A new drug, Cyclobenzaprine hydrochloride (Flexeril), was compared with diazepam (Valium) and placebo in double-blind trials for efficacy in treating spasms and pain in the neck and low back. Complex recording methods involving clinical evaluations (graded), patient self-ratings, goniometry, motion analysis by computer, electromyography of controlled motions and detailed statistical analysis were used. Clinical improvement over two weeks was statistically significant in all treatment groups with a statistically significant preference for Cyclobenzaprine hydrochloride. The most striking improvements recorded were in the electromyographic findings, which showed statistically significant changes for the Cyclobenzaprine group. Clinical muscle spasms are not accompanied by increased myoelectric activity; the reverse is true. With improvement, myoelectric activity in back muscles is augmented during prescribed stressful movements as measured by electromyography and computer analysis combined with complex electrogoniometry


Abstract: A minor tranquilizer, ketazolam, was tested in a double-blind, randomized, crossover study of 50 patients for its effects in neurologic spasticity. The drug was compared with diazepam (widely accepted as an effective
antispasticity agent) and a placebo. The patients with spasticity were almost all cases of multiple sclerosis (24) or stroke (24). Thirty-nine patients completed the study. There was not statistically significant superiority of either diazepam or ketazolam, but both relieved symptoms significantly better than the placebo, as measured clinically and by electromyographic recording of deep tendon reflexes. Ketazolam is a relatively safe and clinically effective antispasticity agent (especially for patients with multiple sclerosis). The well-known "big 3"--dantrolene sodium, baclofen, and diazepam--produce large and small problems in many individual cases; hence, ketazolam now offers a safe and clinically useful alternative.

Basmajian J.V., Shankardass K., and Russell D. (1986) Ketazolam once daily for spasticity: double-blind cross-over study. Arch. Phys. Med. Rehabil. 67, 556-557. Abstract: This double-blind cross-over study of 14 severely spastic inpatients with chronic multiple sclerosis reveals that once-daily doses of ketazolam, a new drug, are effective in reducing spasticity in a significant proportion of patients without significant side-effects. Added to the similar findings of an earlier double-blind controlled study of divided doses, the results suggest that this special feature of ketazolam provides a unique flexibility that may be exploited in individual cases.

Basmajian J.V. (1991) Special considerations for research with pharmacologic agents. Am. J. Phys. Med. Rehabil. 70, 101-106. Abstract: As physical medicine and rehabilitation becomes more and more complicated, the medical rehabilitation research teams are often bewildered by the sweeping changes occurring in the application of therapeutic drugs for rehabilitation. Society, through the instrument of governmental regulations, dictates that all new treatments must be efficacious before "release."

Bass B., Weinshenker B., Rice G.P., Noseworthy J.H., Cameron M.G., Hader W., Bouchard S., and Ebers G.C. (1988) Tizanidine versus baclofen in the treatment of spasticity in patients with multiple sclerosis. Can. J. Neurol. Sci. 15, 15-19. Abstract: Tizanidine (Sirdalud) was compared to baclofen (Lioresal) in a randomized, double-blind, cross-over trial. Each medication was introduced over a three week titration period and then maintained at the highest tolerated dose for five weeks. The two treatment phases were separated by a one week drug withdrawal and a two week washout period. Sixty-six patients entered the trial and forty-eight completed both treatment phases. At the end of the trial, neurologists and physiotherapists thought that baclofen was superior on the basis of perceived efficacy and tolerance (p less than or equal to 0.05). Although the efficacy of tizanidine or baclofen was judged as good to excellent by 24 and 39% of patients respectively, this difference was not statistically significant. Muscle weakness was the most common adverse effect. This was significantly more troublesome in patients treated with baclofen. Somnolence and xerostomia were more common in patients treated with tizanidine. Both baclofen and tizanidine appear to be useful adjuncts in the treatment of spasticity in patients.
with multiple sclerosis. Preference of either drug is tempered principally by side-effects


Abstract: We assessed the repetitive movement (RM) test for measuring the effect of a trial bolus dose of intrathecal baclofen on spasticity. The RM test measures passive range of motion (ROM) by electrogoniometry and stretch reflex activity (SRA) of the flexors and extensors of the knee and ankle by surface electromyography. The SRA has a dynamic component (dynamic stretch reflex, DSR) and a tonic component (tonic stretch reflex, TSR). Four hypotheses were formulated: (a) RM results show a negative relationship between SRA and ROM; (b) values on the RM test are correlated with clinical scores of tonus and spasticity; (c) RM results show a reduction in SRA after administration of the clinically optimal dose of baclofen; and (d) RM results show a dose-dependent effect of intrathecal baclofen on SRA. Twenty-four patients were selected because they had impairments and disabilities caused by intractable spasticity. A bolus of baclofen was administered with incremental doses (25-150 micrograms) until an optimal effect or no effect was obtained. The main outcome measures were RM test and clinical assessments of the Ashworth and spasm score. The results were (a) For the ankle a negative correlation was found between ROM and TSR of the flexor and extensors; for the knee a significant negative correlation was found only with the DSR of the biceps femoris. (b) A positive correlation was found between the Ashworth score and TSR of the extensors and between the spasm score and DSR and TSR of the gastrocnemius muscle. (c) Significant differences were found between baseline measurements and the optimal dose of baclofen for all measures. (d) A significant dose-dependent effect of intrathecal baclofen on the level of SRA was observed. The RM test is thus a useful clinical tool for objectively measuring the effect of intrathecal baclofen administration on spasticity in patients with an upper motor neuron syndrome.


Abstract: Deep venous thrombosis (DVT) of the upper extremity (UE) is an uncommon diagnosis, whereas DVT of the lower extremity is a well-known cause of morbidity and mortality in the rehabilitation patient. Patients with UE DVT secondary to venous stasis, vessel wall abnormalities, hypercoagulability, venous instrumentation and cancer have been previously reported in the literature. To our knowledge no case of DVT in a spastic upper extremity has been noted. A case report of a patient with UE DVT in a spastic extremity
secondary to traumatic brain injury is presented, with a discussion of the aetiology, diagnosis and management of this disorder

Abstract: The inhibitory glycine receptor of mammalian spinal cord is a ligand-gated chloride channel that, on affinity purification, contains two subunits of 48-kilodalton (kD) and 58-kD molecular mass in addition to an associated 93-kD protein. Ligand-binding 48-kD subunit and 93-kD protein were quantified in the CNS of the adult rat using a newly developed dot receptor assay (detection limit less than or equal to 1 fmol/assay) which employs monoclonal antibodies specific for glycine receptor polypeptides. The 93-kD protein was found to codistribute at a fixed stoichiometry with the 48-kD subunit throughout the CNS of the rat. Moreover, the 93-kD protein cofractionated with the ligand-binding subunit on solubilization and affinity chromatography or immunoprecipitation. However, both proteins were separated on sucrose gradient centrifugation of detergent extracts of spinal cord membranes in accord with earlier observations on purified receptor. These data prove that the 93-kD polypeptide is selectively associated with the membrane core of the strychnine-sensitive glycine receptor. The regional distribution of glycine receptor polypeptides was also determined in the CNS of the spastic rat mutant. In contrast to hereditary spasticity in mouse and cattle, no reduction of glycine receptors was found in the spastic rat


Abstract: We have investigated the influence on the excitability of lumbar motoneurons of 5-hydroxytryptamine (5-HT), substance P and thyrotropin-releasing hormone (TRH), three substances which coexist in the same bulbospinal descending pathway and end in large part around motoneurons. We have also studied the effect of clonidine, an alpha 2 noradrenergic agonist. This was done in spinalized rats (T5) treated three weeks before with 5-7-dihydroxytryptamine. Under those circumstances 5-HTP (I.P.), 5-HT (intrathecally) TRH (I.P. or I.T.) and substance P (I.T.) all elicited a strong excitation of motoneurons as measured by integrated EMG of the hindlimb muscles. Substance P reduced by almost half the subsequent response to 5-HTP, 1 hour and 24 hours later. TRH given acutely did not modify the response to 5-HTP but given chronically for twenty one days by means of Alzet minipump, markedly increased the response to 5-HTP. Clonidine by itself decreased the excitability of motoneurons and antagonized the excitatory effect of 5-HTP and
TRH. In a pilot trial, cyproheptadine, a 5-HT antagonist was shown to decrease the manifestations of spasticity in patients with a partial spinal lesion. Clonidine also appears to be of potential use in the treatment of spasticity.

Beliaev V.I. (1988) [Electrophysiologic assessment of the spastic syndrome in patients with a traumatic lesion of the spinal cord]. Zh. Nevropatol. Psikhiatr. Im S. S. Korsakova 88, 91-93. Abstract: In 34 patients general electromyography was used to assess the duration of muscle spastic contraction. H-reflex values ratio before and after vibration was calculated. These 2 techniques allowed a quantitative evaluation of spasticity.


Bennett D.J., De Serres S.J., and Stein R.B. (1996) Regulation of soleus muscle spindle sensitivity in decerebrate and spinal cats during postural and locomotor activities. J. Physiol 495 (Pt 3), 835-850. Abstract: 1. In order to study fusimotor control in reduced preparations, soleus muscle spindle afferents were recorded in premammillary decerebrate cats (n = 15) during crossed extensor reflexes and, after spinalization, during locomotion produced by either clonidine or L-beta-3,4-dihydroxyphenylalanine (L-DOPA). The soleus muscle was oscillated sinusoidally (0.25 mm, 4 Hz) and the afferent mean firing rate and modulation were calculated. An increase in firing rate was assumed to arise from activity in dynamic gamma-motoneurones (dynamic gamma-drive) when associated with an increase in modulation to stretching, and in static gamma-motoneurones (static gamma-drive) when modulation decreased. 2. At rest in all preparations the firing rate and modulation in primary muscle spindle afferents were generally much higher than after de-efferentation (ventral root section), suggesting a predominant dynamic gamma-drive. Clonidine decreased and even eliminated this presumed resting gamma-drive in many afferents, both in the decerebrate (7 of 8) and the spinal (6 of 18) state. This effect on gamma-drive may account, at least in part, for its suppressive effect on spasticity in humans. 3. When locomotion commenced in clonidine-treated spinal cats, primary afferents generally fired with much higher mean rates (+121%) and lower sensitivities (-32%), suggesting a large increase in static gamma-drive (possibly accompanied by a small decrease in dynamic gamma-drive). These high rates were usually maintained tonically throughout the step cycle. However, a third of the afferents were silenced during locomotor contractions, and de-efferentation had no significant effect on their firing rates. Thus, for some spindles alpha-activity can occur without significant gamma-drive. 4. During locomotion in L-DOPA-treated spinal cats the inferred static gamma-drive only occurred phasically, coactivated with the EMG, though it could precede the EMG by 100-500 ms. In the flexion phase both the afferent rate and modulation were lower than before locomotion, suggesting a lack of effective gamma-drive. 5. Crossed extensor reflexes in decerebrate cats also produced a substantial increase in primary afferent firing rate (+187%) and decrease in
sensitivity (-37%), again suggesting increased static gamma-drive (n = 18). This gamma-drive was largely independent of EMG activity and often occurred without alpha-activity. The mean firing rate of secondary muscle spindle afferents increased significantly during locomotion (with L-DOPA) and crossed extensor reflexes, again indicating increased static gamma-drive. Clonidine reduced or eliminated the gamma-drive in seven of eight afferents during crossed extensor reflexes. In conclusion, although there are some common features, such as a predominant static gamma-drive in all walking preparations, the pattern of static and dynamic gamma-drive is not closely linked to alpha-activity under the conditions studied. As well as gamma-drive without alpha-activity, we have shown for the first time that alpha-motoneurones can be activated without significant gamma-drive to many spindles during behavioural tasks.


Abstract: Staphylococcal meningitis associated with implantation of an intrathecal drug pump for spasticity was successfully treated by intrathecal vancomycin delivered by the same pump. This produced high CSF antibiotic levels, and the pump and catheter system did not have to be removed. We are unable to identify a similar case reported in the literature to date.


Abstract: BACKGROUND. Amyotrophic lateral sclerosis is a progressive motor neuron disease for which there is no adequate treatment. Some research suggests that the excitatory amino acid neurotransmitter glutamate may be involved in the pathogenesis. METHODS. To evaluate the efficacy and safety of the antiglutamate agent riluzole, we conducted a prospective, double-blind, placebo-controlled trial in 155 outpatients with amyotrophic lateral sclerosis. The dose of riluzole was 100 mg per day. Randomization was stratified according to the site of disease onset (the bulbar region or the limbs). The primary end points were survival and rates of change in functional status. The main secondary end point was change in muscle strength. Analyses were undertaken after 12 months of treatment and at the end of the placebo-controlled period (median follow-up, 573 days). RESULTS. After 12 months, 45 of 78 patients (58 percent) in the placebo group were still alive, as compared with 57 of 77 patients (74 percent) in the riluzole group (P = 0.014). For patients with bulbar-onset disease, one-year survival rates were 35 percent (6 of 17) with placebo and 73 percent (11 of 15) with riluzole (P = 0.014), whereas for those with limb-onset disease one-year survival was 64 percent and 74 percent, respectively (P = 0.17). The survival
advantage with riluzole was smaller (37 percent [29 of 78] with placebo vs. 49 percent [38 of 77] with riluzole) at the end of the placebo-controlled period, but it remained significant in the overall population (P = 0.046) as well as in the patients with bulbar-onset disease (18 percent [3 of 17] vs. 53 percent [8 of 15], P = 0.013). The deterioration of muscle strength was significantly slower in the riluzole group than in the placebo group (P = 0.028). Adverse reactions to riluzole included asthenia, spasticity, and mild elevations in aminotransferase levels. Twenty-seven patients in the riluzole group withdrew from the study, as compared with 17 in the placebo group. CONCLUSIONS: The antiglutamate agent riluzole appears to slow the progression of amyotrophic lateral sclerosis, and it may improve survival in patients with disease of bulbar onset.

Bentivoglio A.R. and Albanese A. (1999) Botulinum toxin in motor disorders. Curr. Opin. Neurol. 12, 447-456. Abstract: Advances in the clinical use of botulinum neurotoxins continue. Of interest to the neurologist is the advanced practice in the treatment of focal dystonia and the new developments on other dyskinesias and on autonomic control of smooth muscle motility. New toxin serotypes are now being tested; their availability will improve clinical practice and will possibly lead to combined treatments. Indications in spasticity and in juvenile cerebral palsy are now under scrutiny. The combination of focal chemodenervation with specific rehabilitation procedures enables new development in this field.

Berg-Johnsen J., Roste G.K., Solgaard T., and Lundar T. (1998) [Continuous intrathecal infusion of baclofen. A new therapeutic method for spasticity]. Tidsskr. Nor Laegeforen. 118, 3256-3260. Abstract: Intrathecal administration of baclofen is now generally accepted as a powerful treatment of spasticity caused by spinal lesions. 35 patients with severe spasticity, 29 of spinal origin and six of supraspinal origin resistant to conservative treatment, had a programmable pump (Synchromed, Medtronic) for continuous intrathecal baclofen infusion implanted. The patients were followed-up for an average of 29 months (0- 68). The initial effect of the treatment was positive for all patients; spasms were less frequent, there was remission of pain caused by cramps, and in some cases improved ambulation. In five patients, however, the pump was later removed: in two patients the pump ceased to be effective, two patients became infected, and one experienced multiple catheter problems. Problems with the catheter was the most common complication experienced, and this was seen in nine patients. Three patients died of the underlying disease. The majority of patients became accommodated to intrathecal baclofen and it was necessary to administer increasingly larger doses to maintain the clinical effect. Long-term control of spinal spasticity by intrathecal baclofen can be achieved in most patients, but close follow-up is necessary for assessing efficacy and refilling the pump.

Abstract: A case of cervical radiation myelopathy following telecobalt-radiation therapy to the cervical lymph-nodes in Hodgkin’s disease is described. After a latent period of 3 months neurological symptoms presented with a pure spastic paraparesis of the upper extremities. Diagnosis was confirmed neuropathologically. A review is given on clinical signs of cervical radiation myelopathy

Abstract: After a clarifying outline on the most recent anatomo-physiopathologic acquisitions about muscular tone and spasticity, the Author presents the results of a prolonged administration (three months) which was daily controlled, in an Institute for dyskinetic subjects. At the dose of 1 mg/kg/die during the first week, 2 mg/kg/die during the second week and 3 mg/kg/die during the third and the following ones (total posology pro die divided into 3 post-prandium administrations), Dantrolene was administered to 16 subjects of both sexes, whose average age was 13, who presented marked spasticity sometimes accompanied by dystonia. An evaluation was given on these parameters: 1) spasticity estimated in three degrees according to Morosini, 2) passive articular movement (wideness and easiness of maximum excursion), 3) capability of voluntary decontraction, 4) motoricity of relation (motorial difficulty) and 5) dystonic component if present. As a global results, out of 16 cases, nine improved (56%) and seven (44%) remained unaltered. Since the drug resulted to be inefficacious in all cases with dystonia, the global improvement recorded among "pure spastics" rised to 66% of cases. Neither intolerances nor negative secondary effects were noticed

Abstract: Baclofen is particularly effective in treating spasticity of spinal origin in humans. However, most investigations of this drug in animals have only assessed its antinociceptive effect, presumably because of the difficulty in developing animal models of spasticity. This study attempted to evaluate both, the antinociceptive and antispastic action of (-)-baclofen (the more active enantiomer) by incorporating the chronic spinal preparation, in which spasticity gradually develops following spinal transection. Separate groups of intact, acute (1 day) or chronic (20-25 days) spinal rats were pretested on the nociceptive tail-flick (TF) assay prior to either subcutaneous (SC; 1-30 mg/kg) or intrathecal (IT; 0.1-12 micrograms) injection of (-)-baclofen and retested at specific post-injection intervals. Hindlimb spasticity was elicited in chronic spinal rats by mechanical stimulation to the abdomen. Because the clinical use of baclofen generally involves chronic administration, both responses were tested for 3 successive
days to assess tolerance. Results confirmed the analgesic effect of SC and IT (-)-baclofen in intact rats. As previously reported, the antinociceptive effect of IT (-)-baclofen was increased in acute spinal rats. However, three weeks after spinalization there was a profound decrease in this response. In contrast, antinociception produced by SC (-)-baclofen was reduced in acute and chronic spinal rats compared to intact animals; but there was no difference between the acute and chronic conditions. In spite of this differential decrease in antinociception after IT, relative to SC, administration, both routes of administration produced an antispastic effect in chronic spinal rats. There was no antinociceptive tolerance to SC administration and only minimal tolerance to IT (-)-baclofen (in intact rats); the antispastic effect did not become tolerant. A peripheral action might explain the dichotomy between SC and IT (-)-baclofen in regard to antinociception. However, further research is needed to determine why both routes of administration were effective against spasticity while only SC (-)-baclofen retained an antinociceptive action in chronic spinal rats.


Abstract: A double-blind study was carried out in 105 patients with chronic spasticity associated with hemiplegia in order to compare the efficacy and tolerability of tizanidine with that of diazepam. Dosage was increased progressively, if tolerated, to a maximum of 24 mg tizanidine or 30 mg diazepam per day at the end of 2 weeks. The optimum dosage was then maintained for 6 weeks. Efficacy and tolerability parameters were assessed after 2 and 8-weeks' therapy. Patients on tizanidine but not those on diazepam showed a statistically significant improvement in functional status, as assessed by walking distance on flat ground. Analysis of the stretch reflex in four groups of muscles showed that both tizanidine and diazepam reduced the duration of contractions and increased the angle at which contraction occurred, but there were no significant differences between the two drugs. Clonus of the triceps surae resolved in 48% of tizanidine and 40% of diazepam patients. Evaluation of the effect of therapy revealed an improvement with each drug in approximately 83% of patients, with the overall evaluation being slightly (but non-significantly) in favour of tizanidine. There were fewer discontinuations of treatment in the tizanidine group as a result of side-effects. It would appear, therefore, that tizanidine is an effective and well-tolerated drug in the treatment of cerebral spasticity.


Abstract: OBJECTIVES--Spasticity can contribute to poor recovery of upper limb function after stroke. This is a preliminary evaluation of the impact of botulinum toxin treatment on disability caused by upper limb spasticity after stroke. METHODS--Seventeen patients with severe spasticity and a non-functioning arm were treated with intramuscular botulinum A neurotoxin (median age at treatment
54.5 years; median time between onset of stroke and treatment 1.5 years). Baseline and assessments two weeks after treatment were compared to assess efficacy. The duration of improvement in disability was documented. Outcome measures used were; passive range of movement at the shoulder, elbow, wrist, and fingers; modified Ashworth scale to assess spasticity of biceps and forearm finger flexors; an eight point scale to assess the degree of difficulty experienced by the patient or carer for each functional problem defined before treatment; the presence of upper limb pain. The biceps, forearm finger flexors, and flexor carpi ulnaris were treated with intramuscular botulinum toxin. Up to a total dose of 400-1000 mouse units (MU) of Dysport (Speywood) or 100-200 MU of BOTOX (Allergan) was used in each patient. RESULTS--Functional problems reported by the patients before treatment were difficulty with cleaning the palm, cutting fingernails, putting the arm through a sleeve, standing and walking balance, putting on gloves, and rolling over in bed. Hand hygiene improved in 14 of 17 patients; difficulty with sleeves improved in four of 16; standing and walking balance improved in one of four; shoulder pain improved in six of nine; wrist pain improved in five of six. Passive range of movement at shoulder, elbow, and wrist improved after treatment. Benefit was noted within two weeks and lasted one to 11 months. No adverse effects occurred. CONCLUSION--This preliminary study suggests that intramuscular botulinum toxin is a safe and effective treatment for reducing disability in patients with severe upper limb spasticity.


Abstract: OBJECTIVES: After stroke, abnormal arm posture due to spasticity in a functionally useless arm may interfere with self care tasks. In these patients botulinum toxin treatment presents an opportunity to reduce disability. The purpose was to investigate whether reduction in spasticity after botulinum toxin treatment translates into reduction in disability and carer burden. METHODS: Forty patients with stroke with spasticity in a functionally useless arm (median duration 3.1 years) were randomised to receive intramuscular botulinum toxin type A (BT-A; Dysport) (n=20) or placebo (n=20) in a total dose of 1000 MU divided between elbow, wrist, and finger flexors. Spasticity (using the modified Ashworth scale), muscle power, joint movement, and pain were assessed. Disability and carer burden were measured using an eight item and a four item scale respectively. Two baseline and three post-treatment assessments (weeks 2, 6, and 12) were made. Concurrent treatments as far as possible remained unchanged and not optimised. RESULTS: Disability improved at week 6 with BT-A compared with placebo. This effect, present at week 2, wore off by week 12. Reduction in carer burden was seen at week 6 with BT-A and continued for at least 12 weeks. Forearm flexor spasticity was reduced with BT-A up to 12 weeks after treatment. Although significant improvement in elbow flexor spasticity was seen at week 2 with BT-A compared with placebo, this effect was not evident at weeks 6 and 12. Arm pain was not improved after BT-A. Grip strength was
reduced with BT-A. No serious BT-A related adverse effects were reported.

CONCLUSION: BT-A is useful for treating patients with stroke who have self care difficulties due to arm spasticity. The decision to treat should also include relief of carer burden. As muscle weakness may occur, its potential impact on functional activities must be assessed before intervention.


Abstract: Since Botulinum toxin A became a mainstay therapy for blepharospasm, its use in treating other dystonic conditions, spasticity disorders, as well as hyperfunctional lines of the face has increased exponentially in recent years. The following article summarizes our experience in establishing a safe and reliable method of administration of botulinum toxin A for treating hyperfunctional lines of the face.


Abstract: Spasticity, flexion and extension spasms occur after lesions of motor descending pathways. Three different mechanisms can explain these disorders of tone: pure muscular alterations, segmental synaptic sprouting and liberation of spinal reflex activity. This last mechanism, which is also the most classically described has been studied long ago. Amongst all hypotheses which can explain spasticity (hyperexcitability of alpha motoneuron, gamma motoneuron, or reduction of presynaptic inhibition) reduction of presynaptic inhibition is the only one to have been clearly demonstrated. A new treatment is proposed: intrathecal Baclofen. It seems to act by reducing the excitability of alpha motoneuron.


Abstract: 1 Full-wave rectification and integration of the EMG signal recorded from the hamstring muscles of the spastic mouse was used to evaluate the actions of a variety of drugs on the muscle rigidity of these mutants, animals in which no histological lesion has yet been found. 2 Profound and long-lasting muscle relaxant responses were consistently observed upon the injection of diazepam (2 mg/kg, i.p.) and flunitrazepam (2 mg/kg, i.p.). Such responses were always greater than those obtained upon injection of 40% (v/v) propylene glycol (10 ml/kg) alone, the vehicle for the benzodiazepines. 3 The muscle relaxant action of a low dose (0.25 mg/kg i.p.) of the benzodiazepine Roll-6896 was not shared by the same dose of its enantiomer Roll-6893. 4 Profound and long-lasting muscle relaxation was caused by sodium valproate (696 mg/kg, i.p.). Consistent muscle relaxant responses were also observed upon the injection of pentobarbitone (30 mg/kg, i.p.), but not phenobarbitone (30 mg/kg, i.p.). 5 Other drugs that had little or no detectable effect on the muscle rigidity of the spastic...
mouse included diphenylhydantoin (30 mg/kg, i.p.) and bromocriptine (10 mg/kg, s.c.) while, in some animals, benztrapine (2 mg/kg, i.p.) and baclofen (10 mg/kg, i.p.) increased muscle rigidity. The development of full muscle relaxant responses to flunitrazepam (2 mg/kg, i.p.) and to sodium valproate (696 mg/kg, i.p.) was shown to depend upon mild warming of the animals with radiant heat, a procedure which can increase muscle spindle afferent input to the spinal cord. The results suggest a hyperactivity of stretch reflexes in the spastic mouse, ameliorated selectively by those drugs that enhance the GABA-mediated presynaptic inhibition of such pathways.

Biscoe T.J. and Duchen M.R. (1986) Synaptic physiology of spinal motoneurones of normal and spastic mice: an in vitro study. J. Physiol 379, 275-292. Abstract: Spinal cord reflexes have been examined in a preparation of the mouse spinal cord maintained in vitro. Responses of the motoneurone population of normal and spastic mutant mice to stimulation of a segmental dorsal root were compared. In the normal spinal cord, a monosynaptic response with very little polysynaptic excitation was typical. In the mutant, the monosynaptic response was typically followed by a depolarizing wave on which asynchronous compound action potentials were superimposed. In some spastic cords, an oscillating depolarizing wave was seen, lasting up to 500 ms. The stimulus range from threshold to maximal response was the same for the normal and mutant. The dorsal root reflex (d.r.r.) and dorsal root potential (d.r.p.) were prominent in both normal and mutant, and no consistent difference could be identified. Intracellular recordings were made from motoneurones using electrodes filled with potassium acetate. Mean resting potentials and input resistances were not significantly different in mutant and normal mice. The voltage-dependent conductances, seen as the after-depolarization and after-hyperpolarizations following antidromic action potentials and the responses of motoneurones to depolarizing current injection were similar in both populations. The synaptic responses of motoneurones following stimulation of the segmental dorsal root were clearly abnormal in the mutant. In the normal mice, a monosynaptic excitatory postsynaptic potential (e.p.s.p.), seen at low stimulus intensities, was followed at higher stimulus intensities by polysynaptic activity lasting up to 100 ms, which rarely reached threshold for action potential discharge. In the mutant mice, the monosynaptic response was typically followed by depolarizing synaptic responses which often evoked action potentials before the monosynaptic response reached threshold. At higher stimulus intensities, the monosynaptic response was followed by at least one and often multiple action potentials generated on prolonged depolarizing synaptic activity. When cells were impaled with potassium-acetate-filled electrodes, very little spontaneous synaptic activity was seen in either normal or mutant mice. Spontaneous depolarizing postsynaptic potentials (p.s.p.s) were prominent in normal motoneurones when potassium chloride was used to fill electrodes and were increased in amplitude by ionophoresis of chloride into the cells. Under these conditions stimulation of a ventral root evoked a depolarizing p.s.p. and the Renshaw i.p.s.p. reversed. The
spontaneous p.s.p.s were blocked by ionophoresis or bath application of the glycine antagonist strychnine. (ABSTRACT TRUNCATED AT 400 WORDS)

Abstract: The previously described anti-spastic effect of oxcarbazepine and 10,11-di hydro-10-hydroxy carbamazepine was found accidentally in 2 patients undergoing a double-blind comparative study for evaluation of antiepileptic effect. In this study oxcarbazepine was given orally in doses of 300-2700 mg daily to one patient with transverse myelitis and to two patients with multiple sclerosis, all of whom had clinically disabling spasticity in the form of difficulty in walking, lower limb rigidity, spastic contractions of the lower limbs and ankle clonus. Anti-spastic effect was observed at doses between 600-1200 mg daily and consisted in a substantial decrease in the above symptoms of spasticity. The anti-spastic effect appears at a dose immediately below that which produces nausea, dizziness and somnolence


Abstract: Cardiac arrest due to hyperkalaemia following suxamethonium in a patient with generalized spasticity due to head injury is reported and discussed


Abstract: Clinically, phenol is used often as a neurolytic agent to treat pain and spasticity. The purpose of this study was to examine the time course of denervation and recovery in several hindlimb muscles following application of a 5% aqueous solution of phenol to the sciatic nerve. Phenol was applied to the sciatic nerve of adult female rats either by intraneural or perineural injection. Axonal degeneration was evident within the sciatic nerve 2 days following phenol application, although variable amounts of damage were observed. By 2 weeks, the soleus and tibialis anterior had atrophied to 63% and 51% of control. Reinnervation of hindlimb muscles occurred between 2 and 4 weeks following the nerve block. Following denervation, the soleus became slower in that all of the fibers expressed the slow myosin heavy chain (MHC). At 5 months,
maximum tension of the soleus was 74% of control and the muscle consisted of more fast fibers on average, some of which expressed IIx MHC. These data suggest that 5% phenol causes an injury to the nerve that is more severe than a crush injury, and that reinnervation of denervated muscles may be by motoneurons other than those that originally innervated the muscles.


Abstract: The treatment of severe tetanus generally requires prolonged mechanical ventilation. We describe two cases managed with continuous intrathecal infusion of baclofen via a subcutaneous tunnelled spinal catheter and an abdominal injection port. Baclofen, by diminishing spasms and spasticity, allowed reduced sedation and paralysis requirements. This potentially decreases the time and resources required for intensive care management. Complications include sedation, hypotension and CSF infection. After appropriate dose adjustment, baclofen improves the management of severe tetanus.


Abstract: Potential advantages of intramuscular botulinum toxin for the treatment of spasticity include the lack of sensory effects, ability to target specific muscle groups, ability to weaken muscles in a graded fashion and absence of caustic chemicals such as phenol. We describe the use of botulinum toxin for the treatment of severe lower extremity spasticity in two subjects with multiple sclerosis. Both subjects showed an improvement in spasticity, as measured by the modified Ashworth scale, and in functional status. Both subjects exhibited reductions in muscle tone not only in injected muscles, but also in noninjected muscles in the region. These more distant clinical effects have not been emphasized in previous studies after therapeutic injections of botulinum toxin. Further research is needed to clarify the cause and prevalence of these regional motor effects, as well as to further examine the safety and efficacy of botulinum toxin for spasticity treatment.


Abstract: Spasticity is a disabling symptom of MS that is enhanced during interferon beta-1b (IFNbeta-1b) treatment. Nineteen patients with primary progressive MS were treated with IFNbeta-1b; an additional 19 patients did not receive this treatment. Thirteen of the 19 patients treated with IFNbeta-1b had increased spasticity requiring increased antispasticity drug administration. This observation suggests that further studies are needed before interferons can be so widely used in primary progressive MS patients.


Abstract: Spasticity is an expression of a damage of the motor neurone associated with velocity dependent increase of the muscle tone. Since 1986 21 patients with severe spasticity mainly in multiple sclerosis were treated with an implantable pump system to administrate continuously Baclofen intrathecally. Even with a very small dosage of Baclofen patients who were previously treated until intoxication without success there was a favorable reduction in spasticity. Therefore we propose to perform this procedure before using surgical methods or stimulating methods.


Abstract: Multiple doses of delta 9-tetrahydrocannabinol (THC) capsules (Marinol) and THC hemisuccinate suppositories were administered in 24-hour intervals to 2 patients with organically caused spasticity. After oral doses of 10-15 mg THC, peak plasma levels from 2.1 to 16.9 ng/ml THC and 74.5 to 244.0 ng/ml 11-nor-9-carboxy-delta 9-tetrahydrocannabinol (THC-COOH, major THC metabolite) were measured by GC/MS within 1-8 h and 2-8 h, respectively. After rectal doses of 2.5-5 mg THC, peak plasma levels from 1.1 to 4.1 ng/ml THC and 6.1 to 42.0 ng/ml THC-COOH were measured within 2-8 h and 1-8 h, respectively. The bioavailability resulting from the oral formulation was 45-53% relative to the rectal route of administration, due to a lower absorption and higher
first-pass metabolism. The effect of THC on spasticity, rigidity, and pain was estimated by objective neurological tests (Ashworth scale, walking ability) and patient self-rating protocols. Oral and rectal THC reduced at a progressive stage of illness the spasticity, rigidity, and pain, resulting in improved active and passive mobility. The relative effectiveness of the oral vs. the rectal formulation was 25-50%. Physiological and psychological parameters were used to monitor psychotropic and somatic side-effects of THC. No differences in the concentration ability, mood, and function of the cardiovascular system could be observed after administration of THC.


Abstract: With the introduction of the antispasticity agent, tizanidine hydrochloride (Zanaflex), physicians have requested information about the optimal way to switch appropriate patients from baclofen to tizanidine. A group of neurologists and rehabilitation specialists with a particular interest in spasticity was therefore asked to draw up a suitable approach to changing treatment.


Abstract: A 65-year-old white male with acute myelogenous leukemia received whole brain irradiation (2550 rads) and intrathecal cytosine arabinoside for CNS prophylaxis. Bone marrow remission had been previously achieved with systemic chemotherapy (vincristine, Adriamycin, prednisone, and cytosine arabinoside). Two weeks following the last intrathecal cytosine arabinoside treatment, the patient developed a spastic paraparesis requiring the use of a walker. A gas myelogram was normal and CSF examination revealed a protein of 50 mg/100 ml but was otherwise unremarkable. Five months later, the patient had improved in that he could stand on his own. A relapse of his leukemia subsequently occurred and the patient died the following month. Striking degenerative changes were found in the spinal cord at postmortem examination. These included microvacuolization, axonal swellings, and loss of myelin with scattered macrophages laden with fat.


Abstract: Botulinum toxin type A (BTX-A) has been shown to be a safe and effective treatment for focal or segmental muscle overactivity, including spasticity. Local injections of BTX-A are particularly valuable in relieving focal spasticity around a joint or a series of joints. When integrated into an overall
spasticity treatment plan with clearly outlined functional goals, BTX-A may offer significant benefits to the appropriately selected adult or pediatric patient. A range of clinical outcome measures are used to evaluate the patient prior to injection. Initial dosing guidelines are offered, though each patient may have a unique drug response profile and set of modifying factors that will be used as a basis for dose adjustments. Clinical benefit usually lasts for approximately 12 weeks, though in some patients the duration of effect may be longer. Assessment of the patient's clinical and functional status is performed at each follow-up appointment, and the contribution of BTX therapy to the goals of the patient and caregiver are evaluated. Other therapeutic options should be considered where appropriate, and the treatment plan revised when necessary. Guidelines for dilution, handling, and office procedure are offered.


Abstract: Diazepam is widely prescribed for persons with spinal cord injury (SCI) to treat muscular spasticity. To assess the current usage of diazepam in those persons with SCI being followed by the Department of Veterans Affairs Medical Centers (DVAMCs), a survey was mailed to all 23 DVAMCs that have specialized SCI Services. We discovered that no policy regarding the prescription of benzodiazepines existed at 65 percent of the SCI Services. At 70 percent of the SCI Services, diazepam or another benzodiazepine was routinely prescribed. One-third of patients were estimated to have taken diazepam for greater than 10 years and an additional 37 percent for six to 10 years. Despite the potential for addiction, only 10 of the 23 SCI Services reported having a program to encourage discontinuation of diazepam use; a 20 percent success rate was reported in withdrawing this medication. A need for greater understanding with regard to the prescription of diazepam exists and strategies for its withdrawal should be considered. Appropriate guidelines for its use in patients with SCI and spasticity should be developed.


Abstract: The administration of baclofen, a GABAb agonist, by direct infusion into the CSF by means of a programmable device, may avoid the undesired side effects of the oral administration of both the same and other antispastic drugs while giving a marked reduction of spasticity. The preliminary results on 12 patients show the total efficacy of this procedure in reducing spasticity markedly

Abstract: The Marinesco-Sjogren syndrome is an autosomal recessive degenerative disorder characterized by congenital cataracts, cerebellar ataxia, spasticity, mental deficiency, and skeletal abnormalities. We studied two adult siblings with Marinesco-Sjogren syndrome using anatomic and metabolic brain imaging techniques to characterize the pattern and nature of abnormalities in the brain. Computed tomographic and magnetic resonance imaging showed diffuse brain atrophy of mild to moderate degree, involving primarily the white matter of the cerebrum, cerebellum, brain stem, and cervical spinal cord. The pattern of atrophy resembled that seen in diffuse leukoencephalopathies. Measurements of local cerebral glucose metabolic rates with positron emission tomography revealed no statistically significant differences from normal control subjects in most regions, but metabolic rate was decreased in the thalamus in one patient. The findings support a diffuse white matter disorder in Marinesco-Sjogren syndrome.


Abstract: On the basis of previous experimental and clinical studies patients with severe spasticity due to spinal cord damage from multiple sclerosis in 8 cases and posttraumatic paraplegia in 6 and resistant to all conservative treatments were selected for a trial with morphine and baclofen administered intrathecally through a catheter placed in the spinal subarachnoid space rostral to the affected segments and attached to a subcutaneous reservoir. Whereas morphine single injection did not show any benefit, baclofen bolus injection 30 to 60 micrograms, revealed a marked decrease of spasticity and associated symptoms in 8 cases. After checking the clinical effect during 3 weeks and changes in electroneurophysiological studies and bladder manometry the catheter was attached to a subcutaneous programmable pump able to be refilled percutaneously and administered baclofen continuously or more often following a multistep complex programme in total doses of 90 to 150 micrograms per day. After a mean follow-up of 5 months all cases showed an absence of spasms and pain, a notable improvement for bettering of sphincter functions and a marked muscle relaxation that improves motor capacity, leading to increased ambulation or mobility. Neither complications nor side-effects were observed.


Abstract: On the basis of previous experimental and clinical studies, 14 patients with severe spasticity due to central or spinal cord damage, resistant to all
conservative treatments, were selected after a percutaneous trial period for chronic intrathecal baclofen infusion by programmable pumps. The agent was delivered at C4 in quadriplegic patients or in cases with central spasticity and in the neighbouring areas on the affected segments in paraplegic patients. The daily baclofen dose varied from 25 to 260 micrograms and was infused in a bolus, continuously infused or both combined according to the results during the trial period. After a mean follow-up period of 11 months, constant decrease of rigidity, absence of spasms, improvement of bladder function, cramping pain remission, and moderate improvement in walking capacity and transfer activities were usually observed. Neither complications nor side effects were noted.

Abstract: A regional technique for the study of curare sensitivity has been applied to patients with Duchenne type muscular dystrophy, myotonic disorders, certain lower motor neurone disorders, to patients with weakness in the arm after hemiplegia, to patients with hyper-reflexia and hypertonia without weakness, and to Parkinsonism. In the dystrophy patients, sensitivity to curare differs from normal controls in that the neuromuscular block persists. The possibilities that this latent defect of neuromuscular transmission is the result of acetylcholine deficiency due to a prejunctional defect or the result of alterations in the property of the postjunctional membrane are discussed. In the myotonic and lower motor neurone disorders, curare sensitivity was similar to that of normal controls. After hemiplegia, the affected side shows resistance to curare when compared with the unaffected side. In states of hyper-reflexia and hypertonia, however, the sensitivity to curare is greater than in normal controls. In Parkinsonism, sensitivity is similar to that of the controls. The results in upper motor neurone lesions are discussed in relation to the dependence of neuromuscular transmission upon the motor neurone, which, in turn, is dependent upon descending impulses.

Abstract: Two cases of multiple sclerosis are described, in both of whom the disease started in young adult life. This disability gradually progressed to the stage of paraplegia-in-flexion in which the lower limbs were fixed in adduction-and-flexion. Both patients developed painful muscle spasms which made life intolerable. These patients were treated by intrathecal phenol in glycerine in an effort to convert this spastic paralysis into a flaccid paralysis. The three advantages sought were: 1. To relieve the muscle spasms so that the patient could sit in a wheelchair and propel herself. 2. To relieve the pain of the spasms. 3. To allow access to the perineum for proper hygienic care of bladder and bowel function. The first patient obtained an excellent result (Figures 1, 2, 3) but blocks had to be repeated after approximately five months. The second patient after the block developed a good result in the right leg, but still had mild, but painless...
spasms in the muscles of the left leg (Figures 4 and 5). However, she was able to use a wheelchair and was discharged to a chronic hospital where she died of bulbar paralysis six months later. Intrathecal phenol thus appears to be a useful method for relieving muscle spasms and pain in the lower extremities in advanced cases of multiple sclerosis.

Bruck J. and Tshabitscher H. (1973) [Open clinical testing of 7-chlor-1-(cyclopropylmethyl)-1, 3-dihydro-5 phenyl-2H-1, 4 benzodiazepine-2-one(Prazepam) in the indication as tranquilizing and antispastic agent]. Nervenarzt 44, 547-549.


Abstract: Myotonic discharges in rats given 20, 25-diazacholesterol hydrochloride and fibrillation discharges in denervated rat muscle both were silenced by procaine hydrochloride, tetrodotoxin or ischemia, or potassium chloride (after initial activation). They both were activated by succinylcholine, but only the fibrillations were silenced by alpha- bungarotoxin or atropine sulfate. It is hypothesized that fibrillations and diazacholesterol-induced myotonia are mediated through mechanisms involving ionic channels, that both can be produced by activation of the junctional/nonjunctional acetylcholine receptors (or some mechanism coupled to the receptors), but that an unfettered alpha- bungarotoxin- binding portion of the acetylcholine-receptor molecule and an unblocked atropine-binding site are obligatory only for production of fibrillations.


Abstract: Denervation, provoked at the turn of the century and abandoned because of inconstant results, has again been taken up in principle, but with a notable change in technique. It is necessary to do a careful examination of the muscles that are to be denervated (of the median and ulnar nerves) and to determine the nature of the spasticity. The incision, longer than in the original technique, allows a better view of the median and ulnar nerves. The nerve branches to each muscle are thus easily identified, and by electric stimulation during the operation one judges how much denervation to subject the muscles to while taking into account the phenomenon of the take-over of the denervated muscles by the remaining nerve fibers. Part of the nerve branches are then sectioned under microscopic control near the muscle, taking care to cauterize the proximal stump. It may be necessary to do associated tenotomies or capsulotomies. This method gives good results if the technique and the contraindications, (athetosis, chorea and cerebral deficits) are respected. It must be emphasized that the results depend on the degree of denervation, which is hardly quantifiable, and is subject to the operator's experience.


Abstract: The neuroprotective effects of the NMDA antagonists MK-801 and ketamine were analyzed in a mutant strain of Han-Wistar rats which develop neurodegeneration in the hippocampus and cerebellum. Previous experiments have shown that the progressive neuronal degeneration observed in this mutant may be the result of a dysfunctional glutamatergic system. For MK-801 studies, mutants were injected in a chronic paradigm with (+)MK-801 or its weaker acting isomer (-)MK-801 at a dose of 1 mg/kg. Ketamine studies consisted of both acute (50 mg/kg once) and chronic (10 mg/kg multiple times) injection paradigms. MK-801-treated mutants exhibited longer life spans (8-23%) compared to saline-injected mutants. Ketamine-injected mutants in both paradigms also lived slightly longer (6-9%) than the saline mutants. Motor skill deterioration was monitored in an open-field test, and after 50 days of age the MK-801 and ketamine mutants displayed over 20% greater motor skill activity than the saline mutants. In the cerebellum, mutants treated with ketamine and both forms of MK-801 had 10-20% more Purkinje cells surviving at 55 days than the saline mutants. Further, the density of CA3c pyramidal hippocampal neurons in ketamine and MK-801-treated mutants as compared to saline mutants appeared to be greater upon qualitative analysis. This study shows that these mutants derive some protective effects from the NMDA antagonists MK-801 and ketamine, confirming glutamate-induced excitotoxicity as a possible cause of neuronal degeneration in this mutant strain of rat. Copyright 2001 S. Karger AG, Basel


Abstract: A large kindred, in which either Leber's hereditary optic atrophy, or a hereditary spastic dystonia, or a combination of both manifested over many generations was restudied after the first report on it in 1964. NMR scans revealed bilateral, and, in two patients with hemidystonia, unilateral necrosis with shrinkage of the putamen, in one case associated with total disappearance of the head of the caudate nucleus. Except for age-appropriate cortical atrophy in one instance, no other changes were observed in the brain, brainstem, and cerebellum. The putaminal necrosis appears as typical "striatal slits" on the NMR scans. It is argued that this rare disease, since the princeps description in 1964 only reported in England (1986) and the U.S.A (1986), is most likely a singular
type of mitochondrial encephalopathy: it is associated with Leber's optic atrophy, and the NMR changes observed have been signalled in other mitochondrial encephalomyelopathies, such as Leigh's disease and MELAS.


Abstract: The implantable pump field is now more than 20 years old. The original goal of developing a totally artificial beta-cell remains unrealized, but programmable insulin pumps that contain all of the elements of the artificial beta-cell except the glucose sensor are involved in clinical trials in the United States and are commercially available in Europe. Currently, both single-rate and programmable implantable pumps are in general clinical use in the United States for the treatment of pain and spasticity, cancer, and osteomyelitis. Only a few of the potential applications of implantable pumps have been developed to the stage of commercial availability. This is, in part, because drug companies have traditionally developed parenteral drug applications only as a last resort and, in part, because of the complexity of the regulatory process for implantable pumps, often requiring review by both the drug and device branches of the Food and Drug Administration.


Abstract: Intramuscular injections of botulinum toxin (Botox) are followed by a dose-dependent focal paresis which can be used to treat several focal movement disorders. Botox injections are recommended as effective for the treatment of blepharospasm, hemifacial spasm, and cervical dystonia (torticollis). Focal dystonias elsewhere (for example, writer's cramp) can often be treated with similar success. Others, such as oromandibular dystonia, are more difficult to treat. In the case of more generalized dystonias, some focal muscle spasms can be treated with success by local intramuscular injections. New indications are still being investigated, for example in focal tremors and spasticity. Side effects are in general slight and disappear at the end of toxin effect. In general, it is necessary to repeat the injections after a couple of months, due to a cessation of effect after regrowth of nerve terminals. New injections have similar effects even over years of treatment.


Abstract: The efficacy of a selective fusimotor suppressant, the phenothiazine (+/-)-10-3-dimethylamino-2-methyl(propyl)-2-valeroylphenothiazine, has been assessed in a double-blind crossover trial in eight patients suffering from cerebral spasticity and one patient suffering from spinal spasticity. Dosage was 40 mg daily. Independent clinical and electromyographic methods of assessment were used. The active agent produced a small but significant reduction in spasticity, although this was of clinical value in only a few patients. There were few side-effects. It is recommended that further studies using higher dosages be undertaken.


Abstract: We report a case of inadvertent overdose of baclofen given intrathecally resulting in coma. This was unresponsive to flumazenil and required supportive intensive therapy. With the increasing use of baclofen intrathecally for spasticity and its wide interpatient dose variability, there is a need to find a safe antagonist to baclofen for routine medical use.


Abstract: The reproducibility of coronary vasospasm was assessed in nine patients with complete remission of vasospastic angina by medical treatment by reexamination at intervals of mean [+/-SD] 5.7 +/- 0.9 years. Twenty-one segments were defined as spastic, demonstrating more than 90% narrowing after acetylcholine injection at the initial angiography. The degree of spasticity, type of spasm (diffuse or focal) and coronary artery diameter in these segments at the initial and follow-up studies were compared. Of the 21 segments, 17 (81%) still had some spasticity (> 25%) at the follow-up study and 8 (38%) of these 17 showed spasticity with greater than 90% narrowing. On the other hand, spasm was not reprovoked in 4 (19%) segments. Luminal diameter of the spastic segments decreased significantly at the follow-up study (2.52 +/- 0.83 vs 2.26 +/- 0.62 mm, p = 0.01), but percentage stenosis was not different between the initial and follow-up studies (9.1 +/- 7.2 vs 10.3 +/- 8.0%, NS). The reproducibility of the type of spasm provoked was 83%. Coronary vasospasticity persists to some
extent in spite of complete remission of angina by medical treatment, and the type of spasm provoked has high reproducibility. Therefore, the cessation of drug treatment should be done carefully.


Calne S. (1993) Local treatment of dystonia and spasticity with injections of botulinum- A toxin. Axone. 14, 85-88. Abstract: The use of botulinum-A toxin will be described in two conditions—the extrapyramidal syndrome of dystonia and the pyramidal deficit, spasticity. There is no cure for dystonia and its cause is unknown. Drug therapy is unpredictable and dose-limiting side effects frequently occur with little or no alleviation of symptoms. Spasticity of adductor muscles in the lower limbs causes profound disability and major nursing problems in patients with chronic disorders of the pyramidal tract. As in the case with dystonia, drug therapy is unsatisfactory. At the UBC Movement Disorders Clinic treatment with botulinum-A has been applied to over 400 patients since 1985. The results of the first studies using this treatment in spasmodic torticollis (the most common form of focal dystonia) and spasticity (in late stage multiple sclerosis) will be discussed. As well the effects of long term treatment will be addressed. Botulinum-A toxin is approved treatment for strabismus, blepharospasm and hemifacial spasm. Approval for its use in other focal dystonias is anticipated. The very nature of the agent used for treatment requires that patients be well prepared and reassured before they undergo their first treatment. There is a wide gulf between the patients' preconceived notions about the treatment and reality.

Campbell S.K., Almeida G.L., Penn R.D., and Corcos D.M. (1995) The effects of intrathecally administered baclofen on function in patients with spasticity. Phys. Ther. 75, 352-362. Abstract: The purpose of this article is to review the literature on the effects of intrathecally administered baclofen on impairment in spasticity and muscle activation patterns, on functional limitations in mobility and self-care, and on disability in daily life roles. We found plentiful evidence of improvement in spasticity, spasms, and bladder function and some reports of improved patterns of muscle activation and kinematics of single-joint movement. Improved ability to accomplish transfers, self-care, and locomotion is less consistently studied but has also been reported in about 60% to 70% of patients. Evidence of improved quality of life is primarily anecdotal but may be found in 10% to 30% of patients.
We conclude that research protocols should be developed to clarify effects on control of voluntary movement, functional limitations, and quality of life.


Abstract: Cat spinal cord monosynaptic activity during slow repetitive stimulation (0.2 Hz) and post-tetanic potentiation was used to evaluate the combination effects of phenytoin and chlorpromazine. The drug effects were compared in anesthetized cats with either high spinal transection or intact central nervous systems to determine whether the drugs were acting segmentally or suprasegmentally. When chlorpromazine and phenytoin were given in combination to intact animals, the depressant effect on the monosynaptic response was limited to 50% of control, which was not more than the maximum effect of either drug given alone. In spinal animals, chlorpromazine reversed the phenytoin-induced depression during 0.2 Hz stimulation, whereas only the effects of phenytoin on post-tetanic potentiation were evident after the drug combination. These results show that although phenytoin and chlorpromazine each have a depressant effect on spinal cord transmission, the combined effect is limited to a 50% decrease in intact animals. It is suggested that this occlusive drug effect demonstrates that the drug combination has a limited depressant action in the intact nervous system, an action which permits the expression of the effects of these drugs on the other elements of the reflex arc. Collectively, these actions of the drug combination are consistent with their known efficacy in treating certain cases of spasticity.


Abstract: The use of intramuscular alcohol in treating cerebral-palsied children has led to reduced spasticity for varying periods of time, although the periods diminish with each subsequent injection. During the period of reduced spasticity there is an opportunity for therapists and orthopaedic surgeons to determine whether corrective surgery is indicated. The injections have produced no adverse effects.


Abstract: BACKGROUND: Idiopathic or HTLV-1 associated progressive spastic paraparesis does not have a clear etiology or treatment. AIM: To assess the
effects of a medication containing cytidinmonophosphate, uridintriphosphate and vitamin B 12 in the treatment of progressive spastic. PATIENTS AND METHODS: Patients with the disease were randomly assigned to receive the Nucleus CMP forte (containing dysodic cytidinmonophosphate 5 mg, trisodic uridintriphosphate 3 mg and hydroxicobalamin 2 Mg) tid or placebo during six months. Gait, spasticity, degree of neurogenic bladder and somatosensitive evoked potentials were assessed during treatment. RESULTS: Forty six patients aged 25 to 79 years old were studied, 24 were female and 29 HTLV-1 positive. Twenty two were treated with the drug and the rest with placebo. Gait and spasticity improved in 7 of 22 patients receiving the drug and 1 of 24 receiving placebo (p < 0.05). Neurogenic bladder improved in 10 of 22 receiving the drug and 4 of 24 receiving placebo (NS) Somatosensitive evoked potentials improved in four of seven patients treated with the drug and in two of seven treated with placebo. CONCLUSIONS: The medication caused a modest improvement in patients with progressive spastic paraparesis and was free of side effects


Abstract: A large epidemic of spastic paraparesis in Mozambique during a drought was attributed to cyanide exposure from cassava. Active surveillance in one of the villages most affected by the epidemic detected four new cases in the first year after the epidemic, and none in the second year. In apparently healthy schoolchildren in the same village, surveillance of urinary thiocyanate concentration, an indicator of cyanide exposure, showed high peak values of 1175 and 673 mumols l-1 in succeeding years, with a gradual return to near-normal values in the third year. A marked seasonal variation in thiocyanate concentration was present, with the highest value coinciding with the dry season, the period of the epidemic, and the cassava harvest. Lower values were found in the neighbouring unaffected semi-urban centre. As cassava cultivation increases in many drought-affected countries, we recommend monitoring urinary thiocyanate concentration to estimate cyanide exposure and identify populations at risk for spastic paraparesis epidemics

Abstract: Spasticity is one of the major problems affecting the outcome of rehabilitation in paraplegic patients. Orphenadrine citrate possesses an effective muscle relaxant action in many pathologies. Nevertheless, despite a recognized central site of action, no controlled data are available on its use in the treatment of spastic hypertonia in patients with spinal cord injuries. Therefore, the effect of intravenous administration of 60mg of orphenadrine citrate versus placebo on
spastic hypertonia after spinal cord injury was studied in 11 patients. The threshold of the flexion reflex of the lower limb was studied as a neurophysiological correlate of spastic hypertonia. Clinical assessment was made using the Ashworth Spasticity Scale. The threshold, expressed in mAmp, was studied for 60 minutes after the treatment. A significant difference was found using the active drug compared with placebo (p < 0.0001). In 9 patients, the reduction of the abnormal flexion responses after orphenadrine appeared to begin only after 30 minutes. In one patient the onset of the therapeutic effect was early but weak. One patient with severe spastic hypertonia leading to triple flexion when the limb was manipulated did not gain any relief with orphenadrine. The clinical and neurophysiological results suggest an efficacy of orphenadrine citrate in the control of spastic hypertonia in paraplegics. This could be relevant in the rehabilitation strategy, although further studies are needed on the duration of its action.

Casparry D.M., Rybak L.P., and Faingold C.L. (1984) Baclofen reduces tone-evoked activity of cochlear nucleus neurons. Hear. Res. 13, 113-122. Abstract: Recent evidence suggests that an excitant amino acid may be a neurotransmitter at acoustic nerve synapses in cochlear nucleus (CN). Release of excitant amino acids is reportedly reduced by baclofen, a lipophilic GABA-mimetic used to treat the spasticity of multiple sclerosis and spinal injury. Microiontophoresis of (-)baclofen suppressed spontaneous and tone-evoked activity in CN neurons. GABA inhibited the responses of most neurons responsive to (-)baclofen. However, iontophoresis of these two substances onto the same CN neuron resulted in dramatic differences in time course to maximum effect and to recovery. Onset and offset of (-)baclofen-induced firing reduction were gradual at all doses (currents), but even the highest doses rarely caused total suppression of firing. Inhibition of firing by GABA was abrupt, and total suppression was frequently observed over the range of doses used. GABA desensitization (fading) commonly occurred while the (-)baclofen response never faded. The same CN neurons were also suppressed by D-alpha-aminoadipate, which blocks certain excitatory amino acid receptors, while the GABA antagonist bicuculline had no effect on the (-)baclofen response. These findings support the hypothesis that an excitant amino acid may be a transmitter at acoustic nerve synapses in CN.


Abstract: In 19 patients with multiple sclerosis and 1 with subacute sclerosing panencephalitis the mean increase in muscle tonus was found to be 3.1 (range 1--4 according to Burke-Ashwort). In 10 controls with multiple sclerosis the mean spasticity was 2.4. Dantrium was given in doses up to 800 mg for 14--16 days and it caused a greater reduction of spasticity than placebo (p less than 0.05). In 12 patients (60%) varying degrees of muscle tonus reduction was observed. In 11 patients the effect of Dantrium was compared with that of other drugs (Clonazepam, Tetradiazepam, Carisoprodol and Lyoresal). In 6 cases Dantrium was a more effective drug than other muscle relaxants and in 5 cases no difference was observed or other drugs were superior to Dantrium.


Abstract: From 1972-1974, 228 children began treatment for acute lymphocytic leukemia and were prospectively assessed for neurologic complications. After CNS irradiation (2,400 rad) and intrathecal methotrexate (MTX), they received weekly intravenous maintenance therapy with MTX alone (40- 60 mg/m2; 20 patients) or MTX (10-30 mg/m2) with other drugs (208 patients). Signs of leukoencephalopathy appeared in 11 children (nine without CNS leukemia) after 4-15 months of IV MTX alone, and included lethargy, seizures, spasticity, paresis, drooling, and dementia. Before or during the clinical onset, EEG frequencies slowed (all ten patients tested). Radionuclide scans showed periventricular accumulation of 99mTc (9/11 patients) and remained abnormal for greater than or equal to six months in eight patients. Cranial computed tomograms or neuropathology findings (five patients each) demonstrated leukoencephalopathy (nine patients) and radiation-related microangiopathy (ten patients). Severe neurologic and neuropsychologic dysfunctions were present in four long-term survivors.

Abstract: Intravenous narcotics increase the latency of somatosensory-evoked potentials (SSEPS), which are decreased but not abolished by epidural local anesthetics. In addition, intrathecal narcotics decrease spasticity in patients with central nervous system disease. This study of the effects of intrathecal fentanyl
on posterior tibial SSEPS and the monosynaptic H-reflex arc found that intrathecal fentanyl had no effect on the latency of SSEPS, indicating the effects of narcotics on SSEPS are likely to exist at a supraspinal level. H-reflexes were not affected, confirming the lack of effect on this spinal motor reflex. In the same group of patients, intrathecal lidocaine administered 1 week later completely abolished SSEPS and H-reflexes. Complete suppression of SSEPS corresponded to full motor blockade, but sensation to pain and temperature was already many dermatomes higher than the S1 level. Return of SSEPS occurred with return of motor but not sensory function, indicating the likelihood that SSEPS are carried at least in part by large A-fibers. The study shows that spinal narcotics neither affect the transmission of SSEPS nor decrease the H-reflex, a spinal motor reflex. In addition, changes in SSEPS after intrathecal lidocaine do not correlate with the level of surgical anesthesia.


Abstract: The reduction of spasticity after administration of intrathecal fentanyl, 35 micrograms, and intrathecal lidocaine, 50 mg, was compared with preinjection spasticity levels in ten subjects with central nervous system disease or injury. Spasticity was objectively assessed by an electronic instrument that simultaneously measures degrees of extension and force during passive knee extension. Duration of spasticity relief and adverse effects were recorded. Both drugs equally reduced spasticity and increased the range of motion. There were no supraspinal side effects from the fentanyl, whereas three subjects became hypotensive after receiving lidocaine. The reduction of spasticity with intrathecal fentanyl lasted at least 3 h. The authors postulate that fentanyl reduced spasticity by an effect on spinal pathways. Intrathecal fentanyl should be considered as an alternative to lidocaine for diagnostic blocks in patients with spasticity.


Abstract: Neuromuscular stimulation may facilitate motor recovery after stroke or brain injury, reduce shoulder pain associated with hemiplegia, and reduce cerebral spasticity. However, the discomfort of surface neuromuscular stimulation significantly limits the clinical implementation of this modality for persons with hemiplegia. The study contained herein tests the hypothesis that stroke and brain...
injury survivors with chronic hemiplegia (>6 mo) and intact sensation tolerate percutaneous intramuscular stimulation better than surface stimulation. Four stroke and two traumatic brain injury survivors participated in the study contained within this article. Each subject received three pairs of percutaneous and surface stimulations of the paretic finger extensors. The order of the type of stimulation within each pair was randomly assigned. The stimulation parameters for each type of stimulation were normalized to produce the same torque at the metacarpophalangeal joint. Subjects rated their perceived level of discomfort using a 10-cm visual analog scale and the McGill Pain Questionnaire. A blinded evaluator administered the pain measures. Percutaneous stimulation was associated with significantly lower discomfort as reflected by the visual analog scale (0.74 v 3.3; 95% confidence interval of difference, -3.84, -1.28). The McGill Pain Questionnaire produced similar results with percutaneous stimulation associated with a significantly fewer number of words chosen to describe the discomfort (0.87 v 3.30; 95% confidence interval of difference, -3.50, -1.30) and significantly lower Pain Rating Index (1.47 v 6.27; 95% confidence interval of difference, -7.77, -1.83). Data suggest that percutaneous intramuscular stimulation is significantly better tolerated than surface stimulation and that percutaneous stimulation may enhance patient compliance with neuromuscular stimulation treatments.

Abstract: Twenty children, with the diagnosis of cerebral palsy (CP) and under classical, physiotherapeutical and pedagogical, treatment, received piracetam (pyrrolidine acetamide) as an auxiliary drug. The goal was to better spasticity, learning and nervous instability problems aiming at better results of over-all treatment of CP. The group that received the drug has been compared to a control group of 20 children treated by the customary treatment only. The comparison showed favourable results for the medicated group. The drug was administered in the dose of 80 mg/kg/day during 10 weeks. The criteria for evaluation have been psychological, clinical, physiotherapeutical and pedagogical. The drug has been given in a new form of presentation: 6% solution for oral use.

Abstract: Similar movement disorders developed in two 8-year-old retarded children while they were receiving phenytoin. Seizures subsequent to a diphtheria-pertussis-tetanus immunization had developed in each child at 1 to 2 months of age. A static encephalopathy ensued, characterized by mental retardation, ataxia, spasticity, and a mixed seizure disorder. Intermittent dystonia and choreoathetosis developed insidiously while serum phenytoin concentrations were in the therapeutic range. Sustained dystonia and choreoathetosis developed
2 hours after an oral provocation with phenytoin. The baseline abnormalities on the electroencephalogram remained unchanged during the choreoathetosis. Recognizable metabolic abnormalities known to be associated with similar movement disorders were excluded. It was concluded from these studies that the movement disorder is secondary to phenytoin and can occur at therapeutic serum concentrations. Phenytoin is a central anticholinergic agent and a central stimulant of serotonin, and may induce movement disorders as a result of altering these neurotransmitters in the brain. The variable expression of these movement disorders may relate to the nature of the preexisting striatal insult.

Abstract: The prognosis of hexacarbon induced polyneuropathy is usually good, though its clinical course after the cessation of exposure has not been described in detail. Eleven patients with moderate to severe n-hexane induced polyneuropathy due to occupational exposure were regularly followed up for a period of four years at the neurological department of the National Taiwan University Hospital. Sensorimotor neuropathy was diagnosed in nine patients and motor neuropathy in two. All were removed from further exposure to n-hexane after aetiological confirmation, but motor disturbance continued to worsen in five cases. Sensory functions were regained earlier than motor functions. All the patients, including one who was tetraplegic and confined to a wheelchair in the early stages, regained their full motor capabilities within one to four years. Three patients with severe neuropathy had residual muscle atrophy in the intrinsic foot and hand muscles. Signs of damage to the central nervous system, including increased tendon reflexes in two patients and leg tightness in six patients, emerged as muscle power was nearing complete recovery. The tightness of the legs gradually disappeared, but muscle cramps of the calves developed and these were still present at the end of follow up. Two patients had mild abnormal colour vision, and the abnormality was still detectable four years later. It is concluded that n-hexane induced neuropathy has a good prognosis, and that spasticity due to damage to the central nervous system is functionally reversible; muscle cramps and dyschromatopsia persist much longer.

Abstract: A 6-week study of a modified release formulation of tizanidine designed for once daily administration was performed in 27 patients with spasticity due to cerebral lesions. The dosage of tizanidine used ranged from 6 to 18 mg/day. At the start of the study all patients had at least moderate spasticity and 20 (74%) patients had severe or very severe spasticity. All had a decrease in muscle strength. After 1 week of treatment 22 (81%) patients showed improvement in overall spastic state and, after 6 weeks, all 27 patients had improved. At the end of treatment 25 (93%) patients showed an improvement in overall disability. The drug was well tolerated. Side-effects were reported in only four patients, and these were minor and mostly mild. Tizanidine had no clinically important effects.
on blood pressure, heart rate, body weight or laboratory values. Overall, once daily treatment with modified release tizanidine is well tolerated and gives good clinical efficacy in patients with spasticity.


Abstract: INTRODUCTION AND OBJECTIVES: The objective of this study was to assess the feasibility, technical data and use of intrathecal catheter implantation with subcutaneous port for clonidine test injections and individual evaluation. METHODS: According to approval of the local ethics committee, 9 consecutive SCI patients (6 men, 3 women) had catheter and port implantation between January 1998 and May 1999. All did not respond to systemic drug therapy in combination to self-clean intermittent catheterisation (SCIC). Implantation was done under general anesthesia. Needle and catheter were Medtronic Infusion Synchromed Intraspinal catheter (Induratrade mark, 8703W). Clonidine test injections were allowed at D5. RESULTS: There were no complications during operation. Follow-up was 8.2 months (0.5-17). After clonidine bolus injection test and validation, 6 patients decided to have permanent pump implantation, 2 chose other therapies and one did not tolerate clonidine intrathecal injections for blood arterial pressure side effects. CONCLUSIONS: Intrathecal clonidine may represent a useful conservative treatment of both severe bladder hyperreflexia and spinal spasticity. Its short-term effects can be individually evaluated through bolus injection in subcutaneous port before definitive pump implantation.


Abstract: This study sought to test the hypothesis that injections of botulinum toxin type A (BTX-A) at the mid belly of the gastrocnemius muscle in spastic hemiplegic adults produce superior clinical results to proximal injections directed toward the muscular origin. We designed a randomized, double-blind, placebo-controlled intervention study at a university tertiary care setting. Seventeen
subjects with chronic spastic hemiplegic gait were enrolled from a volunteer community sample; time range from acute neurologic insult was 0.75 to 31 yr; age range was 19 to 71 yr; gender consisted of 11 men and 4 women; diagnoses were 12 patients with stroke, 2 with traumatic brain injuries, and 1 with a brain tumor. Two subjects were withdrawn from the study because of (1) acute vascular occlusion before intervention and (2) noncompliance with follow-up visits. After baseline measurements, subjects were injected with 50 units of BTX-A (volume, 0.5 cc) into the medial or lateral gastrocnemius: (1) proximally at one site near the muscular origin; (2) distally at three sites along the mid belly. We measured outcome using the Fugl-Meyer score, Ashworth scale, ankle range of motion, and a timed 50-ft fastest walk. No outcome measures showed a significant effect attributable to site of injections. Confounding variables included physical therapy and varying duration of illness in the study cohort. We conclude that the results failed to support the hypothesis that BTX-A injections at the mid belly of the gastrocnemius produced superior functional improvements to injections located near the muscular origin using localization techniques described. Additional research comparing more precise localization methods for BTX-A injections might further establish the importance of electromyographic guidance using BTX-A in management of spasticity

Abstract: Severe post-anoxic spasticity in a 25-year-old female was significantly improved during an open trial of 15 cycle per second CES. The bipolar LISS device with suboccipital electrode placement was used for 40 minutes three times a day. A synergism appeared when dantrolene 50 mg twice a day was combined with the CES, these additive effects being greater than either modality used alone

Abstract: The subscapularis muscle is the primary internal rotator of the shoulder and plays a key role in causing adduction, internal rotation, and pain in the hemiplegic patient. Spasticity and pain can be reduced by performing motor point blocks to the subscapularis. Two patients with spastic hemiplegic shoulder showed reduction in pain and immediate improvement in external rotation, abduction, and flexion after phenol motor point blocks to the subscapularis muscle. This preliminary report describes a method of performing subscapularis motor point blocks using a medial scapular approach


Abstract: Urinary excretion of sulphur compounds was studied in children from a population in Mozambique that had been affected, during a drought, by an epidemic of spastic paraparesis attributed to cyanide exposure from cassava. The children had increased thiocyanate and decreased inorganic sulphate excretion, indicating high cyanide and low sulphur-containing amino-acid intake. Children from a neighbouring cassava-eating area, where no cases of spastic paraparesis had occurred, had lower thiocyanate excretion but higher inorganic sulphate excretion. These results support the hypothesis that the epidemic was due to the combined effects of high dietary cyanide exposure and sulphur deficiency.


Abstract: Thyroid function was studied in a rural population in Mozambique that had been affected by an epidemic of spastic paraparesis attributed to dietary cyanide exposure from cassava. Laboratory investigation on a sample of this population demonstrated very high levels of serum and urinary thiocyanate, indicating a heavy exposure to cyanide. The urinary excretion of iodine was within normal limits, indicating an adequate intake of iodine. The serum levels of FT4I were somewhat decreased and serum FT3I, T3/T4 ratio and TSH were somewhat raised. This hormone pattern suggests an adaptation to the antithyroid effect of thiocyanate, but not overt hypothyroidism. A follow-up study on school children was performed, and it also demonstrated high thiocyanate exposure, adequate intake of iodine, and absence of endemic goitre. The results show that if iodine supply is adequate, the thyroid gland is capable of adaptation to a heavy body burden of thiocyanate without development of overt hypothyroidism or goitre.

Abstract: Botulinum type A toxin (BTA) is an orphan drug used to treat several disorders of muscle spasticity. We report the first known case of systemic botulism-like syndrome induced by BTA therapy which resulted in respiratory arrest. Clinicians should be aware that systemic effects may occur with localized BTA therapy and may be life-threatening.


Abstract: A total of 93 patients with intractable spasticity due to either spinal cord injury (59 cases), multiple sclerosis (31 cases), or other spinal pathology (three cases) were entered into a randomized double-blind placebo-controlled screening protocol of intrathecal baclofen test injections. Of the 88 patients who responded to an intrathecal bolus of 50, 75, or 100 micrograms of baclofen, 75 underwent implantation of a programmable pump system for chronic therapy. Patients were followed for 5 to 41 months after surgery (mean 19 months). No deaths or new permanent neurological deficits occurred as a result of surgery or chronic intrathecal baclofen administration. Rigidity was reduced from a mean preoperative Ashworth scale score of 3.9 to a mean postoperative score of 1.7. Muscle spasms were reduced from a mean preoperative score of 3.1 (on a four-point scale) to a mean postoperative score of 1.0. Although the dose of intrathecal baclofen required to control spasticity increased with time, drug tolerance was not a limiting factor in this study. Only one patient withdrew from the study because of a late surgical complication (pump pocket infection). Another patient received an intrathecal baclofen overdose because of a human error in programming the pump. The results of this study indicate that intrathecal baclofen infusion can be safe and effective for the long-term treatment of intractable spasticity in patients with spinal cord injury or multiple sclerosis.

Abstract: The efficacy of phenytin sodium and chlorpromazine hydrochloride in the reduction of spasticity was evaluated in both open and controlled studies. In each study, the majority of patients exhibited both objective and subjective signs of improvement. Reduction of motor tone in spastic muscles, as well as improvement in functional status, was observed. Most patients experienced greater benefit from the combination of phenytin and chlorpromazine than from either drug alone. The use of the drugs in combination permitted decreased chlorpromazine doses and reduced unwanted side effects such as lethargy and
somnolence. These drugs may exert their action by suppressing fusimotor efferent as well as afferent discharged from muscle spindles. The results suggest that the fusimotor system is an important pharmacologic target in the treatment of spasticity.

Abstract: To determine the usefulness of EMG-assisted botulinum toxin (BOTOX) injections for the treatment of spasmodic torticollis (ST), we randomized 52 ST patients into two groups and studied them prospectively. In one group [(E+C)RX, N = 28], the muscles were selected for BOTOX injection using both clinical and EMG examination and then injected with EMG assistance. In the second group [(C)RX, N = 24] the muscles were selected for BOTOX injection based solely on clinical examination and injected without EMG assistance. The percentage of patients showing any improvement after BOTOX as similar in both the (E+C)RX and (C)RX groups. A significantly greater magnitude of improvement was present in the (E+C)RX group, as well as a significantly greater number of patients with marked improvement. In particular, patients with retrocollis, head tilt, and shoulder elevation demonstrated additional benefit with EMG-assisted BOTOX injection. EMG assistance may be effective because the technique increases the ability to effectively identify and treat the deep cervical muscles.

Abstract: Cannabidiol (CBD), a nonpsychoactive cannabinoid of Cannabis, was given to 5 patients with dystonic movement disorders in a preliminary open pilot study. Oral doses of CBD rising from 100 to 600 mg/day over a 6 week period were administered along with standard medication. Dose-related improvement in dystonia was observed in all patients and ranged from 20 to 50%. Side-effects of CBD were mild and included hypotension, dry mouth, psychomotor slowing, lightheadedness, and sedation. In 2 patients with coexisting Parkinsonian features, CBD at doses over 300 mg/day exacerbated the hypokinesia and resting tremor. CBD appears to have antidystonic and Parkinsonism-aggravating effects in humans.

Abstract: Unprecedented developments in cannabinoid research within the past decade include discovery of a brain (CB1) and peripheral (CB2) receptor; endogenous ligands, anandamide, and 2-arachidonylglycerol; cannabinoid drug-induced partial and inverse agonism at CB1 receptors, antagonism of NMDA receptors and glutamate, and antioxidant activity; and preferential CB1 receptor localization in areas subserving spasticity, pain, abnormal involuntary movements, seizures, and amnesia. These endogenous structures and
chemicals and mechanisms are potentially new pathophysiologic substrates, and targets for novel cannabinoid treatments, of several neurological disorders.


Abstract: Data are presented for the first 50 patients with cerebral palsy who underwent chronic cerebellar stimulation for symptom alleviation. We observed significant shorter and longer term improvement in spasticity as well as athetosis, speech, and functional status. Continuing increments in improvement were noted as a function of time on stimulation. In many instances, psychometric test scores and behavior also were improved. There was one death in this series. There were no neurologic complications due to cerebellar stimulation. The results of this study warrant the judicious use of cerebellar stimulation for symptomatic and functional relief in cerebral palsy.


Abstract: 1. Using guinea-pig isolated trachea, we have studied how phorbol 12,13-diacetate (PDA) modulates mechanical responses of the tissue to methylxanthines, isoprenaline and ryanodine. 2. Caffeine (10 microM-5 mM), theophylline (10 microM-5 mM) and isoprenaline (1 nM-1 microM), each inhibited the spontaneous tone of the trachea. Pretreatment with PDA (0.1-10 microM) converted relaxant responses to high concentrations of the methylxanthines into contractions. PDA produced no equivalent effect against isoprenaline. Pretreatment with verapamil (1 or 10 microM), nifedipine (0.1 microM) or incubation with Ca(2+)-free, EGTA (0.1 mM)-containing physiological salt solution (PSS) suppressed the contraction produced by caffeine or theophylline in PDA (5 microM)- treated tissues. 3. The ability of PDA (5 microM) to convert...
caffeine-induced relaxation into caffeine-induced contraction was retained in tissues pretreated with a combination of atropine (1 microM) and mepyramine (1 microM) and in tissues denuded of the airway epithelium. 4. Caffeine (10 microM-5 mM), theophylline (10 microM-5 mM) and isoprenaline (1 nM-1 microM), each relaxed trachea contracted with histamine (0.1 mM). The relaxation induced by caffeine, theophylline and isoprenaline was markedly reduced in the presence of PDA (5 microM) and the responses to high concentrations of caffeine and theophylline, but not those to isoprenaline, were reversed to contractions. Verapamil (10 microM) prevented the effects of PDA against caffeine- or theophylline-induced relaxation. 5. PDA (1 microM) enhanced the tracheal spasm produced by caffeine (10 mM) and theophylline (10 mM) in indomethacin (2.8 microM)-treated trachea maintained at 20 degrees C. This enhancement was reduced in the presence of verapamil (10 microM). (ABSTRACT TRUNCATED AT 250 WORDS)

Abstract: The hereditary spastic mouse was studied as a model of cerebral palsy in childhood to test the hypothesis that intramuscular botulinum toxin A would prevent the development of calf-muscle contractures. A prospective randomised controlled trial of calf injection with botulinum A compared with injection of normal saline was performed on juvenile mice. At maturity, the calf muscles of the spastic mice were 16 per cent shorter than those of their normal siblings. The calf muscles of spastic mice injected with botulinum toxin A grew to within 2 per cent of normal length. This difference in mature muscle length was highly significant.

Abstract: Portal-systemic shunts, either spontaneous or artificial, are occasionally complicated by the development of spastic paraparesis. We report on 2 young patients who developed this complication following splenorenal shunts which were made for the treatment of oesophageal varices associated with cirrhosis of the liver and portal hypertension.


Abstract: The central muscle relaxant activity of the antispastic agent tizanidine was compared with that of two novel clinical agents, afloqualone and eperisone, in the mouse and rabbit. Oral tizanidine strongly inhibited morphine-elicited Straub tail induction in the mouse, showing a median effective dose (ED50) of
1.2 mg/kg. Intravenous tizanidine also inhibited hind limb extensor reflex activity in the rabbit with an ED50 of 0.02 mg/kg. Afloqualone and eperisone, however, were much weaker in the mouse assay with ED50 values of 8.2 and 58.1 mg/kg, respectively. At respective intravenous doses of 2.0 and 1.0 mg/kg, afloqualone and eperisone caused maximally 32% and 41% inhibition of reflex activity in the rabbit. On this basis, afloqualone might be expected to exhibit moderate myotonolytic activity in rheumatological indications, but to be of questionable value in spasticity. Similarly, clinical myotonolytic activity of eperisone would only be expected at high doses unless its functional bioavailability were to be much better in man than in either the mouse or rabbit.


Abstract: Pharmacologic and electrophysiologic studies over the past 20 years have shown tizanidine to be a potent, central-acting myotonolytic agent that principally affects spinal polysynaptic reflexes. This action arises from agonistic activity of the compound at noradrenergic alpha 2 receptors, resulting in both direct impairment of excitatory amino acid release from spinal interneurons and a concomitant inhibition of facilitatory coeruleospinal pathways. Similar alpha 2-receptor-mediated inhibition of interneuronal activity appears to underlie the additional antinociceptive and anticonvulsant activity of tizanidine reported in several species and test paradigms. Despite its structural and biochemical similarity to clonidine, the cardiovascular properties of tizanidine are mild and transitory in relation to its activity as a muscle relaxant. These findings, together with a possible greater separation between myotonolytic and general CNS depressant activity than with other agents, make tizanidine a valuable addition in the pharmacologic treatment of spasticity.


Abstract: To determine whether vaginally born breech infants are at increased risk for morbid events as compared with breech infants delivered by cesarean, we studied 1240 singleton breech infants without congenital anomalies delivered in Northern California Kaiser Permanente Medical Care Program hospitals during 1976-1977. Medical record review provided information on indications for method of delivery, delivery complications and injuries, neonatal complications, and neurologic sequelae up to 4 years of age. The relative risk estimates for asphyxia (1.0; 95% confidence interval 0.7, 1.4), head trauma (1.6; 95% confidence interval 0.2, 17.0), neonatal seizures (0.8; 95% confidence interval 0.1, 7.1), cerebral palsy (1.6; 95% confidence interval 0.2, 17.4), and developmental delay (2.0; 95% confidence interval 0.9, 4.4) for vaginally born compared with cesarean-delivered infants indicated that vaginally born infants were not at increased risk for these outcomes. We used multiple logistic regression to control for confounding variables. The adjusted relative risk estimate for the combined-outcome category of head trauma, neonatal seizures, cerebral palsy, mental...
retardation, or spasticity was 0.5 in vaginally delivered infants (95% confidence interval 0.1, 3.2). When all morbid outcomes were considered in combination, the adjusted relative risk estimate was 0.9 for vaginally delivered infants (95% confidence interval 0.6, 1.4)

Abstract: Baclofen, a water soluble drug advocated for the treatment of spinal spasticity, was microencapsulated, using the oil/water emulsion extraction process in an attempt to identify the appropriate experimental conditions capable of producing microspheres releasing baclofen over 2-4 weeks. Individual microspheres ranging in size from 15 to 30 microns were formed exhibiting smooth surfaces at low drug payload (12.8% w/w), irregular and rough surface at high drug content (33.9% w/w). The microencapsulation yield remained practically unchanged (85-90%) up to theoretical payloads of 37.5% w/w, and decreased markedly to 70% when the initial theoretical payload was 50% w/w. The in vitro release profile of baclofen from the poly(D,L-lactide- co-glycolide) microspheres was biphasic only for the high drug payload microspheres with a rapid release of 70% within 48 h, followed by a slower release rate over at least 25 days. In contrast, the microspheres containing low baclofen contents (12.8% w/w) exhibited a gradual and progressive release rate over the course of the experiment. The baclofen release data did not fit either the general equation which describes the diffusional release of dispersed tiny drug particles from spherical micromatrices, or to the kinetic equations which describe the release of dissolved drug from monolithic microspherical devices. It appears that the release of baclofen from the present microspheres is not governed by a unique mechanism. This should be attributed either to the presence of some uncoated drug particles or to the large size of the embedded drug particles compared with the relatively small size of the spherical micromatrices, or to some polymeric erosion occurring after several days incubation in the release medium


Abstract: Functional neuromuscular stimulation (FNS) provides a mechanism for the activation of muscles paralyzed by injury to the spinal cord. Although this technique was first used to treat patients with spinal cord injury over 20 years ago, only recent advances in electronics and biomechanics have made it a promising aid for the rehabilitation of these patients. Thus far, restoration of palmar prehension and lateral prehension in quadriplegics and of standing and biped gait in paraplegics has been achieved under carefully controlled laboratory conditions. This article reviews the current status of FNS and its potential as a
practical tool to aid spinal cord-injured patients. Neurosurgeons who care for these patients might be expected to be involved in the future use of FNS if implantable systems are developed and tested.


Abstract: A case is reported of a 56-year-old woman who suffered from recurrent dislocations of the temporomandibular joint (TMJ) secondary to an exacerbated tetraspastic syndrome of multiple sclerosis. Following chemical denervation of the masseter and pterygoid muscles with injections of type A botulinum toxin, no further dislocations occurred for periods of up to four months. The treatment has been repeated five times. Some of the indications and possible adverse reactions to this therapy are discussed and comparisons made with other, conventional methods for managing recurrent dislocation of the TMJ.


Abstract: The water-soluble benzodiazepine, midazolam, was administered epidurally over the lumbar enlargement 18 times to 9 patients with spasticity due to severe spinal cord injury. Doses of 1.25-3.75 mg produced a rapid decrease of spasticity which lasted 1 h. After the maximal reduction of spasticity, the patients became drowsy. While the results suggest a direct action of midazolam on the spinal cord to reduce spasticity, the effect does not contribute to its usefulness as a therapeutic tool.


Abstract: The paper considers mechanisms of action and clinical efficacy of the drug sirdalud (tizanidine) in painful musculotonic syndromes. Sirdalud is an agonist of alpha 2-adrenergic receptors effective in painful musculotonic syndromes and spasticity of various genesis. The drug exhibits myorelaxative and direct central analgetic effects, is well tolerated and has minimal side effects (drowsiness). The response can be seen as early as the first treatment days. Sirdalud is applicable as alone and in combination with non-steroid anti-inflammatory drugs.


Abstract: The value of locally injected botulinum toxin is emphasised. The toxin was injected directly into the skeletal muscles of eight patients with severe spasticity due to stroke-related hemiplegia. It produced both subjective and
objective improvement. The toxin injections were well tolerated and no significant side effects were noted.

Abstract: Botulinum toxin, a product of Clostridium botulinum, produces presynaptic neuromuscular block by preventing release of acetylcholine from nerve endings. The toxin was injected directly into the skeletal muscles of six patients with severe spasticity due to stroke-related hemiplegia. It produced both subjective and objective improvement. The toxin injections were well tolerated and no significant side effect was reported.


Abstract: Several different drugs are now used, or are potentially useful, to treat patients with spasticity. Although these compounds vary in their actions on spinal neurons and reflex arcs, it is possible to formulate reasonable hypotheses regarding their modes of action. The benzodiazepines bind to specific benzodiazepine receptors linked to classic gamma-aminobutyric acid (GABA) receptors located on the terminals of primary afferent fibers. This binding results in an increased affinity of the GABA receptor for the amino acid, an augmented flux of chloride ions across the terminal membrane, and an increase in the amount of presynaptic inhibition. Baclofen activates GABAB receptors putatively located on the same terminals. Activation of these receptors retards the influx of calcium ions into the terminals, thereby reducing the evoked release of excitatory amino acids and possibly other transmitters. Progabide and its metabolites act on both classic and GABAB receptors. Glycine works on specific inhibitory receptors located on spinal interneurons and motoneurons. The phenothiazines act on the brainstem to alter the function of fusimotor fibers. Phenytoin and carbamazepine reduce the afferent output of muscle spindles. Dantrolene diminishes the activation of the contractile process in muscle fibers by reducing the release of calcium ions from the sarcoplasmic reticulum. This review summarizes the data supporting these concepts.

Abstract: The purpose was to examine whether physiological changes can be found in laryngeal muscles following repeated treatment with botulinum toxin injections in spasmodic dysphonia. Seven patients whose treatment consisted of multiple unilateral thyroarytenoid injections were examined more than 6 months following their most recent botulinum toxin injection fiberoptic laryngoscopy and electromyography. Comparisons were made between injected and contralateral noninjected muscles' motor unit characteristics, muscle activation patterns, and vocal fold movement characteristics. The results demonstrated that motor unit
characteristics differed between injected and noninjected muscles and that these differences were greater in patients less than 12 months since last injection. Motor unit duration differences were reduced and motor unit amplitude and numbers of turns were increased in muscles sampled over 1 year after injection. These results suggest that while the physiologic effects of botulinum toxin are reversible, the reinnervation process continues past 12 months following injection.


Abstract: Over a 7-year period (February 1974 through February 1981), 318 patients underwent the implantation of cerebellar stimulation systems for the reduction of spasticity (98%) or epilepsy (2%). A total of 518 procedures were carried out to implant and maintain the equipment during this period. Fourteen patients developed infections in the tissue around their implanted systems, which represented 4.4% of the patients or 2.7% of the procedures performed. Staphylococcus aureus was the infectious agent in 7 cases (50%), the clinical features of which occurred usually within 1 month. Staphylococcus epidermidis infected 5 patients with features presenting late (more than 2 years) after the initial implantation. The management involved antibiotic therapy for 2 weeks in all 14 patients. In 12 patients, the entire system was removed, with 100% eradication of the infection. In the other 2 patients, the radio receiver and lead wires up to but not including the cerebellar electrode pads were removed. One of these 2 patients has been free of infection for 4 years. The other had S. aureus cultured from removed electrode pads after 6 weeks. Of the 14 cases, morbidity was severe in only 1 patient. Seven patients underwent reimplantation 6 weeks after the infection.


Abstract: In the treatment of spasticity, the therapeutic cerebrospinal fluid levels of (+/-)-baclofen, a gamma-aminobutyric acid (GABA)B receptor agonist, are below 1 microM. However, the mechanism of the therapeutic action of (+/-)-baclofen remains unknown, because, for the most part, the action of (+/-)-baclofen on GABAB receptors requires micromolar concentrations. Using fura-2 fluorescence microscopy, intracellular ionized calcium was measured in cerebellar granule neurons. Stimulation of a high affinity GABAB receptor potentiated by 2-3-fold the rise in intracellular calcium observed after depolarization of the cell with a Krebs-Ringer's buffered solution containing 40 mM K+. Both GABA (100 nM) and (+/-)-baclofen (10-100 nM) stimulated this high
affinity receptor. The potentiation of the depolarization-induced rise in intracellular calcium by (+/-)-baclofen (100 nM) was completely blocked by the GABAB receptor antagonist CGP 35348 (200 microM). Also, the intracellular calcium response induced by the activation of high affinity GABAB receptors was prevented by dantrolene (10 microM). The cerebellar granule neurons contained calcium-induced calcium release (CICR) stores. Caffeine (3 mM) and ryanodine (100 microM) potentiated the depolarization-induced rise in intracellular calcium, and this response to both drugs was blocked by dantrolene (10 microM). Because dantrolene does not prevent the rise in intracellular calcium after cell depolarization (this calcium originated from the influx of extracellular calcium), (+/-)-baclofen acting via the high affinity GABAB receptor indirectly activates the CICR stores, allowing the influx of extracellular calcium to trigger the release of calcium from these dantrolene-sensitive CICR stores. Thus, this high affinity GABAB receptor might become activated during persistent depolarization caused by pathological states and could be a mechanism to be studied for the therapeutic action of (+/-)-baclofen in spasticity.


Abstract: Effects of intra-articular triamcinolone acetonide on pain and passive range of motion (ROM) in the painful hemiplegic shoulder were studied. A Multiple baseline (or AB) design across seven subjects was used. The length of the baseline condition (or A phase) was either 2 or 3 wk, and randomized across subjects. Subsequently, a treatment condition (or B phase) of 4 wk was applied during which three intra-articular injections of triamcinolone acetonide were administered at day 1, 8, and 22. Pain and ROM were the primary outcome parameters and were measured three times each week by means of a visual analogue scale (VAS) and a fluid-filled goniometer, respectively. In addition, a number of secondary outcome parameters were assessed, i.e., spastic muscle activity (Ashworth scale), motor function (Fugl-Meyer index), upper limb function (action research arm test) and signs and symptoms of a shoulder hand syndrome (clinical scoring list). Statistical analysis of the combined time series showed significant effects on pain (P = 0.025). Analysis of the individual time series revealed that five out of seven patients had significant reduction of pain. ROM improved significantly in four out of seven patients. However, improvement of ROM did not reach significance at the group level (P = 0.13). None of the secondary parameters showed significant changes. The correlation coefficient between upper limb function (ARA) at intake and size of treatment effect approaches a level of significance (P = 0.09). The results indicate that intra-articular triamcinolone may be of benefit in reducing hemiplegic shoulder pain...


Abstract: This study is intended to alert the clinician to the insidious symptoms of baclofen overdose, its prevention and treatment. In a group of 43 patients suffering from previously intractable spasticity and a total treatment time of 2,422 weeks, 7 events of intrathecal baclofen overdose happened in 5 patients. On two occasions, a bolus injection caused an overdose (dose 50 and 280 micrograms). The 5 events during continuous infusion intoxication only happened in high dosed patients. The overdose symptoms occurred in one patient when she was lying in supine position (800 micrograms/24 h), in another patient after repair of CSF leakage by an autologous epidural bloodpatch (1,920 micrograms/24 h) and in tolerant patients, once during maximal dose adjustments (2,400 micrograms/24 h) and twice ca. 6 hours following reinitiation of the intrathecal baclofen infusion after a "drug holiday" treatment (27 and 55 micrograms/h). We could not confirm the reported similarity of baclofen overdose with the anticholinergic syndrome. Especially, the bradycardia and hypotension are more in accord with the reported clinical picture of oral baclofen overdose. In the absence of a pure baclofen antagonist and the varying symptoms of intrathecal baclofen, intoxication make rational treatment difficult. We observed that the advised physostigmine therapy is not always effective and safe. The occasionally doubtful antidotal benefits of physostigmine must be weighted against major side-effects. The classical approach of decreasing the absorption of a drug by lowering baclofen levels in the CSF by lumbar puncture drainage was successful. This approach together with conservative symptomatic treatment in an intensive care environment is probably a better and safer alternative than physostigmine alone as an antidote.

Abstract: A report on pregnancy in a quadriplegic patient treated with a high dose of 1000 mcg/24 h continuous intrathecal baclofen infusion using an implanted drug delivery system (Synchronomed, Medtronic, USA). Spasticity could be managed up to the 35th week of gestation. However, uterine contractions evoke enormous spastic symptoms which we, even with maximum values of the spasticity scales, could not classify. The recurrence of spasticity was associated with autonomic dysregulation. With continuous epidurally infused bupivacaine (11.25 mg/h) adequate relaxation could be reached and gestation was
terminated by a primary caesarean section. A healthy girl was born (2040 g, Apgar 9 and 10)

Abstract: The Seldinger technique was developed using a plastic introducer through which introduction and manipulations of a silicone spinal catheter, an extradural stimulation lead or a small diameter fibreoptic scope are possible without the risk of damage to the vulnerable devices. It is not intended as a replacement of the standard technique of introducing a spinal catheter through a Tuohy needle in general anaesthetic practice. Silicone spinal catheters and stimulation leads are used for long-term therapy in intractable chronic pain and spasticity. A fibreoptic scope is used for endoscopic examination of the subarachnoid or extradural space. Using a standard Tuohy needle the soft silicone extradural lead can be damaged easily by manipulations during insertion. For this reason the manufacturer modified the Tuohy needle for extradural silicone lead introduction. The disadvantages of this modified Tuohy needle are: first, difficulty in localization of the extradural space, second, the needle is unsuitable for a subarachnoid catheter or introduction of a fibreoptic scope. The Seldinger technique was performed 25 times in 18 patients, introducing a spinal silicone catheter (n = 14), an extradural silicone stimulation lead (n = 2) or a small diameter fibreoptic endoscope (n = 9). Paraesthesiae caused by neural irritation occurred in awake patients. This did not differ from the technique using a Tuohy needle only. Neural damage or trauma did not occur with the Seldinger technique. The incidence of post-spinal headache was the same for both techniques. No further complications were noted

Abstract: Spasticity, a common symptom of upper motor neuron lesions, may actually aid the patient and should be treated only if it interferes with function, comfort or nursing care. Stretching exercises and elimination of nociceptive stimuli are the first steps in management. If problems persist, medication should be considered. Tenotomies are useful. Motor-point blocks and peripheral nerve blocks are temporary aids, while neurectomies usually provide permanent relief. More drastic neurosurgical procedures are reserved for uncontrolled, incapacitating cases


Abstract: Spasticity results from various pathophysiologic abnormalities in spinal cord neuronal circuits. Noninvasive electrophysiologic techniques can be used to study these circuits in humans. The best correlation between briskness of reflexes and results of electrophysiologic testing is found with reduction in vibratory inhibition, a test that reflects presynaptic inhibition. For increase in muscle tone, the best correlation is found with reduction of Ib nonreciprocal inhibition. These test results, which are stable under controlled conditions, are influenced by myorelaxant drugs and may be used to analyze the mode of action of new products because the tests study specific circuits involving known neurotransmitters. Tizanidine reinforces presynaptic inhibition and two types of postsynaptic inhibition: Ia reciprocal and Ib nonreciprocal. It also markedly reduces flexor reflexes. These effects are explained by an action exerted on spinal interneurons deprived of their normal monoaminergic descending innervation. The spectrum of activity for tizanidine is thus broad, making it likely that tizanidine corrects more than one pathophysiologic abnormality. Because tizanidine reinforces presynaptic as well as Ib nonreciprocal inhibition, it may reduce both brisk tendon jerks and muscle hypertonia.


Abstract: PURPOSE: We assessed the urodynamic effect of various doses of intrathecal clonidine on refractory detrusor hyperreflexia in spinal cord injured patients. MATERIALS AND METHODS: Doses of 15, 30 or 45 microg. intrathecal clonidine or placebo were given to 5 chronic complete spinal cord injured patients with detrusor hyperreflexia. Two cystometries were performed before and 5, 30, 60, 90, 120 and 180 minutes after each injection. RESULTS: A statistically significant dose dependent decrease in detrusor hyperreflexia was observed in each patient without significant side effect. CONCLUSIONS: Intrathecal clonidine may represent a conservative reversible treatment for detrusor hyperreflexia via a subcutaneous programmable pump, like that used for baclofen, for spasticity. The long-term efficacy needs to be evaluated.


Abstract: OBJECTIVE: Assess modifications of sexual function in men treated with intrathecal baclofen for spinal spasticity. DESIGN: Prospective before- after trial. SETTING: A rehabilitation department of a university hospital; follow-up was on an outpatient basis. PATIENTS: A convenience sample of nine consecutively recruited men with spinal cord injury or multiple sclerosis who were receiving intrathecal baclofen by an implantable pump; average follow-up was 44.4
months. MAIN OUTCOME MEASURES: A questionnaire focusing on: libido; ability to sustain reflexive and psychogenic erections; rigidity, evaluated by a visual analog scale; maximum duration of erection; possibility of ejaculation.

RESULTS: Libido and the ability to obtain psychogenic or reflexogenic erections were not modified. However, eight patients reported a decrease of erection rigidity and/or duration. Ejaculation was possible in three cases before implantation. It disappeared in two patients, and was more difficult to obtain in the last one. It reappeared after treatment withdrawal. No differences were found between multiple sclerosis and spinal cord injured patients. CONCLUSION: Intrathecal baclofen may compromise erection and ejaculation. This effect is reversible. Patients should be informed of this effect.


Abstract: An in vitro mammalian model neuronal system to evaluate the intrinsic toxicity of soman and other neurotoxicants as well as the efficacy of potential countermeasures was investigated. The link between soman toxicity, glutamate hyperactivity and neuronal death in the central nervous system was investigated in primary dissociated cell cultures from rat hippocampus and cerebral neocortex. Exposure of cortical or hippocampal neurons to glutamate for 30 min produced neuronal death in almost 80% of the cells examined at 24 h. Hippocampal neurons exposed to soman for 15-120 min at 0.1 microM concentration caused almost complete inhibition (> or = 90%) of acetylcholinesterase but failed to show any evidence of effects on cell viability, indicating a lack of direct cytotoxicity by this agent. Acetylcholine (ACH, 0.1 mM), alone or in combination with soman, did not potentiate glutamate toxicity in hippocampal neurons. Memantine, a drug used for the therapy of Parkinson's disease, spasticity and other brain disorders, significantly protected hippocampal and cortical neurons in culture against glutamate and N-methyl-D-aspartate (NMDA) excitotoxicity. In rats a single dose of memantine (18 mg/kg) administered 1 h prior to a s.c. injection of a 0.9 LD50 dose of soman reduced the severity of convulsions and increased survival. Survival, however, was accompanied by neuronal loss in the frontal cortex, piriform cortex and hippocampus.


Abstract: Various 4- and 8-aminoquinolines, which are effective antimalarial agents, were examined as potential pretreatment compounds for prolongation of the time to 50% block of nerve-elicted muscle twitches in isolated mouse diaphragms exposed to botulinum type A neurotoxin. The 4-aminoquinolines (chloroquine, amodiaquine) and quinacrine, an acridine derivative similar to chloroquine, prolonged the time required for botulinum type A neurotoxin to block neuromuscular transmission by more than 3-fold; 8-aminoquinolines (primaquine and WR242511) had no antibotulinum type A neurotoxin activity. Pyrimethamine,
an antimalarial drug lacking the quinoline ring structure, was also ineffective. Rank order potencies based on equimolar effective concentrations for the test compounds were quinacrine > amodiaquine > chloroquine > quinine or quinidine. Maximum protection from botulinum type A neurotoxin-induced neuromuscular block was achieved when muscles were exposed to drug prior to or simultaneously with the toxin. A delay of more than 20 min abolished the protective ability of the antimalarial agents, presumably owing to the release of the toxin from endosomes in quantities sufficient to initiate neuromuscular block. All of the test compounds except quinine and quinidine depressed muscle contractions when concentrations exceeded 20 microM. In addition, amodiaquine at 50 microM induced muscle contracture. A combination of agents at low concentrations that act at different steps of botulinum type A neurotoxin poisoning potentiated the prolongation of time to 50% block in an approximately additive fashion. Thus N,N,N',N'-tetrakis(2-pyridylmethyl)ethylenediamine (2 microM) and quinacrine (5 microM), when administered in combination, produced up to a 4-fold increase in time to 50% block. A similar level of protection with quinacrine alone required a 4-fold increase in the aminoquinoline concentration. Although the mechanism of protection by these antimalarial agents is probably through the raising of endosomal pH, the possibility that some of these drugs could also act by inhibiting toxin-induced channel formation cannot be ruled out.

Detrembleur C., Lejeune T.M., and Plaghki L. (1998) [Objective measures of muscle stiffness in the ankle. Evaluation of the effect of intrathecal injection of baclofen in spastic patients]. Neurochirurgie  44, 197-200. Abstract: This paper presents the objective and quantitative measurement of muscle stiffness described by Rack and Lehmann. This method allows analysis of the pathophysiological mechanism of spasticity and assessment of anti-spastic treatment. This is illustrated by a case report, showing the objective effect of intrathecally administered baclofen in a spastic patient.

Detrembleur C. and Plaghki L. (2000) Quantitative assessment of intrathecally administered baclofen in spasticity. Arch. Phys. Med. Rehabil. 81, 279-284. Abstract: OBJECTIVE: To quantitatively assess the antispastic effect of intrathecally administered baclofen on muscle stiffness in spastic patients. DESIGN: Case-control study. SETTING: Clinical laboratory in a university hospital of a city of more than 1,000,000 inhabitants. PARTICIPANTS: Eighteen healthy adult volunteers (9 men, 9 women) were recruited for establishing the normal values. Eleven spastic patients (8 men, 3 women) comprised the study group. MAIN OUTCOME MEASURES: The resistance to passive sinusoidal displacement of 5 degrees imposed to the ankle joint was measured at frequencies from 3 to 12 Hz. Torque and displacement signals were subjected to a Fourier analysis to isolate the elastic and viscous components of the total muscle stiffness. RESULTS: In comparison with the period before intrathecal injection, and with the control group, it was shown that at 4 hours after injection, stretch reflex activity was abolished and elastic and viscous muscle stiffness approached control values. The abnormal residual stiffness concerned only the
elastic component due to chronic transformations of the spastic muscle and/or
due to changes in joints and periarticular connective tissue. This antispastic
effect was completely reversed 36 hours after injection. CONCLUSION: The
present study shows that the antispastic effect of intrathecally administered
baclofen in spastic patients can be quantitatively assessed by a sensitive method
allowing measurement of elastic and viscous components of muscle stiffness

(1996) Intrathecal morphine for analgesia in children undergoing selective dorsal
Abstract: Selective dorsal root rhizotomy is performed for relief of spasticity in
children with cerebral palsy. Postoperative pain relief can be provided by
intrathecal morphine administered at the time of the procedure. We sought to
define an optimal dose of intrathecal morphine in children undergoing selective
rhizotomy, through a randomized, double-blinded prospective trial. After
institutional approval and parental written informed consent, 27 patients, ages 3-
10 years, were randomized to receive 10, 20, or 30 micrograms.kg-1 (Groups A,
B, and C, respectively) of preservative-free morphine administered intrathecally
by the surgeon after dural closure. Postoperatively, vital signs, pulse oximetry,
and pain intensity scores were recorded hourly for 24 hr. Supplemental
intravenous morphine was administered postoperatively according to a
predetermined schedule based on pain scores. There was considerable
individual variability in the time to initial morphine dosing and cumulative
supplemental morphine dose. Time to first supplemental morphine dose was not
different between groups. When compared to Groups A and B, cumulative 6-hr
supplemental morphine dose was significantly lower in Group C (38.6 +/- 47
micrograms versus 79.1 +/- 74 and 189.6 +/- 126 for Groups A and B,
respectively). By 12 hr, cumulative supplemental morphine dose was similar in
Groups A and C. Group B consistently had a higher supplemental dose
requirement than Groups A and C at 6, 12, and 18 hr. By 24 hr, there was no
difference in cumulative dose among groups. Postoperative pain scores and the
incidence of respiratory events, nausea, vomiting and pruritus were comparable
among groups. These data suggest that intrathecal morphine at 30
micrograms.kg-1 provides the most intense analgesia at 6 hr following selective
dorsal root rhizotomy, but was otherwise comparable to the 10 micrograms.kg-1
dose

Di Rocco A., Tagliati M., Danisi F., Dorfman D., Moise J., and Simpson D.M.
Abstract: The pathogenesis of AIDS-associated vacuolar myelopathy (VM) may
be related to abnormality of transmethylation mechanisms in the nervous system.
To evaluate the safety and potential efficacy of the methyl-group donor L-
methionine in AIDS-associated VM, we conducted a pilot clinical trial in 12
patients with VM. Seven of the nine patients who completed the study had
clinical and electrophysiologic improvement. Controlled studies may be indicated to assess the efficacy and safety of L-methionine in AIDS-associated VM


Dietz V. (1990) [Spasticity: therapy of increased reflexes or movement disorder?]. Nervenarzt 61, 581-586.


Abstract: The effectiveness of spinal cord stimulation for control of spasticity was studied in 59 spinal cord injury patients. SCS was markedly or moderately effective in reducing spasticity in 63% of the patients. We found that control of spasticity by SCS was not correlated with the severity of spasticity, the type of spasticity (flexor or extensor), or the ability to ambulate. However, stimulation was more effective in patients with incomplete cervical lesions than in complete cervical lesions. Stimulation below the lesion was more effective than above. We conclude that SCS was effective when electrodes were properly positioned below the lesion over the posterior aspect of the spinal cord in patients with some residual spinal cord function. We hypothesize that SCS controls spasticity by modification of activity of spinal-brainstem-spinal loops and by suppression of segmental excitation through antidromic activation of propriospinal pathways


Abstract: We report the case of a patient who developed dantrolene-induced pleurisy. Dantrolene (Dantrium) is a muscle relaxing agent used for the treatment of spastic neurological manifestations which has known liver toxicity. Lung
toxicity is rarely reported. Six cases of dantrolene-induced pleurisy occurring after chronic administration (> 60 days) have been described in the literature. The pleurisy is associated with pleural and peripheral eosinophilia. Spontaneous regression a few days after withdrawal and radiological cure a few months later is the rule. The precise mechanism of this drug-induced pleural reaction remains unknown.


Abstract: We have investigated the effect of phenothiazine, a compound known to inhibit calmodulin, on the responses of normal and spastic cerebral arteries, using the canine "two hemorrhage" model of cerebrovascular spasm. Ring preparations from control vessels or vessels removed three or seven days after injection of blood, were contracted with either 5-hydroxytryptamine (5-HT) or prostaglandin F2 alpha (PGF2 alpha) and then exposed to increasing concentrations of phenothiazine. In normal arteries, low concentrations of phenothiazine enhanced the response to PGF2 alpha, while higher concentrations caused relaxation. Responses to 5-HT were inhibited by all concentrations of phenothiazine tested. When normal arteries were compared with arteries from animals injected with blood, in the case of 5-HT, phenothiazine was a less effective antagonist at low doses, but equieffective at higher doses. Similar experiments conducted with PGF2 alpha showed that phenothiazine was a more effective antagonist in spastic vessels. We conclude that 5-HT and PGF2 alpha have significant differences in the mechanism by which they produce contraction of cerebral vessels, that phenothiazine has secondary effects on contraction independent of inhibition of calmodulin, and, finally that the effects of phenothiazine in clinical vasospasm may be insufficient to reverse the condition, despite the observation that vessels in spasm may be more sensitive to this agent.


Abstract: Fifty-five patients were treated with botulin injections into the muscles showing dystonia, contracture or tremor. Twenty two of them had torticollis, 21 had blepharospasm, 10 had hemifacial spasm, and 2 had tremor. In all, 112 injections were done with good result in 64%, slight effect in 27% and without effect in 9% of the cases. Similar results have been reported from other centers in the world. Adverse effects were not significant and disappeared after several days or weeks. They included ptosis, speech and deglutition disturbances, general weakness and neurotic reactions. These adverse effects developed in 12 cases. In cases of tremor the dose as well as the technique of injections must be individualized. The method is an important therapeutic advance and can be applied in outpatient clinics.
Abstract: Intrathecal baclofen is at present the best treatment for severe spasticity of various etiologies. In walking patients affected by severe spasticity a careful evaluation of the motor performance is needed for a correct indication for this treatment. The examination should focus on the delicate balance between spasticity and voluntary muscle activation which is crucial for an improvement of motor performance during gait. Seven patients have been neurophysiologically evaluated by the use of a Cibex apparatus measuring torque and movement velocity of the lower limbs simultaneously with static and dynamic recordings of the EMG.

Abstract: Clonidine was used as an adjunct to baclofen in 55 patients with spasticity due to spinal cord injury. Dosage was held at the minimum effect amount for those who responded. No effect was seen in 24 patients (44%), although 31 (56%) benefitted from the drug. Patients were grouped as quadriplegics or paraplegics, having complete or incomplete lesions. Of all quadriplegics, seven of 11 complete (64%) and 17 of 25 incomplete patients (68%) responded; among the paraplegics, six of 15 complete (40%) and one of four incomplete patients (25%) improved. Side effects were limited to postural hypotension necessitating reduction in dosage in three patients that were successfully treated; in the unsuccessfully treated group, one patient had insomnia, one had dizziness, and one had drowsiness.

Abstract: STUDY DESIGN: A prospective double blind cross over trial of intravenous 4-Aminopyridine (4-AP). OBJECTIVE: To determine the efficacy of this drug in the treatment of spinal cord injured (SCI) patients for neurologic impairment, pain and spasticity. SETTING: The post anesthesia care unit (PACU) of a tertiary care acute hospital. METHODS: Twelve paraplegic patients were enrolled in a double blind cross over intravenous trial of 4-Aminopyridine (4-AP). Thirty milligrams of 4-AP or placebo were administered over a 2 h period. Patients were serially examined during and after the infusion clinically for pain, sensorimotor function, hypertonicity and motor control using electromyography (EMG). Samples of blood and cerebrospinal fluid (CSF) were also analyzed at similar intervals. RESULTS: Despite penetration of 4-AP into the CSF, no significant differences were noted in the clinical and EMG parameters at the times measured. Individual changes in sensory function were reported by some patients in both the placebo and 4-AP trials, however mean values were not robust. Frequently, patients complained of unpleasant symptoms during the 4-AP
infusion. CONCLUSION: The intravenous route may not be the best way to administer this drug as no short term benefits were observed

Abstract: The purpose of this article is to describe the usual procedure and postoperative recovery after an allogeneic bone marrow harvest and to present a case study of an unusual complication of hemorrhage. The case study describes a donor who experienced hemorrhage with severe pain, muscle spasms, and prolonged limitations in range of motion and ambulation. Oncology nurses should inform donors to promptly report persistent pain, spasms, and muscle weakness. Should hemorrhage occur, blood loss should be evaluated, bedrest should be maintained, and cold packs should be applied to the area. Although excessive bleeding is a rare occurrence, nurses should be alert for this complication to prevent pain and activity impairment


Abstract: Intrathecal baclofen dramatically improves severe spastic syndromes. This improvement is likely related to reduced excitability of alpha- motoneurons. To investigate the influence of baclofen upon the alpha- motoneuron, we analyzed F-waves before and after intrathecal baclofen bolus injection (usually 50 micrograms) as well as after administration of different, constantly delivered doses (60-200 micrograms/day). Intrathecal baclofenbolus decreased the maximum F-wave amplitude (Fp) from an initial value of 9% of the maximum M amplitude (Mmax) (= F/M- ratio) to 2.4% of the Mmax after 130-180 min, reduced the mean F-wave amplitude 60% within 150 min, and shortened the mean duration by 40-60% after 130-180 min. Constantly delivered baclofen of 100 micrograms/day reduced the F/M-ratio from 5% to 2%, the mean F-wave amplitude by 40-80%, and the F-wave mean duration by 40-80%. The minimum F-wave latency did not change after bolus or during steady state administration. The findings indicate that the F-wave mean and maximum amplitude as well as the mean duration are altered in a quantifiable manner following intrathecal baclofen application

Abstract: OBJECTIVE--To investigate whether the dose of intrathecal baclofen
necessary for a sufficient reduction of muscle tone and spasms changes during
treatment of severe spasticity. METHODS--A group of 27 patients received
intrathecal baclofen for 61 (SD 18) months. RESULTS-- Spasticity remained
absent or strongly reduced after stopping the intrathecal baclofen infusion in
seven patients. The dose of baclofen could be reduced to 40% of that dose
which was originally necessary in 10 patients. The dose remained the same or
increased slightly in 10 patients. Possible reasons for the continuing reduction of
spasticity after terminating long term intrathecal baclofen infusion in some
patients could be: lasting morphological changes in spinal cord neurons by
second messenger controlled modulation of gene expression, a toxic effect of
baclofen on spinal neurons, muscular atrophy, inflammation due to the catheter,
or progression of multiple sclerosis. CONCLUSIONS-- A higher initial daily dose
of intrathecal baclofen might lead to a faster, lasting suppression of spasticity and
the development of spastic symptoms might even be prevented by pre-emptive
treatment with baclofen in patients with newly acquired lesions of the spinal cord


treatment for certain symptoms in patients with spinal cord lesions. A double-
blind, cross-over study. Neurology 26, 441-446.
Abstract: Baclofen (a gamma aminobutylic acid derivative) and a placebo were
compared for their efficacy in relieving certain symptoms in patients with long-
standing spinal cord lesions and "spinal spasticity." In a double-blind, cross-over
clinical investigation, 22 patients with chronic spinal cord disease were studied.
Baclofen regularly alleviated involuntary flexor or extensor spasms and increased
resistance to passive movement of the legs but did not alter strength, gait, stretch
reflexes, or clonus. Side effects were mild and transient. This study demonstrates
that (1) baclofen is useful for the treatment of flexor spasms and (2) in evaluating
a new mode of therapy, one must consider selectively the response of individual
components of such global syndromes as "spasticity."

Abstract: The use of a recently released anticonvulsant, gabapentin, in the
treatment of spasticity in two patients with multiple sclerosis is reported.
Gabapentin was chosen because of its GABA-ergic effect and because
previously reported studies have shown that it is well tolerated compared with
other GABA-mimetic medication. Satisfactory release of spasticity with significant
improvement of functional outcome was noted in both cases. Both patients were
first treated with gabapentin for one month at 300 mg per day and then, with no
reported side-effects, at 400 mg per day. Before treatment, spasticity (graded
with modified Ashworth Scale) in one patient was 3 for left lower and 2 for right
lower limbs, and Expanded Disability Status Scale (EDSS) was 7; ambulation
was limited to a few steps with a standard walker. After two weeks of treatment,
spasticity was 2 and 1 for the left and right lower limbs, respectively. At three-month intervals, spasticity was +1 for left and 1 for right lower limbs, and EDSS was 6; the patient could ambulate 75 to 100 m with a standard walker. In the second patient, spasticity before treatment was 2 for both lower and left upper limbs. EDSS was 5.5, and ambulation was confined to 100 m with a cane. Spasticity improved to +1 in lower and 1 in left upper limbs after two weeks and to 1 and normal after three months. At three months, EDSS was 3 and the patient could ambulate for long distances without an assistive device. We suggest that gabapentin can be used effectively to decrease spasticity without significant side effects in patients with multiple sclerosis.


Abstract: Normal development of the CNS requires adequate thyroid hormone exposure. Since iodine is an essential component of the thyroid hormone molecule, its deficiency during fetal development can cause hypothyroidism and irreversible mental retardation. The full-blown syndrome, called cretinism, includes deaf-mutism, short stature, spasticity, and profound mental retardation. The clinical spectrum can vary in degree and combination of these features. Screening programs in iodine-deficient countries show that up to 10% of neonates have elevated serum TSH levels, putting them at theoretical risk for permanent brain damage. About one billion people worldwide risk the consequences of iodine deficiency, all of which can be prevented by adequate maternal and infant iodine nutrition. Iodized salt is usually the preferred prophylactic vehicle, but iodized vegetable oil, iodized water, and iodine tablets are also occasionally used. The United Nations and the heads of state of most countries have pledged the virtual elimination of iodine deficiency by the year 2000. This goal is technically feasible if pursued with sufficient vigor and resources.


Abstract: Dantrolene sodium (Dantrium) is a skeletal muscle relaxant, unique in that it acts on the muscle itself. It should be considered for use in patients with skeletal muscle spasticity who are in a stable neurological state. After careful adjustment of the dose, a substantial number of such patients will experience one or more of the following benefits: (1) a reduction in pain, (2) an increased ability to make use of residual motor function, (3) a reduction in the level of nursing care required, (4) an increased ability to utilize devices, and (5) an increased ability to participate in rehabilitation. The drug should not be used
when reduced spasticity will decrease functional ability. The adverse effects generally are transient; some are the result of central nervous system depression.


Abstract: The ability of botulinum A toxin to denervate and relax a spastic external urethral sphincter was evaluated in a double-blind study involving five men with high spinal cord injuries and detrusor-sphincter dyssynergia. The sphincter was injected with either a low dose of botulinum A toxin or normal saline once per week for three weeks. Electromyography of the external urethral sphincter indicated denervation in the three patients who received toxin injections. The urethral pressure profile decreased an average of 25cm of water, postvoiding residual volume of urine decreased an average of 125cc, and bladder pressure during voiding decreased to an average of 30cm of water. Bulbosphincteric reflexes were more difficult to obtain, and they showed a decreased amplitude with normal latency. In the two patients who received normal saline injections, parameters were unchanged from baseline values until subsequent injection with botulinum A toxin once per week for three weeks when their responses were similar to those of the other three patients. Mild generalized weakness lasting two to three weeks was noted by three patients after initial toxin injections. The duration of the toxin's effect averaged two months. The results suggest that botulinum A toxin, an inhibitor of acetylcholine release at the neuromuscular junction, may be useful in the treatment of detrusor-sphincter dyssynergia.


Abstract: Thirty-nine ambulant children (22 with hemiplegia, 17 with diplegia) with spastic cerebral palsy receiving isolated gastrocnemius muscle injection with botulinum toxin A were studied prospectively. The children had a mean age of 6 years (range 3 to 13 years). Measurement of gastrocnemius muscle length was used to estimate the dynamic component of each child's spasticity and to quantify the response. There was a strong correlation between the dynamic component of spasticity before injection and the corresponding magnitude of the response after injection. Children undergoing repeated injections showed similar correlations. A strong correlation was found between the duration of response and the dynamic component. Children with hemiplegia showed twice the duration for a given dynamic component compared with those with diplegia when injected with the same total dose per unit body weight. Long-term lengthening did not occur for the cohort, although some patients showed a response at a 12-month follow-up. By delaying shortening, the injections may have a role in delaying the need for surgery. Injections were well tolerated with few side effects.

Abstract: Temporary but considerable increase in spasticity following myelography using metrizamide at 300 mgs l/ml concentration occurred in 4 patients. In 3 of the patients the diagnosis is uncertain, but it is likely to be some form of degenerative disease involving motor pathways in two of them; the fourth case has cervical spondylotic myelopathy. The spasticity might be related to the anticholinesterase activity of metrizamide or to competitive inhibition of endogenous glucose metabolism by the deoxyglucose component of the metrizamide molecule.


Abstract: Intramuscular neurolysis with phenol has been used for 10 years in the management of spasticity in children. Best results depend on fastidious technique and realistic use of the procedure. Sedation or anesthesia was used in all cases -- 5% phenol in water was used for all procedures. The main indications were spasticity which interfered with function, either actual or potential, or with care. Where uninhibited vestibular or tonic neck reflexes affect muscle tone, or there is dystonia or athetosis, the procedure is less effective than where spasticity alone is present. Duration of relief of spasticity ranged from 1 month to more than 2 years. About one half of the lower extremity muscle treated required tenotomy later. Generally training was required after the procedure to obtain improved function. A representative sample of muscles treated, repeat procedures, and later surgery is discussed. The procedure is recommended for use in the management of spasticity in children as a way of improving function and/or care.


Abstract: The pharmacology of hydrated 1 less than ([5-(3,4-dichlorophenyl)-2-furanyl]methylene) amino greater than-2,4,-imidazolidinedione sodium salt (clodanolene sodium), as skeletal-muscle contraction antagonist, is presented. Clodanolene sodium is remarkable in that it has no measurable direct effect on the peripheral or central nervous systmes. Skeletal muscle relaxation can be achieved with this drug at doses that do not affect motor coordination. Rats receiving clodanolene sodium for up to 30 days evidenced a downward trend in gross observation score of skeletal muscle relaxation, but the extent of twitch inhibition was the same on day 30 as on day 1. In an animal model of muscle spasticity (Straub-tail mouse), clodanolene sodium has been shown to be more efficacious for induction of skeletal muscle relaxation than neuromuscular...
blocking agents, local anesthetics, or centrally-acting muscle relaxants. Clodanolene sodium's mode of action has been identified as specific for skeletal muscle. It has no measurable effect on neuromuscular transmission or on the electrically excitable surface membrane. Indirect evidence indicates that the site of action of clodanolene sodium, like that of dantrolene sodium, is within the muscle cell and is related to caffeine-sensitive calcium stores. Its skeletal-muscle relaxant activity, we suggest results from a decrease in the release of calcium from the sarcoplasmic reticulum.


Abstract: In a double blind, placebo controlled, cross over study the correlations between single doses (2, 4, and 8 mg), plasma concentrations, and antispastic action of tizanidine were investigated in 16 patients with extensor spasticity of the legs due to multiple sclerosis. An electrogoniometer was used to assess muscle tone at knee extensors, applying Wartenberg's pendulum test. Blood samples, a clinical assessment of muscle tone by the Ashworth scale, and muscle strength by the British Medical Research Council scale were obtained concomitantly. Confirmatory analysis using the change in the relaxation index (R2 value) 1.5 hours after each treatment, showed a statistically significant (p = 0.0123) linear dose-response relation between single doses and antispastic action of tizanidine. Further statistical analysis showed a strong within patient linear correlation between plasma concentrations and antispastic action at 4 and 8 mg doses (p = 0.014 and 0.004 respectively), but only weak between patient correlations. The analysis of the dose-plasma concentration relation showed results consistent with linear pharmacokinetics. The comparison of changes in the R2 ratio with concomitant Ashworth scores showed a significant correlation between the two. It is concluded that there are linear correlations between single doses, plasma concentrations, and antispastic action of tizanidine. Because of the strong within patient but weak between patient correlation between plasma concentrations and antispastic action of tizanidine the effective doses should be determined individually.


Abstract: Very high intravenous doses (2-19 mg/min) of thyrotropin-releasing hormone (TRH, L-pyroglutamyl-L-histidyl-L-prolinamide) given to 12 patients with amyotrophic lateral sclerosis (ALS) produced a moderate to marked improvement of functions caused by deficiency of lower motor neurons (weakness) and upper motor neurons (spasticity). The improvement was sustained throughout the infusion and for about 1 h thereafter; sometimes a slight improvement was evident 20 h after infusion. At a given dose benefits and side-effects were more evident in men than in women. Whether TRH is replacing an ALS-associated deficiency or is simply a symptomatic treatment is unknown. The
results of this study raise the possibility of a treatment for ALS, and may provide new insight into its pathogenesis. The potential response to TRH of spasticity and/or lower motor neuron involvement of other causes is proposed

Abstract: A 43-year-old male with bronchogenic carcinoma was treated with continuous morphine via a thoracic epidural catheter. On the fifth day, after a total dose of 24 mg morphine chloride in 10 or 20 ml saline, he developed hallucinations, hyperthermia, spasticity, narcolepsy and opisthotonos. Respiratory rate and blood pressure were unaffected. Intravenous naloxone reversed all neurological abnormalities. This unusual syndrome was probably caused by a rostral spread of morphine. The location of the catheter and volume seem to be important variables. Hallucinations are important signs of impending intoxication

Abstract: Continuous flow pumps are being used for the delivery of morphine sulfate to the intrathecal and epidural space for control of pain. We have encountered several patients who had a combination of pain and spasticity or who had spasticity so intense that it was the source of pain. One to two milligrams of intrathecal morphine dramatically relieved their spasticity and pain. Three such patients have subsequently undergone pump implantation with prolonged control of their spasticity. This has initiated a formal clinical investigation directed at determining the physiological mechanism of this phenomenon, as well as its long term efficacy

Abstract: Three years ago we reported our preliminary results regarding treatment of intractable spasticity with use of intrathecal morphine. This paper is a follow-up report of 12 patients who underwent implantation of a pump or reservoir for delivery of intrathecal morphine sulfate for control of spasticity. Our primary concern initially was that patients would ultimately become drug tolerant and lose the beneficial effect of the morphine. Only one of these 12 patients has developed drug tolerance. The longest follow-up period has been 4.3 years, and this patient has maintained excellent control of his spasticity with a stable dose of 2 mg of morphine daily


Abstract: A multi-centre, double-blind study was carried out in 100 patients suffering from chronic spasticity due to multiple sclerosis to compare the effectiveness of tizanidine hydrochloride with that of baclofen. Patients were allocated at random to receive treatment initially with daily doses of either 6 mg tizanidine or 15 mg baclofen and the dose was increased during the first 2 weeks up to a maximum of 24 mg tizanidine or 60 mg baclofen per day. Patients were then treated with the optimum dose for 6 weeks. Efficacy and tolerability parameters were evaluated after 2 and 8 weeks. Tizanidine and baclofen improved the functional status of patients in 80% and 76% of cases, respectively, but there were no significant differences between the two drugs. The antispastic efficacy of tizanidine was greater after 8 weeks than after 2 weeks, whereas the efficacy of baclofen decreased slightly with time. Both drugs showed good overall tolerability in more than 60% of patients. Thus, tizanidine is a well tolerated and effective muscle relaxant, the antispastic efficacy of which is well maintained over time, and it promises to be particularly useful in the treatment of spasticity due to multiple sclerosis.


Abstract: Naloxone treatment improves neurologic outcome after experimentally induced spinal trauma, but this opiate-receptor antagonist may increase post-traumatic pain. In contrast, thyrotropin-releasing hormone appears to act in vivo as a partial physiologic opiate antagonist that spares analgesic systems; this activity prompted us to evaluate its effect in spinal injury. Cervical-spine trauma was produced in anesthetized cats by the Allen method. Six animals each received thyrotropin-releasing hormone, saline, or dexamethasone as an intravenous infusion over four hours, beginning one hour after injury. Neurologic recovery was significantly better after treatment with thyrotropin-releasing hormone than after saline or dexamethasone (P less than 0.01): at six weeks, the average animal given thyrotropin-releasing hormone was normal, whereas average control animals had marked spasticity. The beneficial effect of thyrotropin-releasing hormone in experimental spinal injury and its lack of effect on nociception indicate that it may have unique therapeutic potential in spinal trauma in human beings.


Abstract: The behavioural effects of selective serotonin reuptake inhibitors (paroxetine, sertraline, citalopram, fluvoxamine, fluoxetine) and reference compounds (N,N'-di(o-tolyl)guanidine, haloperidol, 3-(3-hydroxyphenyl)-N-((I-propyl)piperidine and chlorpromazine) were studied for their ability to produce
dystonia and torticollis following direct micro injection into the left red nucleus of
the rat, an area of the brain containing a high density of sigma2 receptors but
relatively devoid of biogenic amine receptors. Each animal was monitored for
abnormalities in posture and movement for a period of 30 min and then sacrificed
40 min following drug administration. Only fluvoxamine (100 nmol) and fluoxetine
(100 nmol) elicited acute dystonic behaviour (1-5 min). The onset of dystonia was
accompanied by facial spasticity, vacuous chewing movements and grooming
behaviour which reflected the extent of dystonia. The dystonic behaviour
following the direct intrarubral injection of fluvoxamine and fluoxetine suggest the
possible activation of sigma2 receptors while citalopram, sertraline and
paroxetine were without effect. The results of this study support the role of
sigma2 receptors in the regulation and control of movement and coordination and
provides preliminary evidence to suggest the in vivo activity of sigma receptors
by fluoxetine and fluvoxamine

sigma receptors following chronic selective serotonin reuptake inhibitor
Abstract: The purpose of the present study was to investigate the potential
impairment of normal motor function following chronic selective serotonin
reuptake inhibitor treatment that may result from sensitisation of sigma receptors.
Rats were chronically treated with either sertraline, citalopram, paroxetine or
fluvoxamine and a selective sigma receptor ligand, di-o-tolyguanidine (DTG), for
28 days. All animals then received an acute intra-rubral injection of either DTG or
saline. Following the direct injection of DTG into the red nucleus, rats chronically
treated with DTG exhibit a maximal behavioural response characterised as a
pronounced dystonia. Animals chronically treated with sertraline and citalopram
elicited a response similar to that of control animals following the acute DTG
challenge, whereas chronic treatment with paroxetine and fluvoxamine
significantly decreased and increased the dystonic response, respectively. Facial
spasticity and vacuous chewing movements were associated with, and reflected
the extent of, the DTG-induced dystonia. Changes in regional biogenic amine
concentrations were also determined. The concentrations of serotonin and
noradrenaline were determined in the brain stem and cerebellum following the
intra-rubral injection of either saline or DTG in animals that had been chronically

treated with a selective serotonin reuptake inhibitor or DTG. There was a
significant increase in serotonin concentration in the brain stem as a result of
chronic DTG and fluvoxamine treatments. The increase in serotonin correlated
with the reported potentiation of dystonia in animals that received 28 days
treatment with these drugs. The potentiation of dystonia following chronic DTG
and fluvoxamine treatments suggests that these drugs sensitise the sigma2
receptors, an effect that does not appear to be shared by citalopram, sertraline or
paroxetine

Fakhoury T., Abou-Khalil B., and Blumenkopf B. (1998) EEG changes in
intrathecal baclofen overdose: a case report and review of the literature.
Abstract: OBJECTIVE: To review the clinical and EEG manifestations of intrathecal baclofen overdose. METHODS: We identified one patient who had received an overdose of intrathecal baclofen. Information about the clinical course was obtained by reviewing the patient's medical record. EEGs were recorded with the use of the standard 10-20 electrode placement system. RESULTS: The patient received 30 mg baclofen intrathecally. Shortly after the injection he developed respiratory insufficiency and quadriparesis and later became comatose. The first EEG obtained 20 h after the injection showed very frequent quasiperiodic generalized epileptiform discharges. The patient gradually improved clinically and a second EEG obtained 24 h later showed only intermittent bursts of generalized slow wave activity. A repeat EEG study 1 week later was normal. CONCLUSIONS: The EEG in intrathecal baclofen overdose can show quasiperiodic generalized epileptiform discharges. This does not necessarily indicate the presence of underlying potential epileptogenicity, and treatment with an antiepileptic medication is not necessary.

Abstract: Succinylcholine-induced potassium efflux was studied in two groups of healthy adult patients presenting for elective surgery. One group (Group 1) of 12 patients received alfathesin induction followed by succinylcholine. The other group (Group 2) of 12 patients were pre-treated with fazadinium 0.075 mg.kg⁻¹ about three minutes before administration of alfathesin and succinylcholine. Serial blood samples were taken pre-induction, post-induction and after succinylcholine for estimation of plasma potassium. The results show that pre-treatment with fazadinium 0.075 mg.kg⁻¹ was effective in preventing succinylcholine-induced potassium efflux.

Abstract: The effects on muscle fasciculations and ease of tracheal intubation of pretreatment with fazadinium before administration of succinylcholine were evaluated in 85 patients. Four dose levels of fazadinium evaluated were 0.05 mg.kg⁻¹, 0.075 mg.kg⁻¹, 0.10 mg. kg⁻¹ and 0.15 mg. kg⁻¹. The 0.05 mg.kg⁻¹ dose did not always prevent succinylcholine-induced muscle fasciculations. The 0.15 mg. kg⁻¹ dose gave poor conditions for tracheal intubation and was therefore discontinued. The 0.075 mg. kg⁻¹ dose seemed optimal. Most patients felt transient pain at the site of the injection during administration of fazadinium, and many had a sensation of drowsiness.

Abstract: OBJECTIVE: In a randomized, controlled, single-blind trial, to test the hypothesis that botulinum-A toxin (BTA) injections into the upper extremity of
children with spastic hemiplegia improve upper extremity function. STUDY DESIGN: Thirty children with hemiplegia, aged 2.5 to 10 years, were randomly assigned to receive: (1) a BTA injection into 1 or more of 3 muscle groups (biceps, volar forearm muscles, adductor pollicis) plus occupational therapy or (2) occupational therapy alone. Blinded outcomes obtained at baseline and at 1, 3, and 6 months included the Quality of Upper Extremity Skills Test (QUEST), goniometry measurements, grip strength, and Ashworth scores. The caregiver completed the self-care domain of the Pediatric Evaluation of Disability Inventory. RESULTS: Twenty-nine subjects completed the study. The QUEST demonstrated a significant improvement favoring the treatment group on a 2-way analysis of variance (F = 4.69, df = 1,83; P = .039). BTA treatment was also associated with an improvement in score on the self-care domain of the Pediatric Evaluation of Disability Inventory (F = 4.68, df = 1,82; P = .04). CONCLUSIONS: This study supports the effectiveness of BTA injections to improve upper extremity function of children with hemiplegia who have at least moderate spasticity.

Abstract: Baclofen is a safe and effective means for treating spasticity associated with multiple sclerosis. We found no toxic effects on hepatologic, hematopoietic, or renal function, acutely or for over 3 years of follow-up. A statistically significant reduction was noted in frequency of spasms, and clonus, and there was improved range of joint movement, which enabled patients to maintain functional status for prolonged periods. For the more disabled patients, treatment with baclofen gave symptomatic relief of painful spasms and made immobility more tolerable. Optimum effect was achieved when baclofen was administered in the early stages of disease, before major disabilities became permanent.

Abstract: A case of stiff-man syndrome (SMS), a rare and dramatic CNS disease characterized by continuous muscle activity and painful spasms resembling a chronic form of tetanus, occurring in a patient with Hodgkin's disease (HD) is reported. The patient developed the clinical features of SMS at the same time as the HD relapse. A satisfactory improvement was obtained with diazepam, but the complete recovery from stiffness was achieved only after chemotherapy was started. Cerebellar autoantibodies were found in the serum of the patient. With chemotherapy the patient achieved a second complete remission (CR). Eighteen months later the patient developed a second HD relapse, and at that time no signs of SMS were detected.

Abstract: Botulinum toxin injections are a new treatment for limb spasticity. Intramuscular injections can be performed in spastic muscles; efficacy occurs one or two weeks later, with a mean duration of three months. Clinical action is related to chemical denervation of presynaptic motor end nerves by the botulinum toxin. Double blind studies versus placebo have demonstrated the improvement of limb spasticity after injections of botulinum toxin. Ashworth scales, articular angulations, pain and spasms improve both in upper and lower limb spasticity. Functional scores are not changed in the upper limb, but quality of life improves. Kinematic parameters of gait are improved in lower limb spasticity, especially in children with cerebral palsy disorders. There were no reports of serious side effects. Botulinum toxin is a safe and effective treatment of localized spasticity in adults and children.


Abstract: Succinylcholine, a depolarizing muscle relaxant with both activating and desensitizing effects, is used to facilitate endotracheal intubation. The activating effects were found to be above-normal on induction of anesthesia in 7 neurological patients: generalized muscle spasm in 1 myotonic patient, contractures or prolonged contractions in "anatomically" denervated muscles (1 patient), in "functionally" denervated muscles (1 patient) and in "centrally" denervated muscles (4 patients). One of these four presented hyperkalemia and cardiocirculatory collapse. It is important to differentiate these anomalous responses to succinylcholine from those occurring as early signs of rhabdomyolysis or malignant hyperthermia.


Abstract: Conventional electromyographic (EMG) guidance in botulinum toxin therapy can localize a muscle, but the amount of electrical activity is assessed only subjectively. We wanted to introduce a quantitative EMG criterion, according to which the decision for/against toxin application could be made. Turn/amplitude analysis (TAA) was applied to nine patients with severe paraspasticity (n = 5), right upper or lower limb spasticity (n = 3), or tetraspasticity (n = 1) before and after toxin administration. Muscles were selected for toxin application if both mean turns/second and mean amplitude/turn exceeded the level of 150. A mean Dysport dose of 116 mouse units (mu) (range 40-240 mu) was administered to each of the 26 muscles that met the EMG criterion. Thirty days after the injection, activities of daily living, pain, and TAA count improved in 89%, tone in 78%, and range of motion in 56% of the patients by at least 1 point on corresponding 5-point rating scales. TAA provides a useful EMG criterion for/against botulinum toxin application. Muscle selection according to this criterion leads to a significant subjective and objective toxin effect. TAA is a valuable tool to determine the
benefit of single and subsequent botulinum toxin injections in the treatment of spasticity

Abstract: A two-year follow-up study of 73 low-birth-weight (less than 1,501 gm) infants treated with positive pressure ventilation as neonates revealed the following: 24% incidence of lower respiratory tract infections during the first year; weight and height at two years averaging between tenth and twenty-fifth percentiles; major neurologic defects diagnosed in 14 boys (39%) and seven girls (18%) with one-year Bayley scores of less than 80. Major neurologic sequelae were closely associated with a neonatal history of seizures and intracranial hemorrhage and were more common in boys, survivors weighing more than 1,000 gm and following high-risk pregnancies


Abstract: Intrathecal drug administration via implanted pump is an effective treatment for intractable pain and spasticity but can be compromised by catheter-related complications. To determine the etiology of catheter-related complications, we have conducted a multicenter, prospective study of the long-term performance of a one-piece catheter system. Data pertaining to catheter-related complications were collected at implant and at specified times during the follow-up period. Catheter implantation characteristics that might affect complications were assessed. Two hundred nine patients were studied at 22 participating centers, with 1764 cumulative patient-months of catheter experience. Forty-nine catheter system complications occurred in 37 patients (7 complications related to the catheter itself, and 42 complications related to the implantation procedure). The 9-month complication-free "survival" rate was 78.9% overall (95.5% for the catheter itself). No specific catheter implantation characteristics were associated with the occurrence of complications. These data indicate that the incidence of complications for a one-piece catheter system is similar to that of commercially available two-piece systems, and highlight the need for careful surgical technique during implantation

Abstract: BACKGROUND: Continuous infusion of intrathecal (IT) baclofen is a highly effective standard therapy for severe spasticity of spinal origin. By
contrast, there is limited clinical experience regarding the use of IT baclofen in treating patients with dystonia, and little is known regarding the indications for treatment, efficacy, and safety of IT baclofen in this disorder. OBJECTIVE: To study retrospectively the effects of IT baclofen in treating 25 patients with severe segmental or generalized dystonia. SETTING: Neurological Institute, Columbia-Presbyterian Medical Center, New York, NY. PATIENTS: Twenty-five patients with severe segmental or generalized dystonia that was refractory to oral medications underwent IT baclofen test dosing. In addition to dystonia, 17 patients had spasticity or painful spasms. Thirteen of 25 patients responded to the test doses of IT baclofen, according to unblinded neurological assessments that included the patient's subjective report; all 13 underwent implantation of a pump for continuous IT baclofen infusion. RESULTS: In contrast to reports of patients with spasticity of spinal origin, those with dystonia in the present series had a lower response rate to bolus IT baclofen doses and a smaller degree of clinical improvement. For 10 of the 13 responders to the test doses of IT baclofen, dystonia rating scale scores of videotaped examinations by blinded observers detected no significant change (P < .07) in severity of dystonia. Retrospective data from 11 of 13 patients with implantable pumps, followed up for a mean interval of 21 months after pump insertion, showed continuing efficacy in 6 individuals (55%), based on a determination of patient satisfaction; however, only 3 patients (27%) reported a sustained improvement in functional capacity. Five (38%) of the 13 patients with implantable pumps experienced severe complications that required hospitalization. CONCLUSIONS: Despite recent reports that have described the benefit in small numbers of patients with dystonia, we concluded that the role of IT baclofen in treating severe dystonia remains uncertain. Intrathecal baclofen may be more effective when dystonia is associated with spasticity or pain. In the present series, we detected no significant difference in the response to IT baclofen in patients with or without spasticity or pain, perhaps owing to the small sample size.

Abstract: Propriospinal myoclonus is a rare and relatively little studied complication of spinal cord injury. We report two patients with an extension-producing myoclonus presenting with tetraplegia caused by cervical trauma. Rhythmic extension jerks of the trunk and lower limbs appeared several weeks after their injury in a context of severe spasticity. The characteristics of these jerks were determined by polymyography of 12 muscles. They lasted between 306 and 1127 ms with a frequency of 0.3 to 0.5 Hz. By comparing latencies their origin was found to be in the lumbar cord from which there was a slow (2 m s-1) upward and downward spread. Oral treatment with baclofen and sodium valproate was partially successful in one patient, but ineffective in the other. Intrathecal 75 or 100 micrograms baclofen produced a striking, complete disappearance of myoclonus prompting the implantation and successful use of a baclofen pump in one patient. These two new cases suggest the existence of a
lumbar generator in which myoclonic extension jerks originate, and demonstrate a new therapeutic alternative in intrathecal baclofen for patients resistant to oral medication.


Abstract: Because diazepam appeared to affect body weight, spastic myelopathy patients for whom this drug had been prescribed but in whom the dose was altered were compared with similar patients, without changes in antispastic medication. A retrospective survey averaging 10 months was conducted for these two groups to determine weight changes of 10 pounds or more. After reduction or discontinuation of diazepam in seven patients, all lost weight -12 to 35 lbs at rates of 0.9 to 3.5 lb per month. On unchanged medication, only one of twelve patients lost as much as 10 lb, p < 0.001. After partially or fully restoring diazepam in four patients, all gained weight -7 to 26 lbs-at rates of 1.8 to 4.3 lbs per month. Three of the four patients and two of the 12 without medication change gained as much as 10 pounds, p = 0.03. We conclude that body weight in myelopathy patients is affected by the use of diazepam. The effect of other medications used for spasms was not assessed.


Abstract: GABAB (gamma-aminobutyric acid)-receptors have been implicated in central nervous system (CNS) functions, e.g. cognition and pain perception, and dysfunctions including spasticity and absence epilepsy. To permit an analysis of the two known GABAB-receptor splice variants GABAB-R1a (GB1a) and GABAB-R1b (GB1b), their distribution pattern has been differentiated in the rat brain, using Western blotting and immunohistochemistry with isoform-specific antisera. During postnatal maturation, the expression of the two splice variants was differentially regulated with GB1a being preponderant at birth. In adult brain, GB1b-immunoreactivity (-IR) was predominant, and the two isoforms largely accounted for the pattern of GABAB-receptor binding sites in the brain. Receptor heterogeneity was pronounced in the hippocampus, where both isoforms occurred in CA1, but only GB1b in CA3. Similarly, in the cerebellum, GB1b was exclusively found in Purkinje cells in a zebrin-like pattern. The staining was most pronounced in Purkinje cell dendrites and spines. Using electron microscopy, over 80% of the spine profiles in which a synaptic contact with a parallel fibre was visible contained GB1b-IR at extrasynaptic sites. This subcellular localization
is unrelated to GABAergic inputs, indicating that the role of GABAB-receptors in vivo extends beyond synaptic GABAergic neurotransmission and may, in the cerebellum, involve taurine as a ligand.

Abstract: In 17 in-patients suffering from spasticity due to multiple sclerosis, the effect and tolerability periods were 4 weeks each. As to efficacy, the variables: spasticity, clonus, flexor spasms, gait and bladder function were evaluated clinically. No significant difference was found between the two drugs. As far as side-effects are concerned, sedation was specifically inquired about. Apart from that, spontaneously reported side-effects were recorded. Sedation was more often seen during treatment with diazepam, while the side-effects during baclofen treatment were more varied. The total number and severity of side-effects were equal in the two treatment groups. A preference for one of the two treatment periods was stated by the investigator before the code was broken. A significant difference (p less than 0.001) in favor of Lioresal was found. This is discussed in the light of the fact that no significant difference was found for the individual symptoms or side-effects.

Abstract: Baclofen is a gamma-aminobutyric acid (GABA) agonist approved for the treatment of spasticity and commonly used in the management of many types of neuropathic pain. Controlled studies have demonstrated the efficacy of this drug in trigeminal neuralgia. Although its precise mechanism of analgesic action is unknown, it is likely that a drug-induced increase in inhibitory activity is sufficient to interrupt the cascade of neural events that culminates in aberrant activity of wide dynamic range neurons, or more rostral neurons in nociceptive pathways, that is the substrate for some types of neuropathic pain. The optimal use of baclofen as an adjuvant analgesic requires an understanding of its pharmacology, side effect spectrum, and dosing guidelines that have proven useful in clinical practice. Failure of baclofen therapy following a prolonged trial requires dose tapering prior to discontinuation due to the potential for a withdrawal syndrome.

Abstract: Intrathecal administration of Baclofen, a GABA agonist, through an implantable drug delivery pump has been demonstrated to be effective in the treatment of limb spasticity in patients with myelopathy. Three patients, followed before and after pump placement, experienced satisfactory spasticity relief and improvement in areas of self-care and mobility. Improvement in the bladder management programs of each patient was noted. These changes coincided with
improvement on urodynamic studies, defined as either an increase in bladder capacity or a decrease in sphincter dyssynergia. Changes in bladder function were associated with the initiation of intrathecal therapy and with changes in pump-delivered dosages. In selected patients, intrathecal baclofen infusion can have a beneficial effect on bladder management programs.


Abstract: OBJECT: Previously, we reported the efficacy of pentoxifylline (PTX) treatment in human T-lymphotropic virus type I (HTLV-I)-associated myelopathy (HAM). Here, we clarify the relationship between the clinical efficacy of PTX treatment and elevation of T helper type 2 (Th2) cytokine levels in HAM patients.

PATIENTS AND METHODS: PTX (300 mg) was administered daily by the oral route to 12 HAM patients for 4 weeks. We assessed the relationship between the changes in neurological status (motor disability scores, the degree of spasticity on neurological examination, and the time required to walk 10 m) and the changes in serum and cerebrospinal fluid (CSF) levels of interferon-gamma (IFN-gamma) as a Th1 cytokine and interleukin-4 and -10 (IL-4 and -10) as Th2 cytokines measured by an EASIA (enzyme-amplified sensitivity immunoassay) kit.

RESULTS: PTX treatment induced incremental increases in the levels of IL-4 and IL-10 in both sera and CSF of 6 HAM patients. Clinical improvement was associated with this elevation in IL-4 and IL-10. PTX treatment also induced a decrease in IFN-gamma levels in the sera of 6 HAM patients, but this was not correlated with clinical improvement.

CONCLUSION: These results suggest that the correction of the immunological imbalance in Th1 to Th2 cytokine responses, with upregulation of IL-4 and IL-10, may account for the clinical improvement in HAM patients treated with PTX.


Abstract: The combined effects of a noradrenergic agonist, clonidine, and a serotonergic antagonist, cyproheptadine, together with an interactive locomotor training program incorporating progressive body weight support and treadmill walking exercise, were investigated in two chronic spinal cord injured subjects. Both subjects had no independent locomotor ability due to severe spasticity. Kinematic, temporal distance and electromyographic (EMG) data were collected during treadmill walking. The EMG activity of the lower limb muscles, initially characterized by tonic discharge and abnormal timing, became more phasic with less clonus following medication, which was related to a change in the kinematic pattern. Further kinematic and functional improvement were gained by training. Previously wheelchair-bound, both patients became functionally ambulatory overground with the aid of Canadian crutches. Thus, a potentially effective
strategy for facilitating the expression of the locomotor pattern following spinal cord injury is proposed. This preliminary study showed that such a treatment strategy could possibly lead to a recovery of locomotor function in some chronic, wheelchair-bound spinal cord injured patients who had previously been stabilized on conventional therapies.

Abstract: Between April 1982 and June 1983 four children 3 to 24 months of age were referred for evaluation of neurologic abnormalities found to be compatible with vaccine-related poliovirus infection, which had not been suspected by referring physicians. Patients were epidemiologically unrelated residents of Indiana, and none had prior symptoms suggestive of immunodeficiency. All had received poliovirus vaccine orally (first dose in three, fourth dose in one) and a diphtheria-tetanus-pertussis injection in the left anterior thigh within 30 days of symptoms. A vaccine-like strain of poliovirus was isolated from each patient, and each had symptoms (left leg paralysis in three; developmental regression, spasticity, and progressive fatal cerebral atrophy in one) persisting for at least 6 months. Immune function was normal in two with poliovirus type 3 infection, and abnormal (hypogammaglobulinemia, combined immunodeficiency) in two with type 1 and type 2 infection, respectively. The incidence of observed vaccine-related poliovirus infection in Indiana recipients of orally administered poliovirus vaccine was 0.058 per 100,000 per year, significantly greater (P less than 0.001) than predicted.

Abstract: OBJECTIVE: To describe the use of intra-reservoir gentamicin for the treatment of a Pseudomonas aeruginosa infected baclofen pump. SETTING: Regional Spinal Injuries Centre, Hexham, Northumberland, England. SUBJECT: Male patient aged 32 years with progressive multiple sclerosis and severe bilateral spasticity. RESULTS: Intra-reservoir gentamicin proved successful in treating infection with Pseudomonas aeruginosa. CONCLUSION: Intra-reservoir gentamicin may be successful in treating pump infection with Pseudomonas aeruginosa without the need for pump removal.

Abstract: One goal of pharmacology is to break a cycle of pain and spasms. In this cycle, pain leads to muscle spasms, and spasms lead to pain with no physiologic feedback control occurring. A second goal is to break another interacting cycle of pain and inflammation. In this cycle, pain mediators can lead to inflammation and the inflammation itself can contribute to pain. The two cycles
perpetuate each other because they have many interacting factors in common. Drugs are useful either alone or to supplement other forms of therapy that can break the pain/spasm cycle, as well as the pain/inflammation cycle. This article discusses the many types of drugs available to the clinician today. Although the original version of this article was published by the first author in 1973, the number of new drugs (including some new classes of agents) and newer concepts of pain that have been introduced have required further updating.

Garabedian-Ruffalo S.M. and Ruffalo R.L. (1985) Adverse effects secondary to baclofen withdrawal. Drug Intell. Clin. Pharm. 19, 304-306. Abstract: Drug therapy is now the preferred method of treatment for spasticity, and several effective agents have been developed. The safety and efficacy of these drugs has been established in short-term studies. Overall, due to its low incidence of sedation and serious side effects, baclofen appears to be the drug of choice in the treatment of spinal cord-related spasticity. It is, however, not without its side effects due to both its administration and abrupt withdrawal. This case illustrates some significant problems associated with the abrupt withdrawal of long-term baclofen therapy in a patient with multiple sclerosis.

Garcia Ruiz P.J., Pascual P., I, and Sanchez B., V (2000) Progressive response to botulinum A toxin in cerebral palsy. Eur. J. Neurol. 7, 191-193. Abstract: Botulinum A toxin (BT) has been successfully used for the management of spasticity in cerebral palsy (CP). However, the long-term results of BT have not yet been determined. We have studied the evolution of a homogeneous group of patients with CP treated with BT. All these patients had an equinus gait resulting from calf muscle spasticity without other muscle group involvement. All of these patients were treated with the same total dose (4 microg/kg) at the same time interval (three months). The mean follow-up time was 33 months. Gait evaluation was made blind on videotape recordings by two independent physicians according to five point scale. All our patients exhibited a progressive improvement in their gait pattern. None of our patients developed fixed contractures nor did any of them need surgical correction. No significant side-effects were seen. The response observed in our study could be due to a progressive symptomatic effect of BT, but it might be also explained by a change in the natural history of the spasticity related to CP, at least in this selected group of patients.

Gardner B., Jamous A., Teddy P., Bergstrom E., Wang D., Ravichandran G., Sutton R., and Urquart S. (1995) Intrathecal baclofen--a multicentre clinical comparison of the Medtronic Programmable, Cordis Secor and Constant Infusion Infusaid drug delivery systems. Paraplegia 33, 551-554. Abstract: A retrospective review was carried out of 34 consecutive traumatic spinal cord damaged patients who have had the Medtronic Programmable, Cordis Secor or Constant Infusion Infusaid intrathecal baclofen drug delivery systems inserted between July 1987 and 1992. The results indicate that whilst this treatment has many benefits there is a significant risk of complications, some
potentially fatal. It should only be provided by a skilled and experienced team. The Medtronics Programmable pump is an excellent pump. It is of particular benefit where the therapeutic window is small or fine-tuning required. The Constant Infusion Infusaid is adequate if less precise control and continuous infusion is sufficient. It is of particular benefit in financially disadvantaged countries. The Cordis Secor device is helpful when unpredictable intermittent relief of spasticity is required but is otherwise limited by its complication rate.


Abstract: The motor points of spastic wrist and finger flexors were identified using a nerve stimulator. These motor points were injected percutaneously with either a 3% or 5% aqueous solution of phenol in 11 patients with brain injury. The effectiveness of the blocks was assessed by recording the resting angle of the wrist, active extension of the wrist, and passive extension of the wrist--first with the fingers flexed and then with the fingers extended. The blocks were repeated once in two patients and twice in one patient for return of muscle tone which interfered with hand function. Relaxation of muscle tone persisted for up to two months following the injections. The resting angle of the wrist improved a mean of 25 degrees. Active wrist extension improved an average of 30 degrees. The changes in wrist measurements represent the effects of different processes: 1) the neurolytic effect of the phenol block; 2) improvement in the neurologic status of the patient; and 3) regeneration of the motor end plate. This procedure is an effective method of temporarily controlling spasticity and allowing functional hand training while neurologic recovery is occurring.

Gawade S., Bon C., and Bizzini B. (1985) The use of antibody Fab fragments specifically directed to two different complementary parts of the tetanus toxin molecule for studying the mode of action of the toxin. Brain Res. 334, 139-146.

Abstract: The injection of 500 minimal lethal doses (MLDs) of tetanus toxin into mice routinely causes a flaccid-type paralysis and death within 8 h. Non-precipitating antibody fragments (Fab) directed against each of two papain cleavage products of tetanus toxin (Ibc and IIc) were used to study this botulinum toxin-type effect of tetanus toxin. Ibc (100,000 daltons) is a toxic fragment which does not bind to gangliosides but will produce a flaccid type paralysis when injected into mice. Treatment of intact tetanus toxin (500 MLDs) with Fab-Ibc prevents the flaccid type paralysis and such mice will die from a spastic paralysis after about 24 h. IIc (50,000 daltons) is an atoxic fragment of tetanus toxin which binds tightly to gangliosides. Treatment of tetanus toxin with Fab-IIc prior to intracerebral injection converts the characteristic spastic paralysis to a flaccid paralysis. It is proposed that the botulinum toxin-type effect of tetanus toxin complexed to Fab-IIc results from the inability of such complexes to be transported to the central nervous system. Moreover, the ability of Fab-Ibc to prevent flaccid paralysis, but not spastic paralysis, suggests that both types of paralysis may be mediated by the same portion of the tetanus toxin molecule.

Abstract: Selective dorsal rhizotomy (SDR) is a neurosurgical procedure used for treating lower extremity spasticity in patients with cerebral palsy. The purpose of this paper is to present a review of our institution's first three years' experience with postoperative pain and spasticity management in patients who have undergone SDR. The medical records of the 55 patients who had an SDR during the study period were reviewed. The basis of postoperative analgesia was morphine, with the majority of patients receiving continuous morphine infusions (20-40 micrograms.kg-1.hr-1 (n = 49), 60 micrograms.kg-1.hr-1 (n = 1)). Four patients used a patient-controlled delivery system. One patient had successful analgesia with epidural morphine. Ketorolac (1 mg.kg-1 i.v. loading dose followed by 0.5 mg.kg-1 i.v. every six hr for 48 hr) was used as an adjunct to morphine in six patients. For management of postoperative muscle spasm, an intravenous benzodiazepine was used (diazepam 0.1 mg.kg-1 (n = 2), or midazolam infusion 10-30 micrograms.kg-1.hr-1 (n = 51)). All patients were cared for on a ward where nurses were familiar with the use of continuous opioid and benzodiazepine infusions. All patients received continuous cardiorespiratory monitoring as well as frequent nursing assessment. There were no episodes of postoperative apnoea or excessive sedation. We have found the use of continuous infusions of morphine and midazolam, along with adjunct ketorolac, to be effective in treating postoperative pain and muscle spasms following SDR


Abstract: The paper presents the results of clinical and neurophysiologic study of muscular tonus in 94 patients aged 42-70 years in early recovery after ischemic stroke. Selective role of spasticity was estimated in clinical pattern of motor disorders in groups of the patients with different disorders of muscular tonus with the same degree of paresis. Efficiency of antispastic preparation sirdalud was analyzed in 28 patients from this group. Sirdalud in daily dose of 6-12 mg in patients with prevalence of a spasticity in a clinical picture of the paresis and with either moderate or manifested degree of paresis of the extremities has significant antispastic effect without any decrease of muscular strength, which, in turn, increases the degree of restoration of motor functions


Abstract: Based on examining 20 patients with infantile cerebral paralyses (ICP) and 18 epileptic patients aged 6 to 14 years it has been demonstrated that the effective doses of carbamazepine do not differ (14-27 mg/kg/day) in both the groups, whereas the effective doses of phenobarbital are higher (5.3 mg/kg/day) in ICP patients than in those suffering from epilepsy (3.65 mg/kg/day; P less than 0.05). In this case the blood concentration of both carbamazepine and phenobarbital was lower in ICP patients (5.1 and 23.1 mg/l, respectively, than in epileptic patients (8.2 and 28.8 mg/l). The drug levels in the blood serum were measured by high-effective liquid chromatography. It was assumed that the efficacy of the lower drug concentrations in ICP patients was related to greater permeability of the blood-brain barrier or with higher sensitivity of "epileptized" neurons in them as compared to epileptic patients. The comparison of the doses and blood concentrations may point to more intense biotransformation of the antiepileptic agents in the body of ICP patients than in patients suffering from epilepsy.


Abstract: Intrathecal baclofen (ITB) infusion has been shown to be an effective treatment for spasticity secondary to both cerebral palsy and spinal cord injury. Its effect on the ambulatory status of individuals with cerebral spasticity, however, has not previously been addressed. We reviewed the effect of ITB on functional ambulation in 24 patients who were ambulatory to some extent, either with or without assistive devices. Twenty-one pumps were placed in patients with spastic cerebral palsy and 3 in patients with spasticity secondary to traumatic brain injury (13 boys and 11 girls, mean age 18 years). The mean ITB dose was 200 microg/day (range 22-550 microg/day) and the mean length of follow-up was 52 months. Ambulation was retrospectively graded on four functional levels: community, household, non-functional, and non-ambulatory. The level of ambulation improved by one functional level in 9 patients, did not change for 12 patients, and was worse in 3 patients. Gait was considered to be improved in 20 of 24 patients by the patients or their families. The overall functional improvement not directly related to ambulation was found to be improved in 20 patients, unchanged in 2 patients, and worse in 2 patients. ITB allows for improved ambulation in a certain subset of patients with lower extremity spasticity. It is not contraindicated in patients who rely upon their spasticity for support during ambulation. ITB infusion allows for baclofen dosage titration to balance between extensor tone for support and suppression of hyperactive reflexes which may impede normal locomotion.


Abstract: Intrathecal baclofen infusion (IBI) is an effective treatment for spasticity secondary to cerebral palsy (CP). OBJECT: To assess the need for orthopedic surgery of the lower extremities in such cases, the authors retrospectively
reviewed the outcome in 48 patients with spastic CP who were treated with IBI.

METHODS: Pumps were placed in 40 patients (84%) suffering from spastic quadriplegia and eight patients (16%) with spastic diplegia. The patients’ ages ranged from 5 to 43 years (mean 15 years). The mean follow-up period was 53 months (range 24-94 months). The mean baclofen dosage was 306 microg/day (range 25-1350 microg/day). At the time of pump placement, subsequent orthopedic surgery was planned in 28 patients (58%); however, only 10 (21%) underwent surgery after IBI therapy. In all 10 cases, the surgical procedure was planned at the time of initial evaluation for IBI therapy. In the remaining 18 patients, who did not subsequently undergo their planned orthopedic operation, it was believed that their lower-extremity spasticity had improved to the degree that intervention was no longer indicated. In addition, although six patients had undergone multiple orthopedic operations before their spasticity was treated, no patient required more than one operation after IBI treatment for spasticity.

CONCLUSIONS: The authors conclude that IBI for treatment of spastic CP reduces the need for subsequent orthopedic surgery for the effects of lower-extremity spasticity. In patients with spastic CP and lower-extremity contractures, spasticity should be treated before orthopedic procedures are performed.

Abstract: A 39-year-old female patient who had been receiving 30 mg of baclofen daily for 5 months was admitted to the hospital about 12 hr after overdose of this drug (450 mg). On admission, she was comatose, flaccid, and in respiratory failure. Later she developed muscle twitchings and had several epileptic fits. She was treated symptomatically and became conscious within 36 hr. However, approximately 65 hr after the overdose she developed sinus tachycardia which was successfully treated with oral propranolol. Plasma concentrations, as measured on days 2 and 3, were within the therapeutic range but the elimination half-life was prolonged.

Abstract: Treating severe spasticity with the continuous infusion of intrathecal baclofen through an implantable delivery system is a new and successful alternative to oral medications and ablative surgical procedures. Nurses have a vital role in patient care throughout all phases of therapy. Advances in this technology hold promise for our future in treating other neurologic disorders.

Abstract: Injection of dilute phenol to peripheral nerves or motor block areas when there is spasticity, can, by damage to the nerves or motor areas, relieve the spastic condition, allow better nursing care, free the patient from the embarrassment of a contorted limb and may allow voluntary movement to take place.

Abstract: Intrathecal baclofen infusion has demonstrated effectiveness in decreasing spasticity of spinal origin. Oral antispasticity medication is minimally effective or not well tolerated in cerebral palsy. This study assessed the effectiveness of intrathecal baclofen in reducing spasticity in cerebral palsy. Candidates were screened by randomized, double-blind, intrathecal injections of baclofen and placebo. Responders were defined as those who experienced an average reduction of 1.0 in the lower extremities on the Ashworth Scale for spasticity. Responders received intrathecal baclofen via the SynchroMed System and were followed for up to 43 months. Fifty-one patients completed screening and 44 entered open-label trials. Lower-extremity spasticity decreased from an average baseline score of 3.64 to 1.90 at 39 months. A decrease in upper extremity spasticity was evidenced over the same study period. Forty-two patients reported adverse events. Most common reports were hypotonia, seizures (no new onset), somnolence, and nausea or vomiting. Fifty-nine percent of the patients experienced procedural or system-related events. Spasticity in patients with cerebral palsy can be treated effectively by continuous intrathecal baclofen. Adverse events, although common, were manageable


Abstract: Thirteen paraplegias after decompression have been treated in the 5 centres of Lyons, Geneva, Mulhouse, Basel and Strasbourg. All these cases are somehow comparable: 12 males, 1 female, skilled and well-trained divers are involved from 27 to 50 years. Submersion between 30 and 42 metres, during 15 to 30 minutes. Ascension with or without decompression stops. Beginning with sudden posterior thoracic, 4 feeling sick, 2 becoming briefly unconscious, paralysis after a while (until 1 hour). All have received hyperbaric oxygenation (from 1 to 5 hours later), with an improvement for 10. Neurological findings. 5 tetraplegics, 7 para-(5 with Brown-Sequard), and one L1. Quickly, the tetraplegics improved to a thoracic level. In two cases, paraplegia remained complete at thoracic level. The others had a better evolution; the paralysis improved slowly, with marked spasticity, impaired sensation did not improve to such an extent, often localised at a lower level, with sexual impotence. Micturitions became normal but with often urine leakages. This rather favourable evolution allowed 11 to go back to work


Abstract: We describe a patient presenting with progressive bulbar dysfunction
and spasticity that clinically mimicked amyotrophic lateral sclerosis (ALS). Electromyography, however, showed no evidence of denervation and revealed a rare combination of peripheral and central myokymia. We feel that this pattern of myokymia represented a marker of neural injury from remote radiation therapy. Nervous system disorders resulting from therapeutic radiation are described, and potential pathophysiologic mechanisms underlying myokymia are discussed.


Abstract: A case report of an infant whose mother used phencyclidine (PCP, "angel dust") during pregnancy is presented. As a neonate, the infant showed abnormal behavior and an unusual appearance, and later, spastic quadriparesis. Based on previous animal studies, it is likely that this infant had prolonged exposure to PCP as a fetus. His abnormal neonatal behavior was consistent with previously reported effects of this drug. The relationship between his exposure to PCP and his dysmorphology and spasticity remains speculative. It is suggested that clinicians be alert to further cases of these associations.

Abstract: Diconium bromide, 2-(3,4-dichloroanilino)-quinolizinium bromide, a potent antispasmodic in the lower bowel of the dog, was found in the present study to exert gastric acid-antisecretory and antiulcerogenic activities in the rat stomach. These effects were demonstrated by means of short- and long-term pyloric ligation, acetylsalicylic acid (ASA)- induced ulcerogenesis, and cold-and-restraint stress studies. A reduction of gastric acid concentration by the drug was probably responsible for the decrease in the degree of ulceration and hemorrhagic lesion formation. The drug's inhibition of stress hemorrhagic lesions may be related to an effect both on gastric HCl secretion and on the vasculature in the glabular mucosa. The delay of gastric emptying by diclonium bromide results from its known antispasmodic or smooth-muscle depressant action. The toxicity of diclonium bromide, perorally, was low in rats and overt signs of drug effect were not evident until toxic doses were administered. It is concluded that diclonium bromide may represent a useful non-anticholinergic drug effective in treating both peptic ulcers and spasticity of the colon (irritable-colon syndrome) in man.

Abstract: We have investigated the effects of various dopamine (DA) agonists on
induction of abnormal involuntary movements (AIM) in a group of monkeys which had denervated nigro-striatal DA neurons for 10-14 years rendered by a unilateral surgical ventromedial tegmental (VMT) lesion of the brainstem. The surgical lesions were placed when the monkeys were 2-4 years old. The administration of mixed DA agonists, such as L-DOPA, apomorphine (Apo) and abeorphine 201-678, elicit a self-mutilative biting behavior (SMB) of the forelimb digits contralateral to the lesion, and spasticity of the contralateral hindlimb. These dysfunctions resemble, in some aspects, the neurological disturbances associated with Lesch-Nyhan syndrome. The SMB behavior was elicited by mixed DA agonists which predominantly stimulate D1, but not D2 DA receptors, and was prevented or abolished by the D1 DA antagonist SCH 23390 or by the D1 and D2 DA antagonist fluphenazine (Flu), but not by the D2 antagonist (+/-)-sulpiride. These results suggest that DA agonist-induced SMB behavior is mediated by D1 and/or by both D1 and D2 DA receptor pathways. To study the relationships between HPRT, the defective enzyme in Lesch-Nyhan syndrome, and the DA neuronal systems, we have measured the effects of nigro-striatal DA degeneration and intrastriatal neuronal degeneration on HPRT activity. The unilateral 6-OHDA-induced nigro-striatal DA degeneration does not significantly alter the HPRT activity on the lesioned side of the striatum, while the quinolinic acid-induced intrastriatal neuronal degeneration significantly reduces the enzyme activity. These results suggest that HPRT is localized on intrastriatal neurons which are also known to contain DA receptors. It is postulated that HPRT deficiency in Lesch-Nyhan syndrome results in abnormal guanine nucleotide metabolism which may affect the regulation of DA receptors.


Abstract: 1. Monkeys with surgical unilateral ventromedial tegmental lesions of the brain stem served as models for investigating abnormalities in Parkinson's disease and Lesch-Nyhan syndrome. 2. The animals exhibited some neurological deficits which are similar to those observed in Parkinson's disease or Lesch-Nyhan syndrome. 3. In monkeys with unilateral ventrolateral tegmental lesions, the levels of dopamine and the activities of catecholamine-synthesizing enzymes were reduced on the lesion side of the striatum, and hypokinesia and tremor developed on the contralateral extremities. 4. Dopa or dopamine agonists relieve tremor and evoke abnormal involuntary movements which are similar to the responses observed in patients with Parkinson's disease. 5. The antitremor effect of Dopa is potentiated by catechol-O-methyltransferase inhibition, suggesting a therapeutic potential for these types of agents. 6. Evidence was obtained that stimulation of D2 dopamine receptors by selective dopamine agonists exerts antitremor activity and evokes abnormal involuntary movements. 7. Combined administration of D1 and D2 dopamine agonists seems to enhance the antitremor activity. 8. Partial dopamine agonists exert antitremor activity and produce less severe abnormal involuntary movements than full dopamine agonists. 9. In a group of monkeys with unilateral ventromedial tegmental lesions
of the brain stem the administration of mixed D1/D2 dopamine agonists results in the occurrence of self-biting behavior of the forelimb digits and spasticity of the hindlimbs and these symptoms are similar to those observed in patients with Lesch- Nyhan syndrome. The self-biting behavior seems to be associated with the stimulation of central D1 dopamine receptors and therefore the possible involvement of dopamine neuronal abnormalities in Lesch-Nyhan syndrome deserves further investigation.


Abstract: The authors have studied the antispastic action of Dantrium in 50 patients with multiple sclerosis; in all cases, hypertonia, spasms or clonus constituted a severe obstacle to remedial therapy or nursing. After one year, the authors have found that Dantrium is effective in reducing hypertonia in 40% of the patients, in improving spasms in 65% and in reducing clonus in 50% of the cases. Secondary effects are fairly frequent (60%), characterized in most cases by diminished muscular strength and greater fatigability.


Abstract: The cause of postoperative shivering is not known. The theories and possible remedies are reviewed. Five hundred patients were observed for the possible effect of lissive doses of gallamine, and of analgesic or benzodiazepine premedication. Diazepam premedication appeared to reduce the incidence of post-halothane shivering.


Abstract: Strychnine intoxication is manifested by agitation, muscle spasms, and convulsions. We report a case in which intractable convulsions led to severe lactic acidosis which secondarily resulted in visceral (lung, heart, kidney, liver, and brain) collapse and death. Aggressive therapy instituted in the emergency department and aimed at control of seizure activity and lactic acidosis may be lifesaving.


Abstract: OBJECTIVE: In an effort to increase the effect of intrathecal baclofen
on upper-extremity spasticity, the tip of the intrathecal catheter was placed at the T6-T7 level rather than at the traditional T11-T12 level in children with spastic quadriparesis. METHODS: Twelve children with spastic quadriparesis from varying causes had significant reductions in spasticity after a test dose of intrathecal baclofen and subsequently underwent placement of a programmable pump and intrathecal catheter tip placed at the T6-T7 level with fluoroscopic guidance. With the use of Ashworth scores for four muscle groups in both the upper and lower extremities, degrees of spasticity were determined by a physiatrist preoperatively and at 1, 3, 6, and 12 months postoperatively. Mean changes in upper- and lower-extremity Ashworth scores and baclofen dosages for the entire cohort were compared with published results in which the catheter tip had been placed at the T11-T12 level. RESULTS: Spasticity was significantly reduced in all muscle groups (P < 0.001). The lower-extremity reduction in spasticity of 1.6 points at 3 and 12 months was greater than published reductions of 1.1 points at 3 and 12 months. The upper-extremity reduction in spasticity was noticeably greater at 3 and 12 months (1.7 and 2.0 points, respectively) than published results at 3 and 12 months (0.4 and 0.6 points, respectively). At 3, 6, and 12 months, our mean baclofen dosage remained below the dosages administered at the T11-T12 level. There were no complications related either to the positioning of the catheter higher in the spinal canal or to the administration of baclofen at the T6-T7 level. CONCLUSION: Compared with published results, placement of the tip of the intrathecal catheter at the T6-T7 level was associated with greater relief of upper-extremity spasticity without loss of effect on the lower extremities. The mean dosages of baclofen in our study group were lower compared with mean dosages administered at the T11-T12 level. There was no morbidity related to the more rostral location of the catheter.


Abstract: Systemic pharmacologic treatments may be indicated in conditions in which the distribution of muscle overactivity is diffuse. Antispastic drugs act in the CNS either by suppression of excitation (glutamate) enhancement of inhibition (GABA, glycine), or a combination of the two. Only four drugs are currently approved by the US FDA as antispastic agents: baclofen, diazepam, dantrolene sodium, and tizanidine. However, there are a number of other drugs available with proven antispastic action. This chapter reviews the pharmacology, physiology of action, dosage, and results from controlled clinical trials on side effects, efficacy, and indications for 21 drugs in several categories. Categories reviewed include agents acting through the GABAergic system (baclofen, benzodiazepines, piracetam, progabide); drugs affecting ion flux (dantrolene sodium, lamotrigin, riluzole; drugs acting on monoamines (tizanidine, clonidine, thymoxamine, beta blockers, and cyproheptadine); drugs acting on excitatory amino acids (orphenadrine citrate); cannabinoids; inhibitory neuromediators; and other miscellaneous agents. The technique, advantages and limitations of intrathecal administration of baclofen, morphine, and midazolam are reviewed.
Two consistent limitations appear throughout the controlled studies reviewed: the lack of quantitative and sensitive functional assessment and the lack of comparative trials between different agents. In the majority of trials in which meaningful functional assessment was included, the study drug failed to improve function, even though the antispastic action was significant. Placebo-controlled trials of virtually all major centrally acting antispastic agents have shown that sedation, reduction of global performance, and muscle weakness are frequent side effects. It appears preferable to use centrally acting drugs such as baclofen, tizanidine, and diazepam in spasticity of spinal origin (spinal cord injury and multiple sclerosis), whereas dantrolene sodium, due to its primarily peripheral mechanism of action, may be preferable in spasticity of cerebral origin (stroke and traumatic brain injury) where sensitivity to sedating effects is generally higher. Intrathecal administration of antispastic drugs has been used mainly in cases of muscle overactivity occurring primarily in the lower limbs in nonambulatory, severely disabled patients but new indications may emerge in spasticity of cerebral origin. Intrathecal therapy is an invasive procedure involving long-term implantation of a foreign device, and the potential disadvantages must be weighed against the level of disability in each patient and the resistance to other forms of antispastic therapy. In all forms of treatment of muscle overactivity, one must distinguish between two different goals of therapy: improvement of active function and improvement of hygiene and comfort. The risk of global performance reduction associated with general or regional administration of antispastic drugs may be more acceptable when the primary goal of therapy is hygiene and comfort than when active function is a priority.

Abstract: OBJECTIVE: To assess acceptability, effects on swelling, resting posture, spasticity, and active (AROM) and passive range of motion (PROM) of individually tailored upper limb Lycra garments, designed as dynamic splints to exert directional pull on certain limb segments, when worn for 3 hours by hemiplegic patients. DESIGN: Crossover trial. SETTING: Outpatient and inpatient rehabilitation center. PATIENTS: Convenience sample of 16 patients with hemiparesis and upper limb spasticity caused by a stroke more than 3 weeks before the study. INTERVENTIONS: Assessments performed at the start and end of a 3-hour period during a standard rehabilitation day when the patients were and were not wearing the garment. MAIN OUTCOME MEASURES: (1) Comfort assessed by questionnaire; (2) circumference of each limb segment; (3) resting posture at elbow and wrist; (4) spasticity at shoulder, elbow, and wrist using the Tardieu scale; and (5) AROM and PROM at shoulder, elbow, and wrist measured using a goniometer; (6) elbow proprioception using McCloskey’s method; (7) visual neglect syndrome using the line bisection test. Differences between changes occurring with and without the garment were compared using Wilcoxon’s signed rank test for ordinal variables (spasticity grading) and Student’s t test for continuous variables (all other data). RESULTS: During 3
hours, garments worn on the arm by patients with hemiplegia (1) were comfortable, (2) improved wrist posture and reduced wrist and finger flexor spasticity, (3) reduced swelling in patients with swollen limbs (digit circumference decreased by 4%; p<.01), (4) improved PROM at shoulder (mean increase in range, 4.1 degrees +/- 13.0 degrees per shoulder movement; p<.01); and (5) impaired ability to flex fingers (range of voluntary flexion of digit III reduced from 107.3 degrees +/-79.6 degrees to 91.4 degrees +/- 74.1 degrees; p<.05).

CONCLUSION: Lycra garments, designed to produce continuous stretch of spastic muscles when worn for several hours each day, have rapid splinting and antispastic effects on wrist and fingers in patients with hemiplegia. These garments may help severely affected patients with major spasticity or painful swollen limbs.


Abstract: Botulinum toxin type A (BTX-A) is increasingly being used for the treatment of childhood spasticity, particularly cerebral palsy. However, until very recently, all such use in this indication has been unapproved with no generally accepted treatment protocols, resulting in considerable uncertainty and variation in its use as a therapeutic agent. In view of the increasing awareness of, and interest in, this approach to the treatment of spasticity, and also the recent licensing in a number of countries of a BTX-A preparation for treating equinus deformity in children, it would seem timely to establish a framework of guidelines for the safe and efficacious use of BTX-A for treating spasticity in children. This paper represents an attempt, by a group of 15 experienced clinicians and scientists from a variety of disciplines, to arrive at a consensus and produce detailed recommendations as to appropriate patient selection and assessment, dosage, injection technique and outcome measurement. The importance of adjunctive physiotherapy, orthoses and casting is also stressed.


Abstract: Vigabatrin was specifically designed to enhance gamma-aminobutyric acid (GABA) function in the CNS. By increasing brain concentrations of this inhibitory neurotransmitter the drug appears to decrease propagation of abnormal hypersynchronous discharges, thereby reducing seizure activity. At this stage in its development, clinical experience with vigabatrin is limited primarily to patients with refractory seizure disorders. In this difficult-to-treat population, 'add-on' therapy with vigabatrin greater than or equal to 2 g/day has shown impressive...
efficacy, reducing seizure frequency by greater than or equal to 50% in approximately half of patients. Clinical efficacy does seem to vary with seizure type with the best response reported in adults with complex partial seizures with or without generalisation and in children with cryptogenic partial epilepsy or symptomatic infantile spasm. Vigabatrin appears to have a negative effect on absences and myoclonic seizures. Some disorders of motor control may also be amenable to enhanced GABAergic function. In the small number of patients with tardive dyskinesia treated to date, vigabatrin produced mild to moderate improvement in hyperkinetic symptom scores but Parkinsonism or schizophrenic symptoms occasionally worsened. The best response was reported in a study of patients who had been withdrawn from neuroleptic therapy. In a small but well-controlled comparative trial, vigabatrin was as effective as baclofen in reducing spasm and improving some parameters of spasticity in patients with spinal cord lesions or multiple sclerosis. Most adverse reactions to vigabatrin are mild and transient with central nervous system (CNS) changes being reported most frequently. Of particular note, serial evoked potential studies and the few available histology reports have not found evidence of intramyelinic oedema during therapeutic use, as was reported in rats and dogs on chronic high-dose treatment. Thus, vigabatrin is a promising new anticonvulsant drug. Current evidence supports a trial of this agent as adjunctive therapy in patients with refractory seizure disorders, and future investigation of vigabatrin monotherapy and its efficacy relative to established agents is awaited with interest. Wider experience should help to clarify which patients - by seizure type and concurrent CNS pathology - are likely to benefit from vigabatrin and ongoing monitoring should further clarify the potential detrimental effects, if any, of long term use. In the meantime, it is a welcome addition in the difficult setting of resistant epilepsy.

Abstract: The paper describes a system for transcutaneous functional neuromuscular stimulation (FNS) of certain traumatic thoracic-level complete paraplegics for independent unbraced short distance ambulation. The system described has been approved by the FDA in 1994 for that purpose. Its design, control, operation principles and parameters are described. Patient acceptance criteria and contraindications are outlined as is patient's training. Ambulation results are discussed and clinical and medical observations are reviewed. Finally general comments are made on the system's shortcomings and on possible improvements.

Abstract: BACKGROUND: Functional Neuromuscular Stimulation (FNS) for unbraced short-distance ambulation by traumatic complete/near-complete T4 to T12 paraplegics is based on work by Graupe et al (1982), Kralj et al (1980),
Liberson et al (1961), and others. This paper discusses methodology, performance, training, admissibility criteria, and medical observations for FNS-ambulation using the Parastep-I system, which is the first and only such system to have received FDA approval (1994) and which emanated from these previous works. METHOD: The Parastep system is a transcutaneous non-invasive and microcomputerized electrical stimulation system built into a Walkman-size unit powered by eight AA batteries that is controlled by finger-touch buttons located on a walker’s handbars for manual selection of stimulation menus. The microcomputer shapes, controls, and distributes trains of stimulation signals that trigger action potentials in selected peripheral nerves. Walker support is used for balance. The patient can don the system in under 10 minutes. At least 32 training sessions are required. RESULTS: Approximately 400 patients have used the Parastep system, essentially all achieving standing and at least 30 feet of ambulation, with a few reaching as much as 1 mile at a time. Recent literature presents data on the medical benefits of using the Parastep system—beyond the exercise benefits of short distance ambulation at will—such as increased blood flow to the lower extremities, lower HR at subpeak work intensities, increased peak work capability, reduced spasticity, and psychological benefits. CONCLUSIONS: We believe that the Parastep FNS system, which is presently commercially available by prescription, is easily usable for independent short-distance ambulation. We believe that its exercise benefits and its other medical and psychological benefits, as discussed, make it an important option for thoracic-level traumatic paraplegics.


Grenier B., Mesli A., Cales J., Castel J.P., and Maurette P. (1996) [Severe hyperthermia caused by sudden withdrawal of continuous intrathecal administration of baclofen]. Ann. Fr. Anesth. Reanim. 15, 659-662. Abstract: Baclofen is used for the treatment of post-traumatic spasticity. It carries a risk of overdose as well as of an acute withdrawal syndrome. We report two cases of severe hypertonia and hyperthermia (> 42 degrees C), occurring after accidental discontinuation of intrathecal infusion of baclofen. Both hypertonia and hyperthermia ceased when administration of baclofen was resumed. In parallel, the patients developed transient life-threatening alterations of hepatic (cytolysis), haematologic (coagulopathy) and cardiorespiratory functions for some days. It is concluded that the occurrence of such a withdrawal syndrome should be prevented, especially in patients with chronic intrathecal administration and first symptoms should be recognized without delay. Relationships with other malignant hyperthermias are discussed.

Abstract: This paper concerns the "H" reflex in eleven patients with spastic spinal cord injury (C5-T10), treated with Baclofen (50 mg/day) or Diazepam (20 mg/day). The "H" reflex was tested in the tibial nerve before and 15 days after the interrupted use of the drugs. Five patients used Baclofen and 6 patients used Diazepam. The latency time was measured. All the patients showed normal latency time before the use of the drugs. After the use all but one didn't show any significant alterations of the latency time. The patient, who showed a greater latency after use of drugs, presented an improvement of the motor function.


Abstract: This study reviews a nearly three-year experience of intramuscular neurolysis in children with spasticity. Thirteen children aged 3 to 11 years received general anesthesia during 16 procedures. Ten were cerebral palsy patients, one a congenital hydrocephalic, one a familial spastic paraplegic, and one a brain-injured child. Types of preoperative medications, induction and maintenance anesthetic agents are described, with indications for the particular choices of each type of drug. The principal and side effects of these agents during and after the 16 procedures are summarized. A combination of agents such as chloral hydrate; atropine if endotracheal intubation is necessary; pentothal, halothane, or cyclopropane for induction, and halothane- nitrous oxide for maintenance is our current choice of drugs to produce a light surgical plane of anesthesia. Advantages and disadvantages of the operating room method are considered. An overnight hospital stay was sufficient for all but two children, who required an additional evening of observation as the result of anesthetic side effects. No major complications were encountered in any of these elective procedures. The presence of a pediatric anesthesiologist during the procedure is perhaps to most reassuring aspect of the operating room- general anesthesia method.


Abstract: This report describes a patient presenting with a spastic quadriplegia who was found to have both diffuse idiopathic skeletal hyperostosis (DISH) and ossification of the posterior longitudinal ligament (OPLL) in the cervical spine. There was a dramatic worsening of his symptoms during a myelogram examination of the neck. It is suggested that computed tomographic imaging of the neck is the preferred investigative procedure if OPLL is suspected as a cause of cervical myelopathy.


Abstract: Preclinical data indicate that the administration of the amino acid L-threonine increases glycine levels in rat spinal cord. In order to investigate glycineric mechanisms in spasticity, and other signs of the upper motor syndrome, we gave 4.5 and 6.0 g/day of L-threonine to 18 patients with familial spastic paraparesis (FSP) according to a double-blind, crossover protocol. The response to treatment at the end of each 2-week period was based upon three measures: the physician's global impressions; the patients' global impressions; and semiquantitative ratings of strength, muscle tone, DTRs, walking, hopping, and running. Blood and CSF were collected during each treatment period for amino acid analyses. Based upon the severity rating scales, there was a statistically significant (p less than 0.02) decrease in motor impairment and spasticity during L-threonine administration compared to placebo treatment; significant treatment effects were not found on the physician's and patients' global impressions. Plasma and CSF levels of threonine increased significantly during L-threonine treatment but glycine levels did not change. These data indicate that L-threonine significantly suppressed the signs of spasticity even though the benefits were not clinically valuable


Abstract: TRH analogues have a longer half-life than does TRH and enhanced neuropharmacological actions. In motorneurone disease (MND), no benefit was reported with MK771 and DN1417. Focal, transient, and slight improvements in weakness and spasticity were described with CG3509. A controlled trial with a single intravenous dose of RX 77368 showed improvements in dysarthria, tongue movements, respiration, swallowing, and spasticity lasting up to 72 hours. Changes in muscle force were of no functional significance. There was an acute 25-30% increase in mean corrected fiber density and in mean macro-EMG parameters in biceps, but no change in amplitude or area of single macro-EMG motor units followed during the 2-hour infusions. An acute, direct or indirect, central effect of RX77368 on recruitment order or on activation threshold of pathological motor units is suggested. In a subacute open trial with repeated intravenous infusions of RX77368 (median 2 weeks), improvement in bulbar function in 8 of 12 responders, cramps (5 of 9), and spasticity (5 of 8) were maintained for medians of 18, 14, and 7 days, respectively. Side effects were
prominent with doses above 0.2 mg/kg. Disease progression has not been halted with any analogue, but whether it may be usefully slowed down with RX77368 is worth investigating.

Gundlach A.L., Kortz G., Burazin T.C., Madigan J., and Higgins R.J. (1993) Deficit of inhibitory glycine receptors in spinal cord from Peruvian Pasos: evidence for an equine form of inherited myoclonus. Brain Res. 628, 263-270. Abstract: Inherited myoclonus in Poll Hereford calves and spasticity in the spastic mouse (spa/spa) are characterized by myoclonic jerks of the skeletal musculature which occur spontaneously and in response to sensory stimuli, symptoms resembling those in subconvulsive strychnine poisoning. The primary, biochemical defect in these myoclonic animals is a deficit of inhibitory glycine receptors in the central nervous system. We now report the occurrence of similar stimulus-induced myoclonus in individual, pure-bred Peruvian Paso horses and an associated, specific deficiency in the density of [3H]strychnine binding to inhibitory glycine receptors sites in spinal cord of these animals. Specificity of the deficit was confirmed by a demonstrated lack of change in the density of several other receptor types in affected spinal cord, including muscarinic receptors and GABAA/benzodiazepine receptors. In light of the existence of genetically-inherited myoclonus in other species, these results suggest the occurrence of an equine form of the disorder.

Gunduz S., Ogur E., Mohur H., Somuncu I., Acjksoz E., and Ustunsoz B. (1993) Deep vein thrombosis in spinal cord injured patients. Paraplegia 31, 606-610. Abstract: In this study to determine the incidence of deep vein thrombosis (DVT) in spinal cord injury (SCI) patients, we evaluated 30 instances of bilateral ascending venography obtained in 31 patients. Every patient was on prophylactic low dose heparin anticoagulant therapy. The incidence of DVT was found to be 53.3%. Adverse effects due to venography were seen in 10% of patients. No major complications including postvenographic phlebitis and allergic reactions were observed.

Gwartz B.L. (2001) Intrathecal baclofen for spasticity caused by thrombotic stroke. Am. J. Phys. Med. Rehabil. 80, 383-387. Abstract: This study was undertaken to determine the efficacy of intrathecal baclofen therapy in patients who suffer spasticity after a stroke. This case involves a 64-yr-old woman whose thrombotic strokes resulted in severe left-upper and lower-limb spasticity. The patient achieved substantial functional gains as well as improved ease of care, quality of life, and cessation of narcotic use.

Hachen H.J. and Krucker V. (1977) Clinical and laboratory assessment of the efficacy of baclofen (Lioresal) on urethral sphincter spasticity in patients with traumatic paraplegia. Eur. Urol. 3, 237-240. Abstract: A comparative clinical trial with oral and intravenous baclofen (Lioresal) was performed in a homogeneous group of 70 male patients, hospitalized with traumatic paraplegia. The dosage was 75 mg daily by mouth over a period of 10
days or 20 mg daily i.v. for 2 days. Drug efficacy was evaluated both clinically (residual urine; facilitation of micturition) and urodynamically (integrated cystosphincterometry, sphincter electromyography and micturition cystourethrograms). During oral therapy there were no significant changes in any of the studied parameters. Intravenous administration, on the contrary, proved highly effective and better tolerated


Abstract: Autonomic hyperreflexia occurs in spinal cord injured patients. The mechanism involves spasticity of the autonomic nervous system. Somatic stimuli have been infrequently reported as triggering stimuli for autonomic hyperreflexia. This article reports on a patient who experienced autonomic hyperreflexia brought on by dressing changes of pressure ulcers. Also included is a discussion of current treatment modalities with special regard for clonidine, the drug used in the case report


Abstract: STUDY DESIGN: Intrathecal administration of 4-aminopyridine (4-AP) in chronic spinal cord injured (SCI) patients. OBJECTIVE: To determine the safety and effects of intrathecal administration of 4-AP in a small population of chronic SCI patients. SETTING: The post anesthesia care unit of a tertiary care hospital. METHODS: Following animal mode studies to establish dosing safety, six subjects with chronic SCI were examined. In each subject, an intrathecal catheter was placed with the tip as close to the lesion level as possible. 4-AP was infused at 5 microg/h for a period of 4-5 h. Vital signs were recorded and sensory- motor physical examinations and pain questionnaires were administered for 24 h. In two patients, samples of cerebrospinal fluid for analysis were drawn from a second intrathecal catheter. RESULTS: No adverse systemic side effects were noted. One patient showed transient improvement in sensory function; two showed transient increases in spasticity; three showed transient increases in cutaneomuscular reflexes and two showed an apparent small increase in volitional motor control. The concentration of 4-aminopyridine in the cerebrospinal fluid reached a peak of 163 ng/ml at 4 h in one subject and 122 ng/ml at 5 h in the other subject examined. CONCLUSION: Intrathecal administration of 4-aminopyridine at a rate of 5 microg/h does not appear to cause adverse effects and may modify spinal cord function. This route of administration allows local cerebrospinal fluid concentrations equivalent to those
produced by maximum tolerable systemic doses, which require 1000 times more
drug substance to be delivered to the subject as a whole. Intrathecal
administration offers the potential to focus therapeutic effects to the lesion site
while minimizing systemic side effects

Microbiol. 39, 243-245.

Hammock M.K., Milhorat T.H., and Baron I.S. (1976) Normal pressure
Suppl 55-68.
Abstract: Although the syndrome of normal pressure hydrocephalus (NPH) was
described in the adult as early as 1964, it has only recently been recognized in
the child. In this preliminary report, eight myelomeningocele patients with
presumed NPH were evaluated before and after ventricular shunting procedures.
Cranial computed tomography and serial psychological testing have proved to be
particularly valuable both in the pre-operative and post-operative assessment of
these patients and have the distinct advantage of being simple, non-invasive
diagnostic measures. Continuous intra-ventricular pressure monitoring has
shown what promises to be characteristic elevated pressure plateaux imposed
on normal baseline cerebrospinal fluid (CSF) pressures in so-called NPH but is a
more difficult clinical procedure, necessarily associated with potential
complications. Although decreasing response to growth-stimulating hormone can
be demonstrated in patients with long-standing hydrocephalus, this endocrine
malfunction cannot be considered an early indicator of intracranial pathology.
Single IQ scores are inadequate measures of intellectual function in children
with NPH and serial examinations should be carried out. Detailed
neuropsychological testing will document performance IQ scores well below
verbal IQ scores and will generally show failure of psychomotor development to
keep pace with chronological ageing. Initial studies indicate that improved
performance scores can be expected within 1 1/2 to 3 months following
successful ventricular shunting operations, and that any downward trend in pre-
operative test scoring can at least be reversed. Statistically significant
improvements in full-scale IQ scores have not been seen, however, before the
end of the first post-operative year. Clinically, improved attentiveness and
sociability, and decreased spasticity (if present prior to surgery) can be expected
following shunting. Over-all, ventriculomegaly, normal CSF pressure, stable head
size, and non-progressive neurological symptoms cannot be regarded as
sufficient criteria for the diagnosis of an arrested state of hydrocephalus, and
should suggest NPH, especially in those children who demonstrate a
discrepancy between performance and verbal IQ scores and who fail to exhibit
continuing psychomotor development with advancing age

Abstract: The intrathecal administration of baclofen by way of an implanted
A subcutaneous drug delivery system is described in a patient with a severe spastic paraparesis due to multiple sclerosis. Intrathecally administered baclofen is proposed as another therapeutic dimension and adjunct to physical therapy in the management of patients with severe spasticity that is unresponsive to antispasticity agents administered by mouth.


Abstract: The potassium channel blocking drug 4-aminopyridine (4-AP) was administered to eight patients with chronic spinal cord injury, in a therapeutic trial based on the ability of the drug to restore conduction of impulses in demyelinated nerve fibers. The study was performed using a randomized, double-blind, crossover design, so that each patient received the drug and a vehicle placebo on different occasions, separated by 2 weeks. Drug and placebo were delivered by infusion over 2 h. An escalating total dose from 18.0 to 33.5 mg was used over the course of the study. Subjects were evaluated neurologically before and after the infusion. Two subjects returned for a second trial after 4 months and were examined daily for 3 to 4 days following drug infusion. Side effects were consistent with previous reports. Administration of the drug was associated with significant temporary neurologic improvement in five of six patients with incomplete spinal cord injury. No effect was detected in two cases of complete paraplegia and one of two severe incomplete cases (Frankel class B). Improvements in neurologic status following drug administration included increased motor control and sensory ability below the injury, and reduction in chronic pain and spasticity. The effects persisted up to 48 h after infusion of the drug, and patients largely returned to preinfusion status by 3 days. Compared with the more rapid elimination of the drug, these prolonged neurologic effects appear to involve a secondary response and are probably not a direct expression of potassium channel blockade.


Abstract: Three cases developing increasing neurological deficit within 24 hours of lumbar radiculography with Dimer X are reported. All three developed severe low back and sciatic pain, and myoclonic spasms within one hour of the examination. In each a large intervertebral disc prolapse was outlined. Two cases developed near complete paraplegia before surgical decompression. Following surgery, two patients made a complete rapid recovery, and the other has recovered partially.


Abstract: The routine therapy of multiple sclerosis (MS) in world-wide use today is comprised of four measures: Antiinflammatory and antiedematous treatment with ACTH or Synacthen, respectively, and corticosteroids: only during acute episodes. - High dosage, short duration, no long-term therapy.
Immunosuppression with azathioprine (Imurek): Due to the relatively high risk only to use in malignant courses (frequent and severe bouts). Basic therapy with unsaturated fatty acids (sunflower oil, Naudicelle). Influencing circumscribed target symptoms (spasticity, micturition difficulties, constipation, etc.). In addition, physiotherapeutic, psychagogic and, if necessary, nursing and social measures are included. More than a decade's experience with ultrasound therapy of the lymphatic ring as developed by Selzer in over 300 MS-patients gives the impression of a reduction in bout frequency and severity. A statistical evaluation of therapeutic efficiency has so far been impossible for well-known disease-specific reasons, which hold true for all MS-treatment methods. Great practical importance within a foreseeable space of time may be reached by efforts to influence disturbance in nerve conduction and synaptic transmission as specifically caused by the demyelination process. The successful medicinal deceleration of sodium inactivation, inhibition of potassium activation and extension of the action potential, as well as specifically influencing the neurotransmitters responsible for the disturbed synaptic transmission could lead to a total recovery or improvement of dysfunction in a great many cases. Such a "global symptomatic therapy" might indeed not change the course of disease, but bring about great progress to the patient

Abstract: Tropical spastic paraparesis or HTLV-I-associated myelopathy is a progressive spastic disorder associated with the human T-lymphotropic virus type I. Some cases have responded to prednisone. Danazol is an attenuated androgen with minimal virilizing effects. It is used in the treatment of endometriosis and various autoimmune hematologic diseases shown to be responsive to prednisone. Because danazol is anabolic, useful in prednisone-responsive diseases, and less toxic than prednisone, we gave danazol to 6 patients with TSP and 1 with HIV, HTLV- I-associated myelopathy. Five patients had a favorable response. Two became ambulatory after having been confined to a wheelchair. Three were able to ambulate greater distances (in walkers) than
prior to danazol. Three had noticeable decreases in spasticity. Urinary incontinence resolved in two. Physical therapy was variably employed in all except one patient. Two patients who had not responded to physical therapy responded to physical therapy and danazol. One patient did not tolerate danazol and one patient did not improve. Toxicities noted were mild elevations in liver enzymes in 4 patients; these responded to a decrease in dose of danazol; amenorrhea in one and mild fluid retention in one. We conclude that danazol is a useful agent in the management of TSP

Abstract: The effect of baclofen on gamma motoneurones supplying gastrocnemius medialis muscle in the rabbit has been investigated. Baclofen was found to decrease the frequency of firing of tonic gamma motoneurones, and in some cells to inhibit the tonic discharge altogether. Baclofen also increased the regularity of tonic gamma motoneurone discharge. The drug was found to raise the threshold for firing of gamma motoneurones in response to electrical stimulation of the sural nerve, indicating a depression of reflex transmission between the sural nerve and the motoneurones. The results are discussed and brief consideration given to the possible consequences of these results for the action of the drug in human spasticity

Abstract: Methods for detection and quantification of phenol have been developed primarily for use in environmental and industrial monitoring, given the widespread use of phenol as a disinfectant and antiseptic. Little information is available regarding concentrations of phenol in the blood of patients treated with phenol in regional nerve blocks (e.g., intrathecal) for temporary relief of pain or spasticity. We report a specific and sensitive method for quantifying phenol in plasma, using chemical derivatization and high-resolution capillary column gas chromatography in conjunction with mass spectrometry. The assay we describe was developed to monitor plasma concentrations of phenol in children given motor point nerve blocks with dilute phenol


Abstract: 4-Aminopyridine (4-AP) is a potassium channel blocking agent with the ability to restore conduction in demyelinated internodes of axons of the spinal cord. The present investigation sought to obtain electrophysiologic evidence of
the effect of 4-AP in ameliorating central conduction deficits in a group of patients (n = 6) with spinal cord injury (SCI). The group was selected on the basis of having temperature-dependent central conduction deficits. 4-AP (24-25 mg total dose) was delivered intravenously at 6 mg/h or 15 mg/h while somatosensory evoked potentials (SEPs) and motor evoked potentials (MEPs) were recorded as indices of central conduction. Two patients exhibited marked increases in the amplitude of cortical SEPs, and in one of these, 4-AP brought about a reduced central conduction time from L1 to cortex. Four patients revealed increased amplitude MEPs with concomitant reduction in latency indicative of enhanced conduction in corticospinal or corticobulbospinal pathways. Two of these patients demonstrated increased voluntary motor unit recruitment following 4-AP. Clinical examination revealed reduced spasticity (n = 2), reduced pain (n = 1), increased sensation (n = 1), improved leg movement (n = 3), and restored voluntary control of bowel (n = 1). These results support the hypothesis that 4-AP induces neurologic benefits in some patients with SCI. They are also consistent with the emerging concept that pharmaceutical amelioration of central conduction deficits caused by focal demyelination may contribute to the management of a select group of patients with compressive or contusive SCI.


Abstract: Electromyographic (EMG) studies were carried out with the genetically spastic mouse (spa, autosomal recessive), obtained from matings of B6C3a/a, spa/+ heterozygotes. Spastic homozygotes exhibited high amplitude repetitive EMG bursts during spontaneous activity. Following an electrical stimulus to hindlimb or forelimb, high amplitude stereotyped EMG bursts were recorded from contralateral limbs in spastic mice, but were not observed in phenotypically unaffected littermates or normal C57BL/6J mice. The timing and latency of this stereotyped response to an electrical stimulus was consistent with the participation of spinal cord neuronal pathways. In normal C57BL/6J mice the administration of strychnine (0.65 mg/kg), but not picrotoxinin (up to convulsant doses), reproduced all of the behavioral and EMG features observed in spastic homozygotes. We hypothesize that the symptoms in the spastic mutant may result from a deficiency of strychnine-sensitive (presumably glycinergic) inhibition in the spinal cord.


Abstract: Experiments were carried out in awake, unmedicated monkeys to determine the effect of application of current to the cerebellar hemispheres on electrically induced focal motor seizures and surgically induced spasticity. Application of current at various frequencies and pulse amplitudes did not significantly alter focal motor seizures but did significantly reduce spasticity. Analysis of evoked potential recordings carried out during various experimental procedures suggests that application of current to the cerebellar hemispheres may reduce cortical neuronal responsiveness.

Abstract: Chlorocholine chloride (CCC) inhibits neuromuscular transduction of excitation and, consequently, leads to respiratory arrest in cases of acute intoxication. An account is given of the relationships between neuromuscularly blocking activity and acute toxicity of CCC. Several animal species and pharmacological models are used to produce evidence to the effect that CCC-caused inhibition of neuromuscular transmission of excitation is characterised by parameters typical of block due to depolarisation. The differentiated sensitivity of species to depolarising neuromuscular blockers is thought to be the decisive cause of species differences regarding acute toxicity of CCC. Conclusions are discussed which may be derived from the above findings regarding acute CCC toxicity to man and agricultural animal.

Abstract: Baclofen, an analog of the putative inhibitory neurotransmitter gamma-aminobutyric acid is capable of crossing the blood-brain barrier. The drug has been shown to have an antinociceptive action and is used effectively in the management of spasticity. Baclofen was first used in the treatment of trigeminal neuralgia in 1980 and is currently used in the management of various types of neuropathic pain. The effect of baclofen on migraine has not been previously studied. The aim of the present open pilot study was to evaluate the efficacy of baclofen in patients with migraine. Fifty-four patients with migraine with and without aura who experienced 4-8 migraine attacks during a 4-week baseline were included. Baclofen, 15-40 mgs, was given in three divided doses for 12 weeks. Headache frequency and severity were recorded. Fifty-one patients completed the trial. Baclofen was found to be effective in 86.2% with > or = 50% headache reduction from baseline. Three patients could not tolerate the drug due
to adverse events. In this open study, baclofen was found to be effective for prophylactic treatment of migraine


Abstract: In rats the application of 10 mg/kg 6-amino-nicotinamide (6-AN) leads to an accumulation of 6-phosphogluconate, by inhibition of 6- phosphogluconate dehydrogenase in the pentose phosphate pathway, in the cells of the spinal cord. The accumulation reaches its maximum after 18-24 h. It seems that there exists a relationship between the accumulation of 6-phosphogluconate and the lesion of the neuroglia, which is found in electron microscopic studies. Symptoms of a spastic paresis only develop later when the spinal interneurones are destroyed as a consequence of the lesion of the neuroglia. The accumulation of 6-phosphogluconate almost exceeds the 400 fold of the norm. No considerable differences are found between the effects of a dose of 35 mg 6-AN/kg and one of 10 mg 6-AN/kg. Free gluconate is identified enzymically in the cells of the spinal cords of the rats treated with 6-AN. The compound is very probably formed by dephosphorylation and diffuses into the blood. 6-Phosphogluconate is an inhibitor of the phosphoglucose isomerase. Its accumulation shifts the equilibrium towards glucose 6-phosphate. The lactate concentration decreases as compared with the untreated controls. Muscular action potentials are recorded extracellularly with a concentric needle electrode from the musculus gastrocnemius of rats treated with 6-AN. First activations of the electromyograms are found 48 h after the application of 10 mg 6-AN/kg. The electrical activities increase during the time in which a progressive destruction of the interneurones occurs. The electromyogram displays a permanent state of excitation with high amplitudes and an increased frequency. The continuity and intensity of the increased activity recorded by the electromyograph is the most important pathological finding. p-Chlorophenyl-GABA and, still more so, chlorpromazine cause temporary reduction of the excitation processes and an electromyogram nearly at rest. Under the same conditions, haloperidol is only slightly effective. The symptoms developed by the chemical destruction of the interneurones of the spinal cord, with rigidity and spasticity of the hind limbs, are suitable for testing antispastic drugs


Abstract: When administered systemically to spinalized animals, clonidine, the prototypic alpha 2 adrenergic receptor agonist, purportedly acts at spinal sites to
suppress motor responses related to painful peripheral and vesical stimulation and spasticity, and to improve vesicourethral coordination. Hence, the action of clonidine (400 micrograms in three divided doses in a 16-hour span) on spinal vesical and somatic reflexes was examined in five patients with suprasacral spinal cord lesions by assessing volume-induced micturition reflexes and limb motor discharges that occurred spontaneously or were elicited by noxious and nonnoxious cutaneous stimulation. Clonidine caused a significant reduction in (1) blood pressure, (2) amplitude of detrusor contraction, and (3) vesical external urethral sphincter dyssynergia. Limb motor electromyography discharges were not markedly attenuated, although spatiotemporal changes (eg, irradiation, after-discharges) were observed in some of the patients. The results are ascribed to binding to spinal cord alpha 2 adrenergic receptors located on segmental and intersegmental (propriospinal) interneurons, released from descending inhibition, with greater motor system specificity on striated sphincter innervation. Clonidine may be clinically effective in the treatment of hyperactive micturition reflexes in patients with chronic spinal lesions.


Abstract: OBJECTIVE: To assess the efficacy of acute intrathecal (i.t.) baclofen on chronic, dysesthetic, and spasm-related pain (SRP) among patients with spinal spasticity [i.e., multiple sclerosis (MS), spinal cord injury (SCI), transverse myelitis (TMy)]. DESIGN: Double-blind, randomized, and placebo (vehicle) controlled trials (n = 7), and nonrandomized, nonblinded trials (n = 2). SETTING: In-patient program at Samaritan Rehabilitation Institute, Phoenix, Arizona, U.S.A. PATIENTS: MS (n = 4), spinal cord compression (n = 1), and TMy (n = 2) in the double-blind trial, and SCI (n = 2) in the nonblinded trial; all had chronic spinal lesions and function-limiting spasticity refractory to oral medications, including baclofen (p.o.). INTERVENTIONS: i.t. baclofen (50 micrograms) in 1 ml preservative-free normal saline into the L1-2 interspace. OUTCOME MEASURES: Electromyographic (EMG) activity; intravesical and intraurethral pressures; Ashworth Scale and tendon response values; visual analog scales for describing dysesthetic pain intensity; and threshold/EMG relationships after controlled pinch as an indication of nociceptive pain. RESULTS: i.t. baclofen (a) caused marked reduction of segmental reflexes before suppression of intersegmental reflexes; (b) significantly suppressed dysesthetic pain and SRP with temporal dissociation; and (3) did not influence pinch-induced and musculoskeletal (low back) pain. CONCLUSIONS: The suppressive action of i.t. baclofen on spontaneous and evoked (alldynia) dysesthetic pain suggests that a dysfunctional spinal gamma-aminobutyric acidB receptor system, including functional supersensitivity, is associated with the phenomenon of central pain among patients with spinal lesions. Temporal dissociation regarding the action on dysesthetic pain and SRP suggests that disparate central mechanisms subserve the two clinical states.


Abstract: Twelve chronic hemiparetic outpatients with pronounced lower limb extensor spasticity were injected with 400 units of botulinum toxin A, EMG guided into the soleus, tibialis posterior, and both heads of the gastrocnemius muscles. Botulinum toxin A caused a definite reduction of plantar flexor spasticity, in 10 patients two weeks after the injection, as assessed by the Ashworth scale. Four of the patients were able to achieve active dorsiflexion of their affected ankle. Gait analysis including the measurement of vertical ground reaction forces showed a statistically significant ($p < 0.01$) improvement in velocity, stride length, stance symmetry, and the length of the force point of action under the affected foot. Qualitative improvements on the force diagrams indicated a better loading, advancement of the body, and push off of the affected limb in seven patients. Eight weeks after the injection the effects waned

Abstract: The study tested the spasmolytic effect of Botulinum toxin A in two groups of hemiparetic patients with lower limb spasticity: in the first group ($n = 5$) 2000 U Dysport were injected into the soleus, tibialis posterior and both heads of gastrocnemius muscles alone; the second ($n = 5$) received additional repetitive alternating electrical stimulation of M. tibialis anterior and plantar flexors for 30 min six times per day during the 3 days following the injection. Muscle tone, rated by the Ashworth spasticity score, and gait analysis including recording of vertical ground reaction forces, were assessed before and 4 weeks after injection. The combined treatment proved to be more effective with respect to the clinically assessed reduction of muscle tone, gait velocity, stride length, stance- and swing-symmetry ($P < 0.05$). The result is discussed with reference to animal experiments demonstrating enhanced toxin uptake and accelerated onset of its paralytic effect by electrical stimulation

Abstract: Recent open studies and two placebo-controlled studies confirm the potential role of Botulinum toxin A in the treatment of focal spasticity in adults and children. The effect of the toxin might not only be mediated by the paresis of extrafusal, but also intrafusal muscle fibres, thereby altering the afferent
discharge. To enhance its effectiveness, an additional electrical stimulation seems promising. Most patients tolerate the neurolytic agent well. Two individuals, however, suffered from an intermittent tetraparesis after treatment. The repetitive magnetic stimulation and the use of gabapentin might be other new therapeutic options in the management of spasticity.


Abstract: OBJECTIVE: To investigate whether the combined approach of botulinum toxin type A (BtxA) and electrical stimulation was more effective than the toxin alone in the treatment of chronic upper limb spasticity after stroke. DESIGN: Randomized, placebo-controlled study with four treatment groups: 1000 units BtxA (Dysport) + electrical stimulation (A), 1000 units BtxA (B), placebo + electrical stimulation (C) and placebo (D). SETTING: A neurological rehabilitation clinic. SUBJECTS: Twenty-four stroke patients with chronic upper limb spasticity after stroke, six patients in each treatment group. INTERVENTIONS: Intramuscular injection of either toxin or placebo into six upper limb flexor muscles. In group A and C additional electrical stimulation of the injected muscles with surface electrodes, three times half an hour each day for three days. MAIN OUTCOME MEASURES: Muscle tone rated with the modified Ashworth score, limb position at rest and difficulties encountered during three upper limb motor tasks assessed before and 2, 6 and 12 weeks after injection. RESULTS: Most improvements were observed in patients of group A. Cleaning the palm (p = 0.004) differed across groups. Pairwise comparison for this target variable showed that group A differed from group B and D (p <0.01), but not from C. Indicative across-group differences were obtained for elbow spasticity reduction (p = 0.011), and improvement of putting the arm through a sleeve (p = 0.020). CONCLUSIONS: The placebo-controlled trial favours the concept that electrical stimulation enhances the effectiveness of BtxA in the treatment of chronic upper limb flexor spasticity after stroke.


Abstract: Selective dorsal rhizotomy is a surgical procedure with a selective division of posterior spinal nerve rootlets to treat spasticity in children. The extensive surgical procedure with multilevel laminectomies and the nerve root manipulation result in intense pain postoperatively. Two intrathecal (IT) regimes of pain treatment were compared in these children, concerning their pain relief and possible side-effects. In a prospective study, 12 children (3-6 years of age) with six in each group, received either intermittent IT morphine (5 microg x kg(-1) four times a day) or continuous infusion of a mixture of bupivacaine (40 microg x kg(-1) x h(-1)) and morphine (0.6 microg x kg(-1) x h(-1)). Pain score was lower in the bupivacaine/morphine group (0.2 +/- 1.1) compared to intermittent
morphine (2 +/- 2.4) on a scale from 0 to 6 (P less than or = 0.0001).
Bupivacaine/morphine resulted in a lower, but not significant, difference in
pruritus and lower muscle spasm. Haemodynamic and ventilatory parameters did
not differ between the groups. Intrathecal continuous infusion of bupivacaine and
morphine was superior to intermittent morphine in the treatment of pain after
selective dorsal rhizotomy operations.

Abstract: Acute studies. Following oral or intraperitoneal administration, toxicity
was very low (LD50 in rodents greater than 10,000 and greater than 900 mg/kg,
respectively). Subacute and chronic studies in rodents. Signs of toxicity were
seen only at doses of 400 mg/kg or more. Histopathological changes were found
only in the 78-week study. Subacute studies in dogs (intravenous) and primates
(oral). In dogs, doses of 0.1 and 0.3 mg/kg produced ataxia, salivation, and
diarrhoea. In monkeys doses of 7 mg/kg or higher produced ataxia, increased
appetite, hyperreflexive muscular spasms, increase in liver weight, and lipid
depletion of the adrenal cortex. Reproductive studies in the rat and rabbit.
Repeated doses of up to 30 mg/kg were not associated with any disturbance in
fertility; nor were any embryotoxic or teratogenic effects observed. When dams
were treated with 400 mg/kg, litter mortality was markedly increased. Mutagenicity
studies. The four different tests performed gave no indication of any mutagenic
effect. Local tolerance tests in the rabbit. Brotizolam was well tolerated when
administered intramuscularly, intra-arterially, or intravenously. Carcinogenicity
studies in rodents. The mouse study showed no evidence of a tumourigenic
effect. The rat study is still being evaluated. The toxicological studies
demonstrate that brotizolam has an unusually wide therapeutic range. Findings
of toxicological significance, most of which were reversible, were first recorded at
doses of 7-10 mg/kg, i.e. at more than 100-times the intended human therapeutic
dose.

Abstract: Recent studies in the psychiatric literature indicate that baclofen has an
anxiolytic action in certain psychopathologic conditions. Clinical observation has
shown that manifestations of spasticity are increased in anxious individuals,
implying a supraspinal site of mediation for these responses. The purposes of
this study were to determine if baclofen reduced anxiety in individuals with
traumatic spinal cord lesions and whether that reduction was correlated with
decreased spasticity from the baclofen. Five adult males with traumatic spinal
cord injury were randomly assigned to the study protocol. A double-blind,
repeated measures, multiple base-line, single-case research design was
employed. The independent variable was dose of medication with the three
levels being placebo, 40 mg/day of baclofen and 80 mg/day of baclofen, in four
evenly divided doses. The dependent variable was the score obtained on the
Beck Inventory-A anxiety scale (BIA). The subjects were administered the BIA
twice per week for a nine-week period of time, during which they received the doses of medication as described. Quantitative measurements of spasticity were also taken at each session. Visual inspection analysis of the data showed that two subjects had no measurable anxiety of the BIA throughout the study. Three subjects had measurable anxiety on the BIA during the base-line/placebo phase. They showed a decreased level of their BIA scores with 40 mg/day of baclofen, and a further level reduction with 80 mg/day of baclofen. The reduction in BIA scores was statistically significant using the standard deviation band test in one of these subjects. These data indicate that BIA probably has an anxiolytic effect for individuals status post-traumatic spinal cord injury. (ABSTRACT TRUNCATED AT 250 WORDS)


Abstract: Memantine, an amantadine derivative, is therapeutically used for the treatment of various neurological and psychiatric disorders such as Parkinson's disease, spasticity, and dementia. Pharmacokinetics of memantine and its effects on phospholipid content and composition, on membrane properties and functions such as fluidity and beta-adrenergic transmission were studied in cultured human fibroblasts and macrophages. The kinetic behaviour of memantine was characteristic for a lysosomotropic drug. Fibroblasts exposed to 14C-memantine in the microM range accumulated the drug up to 200 fold above initial medium concentrations. Lysosomal drug storage was proven by indirect evidence and by analyses of subcellular fractions. Repetitive exposure to memantine resulted in a cumulative uptake. While memantine uptake after single exposure was fully reversible, the rate and extent of release of chronically accumulated drug was reduced but could be enhanced by the addition of unlabelled memantine or ammonium chloride to the medium. Chronic, but not single, exposure to memantine above 10 microM resulted in a concentration dependent phospholipid accumulation and in a shift in the phospholipid composition. There was an overproportionate increase in phosphatidylinositol at the expense of phosphatidylserine and sphingomyelin. Chronic exposure of cultured cells to memantine increased fluidity in the superficial layers of the plasma membrane and reduced the isoproterenol-stimulated cAMP-response without affecting beta-adrenoceptor density. All these findings were compatible with the kinetic behaviour and the effectiveness expected of a weak lysosomotropic drug.


Abstract: Sixteen patients suffering from spasticity due to multiple sclerosis were
treated with baclofen and tizanidine in a partially blind cross-over study. No significant difference in efficacy was found. The most striking difference was seen in the side-effects: baclofen frequently caused more or less severe muscle weakness and even falling during walking and standing. Treatment with tizanidine produced an apparent improvement of mobility in some patients suffering from moderate or marked paresis associated with a marked spasticity of their legs. Isometric muscle strength did not show any significant changes during either treatment. The different impact of baclofen and tizanidine on mobility and weight support seems to be related to their different site of action in spasticity.


Abstract: BACKGROUND--Syringomyelia is rare in children aged less than 10 years, and bladder dysfunction is an unlikely first manifestation. This report describes a case of repeated episodes of acute urinary retention in a young girl revealing syringomyelia and Arnold-Chiari malformation. CASE REPORT--A 2.5 year-old girl was admitted because she was suffering from acute urinary retention. Her poor appetite had been treated with cyproheptadine, a histamine type I blocking drug. Clinical investigation revealed no local cause for this bladder dysfunction except moderate spasticity of the legs. Cystography showed no vesicoureteral reflux. Because the episodes of urinary retention recurred each day, magnetic resonance imaging (MRI) was performed; this showed the typical features of syringomyelia extending from C5 to T11 plus Arnold-Chiari malformation. The cyproheptadine was discontinued and the urinary retention disappeared. CONCLUSION--Cyproheptadine may have revealed latent neurogenic bladder in this case, although urodynamic studies, performed 3 months later, detected no bladder dysfunction.


Abstract: Conray (meglumine iothalamate), the contrast media frequently used in shuntograms for diagnosing malfunctioning ventriculo-peritoneal shunts, will occasionally cause severe muscular spasms and seizures. In this article, the authors describe anesthetic and critical care management of a case with this complication.


Abstract: The treatment of lumbar cerebrospinal fluid fistula in the presence of an intrathecal catheter is known to be difficult. Open revision surgery is recommended in the literature, although the rate of recurrence is high. The
epidural blood patch technique is well established as a successful treatment for post-dural-puncture headaches. Recent work about the distribution of the injected blood and theoretical considerations about the mechanism of action make this method suitable for the occlusion of spinal leakage even in the presence of an intrathecal catheter. In this note technical details are given for a successful therapy of lumbar cerebrospinal fluid fistula including the right positioning of the opening of the needle (cerebrospinal fluid can be expected intrathecally and epidurally) by injection of contrast medium first for myelography then for epidurography. In this procedure the (epidural) distribution of autologous blood can be indirectly controlled by compression of the dural sac. The method is easy to perform, and the possible risks are small.


Abstract: A group of six subjects with intractable spinal spasticity completed a double-blind cross-over paradigm in which they received two intrathecal bolus injections of baclofen solution five hours apart on two different days and two intrathecal bolus injections of placebo saline five hours apart on two other days. Each subject was repeatedly tested with a battery of clinical and physiological tests. In contrast to the placebo injections, the group responded to the baclofen injections with subjective and objective, clinically significant improvement in parameters of spasticity in their lower limbs, including muscle tone, frequency of spasms, hyperreflexia and passive range of joint motion. Furthermore, this improvement was maintained following thirty consecutive days of intrathecal bolus injections of baclofen at a fixed dose.

Abstract: In a patient receiving intrathecal baclofen injections for intractable trunk and leg spasms, positioning the subarachnoid catheter tip just caudal to the spinal segments innervating the spastic muscles enhanced the spasmolytic effect of bolus injections of intrathecal baclofen on the affected muscles. Such selective positioning of subarachnoid catheters may facilitate segmental spasmolysis with lower intrathecal doses of baclofen and provide an important alternative to relying only on ascending CSF concentration gradients of baclofen from chronic lumbar intrathecal infusion.
Abstract: Over recent years botulinum toxin type A has emerged as a safe and effective treatment for a number of previously refractory conditions associated with excessive muscle activity. The list of indications is expanding, but at present it is generally considered to be the treatment of choice for focal dystonias such as blepharospasm, torticollis, laryngeal dystonia, and oromandibular dystonia, as well as hemifacial spasm, strabismus, and some forms of limb spasticity. Carefully targeted intramuscular injections of a small amount of the toxin block the release of acetylcholine at the neuromuscular junction, producing a chemical denervation, with the aim of reducing excessive muscle activity without producing significant functional weakness. In some situations electrophysiological assessment and localisation of the muscles for injection is necessary. Treatment is symptomatic, with effects lasting 3 to 4 months and most patients requiring up to 4 injections per year to maintain the beneficial effect. Appropriate use of the toxin requires both an understanding of the physiological action of the potential muscles involved in each situation, together with a knowledge of the likely dose necessary to reduce muscle activity to the required level. Botulinum toxin represents a major advance in the management of these conditions, many of which responded poorly to previously available forms of therapy.


Abstract: A man with a balanced translocation between chromosomes 3 and 9 associated with primary hypogonadism and dorsal spine stenosis is reported. The possible significance of this chromosomal abnormality is discussed.

Abstract: The first part of the paper exposes the basic characteristics of the human spasticity which should be modeled: No hypertonia at rest; velocity-dependent myotatic responses, and fatigability. To model a syndrome including these signs is a related but different problem. Results and limits of the clinical neurophysiology concerning the spasticity are briefly quoted. Animal models would better assist the human neurophysiology when having their neuroanatomy closer to the human one. The second part confirms that a local unilateral excision of the ad hoc sensorimotor cerebral cortex of the Baboon induces a permanent palsy of the contralateral foot and leg, and after delay signs of spasticity in the Sol. Neither clasp-knife phenomenon nor fatigability is observed. There is no sign of motoneuron hyper-excitability. A GABA-related pharmacology suggests a significant defect in the presynaptic inhibition of the reflexogenic IA in-put, and possibly a defect in a post-synaptique gabaergic inhibition. Finally the monkey is
considered as a valuable support for modeling the human spasticity, symptom and possibly syndrome

Abstract: A double blind crossover trial of baclofen against placebo in elderly stroke patients was discontinued because the drug produced an unacceptably high level of drowsiness. In a subsequent study baclofen 10 mg was given orally to 12 elderly stroke patients, and drug concentrations measured from a series of plasma samples. A group of healthy subjects given the same dose in a previous study were used as controls. Elderly patients took longer to achieve peak plasma baclofen concentrations, but healthy controls had higher peak values and eliminated the drug more rapidly; areas under the curve were similar in the two groups. Simulations based on mean data suggest that increased drowsiness in the elderly was probably not due to changes in the drug's pharmacokinetic behaviour

Abstract: Intrathecal baclofen is a useful therapy in patients with spasticity. We describe a patient who underwent an intrathecal pump implant, complicated by epidural lipomatosis that ultimately required a single level laminectomy and fat debulking before successful implantation


Abstract: The pharmacokinetic and clinical properties of a modified release formulation of the alpha 2-adrenergic agonist tizanidine are reviewed. Therapy with conventional tizanidine tablets is effective in the relief of spasticity, but it has a short half-life, resulting in it having to be administered three or four times daily. The modified release capsules have retard characteristics which allow the drug to be given as a once-daily dosage. Single- and multiple-dose pharmacokinetic studies in healthy volunteers have shown that the relative bioavailability of the modified release formulation is similar to that of conventional tablets and is unaffected by food. Clinical studies have shown that modified release tizanidine improved spasticity and disability in approximately 94% and 79%, respectively, of spastic patients. Adverse effects were observed in about 33% of patients. Mild, transient muscular weakness was the most common effect, but it did not require termination of treatment. Body weight, blood pressure, heart rate and haematological or biochemical measures were not adversely affected. The initial recommended dose of modified release tizanidine is one capsule per day of 6
mg, which may be increased gradually to 24 mg. A daily dose of 12 mg modified release tizanidine was used in 50% of patients studied.


Abstract: OBJECTIVE: To define a safe and effective dose of Dysport for treating hip adductor spasticity. METHODS: Patients with definite or probable multiple sclerosis, and disabling spasticity affecting the hip adductor muscles of both legs, were randomised to one of four treatment groups. Dysport (500, 1000, or 1500 Units), or placebo was administered by intramuscular injection to these muscles. Patients were assessed at entry, and 2, 4 (primary analysis time-point), 8, and 12 weeks post- treatment. RESULTS: A total of 74 patients were recruited. Treatment groups were generally well matched at entry. The primary efficacy variables-passive hip abduction and distance between the knees-improved for all groups. The improvement in distance between the knees for the 1500 Unit group was significantly greater than placebo (p = 0.02). Spasm frequency was reduced in all groups, but muscle tone was reduced in the Dysport groups only. Pain was reduced in all groups, but improvements in hygiene scores were evident only in the 1000 Unit and 1500 Unit groups. Duration of benefit was significantly longer than placebo for all Dysport groups (p<0.05). Adverse events were reported by 32/58 (55%) Dysport patients, and by 10/16 (63%) placebo patients. Compared with the two lower dose groups, twice as many adverse events were reported by the 1500 Unit group (2.7/patient). The incidence of muscle weakness was higher for the 1500 Unit group (36%) than for placebo (6%). The response to treatment was considered positive by two thirds of the patients in the 500 Unit group, and by about half the patients in the other groups. CONCLUSION: Dysport reduced the degree of hip adductor spasticity associated with multiple sclerosis, and this benefit was evident despite the concomitant use of oral antispasticity medication and analgesics. Although evidence for a dose response effect was not statistically significant, there was a clear trend towards greater efficacy and duration of effect with higher doses of Dysport. Dysport treatment was well tolerated, with no major side effects seen at doses up to 1500 Units. The optimal dose for hip adductor spasticity seems to be 500-1000 Units, divided between both legs.


Abstract: The muscle relaxant effect of phenobarbitone was studied in genetically spastic rats which exhibit spontaneous tonic activity in the electromyogram (EMG) of the gastrocnemius muscle. Phenobarbitone, 10-30 mg/kg i.p., reduced the tonic activity in the EMG of the gastrocnemius muscle of such rats in a dose- and time-dependent manner. The GABA antagonists biczuculline, 2 mg/kg i.p., and picrotoxin, 2 and 3 mg/kg i.p., reduced the muscle relaxant effect of phenobarbitone, 20 and 30 mg/kg. The benzodiazepine receptor antagonists Ro 15-1788, 5 mg/kg, and CGS 8216, 5 mg/kg (doses which do not affect tonic activity in the EMG), failed to alter the depressant effect of phenobarbitone 30 mg/kg, in the EMG. Beta-Carboline-3-carboxylic acid methylester (beta-CCM), 2 mg/kg i.p., while not affecting the tonic activity in the EMG, reversed the depressant effect of phenobarbitone, 30 mg/kg. Both Ro 15-1788, 5 mg/kg, and CGS 8216, 5 mg/kg, prevented the reversal of the depressant effect of phenobarbitone, 30 mg/kg, produced by beta-CCM, 2 mg/kg. The results indicate that the muscle relaxant action of phenobarbitone in genetically spastic rats is mediated via GABA-related mechanisms and add further support to the hypothesis that both Ro 15-1788 and CGS 8216 are specific antagonists at benzodiazepine receptors, devoid of intrinsic activity at moderate doses. The results also suggest that reversal of the muscle relaxant action of phenobarbitone by beta-CCM is mediated via a GABA/benzodiazepine receptor/chloride ionophore complex.


Abstract: Genetically spastic rats were used for studying the effect on muscle tone of beta-carboline-3-carboxylic acid methylester (beta-CCM), an inverse benzodiazepine (BDZ) agonist, and that of Ro 15-1788 and CGS 8216, both putative antagonists of pharmacological actions of BDZs. These animals exhibit pathologically increased muscle tone, which can be recorded and quantified in the electromyogram (EMG) of the gastrocnemius (GS) muscle. beta-CCM, 2.5 and 3.0 mg/kg i.p., augmented the tonic activity in the EMG of GS muscle in spastic rats while it did not modify muscle tone at doses of 1.0 and 2.0 mg/kg. Diazepam, 0.4 mg/kg i.p., and Ro 15-1788, 5 mg/kg i.p., but not CGS 8216, 5 mg/kg i.p., antagonised the effect of the beta-carboline on muscle tone. Ro 15-1788, at doses of 0.1-5 mg/kg i.p., did not affect muscle tone in the genetically spastic rats, whilst at doses of 25-200 mg/kg the imidazodiazepine dose dependently increased the tonic activity in the EMG. The action of Ro 15-1788, 50 mg/kg i.p., was reversed by diazepam, 0.4 mg/kg i.p., and beta-CCM, 2 mg/kg i.p., while CGS 8216, 5 mg/kg i.p., facilitated the effect of Ro 15-1788 on muscle tone. CGS 8216 at doses of 5 and 25 mg/kg i.p. was devoid of any effect on muscle tone, whilst at doses of 50 and 200 mg/kg the pyrazoloquinoline
increased the tonic activity recorded in the EMG from the GS muscle of the spastic rats. (ABSTRACT TRUNCATED AT 250 WORDS)

Illis L.S., Read D.J., Sedgwick E.M., and Tallis R.C. (1983) Spinal cord stimulation in the United Kingdom. J. Neurol. Neurosurg. Psychiatry 46, 299-304. Abstract: All the medical, surgical and engineering personnel in the UK who have used spinal cord stimulation (SCS) in patients, attended a workshop to discuss their results. The major use of SCS has been for multiple sclerosis and intractable pain. It was concluded that the technique benefited up to two thirds of patients with bladder dysfunction, and that pain and possibly spasticity also responded to SCS, but other manifestations of multiple sclerosis did not. Further information on long term benefit is needed and the use of SCS in other conditions, such as spinal injury and peripheral vascular disease, is not yet established. SCS cannot be recommended for use outside large centres as x-ray screening, urodynamic and neurophysiological assessment facilities are required as well as biological engineering assistance.


Ito T., Hori M., Furukawa K., Karasawa T., and Kadokawa T. (1985) Pharmacological studies of 1-(2,3-dimethyl-4-methoxyphenyl)-2-methyl-3- (1-pyrrolidinyl)-1- propanone hydrochloride (AD-2239), a centrally acting muscle relaxant. Arch. Int. Pharmacodyn. Ther. 275, 105-122. Abstract: Centrally acting muscle relaxant properties of AD-2239 were compared with those of tolperisone, eperisone, diazepam and baclofen. AD-2239 dose-relatedly depressed extensor reflex in urethane-chloralose anesthetized intact and spinal rats, the i.v. potencies being similar to those of tolperisone and eperisone. These effects of AD-2239 were long-lasting. When orally administered, AD-2239 was 4 times more potent than eperisone. Diazepam was without effect on the extensor reflex in spinal rats. AD-2239 depressed the flexor reflex without affecting the patellar reflex in anesthetized cats. Baclofen depressed the latter. When orally administered, AD-2239, in a dose-related manner, depressed the flexor reflex in anesthetized cats, with a potency approximately 8 times that of tolperisone or eperisone. AD-2239 produced a dose-related reduction of anemic decerebrate rigidity (alpha-rigidity) in rats. The potency, at the minimum effective i.v. dose, was 4 times greater than that of tolperisone or eperisone, equal to that of diazepam, and one-half of that of baclofen. AD-2239 neither affected spontaneous electroencephalogram (EEG) nor EEG arousal response in immobilized cats, while the other drugs, at comparatively low doses, depressed them. The results strongly suggest that AD-2239 may have advantages over the existing centrally acting muscle relaxants in the treatment of human clinical spasticity and muscle spasm syndromes.

Ito T., Furukawa K., Karasawa T., Kadokawa T., and Shimizu M. (1985) Functional change in the rat spinal cord by chronic spinal transection and

Abstract: Two types of spinal reflex responses, extensor reflex and ventral root potential, were compared physiologically and pharmacologically in acute and chronic spinal cord transected rats. The recovery curve of the extensor reflex, recorded as evoked electromyogram, in chronic spinal rats was strikingly different from that in acute spinal rats. Namely, shortening of the reflex amplitude suppression period (stimulus interval: 20 msec) and appearance of the supernormal period (30-60 msec) were observed in chronic spinal rats. The recovery curves of ventral root potential (monosynaptic reflex) and M wave were almost the same in both preparations. In the frequency depression curve, the amplitude of the extensor reflex in chronic spinal rats was higher at high frequency stimulation than that in acute spinal rats. 5-Hydroxytryptophan, 5-methoxy-N,N-dimethyltryptamine and quipazine enhanced the extensor reflex in chronic spinal rats with a potency of 200-400, 8 and 4 times stronger than that in acute spinal rats, respectively. These drugs did not show consistent effects on the monosynaptic reflex of ventral root potential in chronic spinal rats. These results strongly suggest that the spinal interneurons where descending serotonergic fibers terminate become supersensitive and functionally modified in chronic spinal rats. It is speculated that the supersensitivity of these interneurons may play an important role in spasticity.


Abstract: Spasticity is a common problem following spinal cord injury. The drug of choice to control spasms is baclofen. There would appear to be no reported studies which have evaluated the psychological and emotional effect of this drug. This preliminary study investigated a number of such effects, including depression, anxiety and general mood state. First, we examined 10 subjects before and during the administration of baclofen. They were then compared to a control group of 12 subjects. A second cohort of 12 subjects taking baclofen were compared to a control group of nine subjects at a specific time after injury. Results indicated that whilst some significant differences were found, suggesting an increase in fatigue with use of baclofen, no major adverse psychological effects were noted. The implications of these results were discussed and suggestions for further research were highlighted.


Abstract: The most potent biologic toxin, botulinum toxin (BTX), has become a powerful therapeutic tool in the treatment of a variety of neurologic, ophthalmic, and other disorders manifested by abnormal, excessive, or inappropriate muscle contractions. This review focuses on the use of BTX in the treatment of dystonia.
and other movement disorders. The therapeutic application of BTX, however, extends beyond movement disorders; chemodenervation with BTX has been found to ameliorate spasticity, rigidity, spastic bladder, achalasia, and even some cosmetic conditions. In addition to describing its therapeutic effects, this article also reviews recent advances in the understanding of the molecular and cellular mechanisms of BTX. Few therapeutic agents have been better understood in terms of their mechanism of action or have had greater impact on patients' functioning than BTX. BTX-A has been used in nearly all clinical trials. Blocking anti-BTX-A antibodies have been detected in about 5% of patients chronically treated with this type of BTX. Patients who develop immunoresistance to BTX-A may benefit from other serotypes of BTX, such as BTX-B and -F, currently undergoing clinical trials.


Abstract: We have investigated the effects of beta-lactam antibiotics on isolated preparations of rat fundus, ileum, and the body of feline stomach. Isotonic changes of isolated preparations were recorded. Benzylpenicillin (EC50 = 1.31 +/- 0.13 x 10(-5) M), ampicillin (EC50 = 2.16 +/- 0.15 x 10(-5) M), cefotaxime (EC50 = 1.33 +/- 0.15 x 10(-5) M), ceftriaxone (EC50 = 4.39 +/- 0.13 x 10(-5) M) and ceftazidime (EC50 = 1.42 +/- 0.01 x 10(-3) M) produced concentration-dependent tonic contractions of rat fundus. Rat ileum and feline stomach did not respond on these substances. Lidocaine (2.3 x 10(-5) M) and physostigmine (1.0 x 10(-8) M) significantly potentiated contractions produced by benzylpenicillin. On the other hand, methysergide (1.4 x 10(-7) M) and atropine (9.6 x 10(-9) M) significantly blocked tonic contractions produced by benzylpenicillin. Effects of beta-lactam antibiotics on smooth muscle isolated preparations were tissue and species dependent, indicating selectivity of their action.

Jeavons P.M., Bower B.D., and Dimitrakoudi M. (1973) Long-term prognosis of 150 cases of "West syndrome". Epilepsia 14, 153-164.


Abstract: A case of intoxication with Phytosol (an insecticide) in a 29-year-old man is described. Ingestion of Phytosol (suicide attempt) produced signs of cholinergic crisis followed, after 16 days, by features of peripheral neuropathy and later, with the regression of signs of polyneuropathy, gradually increasing spastic paraplegia. Electrophysiological investigation of nerves which were clinically moderately involved demonstrated sparing of sensory fibers and damage to motor fibers. There was no change in maximal motor conduction velocity. Histology of the clinically involved sural nerve revealed axonal changes together with demyelination, presumed to be secondary in type. This case shows that the susceptibility to delayed nervous system damage in man is greater than
it might be expected from experimental studies and calls for caution in human exposure to these compounds


Abstract: Major neurologic complications secondary to cyclosporine are well documented and are known to include confusion, cortical blindness, seizure, spasticity, paresis, ataxia and coma. Most previous reports attribute these to white matter central nervous system (CNS) lesions or white/grey matter border lesions. Many predisposing factors have been identified, including: elevated levels of cyclosporine, hypomagnesemia, hypocholesterolemia, aluminium toxicity, high dose steroids, hypertension and infection. However CNS events attributed to cyclosporine have been reported without any of these risk factors. We report a case of a child developing multiple white and grey matter thalamic and cortical lesions along with acute neurologic deterioration, and then review cyclosporine mediated CNS injury, including the roles of P-glycoprotein and cyclophilin

Abstract: Centrally acting alpha-2 adrenergic agonists are one of several pharmacologic agents used in the treatment of spasticity related to disorders of the central nervous system. In addition to their effects on spasticity, certain adverse cardiorespiratory effects have been reported. Adults chronically treated with angiotensin converting enzyme inhibitors may have a limited ability to respond to hypotension when the sympathetic response is simultaneously blocked. The authors present a 10-year-old boy chronically treated with lisinopril, an angiotensin converting enzyme inhibitor, to control hypertension who developed hypotension following the addition of tizanidine, an alpha-2 agonist, for the treatment of spasticity. The possible interaction of tizanidine and other antihypertensive agents should be kept in mind when prescribing therapy to treat either hypertension or spasticity in such patients


Abstract: This report summarizes experience with baclofen (Lioresal) in the management of spasticity and muscle spasms in 113 patients treated for up to six years. Baclofen was found to be of little help in nine patients with spasticity of
cerebral origin, but was effective in reducing spasticity of spinal origin in 72 out of 90 patients (80%). It also reduced the number and severity of spasms in 76 out of 87 patients (87%). Side effects necessitating reduction of dosage were experienced by 20% of patients. Baclofen appears to be a safe and effective agent in the management of spasticity, with the advantage that adequate dosage can usually be achieved without sedation. Beneficial effects have persisted throughout the follow-up period.


Abstract: The effect of a new, peripherally acting muscle relaxant drug (Dantrium) on spasticity was tested on 6 patients with spinal cord injuries. The effect was evaluated both by regular clinical examination and with an electromyographic technique. The latter concerned a quantitative analysis of the patients’ ability to voluntarily control fine neuromuscular activity both with and without the drug. The results indicated that the spasticity was initially markedly reduced in all patients; in one case so markedly that the stability of the trunk was lost. Electromyographically it was found that the ability of the patients to relax the muscles was increased with Dantrium.

Abstract: The effect of a new peripherally acting muscle relaxant drug Dantrium, on spasticity tested on 11 hemiplegic patients. The effect was evaluated both with regular clinical examination and with electromyographic technique. The latter concerned a quantitative analysis of the patients’ voluntary control of fine neuromuscular activity both with and without the drug. The results indicated that spasticity was initially markedly reduced in the majority of the patients without, however, meaningfully increasing the daily-living functions of the patients. After a few months, the medication could be discontinued without any immediate increase in the spasticity. No severe side-effects were noted. In some cases, the medication had to be discontinued due to marked tiredness. Electromyographically, it was found that the ability of the patients to control fine neuromuscular activity with the paretic muscles was increased significantly with Dantrium, indicating that the reduction of the spasticity increased the ability for fine control of the muscles.

Abstract: Seventy-seven patients with muscle spasticity secondary to central nervous system pathology were treated with dantrolene sodium for periods of up to two years. The drug was effective in reducing muscle spasms, clonus, muscle
tone, and the force of muscle contraction elicited by Achilles tendon tap and tibial nerve stimulation, but improvement of function was seen less often. The incidence of side-effects was considerable, and poses a problem regarding patient acceptance of drug treatment.

Joynt R.L. and Leonard J.A., Jr. (1980) Dantrolene sodium suspension in treatment of spastic cerebral palsy. Dev. Med. Child Neurol. 22, 755-767. Abstract: A double-blind study was carried out on 20 children with spasticity secondary to cerebral palsy, in order to compare the effects of dantrolene sodium suspension and a placebo. The drug was found to be physiologically active in reducing the force of muscle contraction, but objective functional improvement, as measured by multiple performance tests, was irregular and probably not significant.

Kabalin J.N., Lennon S., Gill H.S., Wolfe V., and Perkash I. (1993) Incidence and management of autonomic dysreflexia and other intraoperative problems encountered in spinal cord injury patients undergoing extracorporeal shock wave lithotripsy without anesthesia on a second generation lithotriptor. J. Urol. 149, 1064-1067. Abstract: Spinal cord injury patients are at increased risk for urolithiasis and many will require treatment, most commonly with extracorporeal shock wave lithotripsy. New, second generation lithotripsy devices allow treatment without tub immersion, and without general or regional anesthesia for most patients. Spinal cord injury patients, with loss of sensation below the level of injury, would seem to be ideal candidates for such treatment. We present our experience with 20 consecutive spinal cord injury patients treated without anesthesia on the Medstone STS second generation lithotriptor. All patients were awake and experienced no direct sensation from the shock waves. All but 1 patient (T12 level), however, experienced autonomic dysreflexia, with significant elevations in systolic blood pressure (mean increase 44 mm. Hg, maximum 74) and diastolic blood pressure (mean increase 24 mm. Hg, maximum 61), with reflex bradycardia (mean decrease -22 beats per minute). Autonomic dysreflexia was successfully treated in this setting with short-acting sublingual nifedipine. Associated bradycardia was treated with atropine in 6 patients. Preoperative bowel preparation proved to be useful in spinal cord injury patients to maximize stone imaging and may decrease autonomic dysreflexia if this is caused by shock waves impacting on the distended bowel. Other problems included uncontrolled skeletal muscle spasms elicited by shock waves, which proved to be troublesome in maintaining patient position and stone localization. Muscle spasms were decreased with benzodiazepines. Care was also observed in spinal cord injury patients to pad all pressure points on the hard, dry treatment surfaces associated with second generation lithotriptors and, thus, prevent skin breakdown.

Abstract: Continuous intrathecal baclofen infusion (CIBI) is a relatively new treatment modality for severe spasticity of spinal cord origin. Literature review suggests relief of severe spasms and rigidity is proven with CIBI, in patients with spinal cord injury and multiple sclerosis, while ongoing research exists for patients with acquired brain injury and cerebral palsy. Criteria for patient selection, the screening trial process, an outline of the surgical procedure, and generalities of maintenance therapies, will be reviewed broadly as per literature, as well as specifically to the Vancouver experience with adults. Additionally, reported patient outcomes and implications for nursing will be shared.


Abstract: Continuous intrathecal baclofen infusion (CIBI) is a relatively new treatment modality for severe spasticity of spinal cord origin. Literature review suggests relief of severe spasms and rigidity is proven with CIBI, in patients with spinal cord injury and multiple sclerosis, while ongoing research exists for patients with acquired brain injury and cerebral palsy. Criteria for patient selection, the screening trial process, an outline of the surgical procedure, and generalities of maintenance therapies, will be reviewed broadly as per literature, as well as specifically to the Vancouver experience with adults. Additionally, reported patient outcomes and implications for nursing will be shared.


Abstract: A 36-year-old woman without overt coronary risk factors was admitted to hospital with coma about 9 hours after mass self-injection of insulin (1,500 units). Laboratory investigation revealed severe hypoglycemia and hyperinsulinemia. During the treatment of her hypoglycemia, circulatory collapse occurred. The ECG, echocardiogram, and elevation in troponin T suggested a diagnosis of myocardial infarction. Although the patient became apallic and developed systemic spasticity due to hypoglycemic brain damage, her hemodynamics improved with supportive care alone. Coronary angiography and myocardial scintigraphy performed later demonstrated a broad area of myocardial damage despite intact coronary artery circulation. The authors hypothesize that temporary coronary arterial narrowing or coronary arterial vasospasm induced by severe hyperinsulinemia contributed to the pathogenesis of the myocardial infarction. The possibility of myocardial infarction should be considered in patients with acute insulin poisoning.


Abstract: Selected examples from three series of isomeric (alkylthio)-1,2,4-triazoles were prepared and examined for anticonvulsant activity versus strychnine-, maximal-electroshock-, pentylenetetrazole-, and 3-
mercaptopropionic-acid-induced seizures in mice. A number of 5-aryl-3-(alkylthio)-4H-1,2,4-triazoles were selective antagonists of strychnine- induced convulsions. The isomeric 3-aryl-5-(alkylthio)- and 5-aryl-3- (alkylthio)-1H-1,2,4-triazoles were essentially inactive as anticonvulsants. The most potent antagonist of strychnine-induced convulsions was 5-(2-fluorophenyl)-4-methyl-3-(methylthio)-4H-1,2,4-triazole (3s), while the most selective antagonist was 5-(3-fluorophenyl)-4-methyl-3-(methylsulfonyl)-4H-1,2,4-triazole (3aa). The anticonvulsant profiles of these 4H-1,2,4-triazoles suggested that they were acting functionally like glycine receptor agonists. Since it has recently been postulated that compounds possessing glycine-agonist-like properties might be useful in the treatment of spasticity, we examined 5-phenyl-4-methyl-3-(methylsulfonyl)-4H-1,2,4-triazole (3c) in an in vivo model of spasticity. In this regard, 3c reduced the occurrence of hyperreflexia in rats that had received spinal transections 5-10 weeks previously. While triazole 3c appeared to possess glycine-agonist-like properties in vivo, it did not displace [3H]strychnine binding from rat brain stem/spinal cord membranes in vitro. On the other hand, 3c enhanced muscimol-stimulated 36Cl influx in a rat cerebellar membrane preparation, indicating a possible interaction of these triazoles with the GABAA receptor


Abstract: BACKGROUND AND OBJECTIVES. Epidural phenol for control of pain and spasticity has been advocated for clinical use. This study determined the histopathologic changes that follow single and repeated epidural administration of phenol in saline in nonhuman primates. METHODS. Nine primates received 0.5 mL of either 3% phenol in saline (n = 4) or 6% phenol in saline (n = 5) via lumbar epidural injection. Two additional primates received three consecutive daily epidural doses of 0.5 mL of 3% phenol in saline. Finally, 5 unoperated primates and 5 primates that received only 2 mL of radiographic contrast material served as control subjects. Two weeks after the epidural injection, spinal cords were removed and processed for histopathologic study by a neuropathologist blinded to the solution administered. RESULTS. None of the control animals demonstrated histopathologic changes. One animal that received 6% phenol died 3 days after injection. All phenol-treated animals demonstrated predominantly posterior root damage. Spinal cord damage was seen in all animals receiving 6% phenol, in 2 animals receiving 3% phenol single doses, and in neither animal receiving 3% phenol multiple doses. Anterior root damage occurred in all phenol-treated animals except the 4 that received single 3% phenol injections. Animals
that received 6% phenol demonstrated greater lower extremity motor weakness than those in the other groups, but no clear correlation existed between extent of histopathologic changes and motor weakness. CONCLUSIONS. Motor weakness, anterior root damage, and direct cord injury were noted in primates following epidural administration of phenol in concentrations below what has been reported for clinical use in humans. Since it is more difficult to control the spread of epidural versus subarachnoid phenol, the risks of epidural phenol may outweigh the benefits relative to subarachnoid administration.

Abstract: Because intramuscular injections of type A botulinum toxin (btx) are effective for idiopathic spasmodic torticollis, they were administered to 3 patients who had neck movements as their only manifestation of tardive dystonia. Each improved, with a decrease in involuntary movement and reduction in pain. None had either systemic or local side effects. Although expensive, btx treatment is recommended for involuntary neck movements of tardive dystonia but not yet for the classic buccolingual dyskinesia.

Abstract: Nalon-Ace and other nonsteroidal anti-inflammatory drugs (NSAID) containing bromvalerylurea (BVU) are sold as over-the-counter (OTC) drugs and are obtainable without prescription in Japan. A 32-year-old woman was diagnosed as having chronic BVU intoxication due to habitual use of Nalon-Ace. In addition to cerebellar ataxia and pyramidal signs well known in this condition, she showed an as yet non-described dystonic posture of the neck. Laboratory tests revealed an elevated concentration of serum organic bromide, iron deficiency anemia, and hyperchloremia. Brain magnetic resonance imaging (MRI) revealed definite cerebellar atrophy. We should consider the possibility of chronic BVU intoxication in peculiar neurological cases like ours.

Abstract: Baclofen, commonly used to reduce severe muscle spasms in patients with spinal cord injuries, is also active in the brain. A patient with pre-existing bipolar affective disorder developed increased depression while on baclofen, which progressed to a delusional depression when baclofen and haloperidol were rapidly decreased. When the dose of haloperidol was increased to a previously well tolerated dose to deal with the depressive delusion, a pseudoparkinson's state developed. This case demonstrates the interactive effects of baclofen and haloperidol on central noradrenergic and dopaminergic systems and suggests a possible neurochemical basis for the difference between...
delusional and nondelusional depression that is consistent with the different therapeutic response to psychotropic drugs of patients with these illnesses. The paradoxical appearance of the pseudoparkinson state in this patient when much higher doses of haloperidol had been free of such side effects, may reflect baclofen-induced alterations in receptor sensitivity. It appears that baclofen should be used with caution in patients with neuropsychiatric problems and that, when used, the withdrawal of baclofen should be continued over several weeks to allow receptor sensitivity to return to normal levels.

Abstract: Memantine, used as a drug for treatment of spasticity and other extrapyramidal disorders as well as dementia, was shown to prevent brain damage caused by the glutamate (N-methyl-D-aspartate, NMDA) receptor agonist, quinolinic acid. Studies were focused on the hippocampal formation which is known to be highly vulnerable to quinolinic. Pretreatment of animals with memantine added to the food led to a reliable protection of hippocampal neurons when the drug was administered chronically for a period of 10 days prior to quinolinic exposure (i.c.v. injected). Additional i.p. administration of memantine (simultaneously with quinolinic acid or up to 24 h later) did not substantially add to the protective potency of the memantine diet. Our findings indicate that memantine may have beneficial effects in the treatment of brain disorders which are mediated by excitotoxic effects of glutamate.

Abstract: Spasticity is a velocity-dependent pathologic increase in muscle resistance to stretch, and occurs in a variety of neurologic disorders. We report our controlled open study using botulinum toxin A for treatment of adductor spasticity in five patients with advanced multiple sclerosis. Clinical evaluation of spasticity and stiffness of joints is based on the Ashworth Scale and grade of passive abduction. Three patients showed no response; the two others experienced an excellent and longlasting effect. We also describe briefly the different spastic conditions where this treatment has been used successfully.

Abstract: Botulinum toxins, exotoxins of Clostridium botulinum, are the most toxic naturally occurring substances known to man. For more than a century they are known to be the cause of botulism, a nowadays rare intoxication with spoiled food that leads to generalized flaccid weakness of striated muscle including pharyngeal and respiratory musculature. The toxins act primarily at peripheral cholinergic motor nerve endings by blocking the release of the neurotransmitter acetylcholine. As a consequence, action potentials in the motor nerve can no longer be transmitted to the muscle. This lack in transmission, clinically appearing as weakness, may disable or actually critically endanger affected
patients. However, in certain neurological diseases characterized by an abnormal increase in muscle tone or activity, for example dystonia or spasticity, a reduction in signal transmission may actually be beneficial. Around 1980 local injections of minute amounts (in the order of 0.5 ng) of Botulinum toxin type A were first successfully used in a neurological disorder named blepharospasm which is characterized by an involuntary squinting of the eyes. Since then Botulinum toxin has developed rapidly from a frightful poison to a safe therapeutic agent with a remarkable beneficial impact on the quality of life of many thousands of patients worldwide. This review tries to outline in brief the characteristics of Botulinum toxins, their mechanism of action and the various indications for clinical use as a therapeutic agent.


King T. and Mallet L. (1991) Brachial plexus palsy with the use of haloperidol and a geriatric chair. DICP. 25, 1072-1074.  
Abstract: An 81-year-old white man was admitted to an intermediate care facility because of increased wandering and confusion secondary to dementia. On the first day after admission, the patient tried to leave the facility and was hitting and kicking the employees. Haloperidol 0.5 mg tid was prescribed to help control his behavior. He became more agitated and confused; haloperidol was then increased to 1 mg qid and the patient was confined to a geriatric chair to prevent injuries. Cogwheel movements, rigidity, and marked sedation were documented. A right brachial plexus palsy was diagnosed. This case demonstrated the hazards of two commonly used interventions in a nursing home: antipsychotic agents and the geriatric chair.

Abstract: Locally acting treatments for spasticity such as nerve and motor point blocks have the advantage of reducing harmful spasticity in one area, while preserving useful spasticity in another area. This randomized, double-blind study is the first trial that was designed to find out whether botulinus toxin Type A and phenol relieves the signs and symptoms of ankle plantar flexor and foot invertor spasticity after stroke and if either of these methods offers any advantages and disadvantages over the other. Twenty patients who were included in this preliminary study were randomly assigned to receive a single treatment of 400
mouse units of botulinus toxin Type A injected into the calf muscles or to receive a tibial nerve blockade with 3 ml of 5% phenol. A combination of subjective and objective measures were used to assess functional change at baseline and at Weeks 2, 4, 8, and 12. At follow-up, significant improvement (P < 0.05) in the Ashworth score for dorsiflexion was observed in both groups. The change in the Ashworth score for eversion was significant in the group that received botulinus toxin Type A (P < 0.05) but not in the group that received phenol (P > 0.05). When those variables were compared between the two groups, the change in the Ashworth score at Weeks 2 and 4 was significantly better in the group that received botulinus toxin Type A (P < 0.05) but there was not a significant difference between the two groups at Weeks 8 and 12 (P > 0.05). The decrease in clonus duration that was detected by electromyography was significant in both groups at all visits, but the decrease in the group that received botulinus toxin Type A was significantly better at Weeks 2 and 4 (P < 0.05). It is concluded that both motor point injections with botulinus toxin Type A and tibial nerve blockade with phenol are effective in plantar flexor spasticity, but the changes were more significant in the group that received botulinus toxin Type A at Weeks 2 and 4, whereas there was not a significant difference between the two groups at Weeks 8 and 12. Future research should explore the long-term effect of these two treatment modalities.


Abstract: To investigate coronary vasospastic activity after percutaneous transluminal coronary angioplasty (PTCA), we performed intracoronary injection of acetylcholine in 55 patients, mean 3.3 months after successful PTCA. Coronary spasm was defined as transient total or subtotal occlusion of the PTCA sites. Sixty-nine lesions of the 55 patients were examined to determine whether spasm was provoked by incremental doses of acetylcholine. Restenosis was defined as coronary luminal narrowing of > or = 50% after nitroglycerin or isosorbide dinitrate. Twenty of the 55 patients (36%) and 23 of the 69 lesions (33%) had coronary spasm. There was no correlation between the incidence of coronary spasm and the interval from PTCA to the acetylcholine test. The spasm was provoked in 17 lesions of the 50 non-restenotic lesions (34%) and was also provoked in 6 of the 19 restenotic lesions (32%). On the other hand, restenoses occurred in 6 of the 23 spastic lesions (26%) and in 13 of the 43 non-spastic lesions (28%). There was no correlation between the incidence of coronary spasm and the occurrence of restenoses. Twenty-four patients had undergone acetylcholine provocative test before PTCA. Among these 24 patients, 11 had coronary spasm before PTCA, and 7 had coronary spasticity after PTCA. Four patients who had positive evidence of coronary spasm before PTCA did not show negative spasm after PTCA. On the other hand, 3 patients who did not show evidence of coronary spasm showed positive evidence of coronary spasm after PTCA. (ABSTRACT TRUNCATED AT 250 WORDS)
Abstract: Spasticity is a disorder of the motor system that occurs after injury to the central nervous system, which may increase the disability of an individual with spinal cord injury (SCI). Treatment options detailed in this review include rehabilitation techniques and modalities, pharmacological options, injection techniques, intrathecal baclofen, and surgery. This review will hopefully help health professionals to be aware of the treatment alternatives available for patients with SCI related spasticity

Abstract: A paraplegic man with no history of psychiatric illness developed psychosis and dyskinesia following abrupt withdrawal of baclofen; the symptoms resolved 72 hours after resumption of the drug. The psychosis and dyskinesia may have been a manifestation of baclofen’s alteration of cerebral dopaminergic mechanisms

Abstract: The effect of coated Mydocalm tablet, given in 3 x 150-mg daily doses for 3 weeks to 47 patients, simultaneously with physiotherapy, has been examined in comparison to the results of 47 patients treated with physiotherapy solely. In the group of patients receiving Mydocalm as an adjuvant to physiotherapy the alleviation of pain and moderation of muscular hypertonia and spasm were observed within a shorter period. On the basis of the results of these examinations the use of Mydocalm is recommended as an adjuvant to complex therapy, in 300-450-mg daily doses, for the treatment of locomotor diseases accompanied by muscular hypertonia, muscular spasticity, and contracture

Abstract: Spasticity is a common and disabling symptom for many patients with upper motor neuron dysfunction. It results from interruption of inhibitory descending spinal motor pathways, and although the pathophysiology of spasticity is poorly understood, the final common pathway is overactivity of the alpha motor neuron. Therapy for spasticity is symptomatic with the aim of increasing functional capacity and relieving discomfort. Any approach to treatment should be multidisciplinary, including physical therapy, and possibly surgery, as well as pharmacotherapy. It is important that treatment be tailored to the individual patient, and that both patient and care giver have realistic expectations. Pharmacotherapy is generally initiated at low dosages and then gradually increased in an attempt to avoid adverse effects. Optimal therapy is the lowest effective dosage. Baclofen, diazepam, tizanidine and dantrolene are currently approved for use in patients with spasticity. In addition, clonidine
(usually as combination therapy), gabapentin and botulinum toxin have shown efficacy, however, more studies are required to confirm their place in therapy. Intrathecal baclofen, via a surgically implanted pump and reservoir, may provide relief in patients with refractory severe spasticity


Abstract: This study was made in order to define risk factors for patients requiring spinal opioid therapy developing painful spastic muscle tone together with myoclonus and spinal jerking (MSJ). The case histories of 75 patients, all receiving morphine spinally, were retrospectively analysed and, of these, 10 suffered from the MSJ syndrome. The following were taken as evaluation criteria: age, sex, performance status, duration and dosage of previous systemic and current spinal morphine therapy, concomitant analgesic and co-analgesic medication, pretreatment of the dorsal column and neurological dysfunction due to damage either of the nerual plexus or of the medulla spinalis. As a result, high spinal morphine doses in conjunction with pathological changes within the spine were shown to be risk factors for this syndrome. Changing from spinal to systemic morphine application or reduction of spinal doses together with the addition of systemic morphine led to complete recovery from MSJ. As underlying mechanism, an imbalance between the activity of spinal and central opioid receptors and/or toxic morphine effects on the medulla spinalis are discussed. In conclusion, great care should be taken when applying morphine to the spine in patients with neurological dysfunction due to an apparent pathology of the medulla spinalis, especially if large amounts of morphine are likely to be required. Some systemic application of morphine might reduce the risk of patients developing MSJ syndrome

Abstract: We compared the severity of ataxic and spastic dysarthria with local cerebral metabolic rates for glucose (ICMRGlc) in 30 patients with olivopontocerebellar atrophy (OPCA). Perceptual analysis was used to examine the speech disorders, and rating scales were devised to quantitate the degree of ataxia and spasticity in the speech of each patient. ICMRGlc was measured with 18F-2-fluoro-2-deoxy-D-glucose and positron emission tomography (PET). PET studies revealed marked hypometabolism in the cerebellar hemispheres,
cerebellar vermis, and brainstem of OPCA patients compared with 30 control subjects. With data normalized to the cerebral cortex, a significant inverse correlation was found between the severity of ataxia in speech and the ICMRGlc within the cerebellar vermis, cerebellar hemispheres, and brainstem, but not within the thalamus. No significant correlation was found between the severity of spasticity in speech and ICMRGlc in any of these structures. The findings support the view that the severity of ataxia in speech in OPCA is related to the functional activity of the cerebellum and its connections in the brainstem.


Knutsson E. and Martensson A. (1976) Action of dantrolene sodium in spasticity with low dependence on fusimotor drive. J. Neurol. Sci. 29, 195-212. Abstract: The effects of dantrolene sodium, an anti-spasticity drug with a site of action within the muscle fibres, were studied in 19 patients with spastic paresis. Oral doses were successively increased from 100 mg/day to a maximal tolerated level or up to 800 mg/day. Trial periods were 8- 13 weeks. The responses of stretch reflexes to local cooling over the spastic muscles were used to differentiate alpha and gamma spasticity. In the knee extensor and flexor muscle groups, cryo-negative alpha- spasticity was seen in 25 and cryo-positive gamma-spasticity in 4 muscle groups. Ankle clonus was cryo-positive in 14 of 15 cases. Resistance to passive knee joint movements, ankle clonus and isometric or isokinetic muscle strength was determined quantitatively. The gait was recorded by intermittent-light photography and the muscle activation patterns in gait were studied in recordings of the average EMG from limb muscles. Functional disability and spasms were assessed from clinical examinations and interviews. Passive resistance at slow (6%/sec) and fast (30 degrees/sec) knee joint movements decreased by 32% in the extensor muscles (p = 0.005 resp. 0.001) and by 23-26% in the flexor muscles (not significant). Reduced passive resistance was observed in 16 of the muscles with alpha-spasticity and in all 4 of the muscle groups with gamma-spasticity. Clonus was diminished or abolished in 14 of 15 patients with this sign. Maximal isometric or isokinetic muscle strength was unaltered in the majority of the patients. In a few the strength was increased, in some it was decreased. The averaged EMG activity during walking as studied in 10 patients were increased in 35 of the 57 muscle groups examined. In some muscle groups, exaggerated activity attributable to spastic reflexes was reduced. Motor disability was decreased significantly in 10 patients. It was not significantly
changed in 5 and deteriorated in 4 patients. Drowsiness and subjective muscle weakness were the most frequent side-effects. SGOT and SGPT were increased in 3 cases


Kofler M., Saltuari L., Schmutzhard E., Berek K., Baumgartner H., Russegger L., and Aichner F. (1992) Electrophysiological findings in a case of severe intrathecal baclofen overdose. Electroencephalogr. Clin. Neurophysiol. 83, 83-86. Abstract: Multimodality evoked potentials were examined in a case of serious accidental intrathecal baclofen overdose in a patient who suffered from severe spasticity due to a traumatic brain lesion. Electrophysiological findings during, before and after the intoxication were compared. Transcranial electrical stimulation up to 750 V did not evoke any responses in thenar muscles on the first day of intoxication. An improvement to normal values was observed within 3 days, paralleled by an amelioration of the patient's clinical condition. Cervical electrical stimulation was largely unaffected by baclofen. Median nerve somatosensory and brain-stem acoustic evoked potentials revealed few or no differences during intoxication compared to pre- and post- intoxication responses


Kofler M., Donovan W.H., Loubser P.G., and Beric A. (1992) Effects of intrathecal baclofen on lumbosacral and cortical somatosensory evoked potentials. Neurology 42, 864-868. Abstract: We analyzed lumbosacral and cortical somatosensory evoked potentials in three spinal cord injury patients undergoing evaluation of intrathecal baclofen infusion for management of spasticity. The cauda equina propagating root wave (R wave) and conus medullaris postsynaptic responses (S and P waves) were analyzed before and during baclofen infusion. Baclofen abolished the concomitantly recorded H-reflex and markedly suppressed the P wave amplitude and area. The S wave amplitude and area were suppressed to a lesser degree. In contrast, there were no significant changes in cortical somatosensory evoked potentials

also suffered a spinal cord injury. Two patients experienced their first seizure following intrathecal baclofen test bolus injection. Another patient had convulsions on two occasions: following postoperative baclofen dose adjustment, and after sleep deprivation. Structural brain disease seems prerequisite for baclofen to exert epileptogenic activity, since seizures have not occurred in patients receiving intrathecal baclofen for spasticity of solely spinal origin. Antiepileptic medication permitted the continuation of intrathecal baclofen treatment in the three patients.

Abstract: A case of Pacemaker-Twiddler's Syndrome is presented. Rotation of a permanent pacemaker can result in a capstan effect, and the lead is drawn out of the right ventricle. Fixing thoroughly the pacemaker and the lead should be an useful prophylactic measure.

Abstract: Use of intramuscular botulinum-A toxin (Botox) to produce neuromuscular blockade has been effective in treating certain ocular and facial muscular imbalances as well as spasmodic torticollis. In this preliminary open study, the effectiveness of intramuscularly injected Botox on the muscular imbalances of cerebral palsy was assessed in 27 pediatric patients. Each patient had "dynamic deformities" unresponsive to other treatment, and operation was the only other realistic alternative. The dose of Botox was calculated on a unit/body weight basis. In ambulatory patients, clinical changes in gait were assessed by a physician's rating scale. Reduction in spasticity became apparent in 12-72 h after injection; the effect of Botox after target threshold was reached lasted 3-6 months. No major side effects occurred. Botox may prove a useful adjuvant in conservative management of the spasticity of cerebral palsy. Successful management with these injections may allow delay of surgical intervention until the child is older and at less risk of possible complications, including the need for repeated surgical procedures.

Abstract: In order to evaluate further the efficacy of local intramuscular injections of botulinum-A toxin (BAT-A) in the management of dynamic equinus deformity associated with cerebral palsy, a randomized, double-blind, placebo-controlled study was undertaken. When evaluated using our Physician Rating Scale, 83% (five of six) of patients receiving toxin showed improvement, versus 33% (two of six) receiving placebo. There were no major complications. BAT-A injections appear to be safe and effective in children, and merit further prospective study.
Abstract: Neuromuscular blocking agents-45% alcohol, 4% to 6% aqueous phenol, local anesthetics, and botulinum A toxin-have been used for many years in the evaluation and management of spasticity and movement disorders in children with cerebral palsy. Recent reports suggest that longer-acting neuromuscular blocking agents may impact positively on the natural history of dynamic deformity and improve health-related quality of life. This review includes the mechanism of action, techniques, indications, complications, and clinical outcomes associated with these agents.

Abstract: 1. We previously reported that volatile anaesthetics produce incidences of a transient opisthotonus in mice, a sign of CNS stimulation. This study was performed to investigate mechanisms by which enflurane-induced opisthotonus (EIO) occurs. 2. The effects of pretreatment of N-methyl-D-aspartate (NMDA) antagonists dizocilpine (MK-801; DIZ) and ketamine (KET), GABA antagonists picrotoxin (PIC), pentylenetetrazol (PTZ) and glycine antagonist strychnine (STR) on the incidence of EIO were determined. Prior to exposure to 2.0% enflurane in air, male ddN mice were given intraperitoneal injections of 0.2 mL saline (control), 0.5-5.0 mg/kg DIZ, 20-80 mg/kg KET, 2.9 mg/kg PIC, 40.0 mg/kg PTZ and 0.75 mg/kg STR. After the injection, the behavioural state of the mice was observed for 20 min (the pre-enflurane period). During the exposure to enflurane the time for immobilization, that is, anaesthetic induction time (IT), and the incidence of EIO were measured. 3. Dizocilpine (1.0-5.0 mg/kg) and KET (80 mg/kg) significantly (P < 0.01) reduced both the incidence of EIO and IT in a dose-dependent manner. During the pre-enflurane period DIZ produced incidences (5-40%) of transient seizures in a dose-dependent manner, while KET did not induce them at all. The two GABA antagonists had no detectable effect on the EIO. Strychnine significantly enhanced the EIO. These CNS stimulants resulted in a 3-10% incidence of transient seizure and/or opisthotonus during the pre-enflurane period, but there was no correlation between DIZ-induced seizure and EIO. 4. These results suggest that the EIO is mediated by the NMDA and the STR-sensitive glycine receptors, but not the GABA receptor. (ABSTRACT TRUNCATED AT 250 WORDS)

Abstract: F responses were recorded in 6 cases with SSP and in 22 normal controls. The present study confirmed that frequency, number of phases, F/M amplitude ratio and duration were significantly increased and CV of onset latencies was significantly reduced in cases with SSP. After intravenous injection
of TRH (2 mg), all the parameters were altered toward normal sides. It was suggested that the hyperexcitability of motor neuron pool in SSP was stabilized by effects of TRH on injured pyramidal tracts and consequently abnormalities of F responses were improved. The Effect of TRH to correct the abnormal F responses in SSP might be consistent with effects of TRH to reduce spasticity in amyotrophic lateral sclerosis described previously.


Abstract: We report a patient with serious organophosphorus-induced delayed neurotoxicity due to malathion. The patient was a 49-year-old male with a history of habitual alcohol drinking, who ingested approximately 100 ml of 50% malathion [S-1,2-bis(ethoxycarbonyl)-ethyl-0,0-dimethyl phosphorodithioate solution], with a large amount of alcohol in a suicide attempt. Following recovery from an acute cholinergic phase 36 hours after ingestion, respiratory muscle weakness, consciousness disturbance and diffuse weakness of the limb muscles occurred, necessitating mechanical ventilation. On the 7th hospital day, glove and stocking type sensory disturbance was observed and weakness of the limbs had progressed to distal dominant flaccid quadriparalysis with moderate muscle atrophy. Two months after onset, neurogenic bladder and spinal automatism became obvious. After 7 months, spasticity of the lower limbs developed, while the weakness of the upper limbs improved. Sural nerve biopsy showed axonal degeneration, loss of large myelinated fibers and increases in Schwann cell clusters. These findings were similar to those seen in patient with triorthocresyl phosphate (TOCP) intoxication. The symptoms of this patient seemed to correspond to Senanayake's "intermediate syndrome". The final clinical features and sural nerve biopsy findings were in close agreement with those in patients with serious organophosphorus compounds induced delayed neurotoxicity due to TOCP intoxication. However, this patient exhibited more severe neuropathy than seen in previously reported cases of organophosphorus compounds induced delayed neurotoxicity caused by less toxic organophosphorus compounds, such as Dipterex. This suggests that alcohol might have been an etiological factor in damage of nervous tissue in this rare case. This is the first case of organophosphorus compounds induced delayed neurotoxicity due to malathion to be reported in Japan.


Abstract: In patients with predominantly focal spasticity, oral antispastic drugs are relatively ineffective or cause unwanted side effects of central origin. Therefore we treated patients by disabling focal spasticity with local injections of Botulinum-Toxin A (Porton Products BOTOX). Efficacy, dosage, side-effects and injection technique were examined. 11 patients (mean age 48 years) with severe focal spasticity of the flexor muscles of the hand and arm (5 patients), the adductor
muscles of the legs (5) or the plantar flexors of the foot (1) due to multiple sclerosis, cervical myelopathy or stroke-related hemi-paresis were treated with BOTOX. Rating scales, including Ashford spasticity scale, pain scale and a hygienic rating scale, were used to evaluate the efficacy. 25 to 30 ng (1000-1200 MU Porton) were injected in the flexor group of the hand or arm and 42 to 50 ng (1680-2000 MU Porton) BOTOX in the adductor group of one leg. 10 of the patients showed an improvement of at least one point on the scales for spasticity, pain and hygiene. Effects could be observed after 4-7 days and lasted for 6-13 weeks. There were no unwanted side-effects. We conclude that BOTOX is an alternative to the systemic application of antispastic drugs. Focal spasticity and pain can be successfully reduced and hygienic care is facilitated.


Abstract: The 1-aminoadamantanes memantine (1-amin-3,5-dimethyl-adamantane) and amantadine (1-amin-adamantane) are clinically used as anti-parkinsonian, anti-spasticity, anti-dementia and antiviral drugs. In the present investigation we have tested a series of 1-aminoadamantane derivatives including memantine and amantadine for their ability to compete with [3H](+)-pentazocine in homogenates of post-mortem human frontal cortex. The Ki values ranged from 0.237 +/- 0.019 microM for 1- N-dimethyl-amino-3,5-dimethyl-adamantane to 20.25 +/- 16.48 microM for amantadine. The Ki value of memantine was 19.98 +/- 3.08 microM and was thus very similar to that of amantadine. Memantine, at therapeutic concentrations, probably does not interact with the sigma binding site. Amantadine, at therapeutic concentrations, probably binds both to the sigma site and to the phencyclidine (PCP) binding site of the N-methyl-D-aspartate (NMDA) receptor.


Abstract: Memantine is an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist with therapeutic potential in dementia, spasticity and Parkinson’s disease. The Ki-value of memantine at the phencyclidine (PCP) binding site of the NMDA receptor is 0.5 microM in human frontal cortex. We investigated whether concentrations of memantine in cerebrospinal fluid (CSF) and serum samples under therapeutic conditions are in the range of its Ki-value at the PCP binding site. The serum levels ranged from 0.025 to 0.529 microM with daily doses between 5 and 30 mg. CSF levels were highly correlated to serum levels and were below serum levels in each patient with a mean CSF/serum ratio of 0.52. Serum and CSF levels were correlated to the daily dose, but not to the duration of treatment. At the concentrations reported here, memantine is expected to specifically interact with the PCP binding site of the NMDA receptor.
Abstract: Glutamate receptor antagonists with selective action at the N-methyl-D-aspartate (NMDA) receptor are promising agents for the neuroprotective and symptomatic pharmacotherapy of various neuropsychiatric disorders. Although NMDA receptor antagonists of the phencyclidine (PCP) type are precluded from clinical use because of their psychotomimetic properties, amantadine and memantine have been administered to human patients with idiopathic Parkinson's disease and spasticity for many years without serious adverse effects. The mechanisms underlying these differences in psychotogenicity of different NMDA receptor antagonist are currently being discussed. Different affinity to the PCP binding site of the NMDA receptor, region-specific pharmacology, as well as different binding profiles to neurotransmitter receptors other than the NMDA type glutamate receptor, most likely play a role in determining whether an NMDA receptor antagonist drug will be tolerated clinically or not.

Abstract: The development of neuroprotective agents for the prevention of neuronal loss in acute conditions such as stroke and epilepsy or chronic neurodegenerative disorders including Parkinson's disease, Alzheimer's disease, Huntington's chorea, and motor neuron disease is currently focusing on drugs that inhibit excitatory amino acid neurotransmission or exhibit antioxidant properties. Unfortunately, potent antagonists at the N-methyl-D-aspartate (NMDA) type glutamate receptor, which is thought to mediate excitotoxic neuronal injury, e.g., MK-801 or phencyclidine (PCP), share a high probability of inducing psychotomimetic side effects. Further, these drugs have been associated with acute neurotoxicity in vitro and in vivo, precluding their clinical use. In contrast, low affinity NMDA receptor antagonists like amantadine and its dimethyl derivative, memantine, have been administered clinically for the management of Parkinson's disease, dementia, neuroleptic drug-induced side effects, and spasticity. These agents have only rarely induced significant psychotomimetic side effects. Recent pharmacologic advances have helped to elucidate how high drug affinity for the PCP binding site of the NMDA receptor may enhance psychotogenicity. Low affinity and associated fast voltage-dependent channel unblocking kinetics are likely to be responsible for the better tolerance of amantadine and memantine compared with MK-801 and PCP. Further factors apparently modulating psychotogenicity of glutamate receptor antagonists include differential actions on neuronal populations in various brain regions and interactions with neurotransmitter receptors other than the NMDA type glutamate receptor.

spectroscopy. Pediatr. Neurol. 8, 60-64.
Abstract: In a 2-year-old boy with Leigh disease, spasticity, dysarthria, and optic atrophy gradually developed. Computed tomography and magnetic resonance imaging disclosed progressive, symmetric basal ganglia lesions. In muscle tissue, a defect of pyruvate dehydrogenase complex was found. Magnetic resonance volume selective proton spectroscopy (MRVS) of the basal ganglia demonstrated an abnormal lactate peak. A ketonemic diet coincided with clinical stabilization and arrest of progressive brain lesions. Lactate could no longer be demonstrated by MRVS. It reappeared with a new brain lesion coinciding with discontinuation of the diet. MRVS, therefore, appears to be a sensitive tool to evaluate pathologic lactate production in metabolic brain disease with disturbed energy metabolism and allows noninvasive therapy monitoring

Abstract: Electromyographic activity was recorded from tibialis anterior during nocturnal polysomnography in six patients with severe spasticity of spinal origin. The patients had a baclofen reservoir system implanted subcutaneously into their lumbar subarachnoid space and were studied for two nights in a double-blind, placebo controlled, crossover design. Tibialis anterior electromyographic activity per hour of sleep was reduced on the night of baclofen infusion. In particular, less electromyographic activity occurred after arousal from sleep

Abstract: Spinal cord injury can lead to an exaggeration of transmission through spinal pathways, resulting in muscle spasticity, chronic pain, and abnormal control of blood pressure and bladder function. These conditions are mediated, in part, by N-methyl-D-aspartate (NMDA) receptors on spinal neurons, but the effects of cord injury on the expression or function of these receptors is unknown. Therefore, antibodies to the NMDA-R1 receptor subunit and binding of [3H]MK-801 were used to assess NMDA receptors in the spinal cord. Receptor density in rats with intact spinal cords was compared to that in rats 1 and 2 weeks after spinal cord transection (SCT) at the mid-thoracic level. At 1 and 2 weeks after SCT, [3H]MK-801 binding was reduced in most laminae in cord segments caudal to the injury, whereas no decrease in amount of R1 subunit immunoreactivity was observed. No significant changes in [3H]MK-801 binding and NMDA-R1 immunoreactivity could be seen rostral to the transection. Since [3H]MK-801 binding requires an open ion channel, the discrepancy between [3H]MK-801 binding and immunocytochemistry may indicate a loss of functional receptors without a consistent change in their total number. Therefore, the exaggerated reflexes that are well established in rats 2 weeks after cord injury must be mediated by a mechanism that withstands attenuation of NMDA receptor function

Abstract: Chronic intrathecal drug infusion for the treatment of neurological diseases, such as spasticity and chronic pain, has become an accepted method of therapy in recent years. Concurrent pharmacokinetic studies have shown that the cisternal cerebrospinal fluid (CSF) drug level is considerably lower than the lumbar CSF level during continuous infusion into the lumbar subarachnoid space. One factor that makes analysis of this decline in drug level difficult to quantify is that it is only feasible to sample CSF at the two extremes of the spinal subarachnoid space. Using a radionuclide technique, we have examined the distribution along the spinal canal of a hydrophilic compound, indium-111 diethylenetriamine pentaacetic acid, that was delivered over 72 hours into the lumbar subarachnoid space in five patients with implanted drug pumps. Over a 20-cm distance of the thoracic cord, radionuclide counts decreased gradually so that the indium-111 diethylenetriamine pentaacetic acid concentration surrounding the cord at the T2 vertebral level was 43% of that at the T12 level in four patients. Therefore, it appears that even with a hydrophilic compound, which minimizes spinal cord capillary losses, there is still a considerable reduction of CSF drug concentration along the spinal canal. The clinical implication of this gradual decline in drug level is that for intrathecal infusion of relatively hydrophilic compounds there may not be any advantage in placing the catheter tip at more rostral locations, such as at the midthoracic or cervical cord.


Abstract: At present, it is not clear why drug tolerance develops in patients receiving intrathecal baclofen for the chronic treatment of spasticity of spinal origin. To investigate the mechanisms of tolerance to the gamma-aminobutyric acid (GABAB) agonist baclofen, rats were implanted with intrathecal catheters and continuously infused with either the drug or saline for 1, 3, or 7 days. The dose chosen, 1 microgram/hr, initially caused profound hindlimb motor weakness, but by Day 7 the rats had adapted to the drug and exhibited only minimal motor impairment. The animals were sacrificed on Day 1, 3, or 7 and quantitative autoradiography was used to determine the binding density and affinity of the GABAB receptors in the substantia gelatinosa of the lumbar spinal cord. After 1 day of drug infusion there was no change in binding parameters, but after 3 and especially after 7 days there was a significant decrease in the GABAB binding density (74% and 66%, respectively) in baclofen-treated rats as compared to saline-treated control rats. This GABAB receptor down-regulation correlated with tolerance to the motor weakness in the baclofen-treated animals and suggests that similar mechanisms contribute to drug tolerance in patients.

Abstract: In the present report there has been pursued an object of studying the efficiency of the preparation dalargine (synthetic preparation, analogous to encephaline) in case of unstable spine and spinal cord injuries. Under the observation there were 32 operated patients. Dalargine was administered endolumbally by 2 mg, dissolved in 2 ml of physiologic salt solution. The results were evaluated by several categories: locomotive function, sensitivity, pelvic organ function, pain, spasticity, trophic disturbances


Abstract: A 20-year-old man was admitted to our hospital because of generalized muscle cramp with pain. At the age of 12 years, he began to have painful muscle cramps in calf muscles, which gradually extended to all limb and truncal muscles and became more severe and frequent. He also had diarrhea and mild hair loss. On admission he had mild baldness, left shoulder deformity, and hypertrophic muscles. Muscle cramps were observed especially in the extremities. Routine laboratory studies revealed moderately high serum CK and low IgG levels. He had been treated with several muscle relaxants and antiepileptic drugs, but with no favorable effect. During his admission he received high-dose intravenous methylprednisone of 1000 mg/day for three days, followed by oral prednisolone tapered over 4 weeks. Soon after the initiation of the treatment, painful muscle cramps were gradually decreased and his activity of daily life apparently improved. In conclusion steroid pulse therapy is a useful treatment for patients who are not responsive to dantrolene sodium administration, and the effectiveness suggests that a certain autoimmune mechanism plays a role in pathogenetic mechanism


Abstract: A single systemic administration of acromelic acid A (ACRO), a novel kainate analogue (kainoid), induces a series of characteristic behavioral changes in association with selective damage of interneurons in the caudal spinal cord in adult rats. When ACRO (5 mg/kg) was systemically administered, rats displayed forced extension of hindlimbs followed by frequent cramps and generalized convulsion. Most rats died during the convulsions without neuropathological change. Two rats developed long-lasting spastic paraparesis which persisted at least 3 months. Neuropathological changes were observed only in the rats with persistent paraparesis, in which neuron damage was identified selectively in small interneurons in the lumbosacral cord. The regional difference between kainate- and ACRO-induced neuron damage suggests the existence of plural kinds of kainate receptor subtypes


Abstract: The few existing neuropathological, neurochemical, and neuropsychopharmacological studies have shed little light on the pathophysiology of spasmodic torticollis (ST). The relevance of experimental ST in animals and drug-induced ST in man to idiopathic ST is unclear. Most pharmacotherapeutic endeavors have focused on drugs affecting basal ganglia function. Unfortunately, problems of sample size, clinical heterogeneity of patient population, research design, objective evaluation of response, documentation of key data, and adequacy of duration of follow-up make interpretation of published results difficult. Because of the heterogeneity of ST, investigations aimed at establishing a neurotransmitter profile for each patient by observing the acute response to a test dose of drugs affecting cholinergic, dopaminergic, serotonergic, and gamma-aminobutyric acid systems may provide a more rational basis to the selection of treatment.


Abstract: Drug-induced diseases constitute up to 5% of hospital admissions, a figure which almost certainly understates the total morbidity due to drugs. Sever drug-induced myopathies are uncommon, but milder forms may be more prevalent than is generally appreciated, since skeletal muscle constitutes some 45% of total body weight and has a major metabolic role in addition to its mechanical function. Knowledge of possible effects of drugs on the neuromuscular system is of increasing importance both because the range of therapeutic agents continues to expand and because the resulting syndromes, through usually reversible at the outset, may progress and lead to grave consequences if the drug responsible is not stopped. Drug-induced neuropathies will not be considered here, but it will be appreciated that muscle weakness may also be feature of such disorders and that some drugs may cause both a neuropathy and a myopathy. The features of the main drug-induced syndromes are summarised in the table. To these one could justifiably add the unwanted effects of drugs given for the treatment of central nervous system or neuromuscular disorders per se-e.g., the cholinergic block which may be produced by anticholinesterases alone or with corticosteroids in the myasthenic,4
and the profound weakness which may supervene after relief of spasticity with dantrolene sodium

Abstract: Plasma amino acid levels were measured following oral glycine loading in 43 patients with motor neurone disease (MND), eight normal subjects and 18 neurological disease controls with wasting or spasticity from a variety of other causes. Levels at baseline and 1.5 h after loading did not differ, but at 4 h, plasma glycine levels in MND patients remained significantly higher than in normal and neurological controls (P < 0.013). Cerebrospinal fluid glycine levels, which were maximal at 2.5 h, were also significantly higher in MND patients than neurological controls (P < 0.04). These observations suggest a defect of glycine 'housekeeping' in the central nervous system in MND which may be relevant to the pathogenesis of the disease

Abstract: Recent electrophysiological studies in patients with cranial dystonia (CD) have demonstrated evidence for hyperactivity of brainstem interneurons. Tizanidine (Tz), a centrally acting skeletal muscle relaxant, is thought to act by antagonizing the activity of excitatory interneurons which mediate hypertonic processes (e.g. spasticity). Theoretically this agent may be effective in patients with CD. Ten patients were enrolled in an open-label study with a single-blind placebo wash-in. Eight patients tolerated doses of between 28-36 mg per day. For the most part tizanidine was ineffective for the symptoms of CD. This failure suggests that the reported brainstem interneuronal disturbances may not be altered by Tz. Further studies using concomitant electrophysiological assessment would be necessary to assess this possibility. Alternatively, these disturbances may not be a principle cause of the dystonic movements. The finding of similar changes in other basal ganglia diseases lacking CD (e.g. Parkinson's disease) favours this latter explanation

Abstract: Dantrolene is used in patients with muscle spasticity and is the only known effective treatment for malignant hyperthermia. However, its effects on muscle relaxation and energetics are unknown and may have important consequences in diaphragmatic function. We studied the effects of dantrolene (10(-8) to 10(-4) M) on diaphragm muscle strips (n = 12) in the hamster in vitro (Krebs-Henseleit solution, 29 degrees C, 95% oxygen/5% carbon dioxide) in response to tetanic stimulation (50 Hz). We studied contraction and relaxation under isotonic and isometric conditions, as well as energetics. Data are mean +/- SD. Dantrolene induced a negative inotropic effect in the hamster diaphragm
(active force at 10(-4) M: 34% +/- 7% of baseline; P < 0.05) but did not significantly modify the curvature of the force-velocity relationship. Dantrolene did not significantly modify isotonic relaxation. Dantrolene, up to 10(-5) M, did not significantly impair isometric relaxation. In conclusion, dantrolene induced a marked negative inotropic effect on diaphragm muscle without affecting myothermal efficiency and relaxation. Implications: Dantrolene induced a significant and concentration-dependent negative inotropic effect on diaphragm muscle but did not modify isotonic relaxation, which suggests no alteration of the calcium reuptake by the sarcoplasmic reticulum; up to 10(-5) M dantrolene did not alter isometric relaxation, i.e., myofilament calcium sensitivity. Dantrolene did not modify the energetics of diaphragm muscle.


Abstract: Spasticity is a frequent and often disabling symptom in MS patients. Current drugs used as antispastic agents include Dantrolene Sodium, Baclofen and Diazepam. Tizanidine (5-chloro-4-(2imidazolin-2 yl amino)- 2,1,3-benzothialdiazole) is a new antispasticity agent that has purported central action. A double blind placebo controlled trial was performed to study the efficacy of this drug in MS patients. Sixty-six patients entered an eight week therapeutic trial and fifty-nine completed the trial. Patients were assessed at 0, 2, 3 and 8 weeks of therapy for clinical effects. Electrophysiologic tests were performed at 0 and 8 weeks. A statistically significant benefit was noted in spastic muscle groups in the legs with concomitant significant reduction in hyperactive stretch reflexes and ankle clonus. Side effects most frequently cited included dry mouth and drowsiness. Two patients developed elevated liver function test that decreased with cessation of therapy. Other clinical details, side effects and electrophysiologic data will be presented. Tizanidine appears to reduce clinical spasticity and hyperreflexia in MS patients although no change in functional status was detected. Tizanidine may well serve as an alternate antispastic agent, alone or in combination with other agents.


Abstract: Dyskinetic, writhing-like movements, similar to those produced in mice after an intraperitoneal (IP) injection of acetic acid, were elicited by intrathecal (IT) injection of GABA, glycine, taurine or beta- alanine. Baclofen and muscimol failed to produce this behavior. While acetic acid-induced writhing is inhibited by
narcotic and nonnarcotic compounds, GABA-induced writhing was found to be insensitive to pretreatment with either morphine or capsaicin. Moreover, acetic acid-induced writhing does not appear to involve GABAergic transmission as IT injections of nipecotic acid did not alter the intensity of response to IP acetic acid while it enhanced the response to IT GABA. Writhing induced by glycine was not inhibited by strychnine at subconvulsive doses, suggesting that it involves an action at strychnine-insensitive receptors. Together these data suggest that while the dyskinetic movements produced by inhibitory amino acids do not appear to reflect an alteration in nociception, they may mimic either the motor response to abdominal pain or spasticity.

Abstract: Despite the frequency of acute poisoning in normal children by oral or rectal phosphosoda laxatives, the rate of clearance of the resultant high level of phosphorus and the rationale for therapy are defined incompletely.
Pharmacokinetic analysis has been made of plasma inorganic phosphate (Pi) in an infant after ingestion of phosphosoda laxative and of data reported for four comparable poisonings in healthy infants to provide a nomogram which predicts the decline in Pi in paediatric phosphate poisoning. Clearance of Pi is exponential; it directly correlates with and approaches the glomerular filtration rate. After single oral or rectal overdoses, plasma Pi at diagnosis is 4-20 mmol/l and has a half-life of 5-11 h that appears independent of therapy. The time for plasma Pi to return to normal can be calculated from the initial Pi as \( t = \frac{\ln \frac{5}{Pi}}{0.1292} \). Neuromuscular and cardiac abnormalities relate to the low serum calcium; the increase of total serum calcium during recovery from phosphate poisoning is linear but is accelerated by intravenous (i.v.) calcium salt. Continued i.v. calcium therapy may be required since restoration of plasma calcium is often delayed.

Abstract: Cerebellar implants have been placed in 62 patients with postoperative follow-up of 4 months to 3 years. Initially currents were applied through electrodes of alternate polarity on the superior surface of the cerebellar hemispheres and subsequently through negative electrodes on the superior surface to positive electrodes on the posterior surface. The amount of current required for clinical improvement was approximately the same as that required to significantly reduce the amplitude of the somatosensory evoked potential. The clinical and electrophysiological effects were proportional to the intensity of current and to the number of electrodes through which the currents were applied. Currents applied through the cerebellum were more effective than those confined near the cerebellar surface. Histological examination of the cerebellum from the chimpanzees and from 1 patient who died of causes unrelated to stimulation
failed to demonstrate any evidence of neuronal damage related to application of current


Abstract: Dantrolene sodium is a drug used in the treatment of spasticity and malignant hyperthermia. It is known to have a myorelaxant effect related to inhibition of the "release" of calcium by the sarcoplasmic reticulum of striated skeletal muscle. A direct cardiac effect which has only recently been suspected was demonstrated in vitro on isolated preparations of sheep Purkinje fibres and ventricular myocardium. Dantrolene caused a spectacular lengthening of the duration of the action potential of Purkinje fibres. This could be due either to an action on the slow calcium current or to stimulation of an ingoing sodium current sensitive to tetrodotoxin (TTX). This effect on the cardiac action potentials could explain the antiarrhythmic properties of dantrolene sodium during attacks of malignant hyperthermia


Abstract: Six patients with long-lasting spasticity resistant to different drug therapies including oral baclofen received a bolus injection of lumbar intrathecal baclofen. Electromyographic (EMG) reactions of leg muscles (soleus, tibialis anterior, quadriceps, and hamstrings) to standard stimuli and during attempts at voluntary activation were recorded before the drug injection and up to 3 h after the injection. Responses to joint movements, H-reflexes, ankle clonus, and defensive reactions were noticeably suppressed within 30-45 min after the injection and had practically disappeared after 2 h. Ankle clonus was seen only in patients with H-reflexes, and clonus disappeared when the reflex responses to the n. tibialis stimuli were absent. A decrease in clonus EMG burst amplitudes was accompanied by a decrease in the clonus frequency. These observations favor the autooscillation hypothesis of clonus. Baclofen injection led to improvement in selective voluntary activation of leg muscles in patients with residual motor control. These results suggest that execution of voluntary motor commands in the patients suffered from functionally abnormal spinal circuitry rather than from changes in the descending motor commands. Intrathecal baclofen appears to be an effective way of eliminating increased muscle tone and spasms which can allow for voluntary motor function when it is present


Abstract: The therapeutic profile of a new antispastic drug cannot be defined solely on the basis of placebo-controlled studies. Its potential advantages must be evaluated in comparison with existing drugs. This review compares the efficacy and tolerability of tizanidine, a newer muscle relaxant, with that of
baclofen and diazepam, the most widely used antispastic agents, for a variety of diagnoses and target symptoms associated with spasticity. More than 20 double-blind, comparative studies were conducted between 1977 and 1987. These included a total of 777 patients suffering from spasticity of various causes. The collected clinical data have been integrated into a combined analysis. Tizanidine emerges from this comparison as a valuable drug in the treatment of spasticity related to cerebral and spinal disorders

Lawhorn C.D., Boop F., Brown R., and Andelman P. (1994) Epidural pain management in the postrhizotomy patient. Pediatr. Neurosurg. 20, 198-202. Abstract: The authors report a randomized double-blind prospective study comparing epidural morphine 80 micrograms/kg to epidural morphine 80 micrograms/kg plus butorphanol 40 micrograms/kg in children undergoing rhizotomy. Up to 50% of children receiving epidural morphine alone will experience side effects of nausea, vomiting, pruritus, urinary retention or respiratory depression. The addition of the narcotic agonist-antagonist butorphanol virtually eliminated these side effects without compromising analgesia or causing undue sedation. Parent satisfaction was greater than 90%

Lawhorn C.D., Boop F.A., Brown R.E., Jr., Andelman P.D., Schmitz M.L., Kymer P.J., and Shirey R. (1995) Continuous epidural morphine/butorphanol infusion following selective dorsal rhizotomy in children. Childs Nerv. Syst. 11, 621-624. Abstract: The authors prospectively evaluated 15 patients who had undergone selective dorsal rhizotomy who were given a continuous morphine/butorphanol infusion, to determine whether variations in the postoperative pain control and side effects seen using a bolus technique could be reduced. Patients had an epidural catheter placed at the end of the operative procedure through which 50-60 micrograms/kg preservative-free morphine and 15-20 micrograms/kg butorphanol was administered. A continuous epidural infusion of 5 micrograms/kg h morphine and 1.2 micrograms/kg h butorphanol was then initiated. Postoperatively, mean pain scores were excellent. No patient required additional systemic analgesics during the 72-h investigational period. A low incidence of nausea, and no vomiting, pruritus, or respiratory depression was reported by the cohort. All patients maintained oxygen saturations above 95%. This indicates that the use of a continuous epidural infusion provides excellent pain control, decreases the occurrence of untoward side effects, and allows the early initiation of occupational and physical therapy postoperatively

Lazorthes Y., Sallerin-Caute B., Verdie J.C., Bastide R., and Carillo J.P. (1990) Chronic intrathecal baclofen administration for control of severe spasticity. J. Neurosurg. 72, 393-402. Abstract: Baclofen, the most effective drug for treating spasticity, is a specific agonist of gamma-aminobutyric acid-B receptors, and is very abundant in the superficial layers of the spinal cord. Given orally, baclofen does not easily penetrate the blood-brain barrier, and is distributed equally to the brain and spinal cord. Direct intrathecal administration was given in order to change the
distribution of the drug by preferentially perfusing the spinal cord. Eighteen patients presenting a severe spastic syndrome were treated with chronic intrathecal infusion of baclofen in the lumbar cerebrospinal fluid. After clinical preselection, 38 patients were implanted with a lumbar access port allowing long-term trials in order to determine the efficacy of baclofen therapy and the effective 12-hour dose. The 18 patients selected for chronic administration were implanted with a programmable pump. The pathology in these cases was: multiple sclerosis (6 cases), posttrauma spastic syndrome (eight cases), and (one case each) cerebral palsy, ischemic cerebral lesion, spinal ischemia, and transverse myelitis. The mean follow-up period was 18 months (range 4 to 43 months). The clinical results were evaluated according to muscular hypertony on Ashworth's scale (changed for occurrence of painful spasms) and functional improvement. Results were better for spastic syndrome secondary to traumatic medullary lesion than for demyelinating disease. Hypertonia was improved in all cases as confirmed by the registration of the Hoffman (H) reflex. Painful muscular spasms disappeared in 14 of the 16 affected patients. Significant functional improvement was noted in nine patients and was considerable in three. The risk of side effects secondary to overdose (such as excessive hypotonia or central depression) and the absence of a specific baclofen antagonist stresses the necessity for accurate determination of the efficient dose. After an initial titration period and adjustment of the therapeutic dose, the individual doses were from 21 to 500 micrograms/24 hrs (mean 160 micrograms/24 hrs). This new conservative method is very effective, perfectly reversible, and safe when administered in conditions favorable to its use.


Abstract: Direct intrathecal administration of baclofen in the treatment of severe spasticity was proposed in 1984 by Richard Penn with the objective to carry out a selective spinal distribution of the active principle thus avoiding supraspinal side effects. We presented our first results at the French Language Association of Neurosurgery in 1985 within the framework of a report on "Functional neurosurgery of cerebral palsy" (Neurochirurgie, 1985, 31 (suppl 1): 1-118). This study aims to specify the selection criteria and current indications of this method for the treatment of severe chronic diffused spasticity of spinal and cerebral origin in adults and in children. This report relates to our experience concerning 60 patients (10 children) that benefit from the use of a totally implantable system for chronic administration. The total follow-up of all patients was 48 months (from 3 to 140 months). The initial effective daily amount of baclofen was 156 micrograms/24 hours and progressed in time to reach in the long run 280 micrograms/24 hours, with a very broad interindividual variability from 36 to 1050
micrograms/24 hours. All the patients benefited from a reduction in muscular hypertonicity as well as painful muscular spasms. On the other hand, the functional improvement was very variable from one patient to another and depended primarily on the initial clinical state and the etiology of the spasticity. The results observed were more significant in post-traumatic paraplegia than those secondary to demyelination disease even if they were stabilized with regard to spasticity of spinal origin. This mode of administration currently plays a significant role in the treatment of spasticity of cerebral origin, in particular in children presenting a motor disorder of cerebral origin with spastic prevalence. The current limitations of this type of treatment are technical because of the frequent catheter malfunctions, but are due essentially to the importance and constraint of the multi-disciplinary organization needed for the out-patient follow-up.


Abstract: Dihydroergotamine (dhe) (or phentolamine), an alpha-adrenergic blocking agent, induced important changes on the CCK-stimulated gallbladder emptying of 70 volunteer subjects. Two cholecystograms were performed with 10-day intervals in each subject. The first cholecystogram showed gallbladder emptying provoked by a test meal (35 subjects or by 0.5 U. CCK Kg. injected intravenously (35 subjects). During the second cholecystogram 1 mg. of DHE was injected intramuscularly 45 minutes before the cholecystokinetic stimulus. The drug counteracted the gallbladder emptying induced by both endogenous and exogenous CCK. The effect was more pronounced when DHE was administered prior to the test meal stimulus than before CCK administration. This difference could be explained by a delayed gastric emptying induced by the alpha-adrenergic blockade. Our results suggest that the lack of gallbladder emptying could be due to the relaxation of this organ, in addition to a duodenal spasticity induced by DHE (or phentolamine).


Abstract: We conducted a double-blind, placebo-controlled, crossover study of oral L-threonine at 6 g/day in patients with spinal spasticity. Muscle tone from selected leg muscles, measured by the Ashworth Scale, was the principal measure of spasticity and was evaluated before and at the end of each treatment period. A 10% reduction in Ashworth score was regarded as a positive response to a treatment. The results were analyzed sequentially, patients being classified as threonine- responders, placebo-responders or non-responders (those who responded to both treatments by either less or greater than 10%) and a level of significance of p = 0.05 was chosen. The trial concluded in favour of L-threonine after 33 patients. Side-effects were minimal. L-threonine has a modest but definite antispastic effect, and its possible role in modifying spinal glycinergic transmission is discussed.


Abstract: 1. Rats, anaesthetized with urethane, were injected intravenously with dantrolene sodium in a carrier solution of 5% mannitol taken to pH 10 with NaOH. This carrier solution itself was without effect on extrafusal muscle contraction. 2. Dantrolene sodium (5 mg/kg) had a greater depressant action on the twitch contraction of the fast extensor digitorum longus (EDL) muscle than on the slow soleus (SOL) muscle. The EDL twitch was depressed to 25.9% +/- 1.2% (mean + s.e. mean, n = 7) of control whereas the SOL twitch was depressed to 31.3% +/- 0.4% (n = 9). These values were significantly different at the P less than 0.001 level. 3. The twitch contraction time to peak was reduced by approximately 35% in both EDL and SOL by dantrolene sodium. However, the drug reduced the half relaxation time of SOL by approximately 30% but that of EDL was hardly affected. 4. The effect of dantrolene sodium on contractions elicited by repetitive stimulation was dependent upon the stimulation frequency. For the SOL muscle the greater depression was produced at a stimulation frequency of 25 Hz and for EDL at 75 Hz. The minimum of depression was produced for a full fused tetanus for both muscles. 5. The significance of these findings is discussed in terms of the action of dantrolene sodium on motor control in the intact animal.


Abstract: Implanted infusion pumps are an effective method for delivering medications into the intrathecal space to reduce spasticity. Complications can occur with the surgical aspect of implantation, as well as with the hardware. We describe an 8-year experience with the implantation of 34 infusion pumps in 30 patients in whom either morphine or baclofen was used to control spasticity. The overall incidence of total complications was 62%; 24% in the Infusaid pumps, and 167% in the Medtronic pumps. The incidence and types of complications are
important in informed consent as well as in the selection of pumps and connectors


Abstract: OBJECTIVE: To evaluate the use of intrathecal baclofen for the treatment of muscle spasticity in patients with spinal cord injury. DATA SOURCES: A MEDLINE search was used to identify relevant and pertinent literature. Information was obtained from open-label clinical trials, abstracts, conference proceedings, and review articles. Index terms in the search included baclofen, spasticity, intrathecal drug infusion, spinal cord disease, and neurosurgery. DATA EXTRACTION: Studies were selected for review if they evaluated intrathecal baclofen in patients with spinal cord injury. Emphasis was placed on human studies published in the English language. Trials were reviewed by dosage regimen, therapeutic response, adverse effects, and complications. DATA SYNTHESIS: Thus far, intrathecal baclofen administration shows promise in the treatment of spasticity resulting from spinal cord trauma. Few complications and adverse effects have been reported. CONCLUSIONS: Muscle spasms and spasticity constitute a significant problem in spinal cord injuries, interfering with rehabilitation and leading to inconveniences and complications in these patients. Oral baclofen is the drug of choice for spasticity due to spinal cord trauma. It often is ineffective, however, because of the large dosages required to cross the blood-brain barrier and the subsequent appearance of central nervous system adverse effects. These adverse effects are not tolerated by many patients. Intrathecally administered baclofen has been approved by the Food and Drug Administration (FDA) for the treatment of spasticity in patients with spinal cord injury who are refractory to or cannot tolerate oral baclofen. It is intended for use only in implantable pumps approved by the FDA for the administration of baclofen into the intrathecal space. Intrathecal administration achieves high concentrations in the spinal cord with small dosages, thus reducing the incidence of central nervous system adverse effects. To date, approximately 350 patients with spinal cord injury have been treated with intrathecal baclofen. Reductions in spasticity have been demonstrated in both open-label and placebo-controlled trials. Patients also often make substantial gains in activities of daily living. Few adverse effects and complications have been reported. However, tolerance to the clinical effects of intrathecal baclofen has been reported. Further studies are needed to determine specific patient populations that may benefit most from intrathecal baclofen
administration. Individual dosage ranges and follow-up care also need to be defined more completely. In addition, the question of whether tolerance detracts from long-term clinical benefits with intrathecal baclofen needs to be addressed.


Abstract: In nine cases of phencyclidine hydrochloride poisoning, early signs of overdose included drowsiness, nystagmus, miotic pupils, blood pressure elevation, increased deep tendon reflexes, ataxia, anxiety, and agitation. In more severe cases, seizures, spasticity, and opisthotonos were seen in addition to deep coma and respiratory depression. Treatment included removal by emetics or lavage, hydration, and a quiet, reassuring environment. Spasticity, agitation, and ocular manifestations responded to diazepam. Psychiatric intervention was instituted after the patients were stable and no longer agitated.


Abstract: Nitric oxide (NO) as well as its donors has been shown to generate mutation and DNA damage in in vitro assays. The objective of this study was to identify that DNA single-strand breaks (SSBs) could be elicited by NO, not only in vitro but also in vivo. The alkaline single-cell gel electrophoresis (SCGE) was performed to examine the DNA damage in g12 cells and the cells isolated from the organs of mice exposed to sodium nitroprusside (SNP). A modified method, in which neither collagenase nor trypsin was necessary, was used to prepare the single-cell suspension isolated from organs of mice. Results showed that the exposure of g12 cells to 0.13-0.5 micromol/ml SNP with S9 for 1 h induced a concentration-dependent increase in DNA SSBs in g12 cells. The significant increase in DNA migration and comet frequency has appeared in the cells isolated from the spleen, thymus, and peritoneal macrophages of mice after injecting i.p. SNP in the dosage range of 0.67-6.0 mg/kg b.wt for 1 h. However, no obvious increase in DNA strand breaks was observed in the cells isolated from the liver, kidney, lung, brain and heart obtained from the same treated mice. These results suggested that DNA SSBs could be induced by NO in some cells both in vivo and in vitro. There were organ differences in sensitivity in the mice exposed to NO. Spleen, thymus, and macrophages might be the important targets of NO.


Abstract: An 81-year-old man with cervical spondylotic myelopathy developed an acute frontal lobe like syndrome with prominent preservation and an abnormal
electroencephalogram after being given seven doses (70 mg) of baclofen for spasticity. The clinical symptoms cleared up in 72 hours after the medication was discontinued.

Abstract: Adductor spasmodic dysphonia (SD) is a speech disorder resulting from involuntary contractions of the laryngeal muscles. Botulinum toxin (BT) injection of the thyroarytenoid muscle is an effective, though temporary, treatment for most SD patients. Though there are reports of objective improvements in voice quality, there are no large studies of patients' subjective responses to treatment over time. In the present study, patients were given voice diaries to rate vocal spasms, hoarseness, breathiness, volume problems, and dysphagia before and the after treatment. Analysis of these diaries revealed that: (1) most side effects had resolved 4 to 6 weeks after injection, whereas vocal spasm relief persisted; (2) vocal spasm relief and severity of side effects peaked within 1 week; and (3) unilateral injections, though as effective in relieving vocal spasms, caused less volume and swallowing problems than did bilateral injections.


Abstract: The authors administered tiaprid (Tiapridal, Delagrange), to six patients with the dyskinetic form of cerebral palsy, mean dose 11.4 mg/kg/day in three portions. In five instances clinical improvement was recorded, all patients improved as regards tests of practical skills. On the EEG during tiaprid treatment reduction of muscular artefacts was recorded. By means of an original testing device the authors revealed that tiaprid exerts a relatively small influence on the reaction time in response to a light stimulus but that it prolongs significantly the time needed for the motor performance proper. More marked undesirable effects were manifested in one patient (subjectively reported short-term change of sensitivity of the lower extremities and increased amplitude of dyskinesias). The authors emphasize the positive properties of the preparation and recommend tiaprid as the drug of first choice for pharmacological inhibition of extrapyramidal hyperkinesias in patients with the dyskinetic form of cerebral palsy in children.

Abstract: A syndrome of rigidity, bradykinesia, spasticity, and often myoclonus and dementia developed acutely in 5 patients who had undergone successful engraftment of bone marrow transplants for the treatment of various hematologic diseases. Magnetic resonance imaging demonstrated widespread changes in white matter; brain biopsy disclosed mild demyelination associated with active phagocytosis of myelin. One patient, who was not treated, remains severely demented. Patients treated with very high-dose methylprednisolone had complete clinical recovery.

Abstract: Idiopathic cerebral calcification can be associated with a progressive neurologic disorder for which there is no known treatment. This report describes a patient with a familial form of this disorder presenting in middle age with progressive Parkinson-like features along with spasticity, dystonia, and ataxia. Disodium etidronate, a bisphosphonate, produced a two-fold improvement in the rate of his speech and gait, but did not affect his spasticity, dystonia, or ataxia. Quantitative analysis of cerebral calcification did not reveal any reduction in the amount of calcification, suggesting other possible mechanisms for this clinical improvement.

Abstract: The aim of the present study was to find out whether haloperidol-induced rigidity was similar to that seen in parkinsonism. Simultaneous measurements of the muscle resistance (mechanomyogram, MMG) of the hind foot to passive flexion and extension in the ankle joint, as well as determination of the electromyographic (EMG) activity of the gastrocnemius and tibialis anterior muscles of rats were carried out. Haloperidol was injected in doses of 0.5-10 mg/kg 1 h before the start of measurements. Haloperidol increased, in a dose-dependent manner, the muscle resistance of the rat's hind leg to passive movements. Muscle rigidity was accompanied with an increase resting, as well as in the stretch-induced long-latency EMG activity (in which supraspinal reflexes are most probably involved) in both those muscles, whereas the short-latency EMG activity (first large bursts of EMG activity, beginning ca. 9 ms after the start of a movement, probably of a spinal origin) was significantly decreased. The obtained results suggest that the haloperidol-increased MMG/EMG activity might be a good model of parkinsonian rigidity.

Abstract: Benzodiazepines are known to reduce increased muscle stretch reflexes. To investigate the relationship between the necessary plasma
concentrations of diazepam and its major metabolite desmethyldiazepam on the one hand and the phasic and tonic ankle reflex activity on the other, 10 mg diazepam was given intravenously to nine patients, seven with spasticity due to multiple sclerosis and two with parkinsonian rigidity. Diazepam and desmethyldiazepam both had a normalizing effect on the increased phasic ankle reflex seen in spasticity. No effect was observed on the increased tonic reflexes in rigidity. The concentrations of diazepam necessary to reduce spasticity ranged between 300-2,200 mg/l and were so high that drowsiness did occur. However, the study may indicate that desmethyldiazepam has a higher potency and a more long lasting effect on the increased phasic reflexes than diazepam.


Abstract: The effects of intrathecal baclofen infusion were studied in 9 spinal cord injury patients whose spasticity had been refractory to oral medications. In a two stage, placebo controlled trial, baclofen was administered into the lumbar intrathecal space and subsequent clinical and neurophysiologic changes were assessed. In stage 1, 9 patients underwent a 5 day percutaneous infusion of baclofen and placebo via an external pump. Ashworth and reflex scores were assessed at time of enrollment, after infusion of that amount of baclofen which provided optimal spasticity control and after intrathecal infusion of placebo. The mean Ashworth grade decreased from 3.78 +/- 1.34 to 1.16 +/- 0.48 (p less than 0.001) while mean reflex score decreased from 3.57 +/- 1.05 to 0.64 +/- 0.87 (p less than 0.001). These values differed significantly from those associated with placebo therapy (Ashworth grade--2.54 +/- 1.04, p less than 0.001; reflex score--2.56 +/- 1.04, p less than 0.01). Objective improvements in functional abilities and independence were noted in 8 patients, while somatosensory and brainstem auditory evoked potentials were unchanged in all patients. Urodynamic evaluation revealed increased bladder capacity in 3 patients, while in 4 no change was observed. In Stage 2, permanent programmable infusion pumps were implanted in 7 patients who demonstrated a good response during Stage 1. In this group, mean Ashworth score decreased from 3.79 +/- 0.69 to 2 +/- 0.96 (p less than 0.001) and mean reflex score decreased from 3.85 +/- 0.62 to 2.18 +/- 0.43 (p less than 0.001). Baclofen dosage increased from 182 +/- 135 to 528 +/- 266 mcg/day over the 3-22 month follow-up period. Most of the dosage increase occurred within the initial 12 months following infusion pump implantation and tended to plateau thereafter. Minor complications such as catheter dislodgement/kinking and nausea occurred infrequently while no device related
infections were observed. There was no clinical evidence of any significant baclofen neurotoxicity either in Stage 1 or 2. The only ambulatory patient developed marked lower extremity weakness during Stage 1 intrathecal baclofen infusion and was temporarily unable to walk. We conclude that continuous administration of intrathecal baclofen is an effective and safe modality for spasticity control in patients who are refractory to oral medications.


Abstract: A 45-year-old man with transverse myelitis developed an unstable neuropathic spinal arthropathy manifesting as a "silent" L1-L2 dislocation after laminectomy and rhizotomies performed for increased spasticity. Treatment consisted of reduction, posterolateral spinal fusion with Cotrel-Dubousset instrumentation utilizing hooks and pedicular screws, and a posterior lumbar interbody fusion. The authors conclude that laminectomy on a chronic paralytic through the insensate area should be coupled with fusion and instrumentation even if the facet joints and capsules are preserved during the laminectomy.


Abstract: Posterior cervical wiring is commonly performed for patients with spinal instability, but has inherent risks. We report eight patients who had neurological deterioration after sublaminar or spinous process wiring of the cervical spine; four had complete injuries of the spinal cord, one had residual leg spasticity and three recovered after transient injuries. We found no relation between the degree of spinal canal encroachment and the severity of the spinal-cord injury, but in all cases neurological worsening appeared to have been caused by either sublaminar wiring or spinous process wiring which had been placed too far anteriorly. Sublaminar wiring has substantial risks and should be used only at atlantoaxial level, and then only after adequate reduction. Fluoroscopic guidance should be used when placing spinous process wires especially when the posterior spinal anatomy is abnormal.


Abstract: Tonsillectomy is accompanied by 7 to 14 days of pain. We entered 36 patients into a double blind placebo controlled study with dantrolene sodium,
lioresal to evaluate modification of tonsillectomy pain and analgesic requirements after tonsillectomy. Patients were randomly assigned either dantrolene or lioresal or placebo orally four times a day for 5 days postoperatively. On a standardized questionnaire the patients recorded pain, activity level, analgesic requirements and side effects. We conclude that there is no significant differences in subjective pain or analgesic requirements between 3 groups. The muscle spasm is not the only factor of tonsillectomy pain. There is the association of other factors: nerve endings, individual sensitivity, local products of inflammation. In conclusion to control tonsillectomy pain we must use drugs with different action

Abstract: The authors report three cases of poisoning with organic phosphate compounds in children. The first case presented a complex of late signs in the form of toxic polyneuropathy, and two had an acute course. The observation confirmed the view that an at least 7-day hospital stay and 4-week follow-up are necessary in view of great fluctuations in the level of cholinesterase which is often not correlated with the clinical status

Abstract: Baclofen was given intrathecally to six patients with severe lower limb spasticity due to traumatic spinal cord injury. The effects of the drug on spasticity and the ratio between the maximum amplitude of the H reflex and the M response from the soleus (Hmax/Mmax ratio) were assessed. In each patient, spasticity was reduced following intrathecal baclofen and in four patients there was a reduction in the amplitude of the H reflex and Hmax/Mmax ratio. These results suggest that the Hmax/Mmax ratio may be helpful in establishing optimum drug dosage, particularly when the drug is used on a chronic basis


Abstract: Botulinum toxin is the most potent neurotoxin known, and has been in
clinical use since the late 1970s. The toxin inhibits the release of acetylcholine from nerve terminals by inhibiting transport of the synaptic vesicles, thus causing functional denervation lasting up to 6 months. Our understanding of the mechanism of action of the toxin and the spectrum of diseases treatable with this agent continues to increase. Efficacy has been demonstrated in hemifacial spasm, dystonia, spasticity, hyperhidrosis and other conditions. Alternative serotypes are used in some centres, generally after the development of immunoresistance to the standard toxin (serotype A), and are likely to be in routine use in the near future. This paper reviews the history, pharmacology and current uses of botulinum toxin.

Abstract: OBJECTIVE: To report a case of pleural effusion associated with chronic dantrolene administration. DESIGN: Case report. SETTING: Private, university-affiliated, teaching hospital. RESULTS: Twelve years after the initiation of low-dose dantrolene therapy for chronic spasticity, a 35-year-old man developed a pleural effusion with pleural and peripheral eosinophilia. This reaction gradually resolved over several months after discontinuation of the dantrolene therapy. CONCLUSIONS: In patients treated with chronic dantrolene therapy, the presence of pleural effusions should raise the suspicion of dantrolene-induced disease. Withdrawal of dantrolene therapy has generally been associated with an alleviation of signs and symptoms within several months.

Abstract: In spastic patients the alpha-adrenergic blocking drug thymoxamine (Opilon Forte) was found capable of depressing most proprioceptive reflex parameters within 1 min after intravenous administration. The action seems to be of CNS origin, probably exerted as a depression of spindle stretch sensitivity through descending alpha-adrenergic bulbospinal pathways, but an additional action on the mechanism of presynaptic inhibition is likely. With oral administration, the drug is also capable of depressing distressing clonus, and it is concluded that it deserves further testing as a spasmolytic.

Abstract: The mode of action of dantrolene sodium was studied in 11 multiple sclerosis patients with spastic paresis of the legs by measurements of changes in electromyographic and mechanomyographic proprioceptive reflex responses and in voluntary power. Dantrolene sodium 0.5 mg per kg body weight given intravenously clearly reduced monosynaptic reflex twitch tension, but voluntary power only moderately so. The electromyographic reflex responses were unchanged or slightly increased. The mode of action of the drug on spindle function is discussed on the basis of the present findings and the literature. It is
concluded that dantrolene sodium does not reduce spindle stretch sensitivity, but probably reduces activity in group II and tonic 1a afferent fibers


Abstract: Three patients with cerebral palsy are described suffering, respectively, of pes equinus, spasm of the m. teres major and flexion spasm of the hand, who were treated with botulinum toxin A. These patients demonstrate not only the local reduction of the muscular hyperactivity following treatment with botulinum toxin A but also the potential functional benefit resulting from such a treatment. Thus, local intramuscular injection of botulinum toxin A in children with cerebral palsy should be considered as part of a multidisciplinary treatment concept, since reduction of the disability and the functional improvements could have high impact on daily living activities.


Abstract: Intramuscular injection of botulinum neurotoxin A is a relatively new method for treating spastic movement disorders in children. One major goal of any therapy for patients with movement disorders is to improve gross motor function. In this study, 18 patients with adductor spasm were treated with botulinum neurotoxin A. Treatment effect was determined with the Gross Motor Function Measure, a standardized, validated instrument designed to assist in assessment of gross motor function. Spastic muscle hyperactivity and joint mobility were evaluated by the modified Ashworth Scale and by range of motion, respectively. Compared to pretreatment values, significant improvement in gross motor function (P < .010), decrease in the modified Ashworth Scale, and increase in the range of motion (P < .010) were achieved. Patients with moderate impairment of gross motor function (classed at level III and level IV in the Gross Motor Function Classification System) benefited most from treatment. In patients with severe handicap (level V), only one of five treated patients showed improvement in gross motor function. Nevertheless, all patients in this subgroup benefited from improved ease in hygienic care. In conclusion, we have demonstrated that for most children with moderate functional impairment, the Gross Motor Function Measure is a useful instrument for objective
documentation of improvements of gross motor function following treatment with botulinum neurotoxin A

Abstract: Hair samples of 20 spastic children and 29 normal children were collected and measured, using neutron activation analysis and X-ray fluorescence techniques, for the concentrations of Al, Sb, As, Ca, Cu, I, Fe, Pb, Mg, Mn, Hg, K, Sr, S, V and Zn. Both groups of children were of ages between 5 and 13. The washing method of using detergent and powder was found to be comparable to that of using ether. Difference in the mean concentration of each element in the two groups was tested by the Student's t-test and the Wilcoxon rank-sums test. Hair concentrations of Al, Sb, Pb, Mn, K, Sr, and V in the 'spasm group' were found to be significantly (P < 0.05) higher than those in the 'normal group'. Attempt was made to interpret the effects of these elements on the nervous and muscular systems of the spastic children

Abstract: Rapid baclofen withdrawal is known to cause markedly increased spasticity, but high fever associated with this complication has not been reported. We describe a 13-year-old boy with sensory incomplete C1 quadriplegia two years after injury who was on 200mg of baclofen per day for spasticity. Concerns about adverse side effects prompted tapering of his baclofen. Severely increased spasticity was noted with associated hyperthermia to 107 degrees F after the dosage was gradually decreased. Sepsis work-up was negative, head computed tomography scan was unchanged, and electroencephalogram showed no epileptiform activity. Cooling blankets, intravenous diazepam, and return of baclofen to 160mg per day decreased spasticity and normalized body temperature without recurrence of hyperthermia. Possible fever etiology is the hypermetabolic state associated with the acute return of spasticity


Abstract: Although many clinical studies suggest the medical utility of marijuana for some conditions, the scientific evidence is weak. Many patients in California are self-medicating with marijuana, and physicians need data to assess the risks and benefits. The only reasonable solution to this problem is to encourage research on the medical effects of marijuana. The current regulatory system should be modified to remove barriers to clinical research with marijuana. The
NIH panel has identified several conditions for which there may be therapeutic benefit from marijuana use and that merit further research. Marijuana should be held to the same evaluation standards of safety and efficacy as other drugs (a major flaw in Proposition 215) but should not have to be proved better than current medications for its use to be adopted. The therapeutic window for marijuana and THC between desired effect and unpleasant side effects is narrow and is a major reason for discontinuing use. Although the inhaled route of administration has the benefit of allowing patients to self-titrate the dose, the smoking of crude plant material is problematic. The NIH panel recommended that a high priority be given to the development of a controlled inhaled form of THC. The presence of a naturally occurring cannabinoid-receptor system in the brain suggests that research on selective analogues of THC may be useful to enhance its therapeutic effects and minimize adverse effects.


Marsala M., Vanicky I., and Yaksh T.L. (1994) Effect of graded hypothermia (27 degrees to 34 degrees C) on behavioral function, histopathology, and spinal blood flow after spinal ischemia in rat. Stroke 25, 2038-2046. Abstract: BACKGROUND AND PURPOSE: We used a rat model of reversible spinal ischemia to assess the effect of spinal cord temperature on the development of neurological and histopathologic changes after 20 minutes of reversible aortic occlusion. Spinal cord blood flow and CO2 reactivity was tested by using laser Doppler before and 60 minutes after ischemia. METHODS: In halothane (1%)-anesthetized rats, the spinal cord temperature as assessed by using thermocouple in the paraspinal muscles was lowered to 34 degrees, 31 degrees, or 27 degrees C. After ischemia, spinal cord temperature was raised to 37 degrees C for the next 30 minutes. Animals were maintained in this normothermic condition for 8 hours, after which motor and sensory function were assessed. All animals were then anesthetized and perfused with 10% formalin for light microscopic analysis of spinal cords. RESULTS: In normothermic animals, 20 minutes of ischemia resulted in a loss of CO2 reactivity and hind limb paraplegia with an attendant allodynia that persisted for the 8 hours of reperfusion. Even mild (34 degrees C) hypothermia resulted in significant improvement of neurological function compared with the normothermic group. In paraplegic animals, lumbosacral interneuronal pools localized primarily in laminae III through VII displayed heavy argyrophilic neurons and areas of localized necrosis. In moderate and deep hypothermic animals preservation of CO2 responsivity and complete recovery of neurological function were seen with no detectable histopathologic changes. CONCLUSIONS: These results show that a slight decrease in spinal cord temperature in the peri-ischemic period provides significant protection as measured by histopathology and neurological function.


Abstract: The efficiency and duration of action of a single oral dose (8 mg) of tizanidine in patients with spinal cord injuries were determined by studying its antispastic, cardiovascular and sedative effects along with its pharmacokinetic profile in five tetraplegic and five paraplegic patients. After the administration of tizanidine, there was a reduction in spasticity in both groups within half an hour, with the effects lasting for 3 to 4 hours. There was no rebound increase in blood pressure. There was a greater increase in sedation in the tetraplegics than in the paraplegics. Plasma tizanidine levels rose within half an hour after dosing and peaked at one hour. The levels had fallen to 15 percent by 6 hours. The plasma half-life was 2.7 +/- 0.06 hours. We conclude that oral tizanidine has antispastic effects in patients with spinal cord injuries without affecting the power of non-involved muscle groups. It has minimal effects on blood pressure and it lowers heart rate. Side effects include sedation and dryness of mouth


Abstract: We report a patient who had generalized painful muscle cramps associated with isolated ACTH deficiency. A 68-year-old woman was hospitalized because of painful muscle cramps present for one year. Neurological examination revealed no abnormalities except for generalized painful muscle cramps. Serum electrolyte and CPK levels were normal. Serum ACTH and cortisol levels as well as urine 17-OHCS were low. An ACTH loading test employing insulin, TRH and LH-RH indicated isolated ACTH deficiency. Just after the muscle cramp, EMG revealed a low amplitude in the biceps muscle. Colon biopsy showed mild fibrosis and inflammatory cell infiltration in the lamina propria. Her muscle cramps improved markedly after two weeks of hydrocortisone replacement therapy and resolved after three weeks, suggesting that this symptom was closely related to isolated ACTH deficiency. Our case suggests that isolated ACTH deficiency may present with very similar clinical symptoms to Satoyoshi disease


Abstract: A double-blind study was performed comparing 5 mg delta-9-tetrahydrocannabinol (THC) p.o., 50 mg codeine p.o., and placebo in a patient with spasticity and pain due to spinal cord injury. The three conditions were applied 18 times each in a randomized and balanced order. Delta-9-THC and codeine both had an analgesic effect in comparison with placebo. Only delta-9-THC showed a significant beneficial effect on spasticity. In the dosage of THC used no altered consciousness occurred.


Abstract: The centrally active, alpha-2 adrenergic receptor agonist clonidine was given to 12 spinal cord injury patients with problematic spasticity not adequately controlled by recognized spasmyolytic drug therapy. Five patients had an excellent reduction and 2 patients had some reduction in clinical spasticity (average dose 0.39 mg daily). Four of the 7 responders discontinued clonidine because of adverse reactions after an average of ten weeks of therapy. Three responders have continued to tolerate the drug well with excellent control of spasticity for 18 to 34 months. Five patients had no change in clinical spasticity (average dose of 0.24 mg daily). Three of the non-responders discontinued clonidine because of adverse reactions after an average of three weeks of therapy. Significant associated adverse reactions included syncopal seizures (3), cerebrovascular accident (1), deep vein thrombosis (1), autonomic hyperreflexia (3), lethargy/drowsiness (3), and nausea/vomiting (1). Possible mechanisms of action for clonidine to affect spasticity and the unstable cardiovascular system of quadriplegics is discussed. While spinal cord injured patients with severe spasticity may benefit from clonidine, great caution is recommended during its use until further study establishes safe parameters of administration and efficacy is confirmed on controlled studies.


Abstract: Changes in the excitability of the soleus H-reflex were studied after oral administration of L-acetylcarnitine, a cholinomimetic substance, in eight healthy control subjects and 23 spastic patients presenting with slowly progressive paraparesis (n = 10), a cord lesion (n = 9) and a cerebral lesion (n = 4). Changes in the amount of recurrent inhibition of soleus motor neurons at rest were also estimated in order to assess the level of activity of Renshaw cells before and after L-acetylcarnitine administration. Recurrent inhibition elicited by a conditioning reflex discharge (H1) was assessed by a subsequent test reflex (H'). Four patients lacked an H' reflex. In approximately 50% of the remaining patients, recurrent inhibition was normal, while in the other half there was evidence of reduced or absent inhibitory activity at rest. Pooling the data relative to the effect of L-acetylcarnitine on the H-reflex in relation to the strength of recurrent inhibition disclosed that the ratio of peak-to-peak amplitude values of the maximum H reflex to maximum M wave responses (Hmax:Mmax) was reduced in all the cases in which the recurrent inhibition at rest was normal, while such a reduction was never observed in the patients in whom recurrent inhibition was found to be decreased at rest. In the former cases, the size of the H' reflex evoked by the same conditioning H1 discharge was further depressed after L-acetylcarnitine, pointing to a potentiating effect of the drug on Renshaw cells; in the latter cases no such effect was seen. A significant decrease in the mean Hmax:Mmax ratio after L-acetylcarnitine intake was also seen in the healthy control subjects. Possible changes in the amount of presynaptic inhibition on Ia terminals on soleus motor neurons after L-acetylcarnitine were ruled out. It is proposed that the differential effect of the drug on the H-reflex excitability is directly related to the level of Renshaw cell activity, a reduction of which probably follows a lesion interrupting reticulo-spinal pathways with tonic facilitatory influences on Renshaw cells. These findings support the hypothesis that Renshaw cell excitability is set via cortico-reticulo-spiral systems.


Abstract: The high-affinity uptake of [3H]serotonin, [3H]glutamate, and [3H]gamma-aminobutyric acid ([3H]GABA) and the Na+-independent binding of [3H]glutamate and [3H]GABA were studied using spinal cord preparations obtained from normal mongrel dogs and from dogs made paraplegic by midthoracic spinal cord crush. Lumbosacral regions of the spinal cord were removed either before (1 week) or after (3 to 8 weeks) onset of spasticity. A myelin-free synaptosomal fraction was obtained by centrifugation and used for studying high-affinity uptake and for preparing synaptic plasma membranes for Na+-independent binding experiments. For the paraplegic groups, the uptake of 30 nM [3H]serotonin was 66 and 18% of control values after 1 and 3 weeks, respectively. Eadie-Hofstee analysis of [3H]serotonin uptake showed a 90%
reduction in Vmax for the paraplegic group relative to control values, thereby indicating the expected loss of descending serotonergic pathways. The high-affinity uptakes of 1 microM [3H]glutamate and [3H]GABA were the same in both the control and nonspastic paraplegic groups after 1 week. However, after 3 weeks, the uptakes of [3H]glutamate and [3H]GABA were 60-70% higher for the spastic group than for the control animals. For both amino acids, Eadie-Hofstee plots revealed no difference in Km and higher Vmax for the spastic group relative to control values. After 1 and 3 weeks, the Na+-independent binding of 5 nM [3H]glutamate was 40-85% higher and the binding of 10 nM [3H]GABA was 40-60% lower for the paraplegic groups relative to the values for the control animals. (ABSTRACT TRUNCATED AT 250 WORDS)

Abstract: A 19 year old male with phenylketonuria (PKU) developed a spastic paresis 8 months after stopping his restricted phenylalanine diet. CT and MRI showed abnormalities of the deep cerebral white matter, and visual evoked response latencies were prolonged. The spasticity gradually improved over several months after resuming the PKU diet. A repeat MRI scan was unchanged. His brother also had PKU and ceased dietary restrictions, but his only neurological abnormality was a slight increase in the deep tendon reflexes of the lower limbs. CT and MRI of his brain was normal. DNA analysis showed that both brothers were homozygous for the same PKU mutation. These patients demonstrate that reversible neurological signs may develop in patients with classic PKU after ceasing dietary restrictions and that these may be associated with abnormalities seen on neuro-imaging.

Abstract: During emergence from anaesthesia, transient neurological signs that would usually be considered pathological may appear. The objective of this randomized, patient (n = 30) and observer-blinded study was to compare prospectively the incidence and duration of post-anaesthetic neurological abnormalities in healthy patients undergoing minor elective procedures following thiopentone and succinylcholine induction, and enflurane-N2O or isoflurane-N2O anaesthesia. Patients were studied for 60 min after anaesthesia. Arousal state, muscle tone, deep tendon reflexes, plantar reflex, sustained clonus, shivering, intense muscular spasticity and temperature were assessed. Results of neurological examination were correlated with the patient's state of arousal. Transient emergent neurological abnormalities occurred more frequently following enflurane-N2O anaesthesia than isoflurane N2O anaesthesia. This was statistically significant (P less than 0.05) for quadriceps hyperreflexia, upgoing toes (positive Babinski reflex) and intense muscular spasticity. Neurological abnormalities occurred most commonly 5-20 min after anaesthesia and all abnormalities resolved within 60 min. Following enflurane anaesthesia, as
patients became more alert the incidence of abnormalities declined, while the arousal state did not affect the incidence of abnormalities after isoflurane. There was no significant difference between axillary temperatures of those patients who shivered and those who did not. In conclusion, temporary emergent neurological abnormalities occurred more often following enflurane-N2O than after isoflurane-N2O anaesthesia.

Abstract: Control of severe spasticity and its associated features with administration of baclofen directly into the CSF via an intrathecal pump has radically improved the management of patients resistant to oral therapy. This article reviews the rationale and clinical indications for this technique, and the outcome and complications encountered.


Abstract: Dogs, surgically implanted with a chronic gastric fistula, were chronically dosed with N-desmethyldiazepam (32 mg/kg/day) in four divided doses to attain N-desmethyldiazepam plasma levels comparable to those observed in dogs dependent on diazepam (60 mg/kg/day). The time course of N-desmethyldiazepam abstinence was studied, beginning not less than 2 weeks after stabilization levels had been achieved. The abstinence syndrome observed after abrupt discontinuation of N-desmethyldiazepam was similar to the diazepam abstinence syndrome but differed in several important aspects. In diazepam-dependent dogs, there was a short burst of tremor very early in withdrawal (approximately 1-2 hr after the last dose of diazepam) that was not seen in N-desmethyldiazepam-dependent dogs. Signs of abstinence such as tremor, hot foot walking and twitches and jerks were more frequently observed in N-desmethyldiazepam-dependent dogs than in diazepam-dependent dogs as were decreases in food and water intake and in body weight. The overall intensity of abstinence, as measured by the Diazepam Withdrawal Abstinence Scale, was greater in N-desmethyldiazepam-dependent dogs than in dogs dependent on either lorazepam or diazepam. Plasma levels of N-desmethyldiazepam and oxazepam were nearly equal in dogs dependent on diazepam or on N-desmethyldiazepam and were 4 to 10 times greater than the plasma levels of diazepam or lorazepam in diazepam- or lorazepam-dependent dogs, respectively. Furthermore, the plasma levels of N-desmethyldiazepam and oxazepam declined much more slowly than the levels of diazepam and lorazepam. These results suggest that physical dependence on diazepam is caused by the accumulation and actions of N-desmethyldiazepam. (ABSTRACT TRUNCATED AT 250 WORDS)

Abstract: Spasticity following upper motor neuron lesion can be alleviated by few treatments such as physiotherapy, drugs and neurosurgery. However, they all have side effects, limitations or lack of selectivity. We tentatively used the paralyzing effects of botulinum toxin. Since the late 1970's the use of this toxin has increased and it has been extended to numerous muscles and diseases of various causes. In this pilot and open study we use botulinum toxin in spasticity. Eight patients (7 stroke, 1 head injury) with longstanding severe spasticity (minimum: 12 months, maximum: 15 years) were included. Spasticity greatly interfered with their activity in daily life and was resistant to oral antispastic medications. Six patients suffered from pain and 4 had cutaneous lesions especially maceration of the palm of the hand. A- botulinum toxin was injected with a 30-gauged needle. The sites chosen for injection were the following muscles: biceps brachii, brachioradialis, flexor digitorum, flexor carpi, tibialis anterior, flexor digitorum longus. Altogether 41 injections were performed. There were no side effects. Spasticity was improved in all patients. Five patients reported significant pain relief on a visual analogical scale. Most of them reported a benefit in their limb tone and referred to subjective improvement in the activity of daily life and nursing. The beneficial effects of one injection lasted more than 5 months. Seven patients received a second course of treatment. A double-blind study of botulinum toxin in spasticity is to be undertaken to assess its effectiveness and safety when prescribed in the required dose to treat this condition


Abstract: Seventeen patients with severe disabling spinal spasticity were selected and treated by chronic intrathecal baclofen infusion using an implanted programmable pump. Nine patients were tetraparetic, seven were paraplegic and one paraparetic. Patients were regularly followed for 5 to 69 months (mean 37.5 months). The clinical efficacy of baclofen was estimated by means of evaluation of: hypertonia, spasms, pain and functional disability. All patients experienced significant amelioration of quality of life secondary to reduction of hypertonia, spasms and pain related to contractures. Neurogenic pain improved in 3 cases and remained unchanged in 3 others. In patients whose motor functions were partially preserved, various degrees of motor improvement were detected. Electrophysiological recordings of Polysynaptic flexion reflexes (FR) were obtained to control conditions, and under intrathecal baclofen, in order to quantify the spinal excitability responsible for spontaneous or induced spasms. Flexion reflex threshold was increased and amplitude proved to be very significantly
reduced by chronic baclofen infusion in all our patients. Twelve patients with neurogenic bladder dysfunction were also evaluated by a clinically oriented questionnaire and by quantitative urodynamic recordings, before and after pump implantation. In patients with normal micturition, this was not changed by intrathecal baclofen. In patients with spastic bladder, intrathecal baclofen produced a decrease of detrusor hypertonia and hyperactivity in 50% of cases, with reduction of leakage and increase in functional bladder capacity.


Abstract: Dantrolene sodium is a muscle relaxant used in the treatment of spasticity. It has been shown to interfere with calcium release from the sarcoplasmic reticulum and thus to inhibit excitation-contraction coupling. The effect of dantrolene sodium on the twitch tension of the tibialis anterior muscle of the rat was measured after 2 mg/kg i.v. or 25 mg/kg orally. Plasma concentrations were estimated at maximum twitch depression and during recovery from the block. In a separate series of experiments the half-life of labelled dantrolene sodium was measured in blood plasma, skeletal muscle and heart muscle of rats. Dantrolene sodium 2 mg/kg i.v. gave a maximal block of approximately 47%, the mean dantrolene sodium concentration was then 5.8 microgram/ml. A half-life for distribution of 1.1 min and an elimination half-life of 31 min after intravenous administration were observed, elimination rate constants in skeletal and heart muscle were comparable. Recovery from the block went much slower, the half-time of the process being approximately 80 min. Dantrolene sodium 25 mg/kg orally gave a maximal block of approximately 38% at a mean plasma concentration of 3.6 microgram/ml after 14 min. The recovery was again very slow. These experiments demonstrated that dantrolene sodium acts according to a two-compartment pharmacokinetic model. There was a discrepancy between duration of effect and plasma concentration of dantrolene sodium in the rat. This suggests that the receptor for dantrolene sodium is not located in the central compartment.


Abstract: Dantrolene sodium is a muscle relaxant, which is used in the treatment of spasticity. Although it is given chronically, little is known about its pharmacokinetic behaviour. The relationship between the effect of a single oral dose of dantrolene sodium and its plasma concentration in healthy volunteers.
was studied by measuring the effect on the twitch tension, and in spastic patients on the decrease in muscle hypertonia. On the twitch tension dantrolene gave a depression of 49.1 +/- 9.4% (+/- DS) within 1.15 and 3.45 h after ingestion of 100 mg. The mean maximal plasma concentration was 1.24 +/- 0.32 microgram/ml (+/- SD). The effect and the plasma concentration were correlated. No relationship between the plasma concentration of dantrolene sodium and its effect could be established in patients, although definite activity in 6 out of 7 patients was observed after a single oral dose of 100 mg, and plasma concentration of dantrolene sodium greater than 0.3 microgram/ml were consistently associated with better results than placebo treatment in 6 out of 7 patients.

Abstract: Continuous intrathecal infusion of the well known antispastic medication baclofen was evaluated in ten consecutive patients. One year after pump implantation the average Ashworth scale for muscle tone decreased, compared with before treatment, 2.32 points (P < 0.0001), reflexes decreased 2.22 points (P < 0.0001) and the spasm score decreased 1.65 points (P < 0.0001). The average dose increased from 92.22 to 290.95 micrograms (P < 0.0001) between the 1st month of treatment and 1 yr of treatment. The dosage for all patients more than doubled (P < 0.0022) between 3 months and 1 yr postimplantation. There was no significant difference for muscle tone, reflexes or spasms at 3 months v 1 yr. Complications were not unusual and included temporary atelectasis, orthostatic hypotension with escalation of baclofen dose, loss of penile erections, postsurgical pseudo-meningocele, catheter disruptions and exhausted pump reservoirs. One patient suffered a seizure apparently related to a rapid withdrawal from intrathecal baclofen as a result of catheter sequestration. All patients required a period of intensive inpatient rehabilitation to benefit functionally from the decreased motor tone and/or increased voluntary motor control. The procedure is expensive and close follow-up is necessary for assessing efficacy and refilling the pump. Intrathecal baclofen infusion by subcutaneous pump is useful in treating the effects of spinal spasticity resistant to oral medications. However, there appears to be accommodation to intrathecal baclofen necessitating escalating doses to maintain clinical effects.

Abstract: Intrathecal baclofen has not been previously evaluated for the treatment of the disabling hypertonia associated with hereditary spastic paraparesis. Muscle tone and deep-tendon reflexes were evaluated in three patients with hereditary spastic paraparesis after a double-blind, cross-over bolus injection of intrathecal baclofen. Patients underwent placement of a subcutaneous pump for continuous infusion of intrathecal baclofen. Three
months after implantation the muscle tone decreased 2.04 points (p less than .0001) and the reflex score decreased 2.25 points (p less than .001). Patients initially reported subjective weakness, but muscle testing revealed either an increase or no change in voluntary motor function. Baclofen doses of 60 to 264 micrograms per day were required for effective control of muscle tone and spasticity. Much of the disability in familial spastic paraparesis may be related to the loss of suprasegmental inhibition of spinal reflexes overwhelming the residual voluntary motor function.

Abstract: Twelve consecutive patients with severe spasticity and hypertonia following acquired brain injury were treated with continuous intrathecal infusion of baclofen via an implanted, programmable infusion pump-catheter system for a minimum of 3 months. In every case intrathecal baclofen therapy resulted in a statistically significant reduction in upper- and lower-extremity tone, spasm frequency, and reflexes, contributing to improved functional abilities. There were no untoward side effects or complications associated with treatment. This preliminary assessment indicates that intrathecal administration of baclofen is effective in treating the disabling spasticity caused by acquired brain injury in selected patients.

Abstract: The objective of this study was to determine whether the continuous intrathecal delivery of baclofen will control spastic hypertonia associated with long-standing hemiplegia from acquired brain injury. Six hemiparetic patients (average age, 50 (range, 42-66) yr) with more than 6 mo of disabling lower limb spastic hypertonia on one side caused by either a unilateral traumatic brain injury or a stroke were recruited in a consecutive manner. The setting was a tertiary care outpatient and inpatient rehabilitation center directly attached to a university hospital. Patients were screened via a randomized, double-blind, placebo-controlled, crossover design to receive either an intrathecally administered bolus injection of normal saline or 50 microg of baclofen. Data for Ashworth rigidity scores, spasm scores, and deep tendon reflex scores were collected on the affected upper limb and lower limb side. Those who dropped an average of two points on their affected lower limb Ashworth scores were then offered computer-controlled pump implantation for continuous intrathecal administration of baclofen. Differences over time were assessed via descriptive statistics and Wilcoxon's signed-rank test. After 3 mo of treatment, the average lower limb Ashworth score on the affected side decreased from 3.7 +/- 1.0 to 1.9 +/- 0.6 standard deviation (SD) (P < 0.0001), the reflex score from 1.8 +/- 1.3 to 0.5 +/- 0.8 SD (P = 0.0208), and the spasm score from 1.3 +/- 1.2 to 0.8 +/- 1.3 SD (P > 0.05). The average upper limb Ashworth score on the affected side decreased
from 3.4 +/- 0.9 to 2.1 +/- 0.9 SD (P = 0.0002), the reflex score from 2.3 +/- 0.5 to 1.7 +/- 0.5 SD (P > 0.050, and the spasm score from 0.8 +/- 1.3 to 0 +/- 0 SD (P > 0.05). The average intrathecally administered dose of baclofen that was required to attain these effects was 205.3 microg, which was continuously infused for 24 h. Continuous intrathecal infusion of baclofen is capable of maintaining a reduction in the dystonia on the hemiparetic side without significantly affecting motor strength on the normal side.


Abstract: OBJECTIVE: To determine if the long-term use of continuously infused intrathecal baclofen (ITB) over a 1-year period will control spastic- dystonic hypertonia in patients with traumatic brain injury (TBI). SETTING: Tertiary care outpatient and inpatient rehabilitation center directly attached to a university hospital. SUBJECTS: Persons with TBI and intractable spasticity and dystonia for more than 6 months' duration recruited in a consecutive manner. DESIGN: TBI patients were admitted to the study after screening via a bolus injection of either intrathecal normal saline or 50 microg of baclofen. Data for Ashworth rigidity scores, spasm scores, and deep tendon reflex scores were collected for both the upper extremities (UE) and lower extremities (LE). Patients whose LE Ashworth scores decreased an average of 2 points were then offered implantation of a computer-controlled pump for continuous ITB. Changes over time were assessed statistically via Friedman’s analysis for ordinal data and ANOVA for linear data. Differences between set points in time were also assessed via Wilcoxon signed rank. DATA SET: Seventeen patients (average age 29+/-11 yrs) with spasticity and/or dystonia treated over 1 year via a computer-controllable intrathecal delivery system for the delivery of ITB. RESULTS: After 1 year of continuous ITB treatment the average LE Ashworth score decreased from 3.5+/-.13 (SD) to 1.7+/-.09 (p < .0001), spasm score from 1.8+/-.13 to 0.2+/-.05 (p< .0001), and reflex score from 2.5+/-.1.1 to 0.1+/-.0.3 (p < .0001). The average UE Ashworth score decreased from 2.9+/-.1.5 to 1.6+/-.0.5 (p < .0001), spasm score from 1.2+/-.1.5 to 0.2+/-.0.6 (p < 0.0001), and reflex score from 2.2+/-.0.5 to 1.0+/-.0.8 (p < .0001). The average ITB dose required to attain these effects at 1 year was 302 microg continuously infused per day. CONCLUSION: Continuous intrathecal infusion of baclofen is capable of maintaining a reduction in spasticity and dystonia in both the upper and lower extremities of TBI patients.


Abstract: Muscle afferent block (MAB) is an intramuscular injection of 0.5% lidocaine and pure ethanol with a volume ratio of 10:1, introduced as an alternative to botulinum toxin injection for focal dystonia and spasticity. As in the case of botulinum toxin injection, the precise localization of target muscles is crucial to obtain the maximal effect from MAB. For this purpose, we performed
ultrasonography of cervical muscles (echomyography) in 20 patients with cervical dystonia (11 men, 9 women; mean age 46.1), with ultrasonograph SSD-5500 (Aloca Co. Ltd., Japan) and a 7.5 MHz linear probe. In untreated subjects, the boundaries of muscles could be easily identified, while they tended to become ambiguous after repeated MAB sessions. At rest, there were involuntary worm-like movements of a specific muscle group observed in all patients. Contrary to our expectation, in all but one patient abnormal contraction was limited only in a part of synergists responsible for the abnormal posture. In normal subjects there was no abnormal contraction at rest, and all the synergists were simultaneously activated by the voluntary neck deviation. Normal subjects could not mimic the pattern of muscle activity in dystonic patients. The echo-guided MAB was performed in 16 patients. We could easily observe the diffusion of lidocaine and ethanol into the targeted muscle, and injected portions of the muscle stopped their activities just after MAB. The effect persisted for 3-4 days in at least 5 out of 10 patients who had follow-up examination. On the other hand, the movement stopped only temporarily after the injection of saline or lidocaine only. In 3 out of 16 patients, some of the uninjected synergists were activated as if to substitute for the treated muscle just after the injection. We conclude that cervical echomyography is useful to investigate the pattern of muscle activity in cervical dystonia and to accurately localize the contracting muscles during MAB.


Abstract: OBJECTIVES: To compare clinical effectiveness and health related quality of life in patients with severe spasticity who received intrathecal baclofen or a placebo. METHODS: In a double blind, randomised, multicentre trial 22 patients were followed up during 13 weeks and subsequently included in a 52 week observational longitudinal study. Patients were those with chronic, disabling spasticity who did not respond to maximum doses of oral baclofen, dantrolene, and tizanidine. After implantation of a programmable pump patients were randomly assigned to placebo or baclofen infusion for 13 weeks. After 13 weeks all patients received baclofen. Clinical efficacy was assessed by the Ashworth scale, spasm score, and self reported pain, and health related quality of life by the sickness impact profile (SIP) and the Hopkins symptom checklist (HSCL). RESULTS: At three months the scores of the placebo and baclofen group differed slightly for the spasm score (effect size=0.20) and substantially for the Ashworth scale (effect size=1.40) and pain score (effect size=0.94); health related quality of life showed no significant differences. Three months after implantation the baclofen group showed a significant, substantial improvement on the SIP "physical health", "mental health", "mobility", and "sleep and rest" subscales and on the HSCL mental health scale; patients receiving placebo showed no change. After one year of baclofen treatment significant (P<0.05) improvement was found on the SIP dimensions "mobility" and "body care and movement" with moderate effect sizes. Improvement on the SIP subscale
"physical health" (P<0.05; effect size 0.86), the SIP overall score (without "ambulation"), and the "physical health" and overall scale of the HSCL was also significant, with effect sizes >0.80. Changes in health related behaviour were noted for "sleep and rest" and "recreation and pastimes" (P<0.01, P<0.05; effect size 0.95 and 0.63, respectively). Psychosocial behaviour showed no improvement.

CONCLUSIONS: Intrathecal baclofen delivered by an implanted, programmable pump resulted in improved self reported quality of life as assessed by the SIP, and HSCL physical health dimensions also suggest improvement.


Abstract: Spasticity and pain are common disabling sequelae following spinal cord injury (SCI) and are often difficult to manage. The two problems are also not infrequently related. A variety of pharmacological and other approaches have been described for management of these problems in SCI. This case study reports a 32-year-old woman with an established incomplete C5 tetraplegia (anterior cord syndrome) who developed severe, intractable anal spasm following a hemorrhoidectomy, which persisted despite very good healing. This prevented evacuation of her bowels and resulted in severe rectal pain and episodes of autonomic dysreflexia. Attempts to modify the rate and mode of delivery of intrathecal baclofen through an existing programmable infusion pump failed to reduce anal sphincter spasm or improve symptoms. A right-sided pudendal block with lignocaine provided some relief. Clonidine was added to baclofen in the pump reservoir and both drugs were administered intrathecally in combination. This resulted in an immediate improvement in anal sphincter spasm and pain relief, allowing rapid reestablishment of her normal bowel pattern without need for any supplemental analgesia. It appears that intrathecal clonidine may have an important role in the treatment of spasticity, either as a single or an adjuvant agent, when intrathecal baclofen alone is ineffective or there is increasing tolerance to baclofen. Intrathecal clonidine may also prove useful in the management of intractable neuropathic pain.


Abstract: Tizanidine, an imidazoline derivative with alpha 2-receptor-mediated central muscle relaxant activity, is in widespread clinical use for the treatment of spasticity. To evaluate its possible role in anesthesia we assessed the sedative and sympatholytic effects of orally administered tizanidine in a double-blind, placebo-controlled, randomized, cross-over study in six healthy male volunteers. Three different doses of tizanidine (4, 8, and 12 mg) were tested and compared to clonidine 150 micrograms. The sedative and sympatholytic effects of tizanidine 12 mg were comparable in magnitude to those of clonidine 150 micrograms, but
the effects of clonidine were longer lasting. Similarly, the observed decreases in arterial blood pressure (diastolic, 13% and 19%; systolic, 10% and 8% for tizanidine and clonidine, respectively) and salivation were comparable in magnitude but of shorter duration after tizanidine 12 mg than after clonidine. Clonidine and tizanidine 12 mg had also similar effects on the secretion of growth hormone. Our results indicate that the effects of a single 12-mg oral dose of tizanidine resemble those of 150 micrograms oral clonidine, but are of shorter duration. Tizanidine may thus be a useful alternative to clonidine as an orally active, short-acting alpha 2-adrenoceptor agonist in the perioperative period.

Abstract: This investigation assessed the mechanisms of Tetrazepam action on spasticity using a battery of electromyographic methods. Thirty patients with post-stroke spastic hemiparesis treated with Tetrazepam took part in the investigation. A questionnaire for assessment of subjective improvement after treatment used a 5-point scale. The 5-point scales were used to assess muscle tone, muscle strength and tendon reflexes. A battery of electromyographic methods was used to analyse different mechanisms of spasticity: for alpha-motoneuron activity—the F-wave parameters; for gamma-motoneuron activity—the TA/H amplitude ratio; for presynaptic inhibition—the ratio of H-reflex maximal amplitudes before and after vibration on the Achilles tendon (Hvibr/Hmax); for common interneuron activity—the flexor reflex parameters. Our results revealed that Tetrazepam reduces tone in spastic muscles and has a slight effect on tendon hyperreflexia. It has no influence on muscle strength, Babinski sign and ankle clonus. Tetrazepam acts by decreasing motoneurone activity and increasing presynaptic inhibition.

Abstract: This investigation estimated the mechanisms of tizanidine action on spasticity using a battery of neurophysiological methods. Thirty patients with old post-stroke spastic hemiparesis took part in the investigation. They were treated with tizanidine-mean daily dose 15.8 +/- 5.6 mg for a mean of 23.3 +/- 4.8 days. A questionnaire for assessment of subjective improvement after treatment used a 5-point scale. For standardization of the neurological examination 5-point scales were used to assess muscle tone, muscle force and tendon reflexes. A battery of neurophysiological methods was used to analyze different mechanisms of spasticity: for alpha motoneuron excitability—the F wave parameters; for presynaptic inhibition—the ratio of H reflex amplitudes before and after vibration of the achilles tendon (Hvibr/Hmax); for common interneuron activity—the flexor reflex parameters. Our results revealed that tizanidine reduces spastically increased muscle tone, but has no influence on muscle force, tendon reflexes, Babinski sign and ankle clonus. Tizanidine is supposed to act by increasing the presynaptic inhibition and decreasing of alpha motoneuron excitability. When
spasticity has decreased presynaptic inhibition and increased motoneuron excitability, it is better to treat with tizanidine

Abstract: The purpose of this investigation was to evaluate the alterations of flexor reflex parameters in spasticity and the possibilities to take advantage of them as a method for assessment of common interneurone activity. Clinical and electromyographical examinations were performed on 120 patients with spastic hemiparesis after stroke. The flexor reflex was obtained after supramaximal electrostimulation of the tibial nerve behind the ankle. The stimulus consisted of 50 msec train of 1 msec duration pulses given at 100 Hz. The reflex activity was recorded from the tibialis anterior muscle. As all patients were with hemiparesis the healthy side was used as a control. The patients were subdivided into four groups, each treated with different myorelaxants (Baclofen, Sirdalud, Myolastan and electroacupuncture). After about 25 days treatment the clinical and electromyographic examinations were repeated. The flexor reflex was recorded with two clearly distinguishable responses on the healthy, as well as on the spastic side. On the spastic side a reflex with prolonged latencies and durations, as well as with decreased amplitudes and thresholds of both reflex responses was found. On the spastic side the first reflex response had higher threshold than the second one, while on the healthy side it was vice versa. Moderate correlations were found between most of the reflex parameters. No correlations were found between the reflex parameters and the degree of spasticity. Only after Baclofen treatment all reflex parameters tended to normalized. After treatment with Myolastan, Sirdalud and electroacupuncture only the second response's duration shortened. In conclusion the flexor reflex is a sensitive method for assessment of altered common interneurone activity in spasticity.(ABSTRACT TRUNCATED AT 250 WORDS)

Abstract: This investigation estimated the mechanisms of baclofen action on spasticity using a battery of electromyographic methods. Thirty patients with old post-stroke spastic hemiparesis took part in the investigation. They were treated with baclofen-mean daily dose 54.3 alpha 11.6 mg for a mean of 26.3 alpha 4.9 days. A questionnaire for assessment of subjective improvement after treatment used a 5-point scale. For standardization of the neurological examination 5-point scales were used to assess muscle tone, muscle force and tendon reflexes. A battery of electromyographic methods was used to analyse different mechanisms of spasticity: for alpha motoneurone activity--the F wave parameters; for gamma motoneurone activity--the T/H reflex amplitude ratio; for presynaptic inhibition--the ratio of H reflex amplitudes before and after vibration on the achilles tendon (Hvibr./Hmax); for common interneurone activity--the flexor reflex parameters. Our results revealed that baclofen reduces spastically increased muscle tone and Babinski sign. It has no influence on muscle force, tendon reflexes and ankle
clonus. Baclofen acts by normalizing the altered interneurone activity and decreasing of alpha motoneurone activity. When spasticity has altered interneurone activity and increased motoneurone activity, it is better to treat with baclofen.

Abstract: A double-blind crossover trial against placebo was conducted to assess the effects of the GABA derivative, baclofen, on the disabilities due to muscle spasticity in twenty children suffering from cerebral palsy. Baclofen performed very significantly better than placebo in reducing spasticity and significantly better than placebo in allowing both active and passive limb movements to be carried out. Notable improvement was also seen in scissoring. Side-effects were minimal and responded promptly to dose reduction. The evaluation of drug effects on muscle spasticity and the pharmacodynamics of baclofen are discussed.
Recommendations are made regarding dosage of baclofen in childhood.

Abstract: A patient developed pulmonary infiltration, pleural effusions and pericarditis three months after starting dantrolene sodium. Peripheral blood eosinophilia and a raised ESR were present. Symptoms and signs resolved after the drug was discontinued. Dantrolene toxicity should be considered in the differential diagnosis of pneumonitis and pleuro-pericarditis.

Abstract: Very little has been published about the characteristics and sequelae of dysphagia in children with neurological impairment. The swallowing difficulties encountered by children with spastic cerebral palsy are particularly debilitating and potentially lethal. However, aggressive evaluation and management of their feeding is typically deferred until they are medically or nutritionally compromised. Reports of the use of videofluoroscopy to analyze the swallowing patterns and presence or absence of aspiration in such children are rare. This paper describes the histories and analyzes the videofluorographic swallow studies of 22 patients with the primary diagnosis of severe spastic cerebral palsy. The ages of the subjects ranged from 7 months to 19 years. All had severe dysphagia and were slow, inefficient eaters. Fifteen patients (68.2%) demonstrated significant silent aspiration during their swallow study. Analysis of specific features of their swallowing patterns indicated that decreased or poorly coordinated pharyngeal motility was predictive of silent aspiration. Moderately to severely impaired oral-motor coordination was indicative of severity of feeding complications. Our data suggest that early diagnostic workup, including baseline and comparative videofluoroscopic swallow studies, could be helpful in managing the feeding
difficulties in these children and preventing chronic aspiration, malnutrition, and unpleasant lengthy mealtimes


Abstract: We reported a case of motor neuropathy with pyramidal sign following prolonged administration of a high dose of muscle relaxant, pancuronium bromide (Myoblock). A 40-year-old male was admitted to our hospital with acute episode of pancreatitis. He was treated with artificial ventilation and Myoblock to manage delirious state, disseminated intravascular coagulation and multiple organ failure. Total dose of 823 mg (24 mg/day) of Myoblock was given intravenously over 36 days. After Myoblock was discontinued, he regained his consciousness and marked muscle weakness with atrophy was noted in both limbs, more severe in distal lower limbs, without any noticeable sensory and sphincter disturbances. Motor nerve conduction studies showed normal nerve conduction velocities with markedly decreased amplitude of compound muscle action potentials. Repetitive nerve stimulation studies revealed decrement response after tetanic stimulation, which disappeared later. Needle EMG showed active denervation potentials and marked polyphasic motor unit potentials. Muscle biopsy revealed neurogenic muscle atrophy with fragmented acetylcholine esterase-positive postsynaptic sites. Sural nerve biopsy showed slight to moderate degree of axonal degeneration of myelinated fibers. Clinical, electrophysiological, and pathological studies above indicated that the main affected sites were neuromuscular junctions including the terminal twigs of motor neurones and postsynaptic membrane, and pyramidal tracts, predominant in lower limbs. About one month after the recognition of the muscle weakness, his muscle strength improved gradually, however, spasticity with hyperreflexia and pathologic reflexes of both legs were found, and became more prominent thereafter. Intensive physiotherapy and rehabilitation led improvement to the point that he became able to ambulate with walking-aids about 7 months later, but marked spasticity persisted.(ABSTRACT TRUNCATED AT 250 WORDS)


Abstract: In a patient with hyperargininemia, oral administration of sodium benzoate or phenylacetic acid together with an essential amino acid mixture was
used to prevent hyperammonemia and to decrease plasma and CSF concentrations of arginine. Sodium benzoate reduced the plasma ammonia levels, which was confirmed by the increase of urinary excretion of hippuric acid. Phenylacetic acid also controlled hyperammonemia, and EEG findings also improved. By these treatments, plasma and CSF concentrations of arginine showed a slight decrease, but were far above the normal range. There was no clinical improvement, and spasticity of the lower and upper extremities was progressive with mental deterioration.

Abstract: A 28-year-old woman with a long history of drug abuse experienced flaccid quadriplegia and bilateral loss of posterior column sensation a few minutes after an intravenous (IV) injection of methylphenidate hydrochloride. Subsequently, spasticity developed and she showed minimal functional improvement during a period of several months. Necropsy performed 8 1/2 months later showed systemic granulomatosis due to talc and two ischemic infarctions, one involving both medial medullary areas and the other involving the left frontal lobe. Deposits of talc, presumably from a medication prepared for oral use, were demonstrated in the small vessels in the area of the medullary infarction. This case is unique in that the medial medullary syndrome was apparently caused by an embolus of talc following its IV administration.

Abstract: Pharmacotherapy of various neurologic and psychiatric disorders is based on amplification of the effects of the inhibitory neurotransmitter GABA in the CNS. Of particular importance is the modulation of GABAA receptors by benzodiazepines. Their effects are activity-dependent and self-limiting. With the development of new ligands for the benzodiazepine receptor site selective activity-profiles with minimal side-effects are sought. Progress is to be expected from partial agonists and in particular from ligands with selectivity for receptor subtypes.

Abstract: A number of new 1-phenyl- (a), 1-(3-chlorophenyl)- (b) and 1-(2-methoxyphenyl)- (c) piperazine derivatives containing 1,4-benzoxazin- 3(4H)-one (2-4), 2,4-benzoxazin-3-(4H)-one (5), 1,2-benzoxazolin-3-one (6) and 1,3-benzoxazolin-2,4-dione (7) were synthesized. Radioligand binding measurements showed that the majority of compounds had a distinct affinity for 5-HT1A (3a, 6a, 2-5b, 6c; Ki = 7.5-81 nM) and/or 5-HT2A (2b, 5-7a,b; Ki = 18-69 nM) receptors. Structure-Activity Relationship (SAR) studies revealed structural
features which seem to favour the binding to either or both of these two receptor subtypes. For evaluation of the functional in vivo profile of the most potent 5-HT1A (5b, 6b) and/or 5-HT2A (5-7b) ligands, the following tests were used: the 8-OH-DPAT-induced lower lip retraction (LLR) and behavioral syndrome in rats--for 5-HT1A receptor antagonistic activity, and the (+/-)DOI-induced head twitches in mice and the (+/-)DOI-induced discriminative stimulus properties in rats--for 5-HT2A receptor antagonistic properties. The obtained results show that compounds 5b and 6c behave like potent 5-HT1A antagonists, whereas 5b, 6b and 7b demonstrate 5-HT2A receptor antagonistic properties. None of the in vivo tested compounds, given alone, mimicked 8-OH-DPAT activity in those tests. It seems that derivative 5b, which has an equipotent 5-HT1A and 5-HT2A affinity and antagonistic properties at both these receptors, is a promising potential psychotropic substance.


Abstract: The author's clinical experience with the use of dantrolene in children with cerebral palsy is discussed. The medication is found to be the drug of choice for children with spastic cerebral palsy.

Abstract: THIP (Lu 2-030) is pharmacologically a specific and potent GABA-receptor-agonist which in animal studies depresses monosynaptic and, to a smaller extent, polysynaptic spinal reflexes. 5 spastic patients were investigated by means of neurophysiological tests comparing the acute effect of a single oral dose of THIP (15-25 mg) to "the test situation without drug administration" with an interval of 2 days. The neurophysiological tests included quantitative studies of proprioceptive reflexes (T-reflex, vibratory inhibition of the T-reflex, resistance to passive movement of a spastic muscle and clonus) and of the flexor reflex (threshold and latency). The voluntary power was measured by a static technique. THIP clearly reduced the monosynaptic T-reflex and reinforced vibratory inhibition of the IA monosynaptic pathway. The flexor reflex threshold was slightly increased during THIP administration, but the changes were not significant. Flexor reflex latency, resistance to passive movement, clonus and voluntary power were unchanged.

Abstract: Selective dorsal rhizotomy is used widely as a means of treating spasticity associated with cerebral palsy. Little is known regarding the effect of the procedure on the development or progression of spinal deformity. The authors reviewed six patients with progressive deformity after rhizotomy. Prerhizotomy and postrhizotomy records of physical examinations and radiographs were reviewed retrospectively in an attempt to identify risk factors for development of and/or rapid progression of, spinal deformity. Detailed preoperative and postoperative evaluation of spinal alignment should be undertaken, particularly in those patients who may be at risk of rapidly progressive deformity.

Abstract: Familiarity with spasticity and its treatment options and a rational approach to care are necessary to achieve an optimal outcome in patients with this disorder. Not all spasticity needs to be treated. Functional problems experienced by the patient and feedback from caretakers should guide decisions of whether and how to treat. Primary care physicians may benefit from maintaining close working relationships with physical medicine and rehabilitation physicians (physiatrists), who are experienced in assessment of spasticity, especially in relation to function, and can help differentiate true spasticity from rigidity and contracture. After underlying exacerbating factors are ruled out, a treatment plan starting with conservative methods and advancing to more aggressive measures should be followed. Consultation with physiatrists may be useful in regard to antispasticity medications, nerve blocks, intrathecal pumps, and postrhizotomy care.


Abstract: In 1930, thousands of Americans were poisoned by an illicit extract of Jamaica ginger ("jake") used to circumvent the Prohibition laws. A neurotoxic organophosphate compound, triorthocresyl phosphate (TOCP), had been used as an adulterant. The earliest reports were of peripheral neuritis, but later it was evident that an upper motor neuron syndrome had supervened. This TOCP poisoning apparently involved various cell groups and tracts in the spinal cord;
the lesions was not peripheral at all. We interviewed 11 survivors of the illness residing in eastern Tennessee. Four were carefully examined. The principal findings showed the spasticity and abnormal reflexes of an upper motor neuron syndrome. One patient had mild disease, despite typical findings, and had lived a normal life

Abstract: Effects of high-dose TRH on the vibratory inhibition of soleus H-reflex have been studied in 9 patients with amyotrophic lateral sclerosis. In 6 of the 9, TRH induced a significant increase in vibratory inhibition. This suggests that the TRH-induced reduction of spasticity might be due to an increase in presynaptic inhibition acting on Ia fibres


Abstract: The expanding use of intrathecal baclofen for spasticity has raised a concern about the treatment of overdose in these patients, since no specific baclofen antagonist is available. Since physostigmine has been reported to reverse the respiratory depression and somnolence due to opiates, the drug was tried for the treatment of baclofen overdose. In three cases, intravenous physostigmine (2 mg) completely reversed the respiratory depression and coma caused by boluses of 80 to 800 micrograms of lumbar intrathecal baclofen. Physostigmine, although not a specific antagonist, should provide increased safety for patients receiving intrathecal baclofen

Abstract: Recent pharmacological investigations have support the hypothesis that spinal modulation of nociception as well as motor coordination is related to the activity of spinal interneurons and that certain spinal transmitters are involved
in the control of both regulatory systems. Opioids and benzodiazepines, i.e. endorphin- or GABA-induced mechanisms, may be of importance for spinal treatment of spasticity in the near future. In order to clinically evaluate the interactions of these spinal processes we performed in vitro-experiments, animal studies and clinical investigations on the compatibility and antispastic efficacy of spinally administered opiates and benzodiazepines. Preclinical studies on tissue- and CSF-tolerance of different benzodiazepines (pH, tonometry, turbidimetry, histological findings in animals) are in favour of midazolam, a water-soluble compound, which is active against pharmacologically induced spasms in animals (strychnine application in cats with chronic catheterization of the subarachnoid space) after lumbar intrathecal injection. Using an appropriate dosage of intrathecal midazolam selective blockade of spasticity of the hind legs may be demonstrated with integrated EMG. Clinical investigations (neurological assessment using rating scores for spasticity) in 16 patients, including a double-blind comparison of epidural morphine or midazolam, indicate that both drugs are effective against spinal spasticity of different origin. Efficacy of spinally applied agents depends on the severity of spasms and on the duration and extent of systemic pretreatment.


Abstract: The efficacy of intrathecally administered baclofen was demonstrated in three patients with different types of muscular hypertonia (supraspinal rigidity, spasms shortly after spinal trauma, spasms for many years induced by multiple sclerosis) using integrated electromyography. Reduction of muscular electrical activity was accompanied by clinical improvement during long-term infusion via an implanted pump. The three patients have been observed for more than 1 year, during which time the antispastic activity of intrathecally infused baclofen has remained stable. Intrathecal application of baclofen may be considered as a possible alternative to surgery.

Abstract: Even in patients with complete loss of sensation and paraplegia after cervical spinal trauma, abdominal operations usually require general or spinal anesthesia due to spasms and increased muscle tone. Both anesthetic types have serious drawbacks under these circumstances, e.g. hyperkalemia induced by relaxation or the impossibility of adequate monitoring of the level of spinal blockade. After an onset time of 1-2 h the intrathecal injection of approx. 100 micrograms baclofen, a spinally acting GABAB-agonist, led to complete and long-lasting suppression of surgically induced spasticity. This could be
demonstrated by neurological examination (spasticity scores: Ashworth score, spasm score, clonus score) during 5 neurosurgical operations in 3 patients with paraplegia. Except for slight sedation, the patients had no discomfort during operation. Intrathecal baclofen was also effective against autonomic hyperreflexia, i.e. vegetative dysregulation such as bradycardia or hypertension, provoked by catheterization or bladder surgery.


Abstract: After incubation of rat cortical cell cultures with the human immunodeficiency virus type 1 (HIV-1) coat protein gp120 for 12 h, cells showed fragmentation of DNA at internucleosomal linkers, the characteristic feature of apoptosis. In a quantitative approach, it was determined that the percentage of DNA fragmentation increased from 7%, in the absence of gp120, to 62% following incubation with 24 ng/ml of gp120. Simultaneously, the percentage of viable cells decreased from 94% to 33%. Memantine (1-amino-3,5-dimethyladamantane), a drug currently used in the therapy of spasticity and Parkinson’s disease as well as the NMDA antagonist MK-801 both prevented the effects of gp120 at micromolar concentrations. In human cultured astrocytes, gp120 was ineffective with respect to DNA fragmentation and cell toxicity. From these data, we conclude that the gp120-induced apoptosis may contribute to the neurological complications frequently associated with the immunodeficiency syndrome. The cytoprotective effect of memantine in cortical cell cultures may qualify the drug for the treatment of AIDS-related dementia.


Abstract: Incubation of highly enriched neurons from rat cerebral cortex with the human immunodeficiency virus type 1 (HIV-1) coat protein gp120 for 18 h results in fragmentation of DNA at internucleosomal linkers, a feature of apoptosis. We report that neurons respond to exposure to gp120 with an increased release of arachidonic acid via activation of phospholipase A2. This process is not inhibited by antagonists of the N- methyl-D-aspartate (NMDA) receptor channels. To investigate the influence of arachidonic acid on the sensitivity of NMDA receptor towards its agonist, low concentrations of NMDA were coadministered with arachidonic acid. Under these conditions the NMDA-mediated cytotoxicity was enhanced. We conclude that gp120 causes an activation of phospholipase A2, resulting in an increased release of arachidonic acid which in turn sensitizes the NMDA receptor. Two compounds were found to act cytoprotectively against the deleterious effect caused by gp120 on neurons: Memantine [1-amino-3,5-dimethyladamantane] and Flupirtine [2-amino-3-ethoxycarbonylamino-6-(4-fluoro-benzyl-amino)- pyridine maleate]. Both compounds have been found to display a potent cytoprotective effect on neurons treated with the excitatory
amino acid NMDA or with the human immunodeficiency virus type 1 (HIV-1) coat protein gp120. The NMDA antagonist Memantine, a drug currently used in the therapy of spasticity and Parkinson's disease, prevented the effects of gp120 at micromolar concentrations. Flupirtine was previously found to be a centrally acting, nonopioid analgesic agent which additionally possesses anticonvulsant and muscle-relaxant activity at doses similar to those producing analgesia. The cytoprotective effect of Flupirtine in vitro was significant (above 10 microM). Considering the fact that both Memantine and Flupirtine display almost no clinical side effects, these drugs may prove useful both in preventing primary infection of brain cells with the HIV virus, as well as in treating the neurological disorders often associated with the immunodeficiency syndrome such as AIDS-related dementia


Abstract: A combined-modality treatment program consisting of botulinum toxin injection (Botox) and voice therapy was used to treat 17 subjects diagnosed with adductor spasmodic dysphonia (ADD SD). Ten subjects with ADD SD served as the control and were given Botox only. Voice therapy after Botox injection was directed toward reducing the hyperfunctional vocal behaviors, primarily glottal overpressure at voice onset and anterior-posterior squeezing. The results indicated that subjects who underwent combined-modality treatment maintained significantly higher mean airflow rates for significantly longer periods. Moreover, there was a carryover effect in these patients when they received Botox only. Adductor spasmodic dysphonia is treated most effectively when intrinsic laryngeal muscle spasms are reduced or eliminated by Botox injection and extrinsic hyperfunctional vocal behaviors are treated with voice therapy


Abstract: The long-term, chronic, paralysis resulting from spinal cord injury in the cat has been reversed by the use of an alpha 2-adrenergic receptor agonist, clonidine. Administration of this drug resulted in "normalization" of sensory-motor and autonomic dysfunctions. Preliminary studies of the clonidine in humans with traumatically injured spinal cord indicate that autonomic dysreflexia can be controlled and spasticity minimized. The data suggest that biochemical and pharmacologic manipulation of receptors may ameliorate paralysis following traumatic injury to the spinal cord as well as to the brain and brainstem


Abstract: The neurotoxicity mediated by alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), an agonist for glutamate receptors, was investigated by infusing adult rats with this agent intrathecally for either a short term (2 hours) or a long term (7 days) using a mechanical pump or a mini-osmotic pump, respectively. In the short-term infusion group, spasticity of the hindlimbs developed during infusion at 0.5 nmol/h or more of AMPA, tremors at 50 nmol/h or more, and flaccidity at 65 nmol/h or more. One day later, flaccid paralysis of the hindlimbs and urinary incontinence were observed in the rats that received 50 nmol/h (total dose: 100 nmol) or more of AMPA. These symptoms were thought to be permanent. On the other hand, in the long-term infusion group, behavioral changes were apparent only after second postoperative day, when rats displayed hindlimb palsy or urinary incontinence. Behavioral deficits became progressively severe, and rats usually displayed both hindlimb paraplegia and urinary incontinence by the 7th postoperative day. These progressive behavioral deficits were induced in a dose-dependent manner in rats that received AMPA at doses greater than 0.1 nmol/h. Gliosis with neuronal loss involving the partial (lumbar segments) and whole (sacral segments) gray matter of the spinal cord was induced in rats that received AMPA at doses greater than 50 nmol/h in the short-term infusion group and greater than 0.1 nmol/h in the long-term infusion group.(ABSTRACT TRUNCATED AT 250 WORDS)


Abstract: A prospective trial to demonstrate the efficacy of intrathecal baclofen therapy by implanted pump for adults with spasticity due to spinal cord injury or multiple sclerosis was initiated in our hospital. Of the 140 patients assessed, 7 met the following criteria for inclusion in the study: a modified Ashworth score > 3, a spasm frequency score > 2, and an inadequate response to oral anti-spasticity drugs, (i.e., baclofen, clonidine and cyproheptadine). All patients responded to intrathecal bolus injection of baclofen in the double blind, placebo-controlled screening phase (mean bolus dose = 42.8 micrograms). Programmable Medtronic pumps were implanted in 4 patients while 3 patients received non-programmable Infusaid pumps. Post-implantation, a marked decrease in spasticity occurred with a significant reduction of the Ashworth score (mean = 1.8, p < .005), a reduced spasm score (mean = 0.8, p < .005), and an improved leg swing in the pendulum test. These effects were maintained during a follow-up of 24-41 months (average infusion dose = 218.7 micrograms/day). The gross cost-savings due to reduced hospitalizations related to spasticity was calculated by comparing the cost for the two year period before pump implantation to the same period after treatment for 6 of the 7 patients. The cost of in-hospital implantation as well as the cost of the pumps were deducted from the gross savings. There was a net cost-saving of $153,120. Our findings agree with
the reported efficacy and safety of intrathecal baclofen treatment, and illustrate
the cost-effectiveness of this treatment


Abstract: Tizanidine, an imidazoline that acts as an agonist at alpha 2-adrenergic receptors, has been shown to be effective in reducing spasticity caused by MS. This multicenter study (14 sites) assessed the efficacy and safety of oral tizanidine in patients who had spinal cord injury of > 12 months' duration. Of the 124 patients admitted to the study, 78 completed it. Tizanidine was titrated to an optimized dosage in each patient to a maximum of 36 mg/d. Muscle tone, assessed by Ashworth score, was significantly reduced (p = 0.0001) by tizanidine treatment in comparison with placebo. Video motion analysis of the pendulum test showed improvement in the tizanidine-treated patients vs placebo (p = 0.04) and showed a significant correlation with the Ashworth score (p < 0.001). No significant alterations in muscle strength or vital signs were noted in either treatment group. The most common adverse events during tizanidine treatment were somnolence, xerostomia, and fatigue. It was concluded that, overall, tizanidine is effective in reducing spasticity in patients with spinal cord injury.


Abstract: BACKGROUND: Spasticity is a serious problem in multiple sclerosis (MS) and many patients do not achieve a satisfactory response to currently available oral antispasticity drugs. Tizanidine hydrochloride, an alpha 2-noradrenergic agonist, has been shown to have an antispasticity effect in single center trials of patients with MS. OBJECTIVE: To compare plasma concentrations of tizanidine with objective measures of muscle tone in patients with MS with moderate to severe spasticity. SETTING: Ten centers, all tertiary referral centers for the specialized treatment of patients with MS, in the United States and Canada. DESIGN: A randomized, double-blind, placebo-controlled, dose-response study of tizanidine hydrochloride (8 or 16 mg). PATIENTS: One hundred forty-two patients with spastic MS who were not taking any interfering medication, such as an antispasticity drug or other alpha-noradrenergic agonist, entered the trial. RESULTS: Tizanidine treatment reduced muscle tone significantly, as shown by improved Ashworth scores and increased knee swing amplitude recorded by the pendulum test, both of which correlated significantly with plasma concentration. Placebo had no significant effect on muscle tone.
Dizziness, drowsiness, dry mouth, and fatigue were reported most often in the group treated with tizanidine at peak plasma concentration. CONCLUSIONS: Tizanidine reduces spasticity in MS, and both therapeutic effects and side effects are related to the plasma drug levels.

Abstract: The article illustrates a practical approach to the challenging management of problematic, generalized spasticity. Use of dose titration to achieve symptomatic relief is described. Currently approved pharmaceuticals used as antispasticity agents and muscle relaxants and other medications with antispasticity effects are reviewed.

Abstract: A programmable baclofen pump was implanted in 7 patients for relief of severe spasticity. The patients experienced improvement in bladder and sphincter function. This system would seem to be of value in improving lower urinary tract function in patients with diseases that produce marked spasticity.


Abstract: Two patients who had severe spinal spasticity with painful flexor spasms were treated with oral baclofen with relief of symptoms. The various drugs to treat severe spastic weakness and flexor spasms and their mode of action are briefly discussed.

Abstract: Pressure, hygiene, spasticity and chronic infection are the important local factors in pressure ulceration. Hypoproteinemia, nutritional deficiency and anemia are the systemic factors. Careful attention to local wound care and dietary supplements is required. Muscle and myocutaneous flaps may provide better coverage than the traditional random pattern flaps. Flaps with sensibility have theoretic advantages but need further investigation.


Abstract: Although the basic rhythm of stepping, walking, and running is present in the spinal cord, it is not manifest in patients with lesions of the spinal cord, on account of spasticity. Spasticity is an over-reaction to every kind of input. Every response is followed by an after-discharge. This affects the muscles which have reacted, and it spreads to involve many other muscles, more ipsilaterally than contralaterally. In the normal this is prevented by the corticospinal tract, by Renshaw inhibition, and by inhibition of the input to the spinal cord. Anything that reduces the input that finally reaches motor neurons reduces general excitability; it reduces spasticity permanently, allowing normal movements to occur.

Abstract: Metoclopramide is a widely used product, which can accidentally cause acute dyskinesia, of which several forms may be observed, including dysarthria, tetany, spasmophilia, false cerebral vascular insult, trismus, hysteriform spell.... In all those cases, one should think of giving an antiemetic and of properly orienting history-taking, thus avoiding a longer stay in hospital that would not be justified. This is demonstrated by two patients recently admitted into the department of maxillofacial surgery and stomatology with maxillofacial signs related with the adverse effects of this kind of drug.


Abstract: A double-blind crossover trial compared tizanidine with baclofen in 36 patients with spasticity. Tizanidine appeared to reduce lower limb spasticity more effectively and to have fewer side effects, but no statistically significant differences emerged when the two drugs were compared. An additional open study of tizanidine confirmed the beneficial action in a selected minority of patients with spasticity. This drug may have an important role in the management of spasticity, but further studies are required.

Abstract: A rare case of suicidal strychnine poisoning that resolved naturally without treatment is presented. The patient first complained of chest pain, which was originally thought to be caused by a dissecting aneurysm; however, nystagmus, dysesthesia, spastic paraplesia, and hyperreactivity to stimuli shortly developed. Diagnosis was difficult because the patient did not disclose the drinking of strychnine or the suicidal intent, and no abnormal signs were seen in the various central nervous system examinations. The natural course was
observed without treatment because the patient's circulatory and respiratory condition was good. Movement disturbances in the upper extremities disappeared after 2 days, nystagmus in 3 days, and dysesthesia and spastic paraplegia in 4 days. The patient was able to stand on the fourth day and walk on the seventh. He was discharged on day 10 without any detectable ill effects.

Abstract: In this two-phase study, 21 pediatric patients with epilepsy and spasticity were initially treated with dantrolene sodium suspension and, after a washout period, began a double-blind portion where one half received dantrolene sodium suspension and the other half received a placebo suspension. The frequency of seizures, serum anticonvulsant levels and electroencephalograms were compared with control values. On dantrolene sodium suspension, there was no persistent change in these parameters. Therefore, it is concluded that dantrolene sodium does not adversely affect the frequency of seizures in children with epilepsy and spasticity, who are being maintained on anticonvulsant medications.

Abstract: Clonidine, a noradrenergic agonist, and cyproheptadine, a serotonergic antagonist, have each been associated with improved walking in SCI subjects. Baclofen, a GABA agonist, is frequently prescribed for spasticity but its effects on walking have not been well quantified. The objective of this study was to compare the effects of clonidine, cyproheptadine and baclofen on walking in SCI subjects with incomplete injuries. A motorized treadmill was used and harness support provided when necessary. A repeated single-subject design was employed for the twelve subjects. The greatest effects were found in more severely disabled subjects. Cyproheptadine was associated with greatly reduced need for assistance, increases in maximum treadmill speed (MTS) and reduced clonus. Clonidine was associated with increases in MTS and a generally more upright posture. Baclofen was associated with minor changes in walking. In many cases of drug effects, MTS increases and other changes were retained following washout of drugs. The significance and implications of the drug effects and the retention of effects during washout periods are discussed. It is concluded that clonidine and cyproheptadine have different effects but both appear useful for severely disabled SCI subjects. The effects of baclofen on walking after spinal cord injury remains unclear.


Abstract: Five patients presented in infancy or early childhood with various combinations of pyramidal and extrapyramidal signs with normal cognitive function. Their perinatal courses were unremarkable. In each patient, initial impressions listed by several examiners included spastic diplegia or cerebral palsy. Later in each course, either extrapyramidal features or progression suggested dopa-responsive dystonia. In 4 of the 5 children, cerebrospinal fluid was obtained and disclosed reduced levels of biopterin, neopterin, and homovanillic acid in all 4. Levodopa therapy resulted in prompt improvement with normal function returning within 6 months. The disappearance of the "spasticity," extensor plantar responses, and extrapyramidal signs, following levodopa therapy, confirmed the diagnosis of dopa-responsive dystonia in these patients. Three had apparently sporadic disease; the other 2 were siblings with an affected paternal grandmother. Three had onset in infancy with delayed sitting and walking before the appearance of overt dystonia; infantile onset is infrequent in dopa-responsive dystonia. The other 2 had normal milestones, but developed gait disorders with prominent imbalance in early childhood. The diagnosis of dopa-responsive dystonia should be considered in children with unexplained or atypical "cerebral palsy."

O'Brien C.F. (1997) Injection techniques for botulinum toxin using electromyography and electrical stimulation. Muscle Nerve Suppl 6, S176-S180. Abstract: Increasing data supports the use of botulinum toxin injection as a therapeutic intervention in the management of spasticity. The avid binding of botulinum toxin (BTX) to presynaptic neuron terminals and the diffusion characteristics of the medication allow relative ease of administration. For many clinical applications, efficacy may be improved, and adverse effects reduced, by more precise targeting of the muscles to be injected. Electromyographic guidance (EMG) is commonly used to confirm appropriate localization of the injection needle in specific muscles immediately before injection. Electrical stimulation (ES) may be more useful in patients who are unresponsive or sedated. Equipment options and technical aspects of EMG and ES are discussed, including some adjunctive imaging methods for injecting difficult-to-localize muscles.

O'Kusky J.R. and McGeer E.G. (1985) Methylmercury poisoning of the developing nervous system in the rat: decreased activity of glutamic acid decarboxylase in cerebral cortex and neostriatum. Brain Res. 353, 299-306. Abstract: The specific activities of glutamic acid decarboxylase (GAD) and choline acetyltransferase (ChAT) were measured in 6 regions of the central nervous system in young rats, following chronic postnatal administration of methylmercuric chloride. These rats exhibited signs of neurological impairment which included visual deficits, ataxia, spasticity and myoclonus. At the onset of neurological impairment, there was a significant reduction in GAD activity in the occipital cortex (43%), frontal cortex (37%) and caudate-putamen (42%). Preceding the onset of neurological impairment, diminished GAD activity was detected only in the occipital cortex. In the cerebellum, thalamus and spinal cord,
GAD activities were normal throughout the experiment. No significant differences in ChAT activity were detected in any of the 6 regions. These results are consistent with a preferential involvement of GABAergic neurons in methylmercury-induced lesions of the cerebral cortex and neostriatum

Oboimov E.I. and Kolesova O.E. (1989) [Spastic torticollis]. Sov. Med. 41-44. Abstract: Fifty-seven cases of spastic torticollis are reported, and its etiologic factors, including stressful situations, are analyzed. Plasma serotonin measurements have added new insight into pathogenetic mechanisms of the condition. The range of "reflex" spastic torticollis has been limited on the basis of biochemical and EMG findings. Fairly high incidence of attendant extrapyramidal symptoms and their polymorphism are pointed out, and, the need for a differential approach to the treatment of spastic torticollis being emphasized, a schedule of combined treatment, incorporating eglonyl and amitriptyline, is proposed for clonic-tonic torticollis

Ochs G., Struppler A., Meyerson B.A., Linderoth B., Gybels J., Gardner B.P., Teddy P., Jamous A., and Weinmann P. (1989) Intrathecal baclofen for long-term treatment of spasticity: a multi-centre study. J. Neurol. Neurosurg. Psychiatry 52, 933-939. Abstract: Twenty eight patients with severe, intractable spasticity have been treated by chronic intrathecal administration of baclofen. An implantable programmable drug-administration-device (DAD) was used with a permanent intrathecal catheter. Infusion of 50 to 800 micrograms/day of baclofen completely abolished spasticity. Follow-up was up to two years. Therapeutic effect was documented by clinical assessment of tone, spasms and reflexes and by electrophysiological recordings of mono- and polysynaptic reflex activity. Complications and untoward side-effects of the procedure were few. This procedure is recommended for spasticity of spinal origin refractory to physiotherapy and oral medication. It is a preferable alternative to ablative surgical intervention

Ochs G.A. (1993) Intrathecal baclofen. Baillieres Clin. Neurol. 2, 73-86. Abstract: The intrathecal application of the GABA-B agonist baclofen has become more and more popular for severe spinal spasticity. Since it was first introduced in 1984 more than 1000 patients worldwide have been treated by this method, using an implantable drug administration device. Clinical data from 48 patients are presented, as well as further experience from a multicentre trial conducted in Europe, in conjunction with a literature overview. The method is now generally accepted as a powerful treatment for spasticity due to spinal lesions of whatever aetiology; improvement in mobility and function as well as relief of spastic pain are the most obvious benefits for the patient. Bladder function is improved in terms of increased bladder volume and lowered residual volume. In patients with supraspinal lesions causing muscle hypertension, where several mechanisms usually contribute besides hyper-reflexia (spasticity), the response has been less pronounced, but intrathecal baclofen still seems to have
clinical effects that are superior to those of any oral drug treatment. The initial technical and methodical problems have been solved and today the procedure is generally assessed as safe.


Abstract: A simple method that can be performed at the bedside using a spring balance was developed in order to quantify spasticity. The effects of tizanidine on spasticity were evaluated in 30 patients with sequelae of cerebrovascular disease using this method. Treatment with tizanidine was effective in 60% of the patients; there were high correlations between spasticity before and after tizanidine administration and the severity of symptoms and also between the degree of improvement in spasticity and in that of the symptoms. Atonic seizures, due to overdose of tizanidine, were observed in only one patient. The simple spasticity quantification method developed was useful for monitoring tizanidine administration in order to prevent drug overdose. The method appears to be very useful for evaluating the degree of spasticity at the bedside and in measuring the effects of antispastic drugs.


Abstract: To clarify the role of thromboxane A2 (TXA2) in evoking coronary spasm, we compared coronary arterial spasticity induced by ergonovine maleate (EM) with coronary sinus thromboxane B2 (TXB2: a stable catabolite of TXA2) in 34 patients with documented variant angina and 11 patients with chest pain syndrome (CPS). We also examined the effect of OKY-1581 (8 mg/kg, i.v.), a TXA2 synthetase inhibitor, on the coronary arterial spasticity of these patients. When blood samples were taken from coronary sinus just before EM test, all patients with variant angina exhibiting markedly augmented TXB2 levels (424 +/- 138 pg/ml), had positive EM test results, while CPS exhibiting lower TXB2 levels (223 +/- 38 pg/ml), had negative EM test. We found that the amounts of EM needed to induce coronary spasm were inversely correlated with TXB2 levels in coronary sinus. In 7 out of these 8 patients, OKY-1581 was found to attenuate the increased spasticity with reduction of coronary sinus TXB2 levels. In 3 patients, an EM rechallenge at symptomatically quiescent stage resulted in negative test with augmented TXB2 levels being markedly decreased. These findings indicate that increased TXA2 in circulating plasma is closely correlated with the hypersensitivity of coronary arteries to EM in patients with variant angina, suggesting a possible role of augmented TXA2 production in the enhancement of coronary vascular spasticity.

paraplegia with a thin corpus callosum. Acta Neurol. Scand. 102, 196-199.

Abstract: We followed-up a Japanese man suffering from hereditary spastic paraplegia with a thin corpus callosum (HSP-TCC) by single photon emission computed tomography (SPECT) using 123I-isopropyl-piodoamphetamine (123I-IMP) over 4 years (25 to 29 years old). Besides the initial symptoms of lower limb spasticity, mental deterioration slightly progressed and upper limb spasticity and slight cerebellar ataxia were developed, during the period. Cranial magnetic resonance imaging (MRI) revealed an extremely thin corpus callosum and medial frontal atrophy, which remained essentially unchanged during the period. 123I-IMP SPECT demonstrated that cerebral blood flow was decreased in the thalamus and the medial frontal, temporal and parietal cortices at the first examination, and that the thalamus showed further reduction but the other involved regions presented essentially no progression during the follow-up period. This is the first report referring to the longitudinal clinical and neuroradiological changes in HSP-TCC


Abstract: This preliminary study was designed to investigate the effects of botulinus toxin Type A and phenol treatments on electrophysiologic tests evaluating spinal afferent and efferent motor pathways involved in spasticity. The questions posed were whether different types of mechanisms act on reducing spasticity with these different treatment modalities and whether the tests are correlated with clinical recovery. Twenty patients with lower limb spasticity secondary to stroke were randomly assigned to receive 400 mouse units of botulinus toxin Type A injected into the calf muscles or to receive a tibial nerve blockade with 3 ml of 5% phenol. The amplitudes of the Achilles tendon response, M response, H reflex response, and maximum H:M ratio and Achilles tendon response to H response ratio were recorded from the soleus muscle at baseline and at Weeks 2, 4, and 12. The most obvious change was a reduction in the amplitude of the tendon response in the group that received botulinus toxin Type A, and it was a reduction in the M response amplitude in the group that received phenol. The decrease in the tendon response amplitude and tendon response to H ratio in the group that received botulinus toxin Type A and the decrease in the M response amplitude in the phenol group were found to be well correlated with clinical recovery as assessed by the Ashworth scale. The findings suggested that botulinus toxin Type A injection decreases spasticity primarily by affecting the fusimotor system and muscle spindle, and the involvement of the alpha-motor fibers within the tibial nerve is the most likely factor contributing to the reduction of spasticity after phenol blockade. The therapeutic effectiveness of these agents could be assessed and followed up by the changes in electrophysiologic responses matching their mechanisms of action. The findings should be supported by further electrophysiologic techniques

Ordia J.I., Fischer E., Adamski E., and Spatz E.L. (2001) Dysesthesia perceived as painful spasticity: A report of 3 cases. Arch. Phys. Med. Rehabil. 82, 697-699. Abstract: Lesions of the central nervous system often involve the pyramidal tracts and the sensory pathways to produce spasticity, paresthesias, and dysesthesia. Three patients with intractable spasticity were treated with intrathecal baclofen. Two had an implanted Medtronic SynchroMed pump for long-term delivery of the muscle relaxant. The third patient had undergone a screening trial in which the baclofen was delivered into the intrathecal space through a lumbar catheter. All had excellent relief of spasms on clinical examination, but they reported painful spasms particularly at night. Two of the patients were successfully treated for dysesthesia.

Orlova O.R. and Golubev V.L. (1986) [Phenomenon of inverted rotation in spastic torticollis]. Zh. Nevropatol. Psikhiatr. Im S. S. Korsakova 86, 348-351. Abstract: The article describes a rare clinical case where a patient with right- side spastic torticollis developed stable left-side spastic torticollis following discontinuation of nacom. On the basis of clinico- physiological analysis of the given phenomenon and having compared their findings with the literature data the authors substantiate the involvement of the nigrostriatal systems of both hemispheres in the pathogenesis of torticollis and in the mechanisms of rotation inversion reported in the given disease for the first time.

Orsnes G.B., Sorensen P.S., Larsen T.K., and Ravnborg M. (2000) Effect of baclofen on gait in spastic MS patients. Acta Neurol. Scand. 101, 244-248. Abstract: OBJECTIVES: To measure gait and postural stability by objective methods in spastic MS patients and to evaluate the effect of baclofen on gait and postural stability. PATIENTS AND METHODS: Fourteen spastic MS patients were examined in a placebo controlled double-blind, cross-over trial of oral baclofen treatment. The gait was measured on a computerized treadmill and postural stability was measured on a computer assisted force-plate. RESULTS: Only insignificant improvements in the clinical measurements during baclofen treatment were found. At baseline gait was characterized by low speed, short steps and unsteadiness. Postural stability was severely impaired. During baclofen treatment only vertical unsteadiness of gait diminished significantly. DISCUSSION: We conclude that patients primarily with spasticity, concomitant with hampering or painful spasms and co-contractions should be offered treatment with baclofen. Only some will experience improvement of their gait disorders, when treated with baclofen.

Abstract: A mechanomyographic response of the hind foot to passive straightening and bending, as well as an electromyographic activity of the gastrocnemius and tibialis anterior muscles were recorded in old (35-44-month-old) and young female rats. In old rats, spontaneous, tonic electromyographic activity patterns were concurrently observed in both antagonistic muscles; they were low-amplitude, dense tonic activity and continuous, high-amplitude, sparse electromyographic activity. The tonic electromyographic activity was correlated with a decline in the strength and mass of muscles, as well as with motor disturbances, including paresis of the rigidly straightened backward hind legs, dragged behind by an animal. In muscles of old rats, morphological features of a chronic denervation atrophy were found. Baclofen (10 and 15 mg/kg, i.p.) diminished the spontaneous tonic electromyographic activity and potently decreased the whole body muscle tone, whereas Madopar (50 mg/kg of L-DOPA+12.5 mg/kg of benzerazide) was ineffective. It is suggested that old rats in which the above-described pathologic alterations are observed might be a useful animal model in the search for basic etiopathological mechanisms of spasticity and similar disturbances found in humans.


Abstract: Intraspinal drug delivery provides agents directly to their site of action. These sites, receptors within the spinal cord, are bound to a greater degree when drugs are administered intraspinally. The purpose for drug therapy, the acute or chronic nature of delivery, and the drug administration system affect the choice of epidural versus intrathecal route of delivery. Pharmacologic properties, such as solubility, pH, and pKa, aid in dictating the drug chosen for administration. Intraspinal opiates and anesthetics have been used extensively since the 1970s in postoperative, postpartum, and cancer populations. Various delivery systems are in use, including external catheters and implanted ports and pumps. Nursing care includes titration of doses, prevention and management of side effects, and maintenance of delivery systems. Intrathecal baclofen is a new treatment for severe spasticity for patients with multiple sclerosis or spinal cord injury. Candidates include patients who experience persistent spasticity unrelied by antispasmodics or who experience unacceptable side effects to those oral drugs. Nurses assess spasticity, titrate the intrathecal baclofen to obtain an acceptable degree of spasticity, and manage side effects associated with intrathecal baclofen. A long-term benefit of intraspinal drug delivery, potentially providing benefit to many patients, is the identification of experimental agents that do not cross the blood-brain barrier but prove effective when delivered intraspinally. Pharmacologists and others then might undertake the costly modifications necessary to improve the solubility of the drug. The analogue then might be given orally. "The feasibility of an operation is not an indication for its performance." These words, attributed to the late Lord Cohen, also apply to
intraspinal drug delivery. As with any therapy, the simplest and least invasive course should be taken. If, for example, the patient experiences good relief without side effects when given oral opiates or baclofen, there is no good rationale for inserting an intraspinal catheter. The potential for increased morbidity and the escalated expense make this an illogical choice. There are, however, many patients who cannot tolerate oral opiates or baclofen but obtain significant benefit from intraspinal drug delivery. Those who benefit should not be denied this therapy. Much research is necessary as this modality develops. Nurses who comprehend the science of intraspinal drug delivery, as well as the art of patient management, can contribute to this advancing field.


spasticity not relieved by these methods. These patients were subsequently treated with intrathecal baclofen delivered by an implanted programmable drug pump. Twenty-one patients have received this form of treatment, and the functional status of eight has been tracked by the Patient Evaluation Conference System (PECS) for at least six months. In most cases, spasticity, performance of bowel and bladder programs, and performance of ADL improved after delivery of intrathecal baclofen. The improvements appear to be due to the decrease in hypertonicity and the increased ease of movement (passive or active) in affected extremities. Intrathecal baclofen should be considered as a treatment method in patients with severe spasticity of spinal origin.

Abstract: A hemiplegic patient with severe upper extremity spasticity 2 years after a cerebrovascular accident received a diagnostic median nerve block below the elbow with bupivacaine. He had been placed on Coumadin as prophylaxis for cerebrovascular arteriosclerotic disease, and prothrombin time was kept at twice the control value. Less than 48 hours after the procedure, a compartment syndrome developed in the volar forearm. Compartment syndrome has not previously been reported as a complication resulting from a nerve block procedure. We conclude that (1) compartment syndrome may develop after a peripheral nerve block procedure for spasticity, (2) prophylactic anticoagulation may increase the risk for hemorrhagic events resulting from percutaneous injection and (3) early recognition is essential and appropriate decompressive fasciotomy may be indicated if a compartment syndrome develops after a nerve block procedure.

Abstract: OBJECTIVE: To review the results and adverse effects to botulinum toxin type A (BTA), Botox, in cerebral palsy (CP) spastic and/or dystonic in an open prospective study. MATERIAL AND METHODS: The first 39 cases treated were analyzed. They received 1-2 doses and were followed up to 12 months. BTA indications were wide: to improve limb function, to avoid surgical orthopedics or improve hygienics or dressing. O'Brien Global Assessment Scale (scored by neurologist, physiotherapist or parents), Ashworth spasticity scale, functional scale for dystonic upper limb (Sindou-Millet) and exam of position of foot, knee and hip, were used. RESULTS: Total doses/session was 1-10 U/kg. We observed adverse effects in 6 cases (15.4%), always mild and lasting only few days (general weakness, tiredness, instability). Positive effects lasted 4 months in upper limbs and 4.5 months in lower limbs. In upper limbs (9 cases injected) it was observed a global positive result of mild grade in 11-40%, moderate without functional improvement in 11- 22%, and moderate-important with functional improvement in 40-78% of patients, being patient's evaluation the...
best and physiotherapist's one the worst. Spasticity improved 2 or more grades in Ashworth scale in 7/9 cases. Dystonia improved in proportion to dose. In lower limbs gastrocnemius muscles were injected in 29 cases (55 sessions), adductors in 14 cases (33 sessions), ischiottibialis in 8 cases (27 sessions), posterior tibialis in 8 cases (12 sessions). It was observed a global improvement null or mild in 20%, moderate without functional change in 35-44%, and moderate or important with functional improvement in 35-44%, with signficative correlation between parent’s, physiotherapist's and neurologist's scores. Spasticity was also significatively reduced after treatment. It went down 2 or more grades in Ashworth scale in 40% of ischiottibialis, 60% of adductors and 65% of gastrocnemius, in general with a doses-effect association. Foot position in walking improved from moderate to important grade in 2/3 of cases, as improved foot position while standing. Knee flexion and hip hyperadduction were reduced moderate-importantly in 60% and 40% of cases respectively.

CONCLUSION: BTA is highly effective in the treatment of CP, and if associate with physiotherapy long and even permanent effect can be achieved.


Abstract: Cases of polyneuropathy due to exposure to industrial solvents have been studied at several shoe factories in the province of Siena. After the screening of 654 employees 98 verified cases were detected. Of these, 16 were rated as moderate to severe, 45 as mild, and 37 were minimally involved but with characteristic electrodiagnostic abnormalities. Follow-up study in 53 patients showed that neurological signs and symptoms as well as electrodiagnostic abnormalities continued for years in several patients. In addition, after a year's observation, some patients showed signs of central nervous system dysfunction such as spasticity of the lower limbs and increased deep tendon reflexes. High percentages of commercial n-hexane were found in all the samples of glues and solvents collected from home-workers and from factories where cases of polyneuropathy occurred.


Abstract: Intrathecal baclofen abolishes spasticity in many patients with neurological diseases but there are few studies on its long-term effectiveness. Since 1986 a manually operated subcutaneous pump has been used to deliver baclofen intrathecally in 21 patients with a follow up of at least one year. Most patients had multiple sclerosis and all were wheelchair-bound. Sixteen patients had a complete and sustained benefit. In four other patients the treatment was effective in the short term but not in the long term. In the remaining patient the pump never worked. Complications included meningitis, pump failure, erosion through the skin, and baclofen overdose. Nevertheless, only three patients have
asked to discontinue the treatment. We conclude that intrathecal baclofen, delivered by a manually operated implanted pump, is an effective treatment for severe spasticity in most patients


Abstract: OBJECTIVE: The aim of this study was to verify the action of Botulinum toxin type-A (BoNT-A) by means of neurophysiological techniques, in patients presenting lower limb spasticity and requiring BoNT-A injections in the calf muscles, due to the poor response to medical antispastic treatment. SUBJECTS AND METHOD: Patients presenting paraparesis were enrolled. They underwent clinical evaluation for spasticity according to the Ashworth scale and neurophysiological recordings including: motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) of the leg area; compound motor action potential (cMAP) to tibial nerve stimulation, F-wave, and H-reflex before the treatment and 24 h, 2 weeks and 1 month after the injection of BoNT-A. In all patients, gastrocnemius was treated and in some cases soleus or tibialis posterior muscles were also injected. RESULTS: In all patients, BoNT-A injections induced a clear clinical improvement as showed by the reduced spasticity values of the Ashworth scale. A significant increment of MEP latency and central conduction time (CCT) duration were observed 2 weeks after the treatment only in the injected muscles. CONCLUSIONS: Prolonged MEP latencies and CCT after BoNT-A injections is probably due to a central alteration in responsiveness of spinal motor neurons to descending impulses from the corticospinal tracts. Such changes represent objective parameters heralding clinical efficacy of treatment


Abstract: An improved method of sphincterometry is described, which is easy to
perform in men and also may be used in women. It gives reproducible results in the individual patient. The maximum pressure was found by radiographic and reflexological examinations of the external urethral sphincter. When 0.5 mg./kg. body weight dantrolene sodium was injected intravenously the resistance of the external urethral sphincter was found to be reduced significantly, presumably reflecting a reduction of reflex activity


Abstract: The effect of the alpha-adrenergic blocking agent thymoxamine by intravenous administration was studied in 25 patients with spastic paraplegia and uninhibited neurogenic bladder. By cystometry a shift to the right of the first desire to void, the threshold of the first uninhibited contraction and a reduction of the pressures of the uninhibited contractions was found, but the bladder capacity was unchanged. The urethral pressure profile studied in 10 patients showed reduction in most and the peak value in all the patients. EMG from the external urethral sphincter in five patients showed damping of anal reflexes in all cases and in basic activity and cough reflexes when appropriate for studies. The site of action on the bladder is most likely adrenergic receptors in the bladder and the unchanged bladder capacity may be related to a too-short duration of the effect of thymoxamine. The effect on the spastic striated pelvic sphincters may be central, whereas the effect on the smooth muscle may be peripheral. Feedback from the drug relaxed proximal part of the urethra to the bladder might also be of importance


Abstract: One of the many causes of enteral feeding (EF) intolerance after traumatic brain injury (TBI) is superior mesenteric artery syndrome (SMAS). Although it is reported in pediatric brain injury, few cases are noted in adults. To increase awareness of this medically treatable condition, we present two patients who developed SMAS after sustaining severe brain injury. SMAS results from compression of the duodenum by the SMA against the aorta and risk factors include acute weight loss, prolonged recumbency, and spasticity—all frequently encountered in severe TBI. After gastric decompression, symptoms often resolve with weight gain achieved by conservative treatment; including feeding in the left lateral or prone position, hyperalimentation, or extension of a feeding tube beyond the obstruction. SMAS should be considered in the presence of EF intolerance in severe adult TBI because multiple risk factors may be present


Abstract: Spasticity is a source of disability for the hemiplegic patient. It leads to
various disorders influencing the quality of gait: at the lower limb varus equinus foot deformity, toe-claw and/or hip adduction with adductors spasticity. At the upper limb, flexion deformity of the wrist and the hand makes grasp and grip ineffective and spasticity of the Pectoralis Major muscle is considered as a main cause of sympathetic dystrophy. Neurolysis with alcohol injection in the nerve trunk or at the motor point destroys the gamma fibers and reduces spasticity, without impairing motor command. The effects on spasticity, motricity, and deformity of 33 chemical neurolysis with alcohol are analysed with a six months follow-up (27 hemiplegic patients, 28 to 62 years old, mean = 54.5). The authors have used 60% alcohol concentration. Sciatic nerve injection significantly reduces triceps spasticity (7/11), improves the range motion of the ankle, and allows the patient to take off the ankle device. Those fair results are still present at the fourth month after injection. Similar results are reported after injection of the obturator nerve for hip adduction deformity (2/3), median nerve injection for wrist and hand deformity (6/6). Pectoralis Major injection in the motor point is effective for 10 of the 13 cases, preventing sympathetic reflex dystrophy or contributing to its dramatic improvement.

Abstract: We describe two cases of an unusual acneiform eruption which occurred in middle aged women being treated with dantrolene for spasticity.

Abstract: INTRODUCTION: Baclofen is frequently used to treat muscle spasticity due to spinal cord injury and multiple sclerosis. Baclofen overdose can lead to coma, respiratory depression, hyporeflexia, and flaccidity. An abrupt decrease in the dose of baclofen due to surgery or a rapid tapering program may result in severe baclofen withdrawal syndrome manifesting hallucinations, delirium, seizures, and high fever. Severe baclofen withdrawal syndrome secondary to intentional overdose, however, has not received mention. CASE REPORT: A 42-year-old male receiving chronic baclofen therapy, 20 mg/d, attempted suicide by ingesting at least 800 mg of baclofen. He was found in coma 2 hours postingestion with depressed respirations, areflexia, hypotonia, bradycardia, and hypotension. Treatment with intravenous fluids, atropine, dopamine, and hemodialysis was associated with restoration of consciousness within 2 days but disorientation, hallucinations, fever, delirium, hypotension, bradycardia, and coma developed during the following week. Baclofen withdrawal syndrome was not diagnosed until hospital day 9, when reinstitution of baclofen rapidly stabilized his condition. Oral overdosage of baclofen causes severe neurological and cardiovascular manifestations due to its GABA and dominant cholinergic effects. Severe baclofen withdrawal syndrome is manifest by neuropsychiatric manifestations and hemodynamic instability. Caution should be exercised after a baclofen overdose in patients receiving chronic baclofen therapy.

Abstract: Implanted drug pumps provide a new way to infuse medication chronically to the nervous system in a selective fashion. They have been of value in treating pain of cancer and spasticity through spinal subarachnoid catheters. Treatment of Alzheimer’s disease is currently being investigated using intraventricular bethanechol

Abstract: Baclofen is the most effective drug for the treatment of rigidity and spasms caused by damage to the spinal cord, but frequently, relatively little relief is afforded and dose is limited by central side-effects. To improve the efficiency of drug delivery 6 patients received implantable programmable pumps with a catheter going into the lumbar subarachnoid space. Baclofen, at doses of 12 micrograms to 400 micrograms per day, was given for up to 7 months. With intraspinal treatment there was an immediate reduction of muscle tone to normal levels, and spontaneous spasms were eliminated. Patients experienced less discomfort, and daily activities were more easily accomplished

Abstract: Seven patients with spasticity of spinal cord origin have been maintained for up to 2 years with continuous spinal intrathecal infusion of baclofen. Prior to treatment, all of the patients had severe rigidity in their lower limbs and most had frequent and extensive spontaneous spasms, all of which greatly interfered with their activities of daily living. Oral antispasmodic medications were ineffective or caused central side effects. The patients underwent implantation of a programmable drug pump connected to a lumbar subarachnoid catheter. Within days of beginning continuous intrathecal baclofen infusion, the muscle tone was reduced to normal levels and spasms were eliminated. Over the ensuing months, muscle tone remained normal, but short-duration spasms could be induced by some activities. The greatest benefits to the patients were improvement in activities of daily living and better sleep due to reduced spasms. The baclofen doses were increased over the first few months but then were stabilized or only increased slightly, with the maximum dose being 650 micrograms/day. The most serious complications were two drug overdoses which took several days to clear up and were due to malfunctions of an earlier pump model. Baclofen clearance from the cerebrospinal fluid occurs with a half-life of 5 hours. The most serious concern in maintaining patients indefinitely on intrathecal baclofen is whether drug tolerance will eventually occur

Abstract: We studied the effect of the intrathecal infusion of baclofen, an agonist of gamma-aminobutyric acid, on abnormal muscle tone and spasms associated with spinal spasticity, in a randomized double-blind crossover study. Twenty patients with spinal spasticity caused by multiple sclerosis or spinal-cord injury who had had no response to treatment with oral baclofen received an intrathecal infusion of baclofen or saline for three days. The infusions were administered by means of a programmable pump implanted in the lumbar subarachnoid space. Muscle tone decreased in all 20 patients (mean [+/− SD] Ashworth score for rigidity, from 4.0 +/- 1.0 to 1.2 +/- 0.4; P less than 0.0001), and spasms were decreased in 18 of the 19 patients who had spasms (mean [+/− SD] score for spasm frequency, from 3.3 +/- 1.2 to 0.4 +/- 0.8; P less than 0.0005). Tests for motor function, neurologic examination, and assessments by the patients correctly indicated when baclofen was being infused in all cases. All patients were then entered in an open long-term trial of continuous infusion of intrathecal baclofen. During a mean follow-up period of 19.2 months (range, 10 to 33), muscle tone has been maintained within the normal range (mean Ashworth score, 1.0 +/- 0.1) and spasms have been reduced to a level that does not interfere with activities of daily living (mean spasm score, 0.3 +/- 0.6). No drowsiness or confusion occurred, one pump failed, and two catheters became dislodged and had to be replaced. No infections were observed. Our observations suggest that intrathecal baclofen is an effective long-term treatment for spinal spasticity that has not responded to oral baclofen

Abstract: Significant advances in the medical and surgical treatment of spasticity have occurred over the last decade. These improvements in treatment and the previous work on which they are based are presented. In particular, Foerster’s pioneering observations and the neuropharmacology of antispastic drugs are discussed

Abstract: A total of 66 consecutive patients with severe spasticity of spinal cord origin were screened with intrathecal baclofen, and all but two responded with a two-point decrease in their Ashworth spasticity scale and/or spasm scale score. Of these, 62 elected to receive chronic intrathecal baclofen administration by means of an implanted delivery system. These patients have been followed for an average of 30 months (the first three for 81 months). Intrathecal baclofen has been well tolerated and all serious side effects were transient and have been
managed by dose adjustments. The pump presently available has worked safely; the only problem has been stalling in 7% of these devices. The catheter system has had to be repaired in just over one-half of the patients and is the main cause of interruption of drug delivery. Of the 62 patients implanted, 52 (84%) continue to be treated adequately for spasticity; there are three poor long-term responders, four deaths due to underlying disease, and three whose participation has been voluntarily withdrawn. It is suggested that long-term control of spinal spasticity by intrathecal baclofen can be achieved in most patients.

Abstract: To test the efficacy of intrathecal baclofen in various movement disorders, 18 patients with dystonia, head trauma, cerebral palsy, rigidity, or painful spasms underwent a trial of intrathecal baclofen. Ten went on to permanent implantation with an infusion pump to provide long-term treatment. Patients with a component of spasticity, painful spasms, or focal dystonias did best, and no response was seen in patients with rigidity due to anoxic encephalopathy. A videotape of responses is provided.

Abstract: A prospective study of intrathecal catheter reliability was performed at Rush-Presbyterian-St. Luke’s Medical Center. All 102 patients who had baclofen administered chronically for spasticity via an implanted drug pump were included. Sixty percent of the patients had no catheter complications; the remaining patients had one to five complications over their course of treatment. Survival analysis demonstrated a steady rate of malfunction up to 80 months, with the mean time to first failure recorded at 20 months. Kinks, holes, breaks, dislodgments, and disconnections were the most common complications. On the basis of their research the authors conclude that the thin-walled silastic catheter does not perform well and that larger, thick-walled catheters should be used.

Abstract: Young animals are resistant to organophosphate-induced delayed neuropathy (OPIDP), although biochemical changes on Neuropathy Target Esterase (NTE) caused by neuropathic organophosphorus esters (OP) are similar to those observed in the sensitive hen. We report here that the resistance of chicks to single doses of neuropathic OPs is not absolute because ataxia was produced in 40-day-old chicks by 2,2-dichlorovinyl dibutyl phosphate (DBDCVP, 5.0 or 10.0 mg/kg s.c.) and by diisopropyl phosphorofluoridate (DFP, 2.0 mg/kg s.c.). However, the clinical picture was different from that usually seen in hens; spasticity and complete recovery being the main features. alpha-Tolyl sulphonyl fluoride (PMSF, 300 mg/kg s.c.) promoted both DBDCVP neuropathy (5.0 or 10.0 mg/kg s.c.) and non-neuropathic doses of DFP (1.5 mg/kg s.c.) or DBDCVP (1.0 mg/kg s.c.). The lowest promoting dose of PMSF given 24 hr after 1.5 mg/kg of
DFP was 30 mg/kg. Higher doses had a more severe effect but no further increase of OPIDP severity was obtained with doses ranging from 90 to 300 mg/kg. PMSF (30 mg/kg) protected 40-day-old chicks from subsequent doses of neuropathic OPs even when a promoting dose of PMSF followed. At 60 days of age, chicks' resistance to OPIDP decreased because lower doses of neuropathic OPs became effective and, similarly to hens, PMSF did not fully protect from subsequent promotion. In 40-day-old chicks the threshold of NTE inhibition for OPIDP development was 95-97% (DBDCVP 5.0 mg/kg). When promotion followed initiation, the minimal effective inhibition of NTE for initiation by neuropathic OPs was about 90%. In 36-day-old chicks, PMSF (300 mg/kg) promoted OPIDP when given up to 5 days after DFP (1.5 mg/kg) when residual NTE inhibition in brain and sciatic nerve was about 40%. We conclude that chicks' resistance to OPIDP might reflect either a less effective initiation by phosphorylated NTE or a more efficient repair mechanism or both, and also that promotion is likely to involve a target other than NTE.


Abstract: BACKGROUND: Baclofen, a lipophilic analog of gamma-aminobutyric acid, is clinically used to control spasticity. We report a mass exposure to baclofen in adolescents seeking intoxication; toxicokinetic data are included.

CASE SERIES: A group of adolescents became symptomatic after ingesting 3 to 30 20-mg tablets of baclofen during a party at a suburban Boys' Club. Several children were noted to be very lethargic by chaperones, ingestion was suspected, and paramedics were called. Some white tablets were found in a couch at the site of the party. The Massachusetts Poison Control Center was called, and the tablets were identified as baclofen (20 mg). Fourteen patients were taken to local hospitals; 9 required intubation. Eight adolescents were transferred to our institution. In these 8 patients, symptoms were noted within 1 to 2 hours after overdose. The most common clinical findings included coma (7), hypothermia (6), bradycardia (5), hypertension (4), and hyporeflexia (8). Mean length of mechanical ventilation was 40 hours. Three patients had unifocal premature ventricular contractions. Two patients had tonic-clonic seizures. A single dose of activated charcoal was given to all patients. Drugs administered included nifedipine (1), flumazenil (1), naloxone (1), lorazepam (2), and phosphenyton (2). All patients recovered and were discharged home within 5 days of ingestion. Serial serum baclofen levels were obtained in all intubated patients (range, 0.049 to 6.0; normal, 0.08 to 0.40 microgram/mL). Levels obtained 14 hours after ingestion showed a linear correlation with length of mechanical ventilation (R² = 0.9863). Persistent symptoms were noted in some patients, despite nondetectable baclofen levels. Toxicologic screening for drugs of abuse was negative except in 2 patients with ethanol levels, both < 5 mg/dL.

CONCLUSION: Baclofen overdose may result in coma, apnea, autonomic disturbances, cardiac conduction abnormalities, and seizures. Levels obtained shortly after overdose correlate with length of mechanical ventilation.
Abstract: It is now known that there are at least two types of cannabinoid receptors. These are CB1 receptors, present mainly on central and peripheral neurones, and CB2 receptors, present mainly on immune cells. Endogenous cannabinoid receptor agonists (‘endocannabinoids’) have also been identified. The discovery of this ‘endogenous cannabinoid system’ has led to the development of selective CB1 and CB2 receptor ligands and fueled renewed interest in the clinical potential of cannabinoids. Two cannabinoid CB1 receptor agonists are already used clinically, as antiemetics or as appetite stimulants. These are D₉-tetrahydrocannabinol (THC) and nabilone. Other possible uses for CB1 receptor agonists include the suppression of muscle spasm/spasticity associated with multiple sclerosis or spinal cord injury, the relief of chronic pain and the management of glaucoma and bronchial asthma. CB1 receptor antagonists may also have clinical applications, e.g. as appetite suppressants and in the management of schizophrenia or disorders of cognition and memory. So too may CB2 receptor ligands and drugs that activate cannabinoid receptors indirectly by augmenting endocannabinoid levels at cannabinoid receptors. When taken orally, THC seems to undergo variable absorption and to have a narrow 'therapeutic window' (dose range in which it is effective without producing significant unwanted effects). This makes it difficult to predict an oral dose that will be both effective and tolerable to a patient and indicates a need for better cannabinoid formulations and modes of administration. For the therapeutic potential of cannabis or CB1 receptor agonists to be fully exploited, it will be important to establish objectively and conclusively (a) whether these agents have efficacy against selected symptoms that is of clinical significance and, if so, whether the benefits outweigh the risks, (b) whether cannabis has therapeutic advantages over individual cannabinoids, (c) whether there is a need for additional drug treatments to manage any of the disorders against which cannabinoids are effective, and (d) whether it will be possible to develop drugs that have reduced psychotropic activity and yet retain the ability to act through CB1 receptors to produce their sought-after effects. Copyright Copyright 1999 S. Karger GmbH, Freiburg

Abstract: Mammalian tissues contain at least two types of cannabinoid receptor, CB1 and CB2, both coupled to G proteins. CB1 receptors are expressed mainly by neurones of the central and peripheral nervous system whereas CB2 receptors occur in certain non-neuronal tissues, particularly in immune cells. The existence of endogenous ligands for cannabinoid receptors has also been demonstrated. The discovery of this endogenous cannabinoid system has been paralleled by a renewed interest in possible therapeutic applications of cannabinoids, for example in the management of pain and in the suppression of muscle spasticity/spasm associated with multiple sclerosis or spinal cord injury. It has also prompted the development of a range of novel cannabinoid receptor agonists.
ligands, including several that show marked selectivity for CB1 or CB2 receptors. This review summarizes current knowledge about the in vitro pharmacological properties of important CB1 and CB2 receptor ligands. Particular attention is paid to the binding properties of these ligands, to the efficacies of cannabinoid receptor agonists, as determined using cyclic AMP or [35S]GTPγS binding assays, and to selected examples of how these pharmacological properties can be influenced by chemical structure. The in vitro pharmacological properties of ligands that can potently and selectively oppose the actions of CB1 or CB2 receptor agonists are also described. When administered by themselves, some of these ligands produce effects in certain tissue preparations that are opposite in direction to those produced by cannabinoid receptor agonists and the possibility that the ligands producing such inverse cannabimimetic effects are inverse agonists rather than pure antagonists is discussed.


Abstract: Fifty-five children with cerebral palsy had multiple-level laminectomies for selective posterior rhizotomies for the relief of spasticity. They were followed up clinically and radiologically to assess their spinal stability and the possible development of post-laminectomy deformity of the spine. The majority of the deformities found were related to cerebral palsy and did not appear to be due to the laminectomy: 16% had scoliosis, 5% kyphosis, 7% lordosis, and 9% spondylolysis/spondylolisthesis. Spondylolysis is the only abnormality that appeared to be more common in this group than in children with cerebral palsy.


Abstract: The dihydropyridine Bay K 8644 exerts a positive modulation of Ca2+ channels. Administration of Bay K 8644 3-5 mg/kg i.p. to rats induces within 15 min a severe spasticity syndrome consisting of stiff tail, arched back, stretching and twisting of forelimbs and hindlegs and backwards motility and rolling over. The syndrome was effectively antagonized by nifedipine 3-30 mg/kg but not by the other Ca2+ channel blockers flunarizine, diltiazem and verapamil. Diltiazem even enhanced the spasticity. Diazepam 10-30 mg/kg i.p. completely blocked the spasticity whereas the other muscle relaxants (−)-baclofen and the beta-carboline ZK 93423 were completely inactive. These findings with Bay K 8644 suggest that spasticity may be caused by changed Ca2+ homeostasis.


Abstract: Ninety-two tibial nerve blocks with phenol were performed in 59 patients for treatment of severe spasticity of the foot. The Achilles tendon reflex was abolished, ankle clonus was eliminated and resistance to passive stretch was reduced substantially following the procedure in all patients. Significant functional gains were observed as a result of decrease in spasticity with long-
term follow-up averaging 28.7 months (range 14-60). The simplicity of the procedure, the functional results observed with long-lasting effects, and the lack of serious complications, would suggest the more widespread use of this procedure in the treatment of the spastic foot.


Abstract: Spasticity is a common neurologic condition in patients with multiple sclerosis, stroke, cerebral palsy or an injured spinal cord. Animal studies suggest that THC has an inhibitory effect on polysynaptic reflexes. Some spastic patients claim improvement after inhaling cannabis. We tested muscle tone, reflexes, strength and performed EMGs before and after double-blinded oral administration of either 10 or 5 mg THC or placebo. The blinded examiner correctly identified the trials in which the patients received THC in seven of nine cases. For the group, 10 mg THC significantly reduced spasticity by clinical measurement (P less than 0.01). Quadriceps EMG interference pattern was reduced in those four patients with primarily extensor spasticity. THC was administered to eight other patients with spasticity and other CNS lesions. Responses varied, but benefit was seen in three of three patients with "tonic spasms." No benefit was noted in patients with cerebellar disease.


Abstract: Chronic pleural effusion occurred in three patients, one of whom also developed acute pericarditis. A fourth patient developed both pleural and pericardial effusions. All patients had been receiving dantrolene sodium for at least two months. The pleural fluid was a sterile exudate with pleural and peripheral blood eosinophilia in all patients. No pulmonary parenchymal involvement was apparent. Pleural biopsy specimens showed nonspecific inflammation. Resolution of the pleural process was prolonged after dantrolene therapy was discontinued. Although a causal relationship between dantrolene and serosal inflammation remains unproved, this association in four patients warrants careful observation of others receiving long-term dantrolene therapy.


Abstract: PURPOSE: Botulinum toxin injection into the external urinary sphincter in spinal cord injured men with detrusor-sphincter dyssynergia has been reported. We expand the clinical use of botulinum toxin for a variety of bladder...
outlet obstructions and to decrease outlet resistance in patients with acontractile detrusor but who wish to void by the Valsalva maneuver. MATERIALS AND METHODS: Prospective treatment was performed for voiding dysfunction in 8 men and 13 women 34 to 74 years old. The reasons for voiding dysfunction included neurogenic detrusor- sphincter dyssynergia in 12 cases, pelvic floor spasticity in 8 and acontractile detrusor in 1 patient with multiple sclerosis who wished to void by the Valsalva maneuver. Using a rigid cystoscope and a collagen injection needle, a total of 80 to 100 units of botulinum A toxin (Botox) were injected into the external sphincter at the 3, 6, 9 and 12 o'clock positions.

RESULTS: Preoperatively 19 of 21 patients were on indwelling or intermittent catheterization. After botulinum A injection all but 1 patient were able to void without catheterization. No acute complications, such as general paralysis or respiratory depression, occurred and none of the patients had dribbling or stress urinary incontinence. Postoperative post-void residual decreased by 71% and voiding pressures decreased on average 38%. Of the 21 patients 14 (67%) reported significant subjective improvement in voiding. Followup ranges from 3 to 16 months, with a maximum of 3 botulinum A injections in some patients. CONCLUSIONS: Urethral sphincter botulinum injection should be considered for complex voiding dysfunction. Encouraging improvement without complications were seen in most of our patients. We have expanded the use of botulinum toxin to treat pelvic floor spasticity and also women

Abstract: A patient with dystrophia myotonica was given dantrolene sodium to try to provide muscle relaxation during a cholecystectomy. Dantrolene was used as it is accepted that the drug has a place in the control of spasticity and also causes muscle relaxation, whereas conventional muscle relaxants are unable to control myotonia of muscle origin. Dantrolene alone did not provide good enough intubating and operating conditions in this subject. Later studies showed that, after dantrolene, EMG recordings from the patient were not significantly altered, although an impression of a slight increase in the myotonic potentials was gained

Abstract: Dantrolene sodium or dantrolene1 is 1(5-(nitrophenyl)furfurylidend] amino) hydantoin sodium hydrate. It is indicated for use in chronic disorders characterised by skeletal muscle spasticity, such as spinal cord injury, stroke, cerebral palsy and multiple sclerosis. Dantrolene is believed to act directly on the contractile mechanism of skeletal muscle to decrease the force of contraction in the absence of any demonstrated effects on neural pathways, on the neuromuscular junction, or on the excitable properties of the muscle fibre
membranes. Controlled trials have demonstrated that dantrolene is superior to placebo in adults or children with spasticity from various causes, as evidenced by clinical assessments of disability and daily activities, and by muscle and reflex responses to mechanical and electrical stimulation. It is somewhat less effective in patients with multiple sclerosis than in those with spasticity from other causes. There has been a general clinical impression in controlled trials that dantrolene caused less sedation than would have been expected from therapeutically comparable doses of diazepam. In 2 controlled trials, there was no significant difference between dantrolene and diazepam in terms of reductions in spasticity, clonus, and hyperreflexia, but side-effects such as drowsiness and incoordination occurred significantly more frequently on diazepam. Long-term studies have indicated continuing benefit for patients taking dantrolene, though the incidence of side-effects has often been high and there has been a suggestion of exacerbation of seizures in children with cerebral palsy. Dantrolene may be of value in the medical treatment of spasm of the external urethral sphincter due to neurological and non-neurological disease, and animal studies suggest a potential use in the management of malignant hyperpyrexia. Chemical evidence of liver dysfunction may occur in 0.7 to 1% of patients on long-term treatment with dantrolene, with symptomatic hepatitis in 0.35 to 0.5% and fatal hepatitis in 0.1 to 0.2%. The drug commonly causes transient drowsiness, dizziness, weakness, general malaise, fatigue and diarrhoea at the start of therapy. Muscle weakness may be the principal limiting side-effect in ambulant patients, particularly in those with multiple sclerosis, and therapy could be hazardous in patients with pre-existing bulbar or respiratory weakness. The dosage of dantrolene has been fixed in most controlled trials, though long-term studies have indicated the need for individualisation of dosage. The initial dose is usually 25mg once daily, increasing to 25mg two, three or four times daily, and then by increments of 25mg up to as high as 100mg two, three or four times daily. The lowest dose compatible with optimal response is recommended.


Abstract: The purpose of this investigation was to determine what implications consistent presentation of food, delivered by an assistive feeding device at a position regarded as optimal, would have for the maintenance of food intake, duration of meals, and efficiency of eating. The trial employed an AB within-subjects design and extended over a 9-month period. Twenty children, aged 7 to 17 years, with severe neurological impairment and associated eating difficulties, were studied. The effects of the intervention were compared by examination of diaries recording the sizes and composition of meals consumed during designated periods and by precautionary measures of growth and weight. Although no statistically significant changes in weight were recorded overall, meals presented consistently were consumed less efficiently and sometimes more slowly than were standard ones, where food was presented by hand. However, no change occurred in the amount of energy and protein consumed,
which suggested that the children's ability to thrive was neither improved nor further compromised by participation in the study. The findings have implications for the way in which children are assisted during mealtimes by their caregivers.


Abstract: Flexor and extensor spasms associated with severe spasticity frequently cause pain and suffering in neurologically impaired patients, and greatly interfere with comfort and activities. When high doses of oral medications are necessary to keep the symptoms under control and are poorly tolerated, the long-term spinal-selective intrathecal infusion of baclofen by means of implanted drug pump and catheter is a safe, efficient and reversible alternative to destructive surgical procedures. Between September 1991 and March 1995, intrathecal baclofen was infused in 18 selected patients out of a series of 42 severely disabled spastic cases. We report here our preliminary experience with the criteria of selection, the initial intrathecal bolus test and the long-term benefit of the selected patients. Our results confirm the dramatic immediate and long-term benefit reported in other series. After a period of treatment of 1 to 42 months, 13 patients had a complete disappearance of their spastic symptoms without any oral treatment, one patient kept unchanged clonus despite the use of low-dose oral treatment and another one a severe, not improved dysuria although in both of them hypertonia and spasms were abolished. Finally, 2 patients had important joint stiffness slightly impairing the benefit from the treatment. None of the 18 patients had central side-effects related to baclofen. With time, a slight increase in daily dose (inferior to 10%) was necessary in most patients.


Abstract: Malignant hyperthermia developed in the 94th minute of anesthesia undergone by a nearly 5-year-old girl. Two minutes after re-filling the halothane vaporizer, muscle rigor and tachyarrhythmia occurred. Massive myoglobinuria setting in on the day of operation reached its peak on the 1st postoperative day. Only following this were the highest CK activities to be recorded. CK-BB could not be detected at any time.


Abstract: Many therapeutic effects of benzodiazepines are mediated by neuronal high-affinity binding sites, i.e. benzodiazepine receptors (BR), located on GABAA
receptors. Recently, endogenous BR ligands have partially been identified which, as agonists, either increase or, as inverse agonists, decrease GABAergic inhibition in the brain. BR antagonists, previously described as intrinsically inactive, induce effects in animals and humans under particular circumstances emphasizing a functional relevance of endogenous BR ligands. Several brain disorders, e.g. anxiety, insomnia, epilepsy, spasticity, alcoholism, coma, dementia, may be associated with a disequilibrium of opposing endogenous BR ligands changing the excitability of neurons implicated in aforementioned diseases. It is proposed that, depending on the relative role endogenous BR ligands play in the pathophysiology of these disorders, BR antagonists might demonstrate a variable efficacy in improving their symptomatology. In fact, such therapy would restore the homeostatic balance among various endogenous BR ligands being disturbed during an illness.

Abstract: During the past year observations have been published that might lead to further improvement in the design of future clinical trials. At the same time, results of clinical trials have become available that suggest that a number of treatments could be of benefit in the care of patients in the various phases of multiple sclerosis. Future multiple sclerosis clinical trials should involve a blinded investigator restricted to assessing the clinical outcome variables, and because current evidence suggests that magnetic resonance imaging gives an objective and sensitive reflection of the biological evolution of the disease, such scanning should also be included. The use of a composite outcome variable in a trial of chronic progressive multiple sclerosis should also be considered in order to increase the percentage of patients reaching the clinical endpoint. In 1994 recommendations were published for the selection of relapsing-remitting patients for treatment with interferon beta-1b; furthermore, large and well performed clinical trials demonstrated that interferon beta-1a and copolymer-1 are also partially effective, though not curative, for these patients. Two smaller studies suggested that low-dose methotrexate and cladribine might have a beneficial effect on the course of the disease in patients with secondary chronic progressive multiple sclerosis, the former drug probably being less toxic. Unfortunately, therapeutic perspectives for patients with primary progressive multiple sclerosis are less promising at present. Several studies suggest that 4-aminopyridine and tizanidine have therapeutic potential for symptomatic treatment; the former by improving neurological deficits, the latter by relieving troublesome spasticity. (ABSTRACT TRUNCATED AT 250 WORDS)

Popovic P., Popovic V., and Schaffer R. (1976) Recovery from experimental paraplegia after levodopa administration. Acta Neurochir. (Wien.) 35, 141-147. Abstract: In decompression sickness and during some surgical procedures, air emboli that form sometimes cause serious damage if the gas bubbles find their way to the vital organs. Paralysis of the spinal cord is one of the most serious manifestations induced by air emboli. Exposure to compression chambers is...
effective in air emboli treatment, but availability of chambers is inadequate and the treatment is lengthy. Until now there has been no fully effective injectable agent that can remedy the damage caused by air embolization. In this work levodopa was chosen as an injectable drug that might help to improve recovery from experimental paraplegia because of the reported effects of levodopa on muscle tone, spasticity and locomotion. To induce air emboli, the descending aorta of rats was chronically cannulated. Two weeks later, after full recovery from surgery, air was injected through the chronically implanted cannula into unanesthetized rats (0.35 ml of air per 100 g, during 4 sec). The paraplegia (paralysis of both hind legs) was manifested 2-10 minutes later. Only animals that had total paraplegia, without any sensation, were used in the experiments. Levodopa was administered 2 minutes after paraplegia was established. The levodopa treatment was repeated each day during one week. After six days, ten levodopa treated (intra-arterially) animals in a group of twelve and six levodopa treated (intraperitoneally) animals in a group of eight recovered completely from paraplegia. In control groups only three from thirteen (untreated), or two from twelve (solvent administration) animals recovered from paraplegia.


Abstract: OBJECTIVE: The purpose of our study was to analyse and evaluate the costs of continuous intrathecal baclofen administration as a modality in the treatment of severe spasticity in the Netherlands. DESIGN: A cost analysis was conducted as part of a prospective, multicentre, multidisciplinary, randomised and placebo-controlled clinical trial. The study covered the period from December 1991 to September 1995. The data on medical consumption and costs were collected over a 3-year period from different sources: administrative databases of health insurance companies, hospital registries and a patient survey. These data were structured by means of a flowchart analysis of the medical decision-making by specialists and general practitioners (GPs). They included data on in- and outpatient care, home care and care in nursing homes. The cost analysis was conducted using data from 18 patients included in the trial and from 15 so-called ‘match’ patients. The latter group are patients with comparable diseases leading to spasticity and living in comparable circumstances. Next to absolute costs (direct and indirect) of care and treatment for the 2 groups of patients, cost differences between the 2 groups were considered (differential cost analysis). SETTING: Per patient cost data, collected prospectively for 2 years during the phase of clinical evaluation, and retrospectively 1 year before implantation. The data were collected on patients from in- and outpatient care, home care and care in nursing home settings. PATIENTS AND PARTICIPANTS: The trial patients (8 men) had a mean age of 46 years; 11 patients had multiple sclerosis and 7 patients had spinal cord injuries. The match patients (7 men) had a mean age of 48 years; 9 patients had multiple sclerosis and 6 patients had spinal cord injuries. INTERVENTIONS: Trial patients were treated with a subcutaneously implanted...
programmable continuous infusion pump (SynchroMed, Medtronic), filled with baclofen (a muscle relaxant) to treat patients with chronic disabling spasticity who did not respond to a maximum dose of oral baclofen, dantrolene and tizanidine. **MAIN OUTCOME MEASURES AND RESULTS:** An analysis of hospital stay between both groups showed a significant difference during the implantation year. The average number of hospital days per patient in the year in the treated group was 31.5 days and in the match group was 18.7 days. Significant cost differences between both groups in the year that started with pump implantation and the following year can be attributed mostly to the costs of implantation of the pump and related hospitalisation days. The total costs of patient selection, testing, implanting the pump and follow-up amounted to $US28,473 for the first year. Savings must be taken into consideration as well. The savings of direct costs were due to withdrawal of oral medication (estimated annual total of between $US1950 and $US2800 per patient). Indirect savings on employment and nursing home costs, amounted annually to $US1047 and $US5814, respectively. Scenarios make it possible to consider policy consequences. The case of ‘extending’ the indications for this treatment to a larger population has been calculated and visualised. **CONCLUSIONS:** The costs of the therapy (continuous intrathecal infusion of baclofen) can be attributed mostly to implantation of the pump and related hospitalisation days. Savings originated from withdrawal of oral medication, job preservation and avoidance or delay of admission to a nursing home.


Abstract: A randomized double-blind dose-titration crossover trial of the safety and efficacy of oral fampridine-SR (sustained release 4-aminopyridine) was conducted on spinal cord injured (SCI) patients at two centers. Twenty-six patients (n = 26) with incomplete lesions completed the trial. These patients all had chronic (>2 years) and stable neurological deficits. They received fampridine-SR 12.5 and 17.5 mg b.i.d. over a 2-week treatment period, followed by a 1-week washout and 2 weeks of placebo, or vice versa. Patients reported significant benefit of fampridine-SR over placebo on patient satisfaction (McNemar's test, p2 < 0.05) and quality of life scores (p2 < 0.01). Sensory scores (p1 < 0.01), including both pin prick (p1 = 0.059) and light touch (p1 = 0.058), and motor scores (adjusted to reflect only paretic segments) (p1 < 0.01) all yielded evidence of benefit of fampridine-SR over placebo. The Ashworth scale of spasticity was significantly (p2 < 0.05) reduced when patients received fampridine-SR. There were no statistically significant benefits of the drug on measures of pain or bowel, bladder and sexual function, or functional independence. Side effects of lightheadedness and nausea were transient and trivial relative to efficacy, and approximately 30% of patients reported a wish to continue to use fampridine-SR. The clinical benefits most likely derive from the K+ channel blocking action of the drug. Potassium channel blockade enhances
axon conduction across demyelinated internodes and enhances neuroneuronal and neuromuscular transmission in preserved axons. These results provide the first evidence of therapeutic benefit of fampridine-SR in SCI patients


Abstract: Preclinical trials of intravenously administered 4-Aminopyridine (4-AP) have demonstrated transient improvements in neurological function in patients with longstanding spinal cord injury (SCI). The present report describes three patients with SCI who responded favourably in preclinical trials and who were subsequently administered oral (capsule) 4-AP (10 mg b.i.d. or t.i.d.) over a 4 month interval. The three patients (two male: 1 female) all had incomplete tetraplegia (ASIA levels C and D) with the neurological level of the lesion between C5-C7. Following the administration of 4-AP the patients demonstrated marked and sustained reductions in upper (n = 1) or lower extremity (n = 2) spasticity. Other clinical benefits of 4-AP were reduced pain (n = 1), restored muscle strength (n = 3), improved sensation (n = 2), voluntary control of bowel function (n = 1), and sustained penile tumescence (n = 2). The patients exhibited improved hand function (n = 1), enhanced mobility in transfers and gait (n = 2), with improved energy and endurance. Only trivial side effects (transient light-headedness) were observed. In one case, the enhanced neurological function allowed the patient to stand with support for the first time post injury (16 years). The time course of therapeutic response to the initial dose matched the pharmacokinetic elimination profile derived from serum and urine analysis. There was no evidence of renal or hepatic toxicity with prolonged use. These results indicate a therapeutic benefit of oral 4-Aminopyridine in the management of various neurological deficits in a select group of SCI patients


Abstract: Argininemia, a rare autosomal recessive urea cycle disorder, is caused by a deficiency of arginase, with resulting elevated plasma arginine and ammonia levels. Reports to date have focused little on the neurology of this disorder or the efficacy of treatments. A MEDLINE search revealed 25 previously reported cases, to which we have added two brothers who presented with late onset progressive spastic diplegia. Though their degree of enzyme deficiency was comparable, the severity of their phenotypic abnormalities differed substantially. With dietary therapy, both showed improved cognitive and motor function. Late metabolic crises occurred in both, resulting in death of the less severely affected brother. Based on analysis of our clinical database, we report on the full spectrum of neurologic abnormalities seen in argininemia with particular focus on the accompanying progressive spastic diplegia and its response to treatment; progressive decline in head growth; distinctive neuroradiologic findings; and life-
threatening later complications. Current and potential future therapies and long-term outcome are summarized.

Abstract: Epileptic seizures are a known complication of metrizamide myelography. To our knowledge, this is the first report of a case of nonconvulsive status epilepticus of the absence type following metrizamide myelography. There was symptomatic and electroencephalographic improvement after intravenous administration of antiepileptic drugs, and there was no neurological residual. Nonconvulsive status epilepticus should be considered when impairment of consciousness supervenes after radiographic procedures using metrizamide.

Abstract: The authors report their experience using dorsal longitudinal myelotomy in treating spasticity in 20 patients with complete spinal cord injuries. These patients suffered from severe painful flexor/extensor spasms that prevented them from wheelchair ambulation and/or their decubitus ulcers healing. All were receiving large doses of various oral drugs, including baclofen, which had failed to control their spasticity, and all underwent a modification of a posterior T-myelotomy as first described by Bischof. All 20 patients enjoyed immediate complete relief of their painful spasms, although two (10%) eventually experienced return of their spasms and are thus classified as long-term failures. Seventeen patients succeeded in markedly reducing, or being completely weaned from, their antispasmodic medications. In 11 of 14 patients, nonhealing decubitus ulcers subsequently healed with treatment. Bladder function was unchanged from the preoperative status in all patients. Chronic intrathecal baclofen infusion has recently been reported as an effective treatment of the spasticity of paraplegia. The results of this study, along with previous reports advocating dorsal longitudinal myelotomy, suggest that this approach is an efficacious alternative to chronic baclofen infusion in reducing spasticity for complete paraplegics. Considering the cost of the infusion pump, along with the fact that chronic intrathecal baclofen therapy necessitates long-term medical supervision, it appears that myelotomy is superior for this select group of patients who have no hope of regaining voluntary motor function.

Abstract: A case is reported of muscle 'gibrillation' following the administration of thiopentone and pancuronium to a patient suffering from metachromatic leucodystrophy and possible mechanisms are discussed.

Abstract: A 15-year-old boy suffered from progressive bilateral optic neuropathy of acute onset at the age of 10 years. Subsequently he developed spastic paraparesis and a predominantly motor type neuro-axonal neuropathy in all limbs. The basic error has been elucidated to be due to an unusual biotinidase Km variant with biphasic enzyme kinetics causing systemic biotin depletion and consequent multiple biotin-dependent carboxylase deficiency. After daily oral substitution with 10 mg biotin metabolic derangements subsided rapidly. Follow-up studies over one year after substitution with biotin demonstrated remarkable recovery from part of the previously present neuro-ophthalmological, motor and cognitive deficits. The previously extinguished flash-evoked visual potentials now showed clear responses after six months of substitution with biotin. In contrast with reports in literature, these findings indicated that neurological damage associated with biotinidase deficiency, rather than being permanent, is to some extent reversible.


Abstract: The medical treatment of spasticity has improved since the introduction of botulinum toxin type A (BTA) for intramuscular injection into spastic muscles. Two not directly comparable preparations are on the market: Botox and Dysport. Botox is four times as potent as Dysport. BTA is especially used for spasticity in legs, arms, and the paravertebral musculature. Surface analgesic cream is applied and an oral or rectal sedative is given after which BTA is injected locally according to strict instructions. In the motor end plate, BTA blocks the release into the synaptic cleft of acetylcholine from vesicles in the terminal nerve fibres, thereby bringing about paralysis of muscle fibre. Blockade lasts for about four months. The treatment must therefore be repeated. Because the treatment is local, side effects are few, mild, and acceptable.


Abstract: OBJECT: The goal of this study was to assess the long-term benefits of managing severe spasticity by using continuous infusion of intrathecal baclofen delivered via an implantable pump. METHODS: Eighteen patients with severe spasticity of cerebral origin, who failed to respond adequately to more
conservative treatments, have been treated with continuous infusion of intrathecal baclofen delivered via an implanted pump. Follow-up review of these patients has lasted between 12 months and 9 years. The patients have been assessed using a variety of tools. Seventeen have had a significant reduction in tone and all have benefited by a reduced need for nursing care or increased function or both. CONCLUSION: Long-term continuous infusion of intrathecal baclofen delivered via an implantable pump offers an effective method for dealing with otherwise intractable spasticity.


Reeves R.K., Stolp-Smith K.A., and Christopherson M.W. (1998) Hyperthermia, rhabdomyolysis, and disseminated intravascular coagulation associated with baclofen pump catheter failure. Arch. Phys. Med. Rehabil. 79, 353-356. Abstract: A 29-year-old man with C6 tetraplegia (ASIA A) using an implanted baclofen pump and intrathecal catheter infusion system for spasticity control developed severe spasticity, hyperthermia, hypotension, rhabdomyolysis, and disseminated intravascular coagulation after catheter disconnection. Tracheal intubation and mechanical ventilation were necessary. Extensive workup for a concurrent infection was negative except for urine cultures. The patient remained febrile for 10 days despite empirical antibiotic trials. Administration of high-dose benzodiazepines was inadequate for spasticity control. Spasticity control and his clinical condition, including body temperature, did not improve until his catheter was surgically replaced and intrathecal baclofen administration was resumed. The pharmacopathology of abrupt baclofen withdrawal and the similarities between this presentation, sepsis, neuroleptic malignant syndrome, and malignant hyperthermia are discussed. High-dose dantrolene was not used; however, based on similarities between this patient's presentation and neuroleptic malignant syndrome, it may have been the drug of choice.


Abstract: The influence of memantine on several properties of a neuronal cell line was tested. The aim was to get some insight into possible mechanisms of action of this drug which is therapeutically applicable in treatment of spasticity, Parkinson's disease, and cerebral coma. In neuroblastoma X glioma hybrid cells, memantine, at micromolar concentrations, blocked the depolarization induced by iontophoretically applied serotonin (5-hydroxytryptamine, 5-HT). In the hybrid cells, receptors of the 5-HT3 type mediated the depolarization, which was frequently accompanied by a series of action potentials. The inhibition by memantine of the serotonin response occurred fast and was completely reversible, irrespective of whether the cell showed a stable membrane potential or spontaneous action potentials. However, memantine did not alter spontaneous or electrically evoked action potential activity in the hybrid cells, and apparently did not block the underlying ionic conductances. Furthermore memantine did not affect either the cation permeability activated by substance P in the hybrid cells or the K+ channel triggered by bradykinin in a glioma cell line. Thus, memantine appears specifically to suppress the ion channel opened by serotonin in the hybrid cells. The interaction of memantine with serotonin receptors and the associated ion channels reported here, might give an important clue, as to a site of action of memantine in the nervous system.


Abstract: OBJECTIVE: To evaluate the efficacy of a combined treatment for spastic foot using selective injections of botulinum toxin (BTA) into the tibialis posterior muscle followed by ankle taping, and to compare it with current BTA treatment procedure. DESIGN: Single-blind randomized control trial. Three-month follow-up after treatment. SETTING: Neurorehabilitation clinic.

SUBJECTS: Eighteen outpatients with equinovarus foot due to severe spasticity after stroke. INTERVENTIONS: (1) Injection of 190 to 320 BTA U into several calf muscles (group A); (2) injection of 100 BTA U into the tibialis posterior muscle, followed by ankle-foot taping (group B). MAIN OUTCOME MEASURES: Ankle range of motion (ROM), Ashworth scale, gait velocity, and step length. RESULTS: Average Ashworth scores decreased 1 point in both groups, but the benefit appeared of shorter duration in group B. Changes in both foot position at rest and passive ankle ROM were observed in all patients, without treatment-related differences, except for gain in passive dorsiflexion that appeared higher in group A. Gait velocity and step length showed similar increases in both groups. CONCLUSION: The combination of selective injections of low BTA doses with ankle-foot taping is as effective as the injection of the current doses for the reduction of foot inversion with positive effects on gait parameters.

Abstract: Scarring around the electrically stimulating electrodes has been of concern since dorsal column stimulation was introduced. This concern resurfaced in the days of cerebellar electrodes and, with the advent of epidural stimulating techniques for the control of pain and spasticity, it again arises as a potential problem. We present a patient who underwent the placement of a C-2-C-4 electrode to treat torticollis; 3 months later, a mild spastic quadriparesis developed and the stimulation became ineffective. At reexploration, dense scar surrounded the electrode and confined the cervical spinal cord. With microdissection techniques, the scar was removed from the dura mater and the dura began to pulsate freely. The quadriparesis reversed. Examination of the scar tissue microscopically showed linearly arrayed fibroblastic nuclei, and we are uncertain whether the exuberant fibroblastic response is a response to electrical stimulation, the materials used in the electrode, or some technical aspects of the operation.


Abstract: We performed a double-blind study to measure the clinical and subclinical effects of an alternative medicine magnetic device on disease activity in multiple sclerosis (MS). The MS patients were exposed to a magnetic pulsing device (Enermed) where the frequency of the magnetic pulse was in the 4-13 Hz range (50-100 milliGauss). A total of 30 MS patients wore the device on preselected sites between 10 and 24 hours a day for 2 months. Half of the patients (15) randomly received an Enermed device that was magnetically inactive and the other half received an active device. Each MS patient received a set of tests to evaluate MS disease status before and after wearing the Enermed device. The tests included (1) a clinical rating (Kurtzke, EDSS), (2) patient-reported performance scales, and (3) quantitative electroencephalography (QEEG) during a language task. Although there was no significant change between pretreatment and posttreatment in the EDSS scale, there was a significant improvement in the performance scale (PS) combined rating for bladder control, cognitive function, fatigue level, mobility, spasticity, and vision (active group -3.83 +/- 1.08, p < 0.005; placebo group -0.17 +/- 1.07, change in PS scale). There was also a significant change between pretreatment and posttreatment in alpha EEG magnitude during the language task recorded at various electrode sites on the left side. In this double-blind, placebo-controlled study, we have demonstrated a statistically significant effect of the Enermed magnetic pulsing device on patient performance scales and on alpha EEG magnitude during a language task.

Abstract: OBJECTIVE: To investigate the benefits of the focal use of botulinum toxin in spasticity in the forearm seen after incomplete spinal cord injury. DESIGN: A single case study with standardized assessment before and at three-week intervals after injection. INTERVENTION: EMG-guided selective injection of botulinum toxin. SUBJECT: A 23-year-old man, 18 months post injury. MEASURES: Rivermead Motor Assessment; grip strength; Jebsen hand tests; visual analogue scale; Ashworth spasticity scale. RESULTS: Weakness was seen as expected with some functional losses, but the patient made gains in the areas of concern: shaking hands, typing, using the hand to drink. These gains were sustained at 12 weeks. CONCLUSION: Selective use of botulinum toxin to weaken muscles can lead to functional benefit


Abstract: Intrathecal application of baclofen is considered the treatment of choice in patients suffering from spinal spasticity insufficiently responding to conventional oral antispastic medication. This approach has also been used successfully in cases with spasticity of supraspinal origin. To achieve a good therapeutic response in the latter condition the amount of intrathecal baclofen has to be approximately twice the dosage required in spinal spasticity. We report on 8 patients suffering from supraspinal spasticity due to severe traumatic brain injury. Intrathecal baclofen reduced spasticity in all patients (mean Ashworth Score from 3.9 to 1.6; mean Reflex Score from 4.0 to 1.4). In some cases improvement of motor performance and in one case recovery of bladder function were noted. In two patients focal epileptic seizures with secondary generalization seemed to be associated with the application of baclofen. The local intrathecal application of baclofen has proven to be an effective therapy in otherwise intractable cases of severe supraspinal spasticity


Abstract: Response to oral and intramuscular emepronium bromide was assessed cystometrically in nine patients with urinary incontinence caused by an uninhibited bladder. Oral therapy had no effect, whereas intramuscular administration increased bladder capacity and significantly delayed the onset of bladder spasm and the desire to void. Plasma-propranolol response was delayed
and concentrations were reduced after an oral 40 mg dose of propranolol in 3 patients who had received oral emepronium bromide. These results indicate that although oral emepronium bromide had some anticholinergic effect--i.e., in reducing gastrointestinal motility--absorption of an oral dose was not sufficient for the bladder to be affected

Abstract: Baclofen is a central nervous system agent that is commonly used for the treatment of muscle spasticity in spinal cord injury patients. Acute withdrawal of this medication can induce the development of neurological symptoms, including seizure disorder, psychosis, hallucinations and visual disturbances. We report 3 cases of acute central nervous system symptoms that developed in spinal cord injury patients. Each patient had been chronically maintained on a baclofen regimen to control muscle spasticity. Symptoms developed shortly after baclofen therapy was interrupted following genitourinary surgery. It is important that urologists become familiar with the symptomatology of baclofen withdrawal, the methods of its prevention and the appropriate therapy should the syndrome develop

Abstract: A 38-year-old man with chronic low back pain underwent myelography and was inadvertently injected with ionic contrast medium. Within minutes, he started complaining of muscle spasms in his lower extremities, followed by respiratory distress and myoclonus. Immediate intravenous treatment with fluids, antihistamines, and supplemental oxygen was started. Within 1 hour after the myelogram, he was intubated and paralyzed with a neuromuscular blocking agent. Shortly thereafter, he began receiving triple anticonvulsant therapy and a lumbar drain was inserted to allow for the evacuation of cerebrospinal fluid. Electroencephalographic monitoring, which initially showed that the patient was in status epilepticus, subsequently showed no more episodes of seizure activity. Massive rhabdomyolysis, renal failure, and metabolic derangement were prevented. He was then extubated and regained full consciousness. He was discharged on the 13th day of hospitalization with mild amnesia and some cognitive dysfunction. A review of the literature reveals descriptions of 9 of 15 patients who survived similar episodes. We conclude that prompt identification of the contrast medium error and prompt intervention are crucial to increase significantly the chances of survival. Elective paralysis, anticonvulsant therapy, and cerebrospinal fluid drainage are the recommended modes of treatment

Abstract: The epidemiological, clinical, electrophysiological and nerve biopsy
findings of 3 cases of n-hexane neuropathy in shoe industry are reported. The disease affects more than 1 person working in the same environment, regardless of their specific role, and occurs in factories where standards of hygiene are low. In the most severe cases the picture of peripheral neuropathy is associated with symptoms suggesting a concurrent involvement of the central nervous system such as dysarthria, disproportionate ataxia of the gait, blurred vision, and sometimes, after the recovery of the peripheral neuropathy, appearance of leg spasticity. Light- and electron microscopic study of peripheral nerve biopsies shows that the toxic produces a primary axonopathy characterized by segmental swellings of the fibers, due to accumulation of filaments. Retraction of the myelin from the node and segmental demyelination are secondary to the axonal changes. Experimental models of hexacarbon neurotoxicity may offer an explanation for the anatomical substrate underlying the symptoms related to the involvement of the central nervous system.


Abstract: Nine children treated for acute leukemia or lymphosarcoma developed subacute encephalopathy starting with listlessness, depression and impairment of speech. Walking difficulties, ataxia, spasticity and sphincter disorders developed later. Transient intracranial hypertension and abnormal movements respectively developed in two patients. EEG frontal slow waves, raised CSF protein, abnormal white matter radioisotope uptake and CT scan hypodensity with patchy contrast enhancement were evident at the onset. Later, dilated ventricles and calcification appeared in the younger patients. Post-mortem neuropathological studies of three patients disclosed predominantly perivascular myelin loss in areas of white matter necrosis, abnormalities of small vessels and numerous axonal swellings. The spinal cord showed secondary degeneration of the corticospinal tracts. Analysis of the aetiological factors in this series points to the prevailing danger of cranial radiotherapy, probably increased by the young age of patients and by associated drug administration.


Abstract: The relationship among tizanidine dose, plasma concentration, and antispastic action is linear in nature. Response to a given dose of this agent varies among patients, and determining the appropriate clinical dose requires individual titration.

Abstract: Postdural puncture cerebral spinal fluid (CSF) leak most often manifests as a postdural puncture headache (PDPH). The reported frequency in young children varies (1-4). Persistent CSF leak may also be present without PDPH. We present a case of postoperative nausea and vomiting resulting from a presumed lumbar CSF leak in a nonverbal child after surgical placement of a permanent intrathecal catheter. Treatment with an epidural blood patch (EBP) via the caudal approach resulted in complete relief of symptoms.


Abstract: Continuous intrathecal baclofen infusion via a subcutaneously implanted programmable pump has been used in the treatment of severe spasticity. Improvement classically concerns the neurological (hypertonia, spasms, hyperreflexia), urological (bladder function) and other clinically relevant outcomes, such as functional status of daily living. This short note reports on another effect of intrathecal baclofen on vasomotor disorders and cyanosis in the lower limbs, described in a patient with spastic paraplegia.


Abstract: INTRODUCTION. Severe spasticity, according to Lance’s definition, is a manifestation of superior motoneurone injury syndrome which is characterized by increased stretching tonic reflexes, osteotendinous hyperreflexia, and release of proprioceptive reflexes. Baclofen (a beta- 4 chlorophenyl derived from gamma-aminobutyric acid) was firstly administered by intradural route in humans by Penn and Kroin in 1985 for the treatment of severe spasticity of muscular and central origin. MATERIAL AND METHODS. We report the results obtained in eleven patients with severe spastic picture, six of medullar origin and five of central origin who were treated with intradural administration of baclofen using an implanted programmable continuous perfusion system (Synchromed 8611H). The age of patients ranged from 12 up to 58 years. Six were males and five females. The duration of the treatment ranged from a maximal period of 36 months to a minimal period of 12 months. The initial dose of baclofen varied from 50 micrograms/day to 144 micrograms/day. RESULTS. The better results were obtained in patients with spasticity of medullar origin. The most marked beneficial effects were the reduction of spasms elicited, or not, by external stimuli. In all cases the doses of baclofen had to be progressively increased, leading to a mean final dose of 235.6 micrograms/day, with a maximal dose of 480 micrograms/day and a minimal dose of 144 micrograms/day. CONCLUSIONS. Baclofen administered by intradural route is more effective than administered by orally and the required doses were lower. Intradural administration was effective even though the oral route was unsuccessful.

Abstract: Electromyographic (EMG) evidence of inappropriate muscle activity (IMA) in the cricothyroid (CT) and vocalis (V) (thyroarytenoid) muscles was correlated with clinical voice measures in 32 patients with spasmodic dysphonia (SD). Subjective voice rating and quantified fluency and laryngeal diadochokinesis measures were obtained prior to botulinum toxin (Botox) injection into the V muscles. Pre-Botox EMG was performed using a monopolar needle electrode. Each muscle was sequentially examined at rest, during vocal click, scale, sustained "E" at different pitches, and repeated "E" voicings for brief periods. A three point EMG severity scale was used to grade the amount of IMA seen in each muscle. EMG evaluation showed no evidence of lower motor neuron involvement but did reveal IMA in 81.3% of the subjects. There were no significant correlations for the patients between different EMG-based IMA severity scales and the measures of voice quality and sound production. EMG did discriminate between predominantly adductor and abductor SD pattern types, but could not correctly differentiate a mixed SD group. Those patients with adductor SD displayed IMA in the V and CT muscles, while those with abductor SD displayed more IMA in the CT than the V muscles. Sequential EMG assessment of CT and V IMA in SD did not predict clinical severity or outcome following Botox injection into the V muscles

Abstract: OBJECTIVE: To assess the outcomes of botulinum toxin injection of spastic finger flexors followed by intensive training of finger extensors. DESIGN: Fourteen subjects with chronic hemiplegia spasticity of the upper limb had electromyographic-guided botulinum toxin injection into the long finger flexors. All patients presented with minimal active finger extension with the wrist flexed, sustained clonus of the finger flexors, functional proximal arm function, and absence of fixed contracture. Cadaver dissections directed selection of two injection sites: the flexor digitorum sublimis and the flexor digitorum profundus. Fifty mouse units of botulinum toxin were injected into each muscle. After injection, the subjects were instructed in a home program of stretching the long finger flexors, upper limb weight bearing with a weight-bearing splint, and exercise to improve finger extension control. RESULTS: Compared with preinjection measures, assessment the first week after the initial injection showed significantly reduced tone, reduced clonus, and greater active finger extension with the wrist in the neutral position. Four months later, the Ashworth scale increased to preinjection levels in the six subjects with repeated injections but was again decreased postinjection. Active finger extension with the wrist in the neutral position and clonus showed a statistically nonsignificant trend toward cumulative improvement after the second injection. CONCLUSION: The greatest change in finger extension and spasticity reduction occurred after the first injection. Continued significant improvement in finger extension was not observed
Abstract: Tropical myeloneuropathies include tropical ataxic neuropathy and tropical spastic paraparesis. These disorders occur in geographic isolates in several developing countries and are associated with malnutrition, cyanide intoxication from cassava consumption, tropical malabsorption (TM), vegetarian diets, and lathyrism. TM-malnutrition was a probable cause of myeloneuropathies among Far East prisoners of war in World War II. Clusters of unknown etiology occur in India, Africa, the Seychelles, several Caribbean islands, Jamaica, and Colombia. Treponemal infection (yaws) could be an etiologic factor in the last two. Tropical myeloneuropathies, a serious health problem, are multifactorial conditions that provide unsurpassed opportunities for international cooperation and neurologic research.


Abstract: Clonidine is being used increasingly for treatment of spasticity in patients with spinal cord injury. Though hypotension, dry mouth, and constipation are well-documented possible adverse effects, the possibility of clonidine-induced bradycardia is less well recognized and is rare. This report describes a patient who developed spasticity following a traumatic spinal cord injury. After clonidine was initiated, the patient’s spasticity improved. However, he developed significant bradycardia. Once clonidine was discontinued, the resting heart rate returned to normal. This case illustrates an unusual adverse effect of clonidine. Possible mechanisms by which clonidine decreases spasticity are described, probable mechanisms of induced bradycardia are reviewed, and specific treatment recommendations for the use of clonidine in spinal cord injured patients are presented.

Roshchin V.A. (1985) [Evaluation of the local effect of the magnetic field on the human body in laboratory studies]. Gig. Tr. Prof. Zabol. 33-36.


Abstract: The effects of magnesium glycerophosphate oral therapy on spasticity was studied in a 35-year-old woman with severe spastic paraplegia resulting from multiple sclerosis (MS). We found a significant improvement in the spasticity after only 1 week from the onset of the treatment on the modified Ashworth scale, an improvement in the range of motion and in the measures of angles at resting
position in lower limbs. No side-effects were reported and there was no weakness in the arms during the treatment.


Abstract: Baclofen (25 to 60 mg per day) and diazepam (10 to 40 mg per day) were evaluated for spasticity reduction in a double-blind, crossover study in 13 patients over a period of 19 weeks. Both drugs produced overall improvement and there was no significant difference in preference for one or other treatment. Side-effects, especially excessive daytime sedation, were more common in the diazepam group. In a companion baclofen long-term study, 18 spastic patients were treated with baclofen for an average of 4 years. Baclofen discontinuation in this group resulted in a worsening of spastic signs and symptoms in 16 patients, with no evidence of drug tolerance even after many years of baclofen therapy.


Abstract: Fourteen patients with spinal cord damage were treated with Ba-34647 (Lioresal, Ciba-Geigy), a new antispasticity drug. The treatment was initiated for excessive skeletal muscle spasticity and voiding difficulty. Seven of the patients had been wearing indwelling catheters and seven were catheter-free. The former were given trials at voiding after removal of catheters; the usual assistive methods common to most bladder training regimens were administered. Despite this, the trials were unsuccessful in reducing residual urine to acceptable levels. With addition of therapeutic doses of the drug without the training regimen, voiding trials were also unsuccessful excepting the response of one patient. The drug plus the training regimen was effective in reducing residual urine to acceptable levels in all patients. On discontinuing or decreasing the dosages of the drug, there was gradual but rapid build-up of residual urine despite the active training regimen. Restoration of effective dosage again led to satisfactory voiding function in all patients. The catheter-free group suffered from frequency, nocturia, and bed-wetting owing to excessive residual urine despite the employment of active training regimens. With addition of optimal dosages of Ba-34647, these problems were markedly reduced. They increased with drug discontinuation or dosage decrease and again improved upon restoration of effective doses. Bladder training, including active assistance to the expulsion of urine, is essential to the evaluation of antispasticity drugs for their effect on voiding.


Abstract: Twelve spastic patients with traumatic transverse myelopathies participated in a two-stage, double-blind crossover study using BA-34647 (a new experimental antispasticity drug by Ciba-Geigy) and placebo. Clinical
measurements of spasticity were performed before, during and after each stage. Six patients had excellent results receiving a regimen of BA-34647 but not when receiving placebo. Four patients had fair-to-good results with both BA-34647 and placebo. One patient had no significant changes when receiving either drug or placebo, the effective dose not being reached due to excessive body weight. One patient had a shortened trial due to pain and diminished function caused by excessive spasticity. Abrupt changes in post-treatment symptomatology (increase in spasticity) occurred in all six patients who demonstrated excellent results and in all four patients with fair-to-good results. In each of these cases, the increase followed the discontinuation of BA-34647. In no case was there an increase of spasticity following discontinuation of placebo. The effectiveness of an antispasticity drug may be too subtle to be perceived subjectively and objectively. The rebound phenomenon is evidence that a pharmacodynamic effect, though minor, was present.

Abstract: Sudden withdrawal of baclofen has been shown to provoke hallucinations. There has been no documented case showing hallucinations persisting during treatment over several years and responsive to subsequent reductions in dosage. Such a case is now reported. The chronicity of the symptoms originally suggested a psychotic illness, but this proved to be incorrect. The literature on baclofen toxicity is reviewed.


Abstract: Thirty-two patients with spasticity due to multiple sclerosis were entered into a randomized, double-blinded, placebo-controlled crossover trial of the gamma-aminobutyric acid agonist, progabide. Each patient was treated with a maximum of 45 mg/kg of progabide during each of two four-week treatment periods, separated by a two-week washout. Twenty-five participants completed the study; seven failed to complete the study due to adverse events. Progabide was associated with lessened spasticity. There was no loss of motor power associated with progabide. The physician, patients, and study nurse coordinator all declared preferences for progabide for treatment of spasticity. Ten participants (40%) chose to remain on progabide in an open, long-term follow-up protocol. Seven serious adverse events occurred. One consisted of fever and weakness without infection; the other six consisted of elevated aspartate aminotransferase and alanine aminotransferase levels, four of which were asymptomatic. All adverse events resolved entirely when the drug was stopped. Progabide is an effective antispastic agent and its antispastic effect is not accompanied by increased motor weakness. The use of the drug, however, is associated with a
high incidence of adverse events, which will likely limit progabide's therapeutic usefulness

Abstract: Pharmacotherapy plays an important part in the overall management of patients with multiple sclerosis. Most therapies directed at altering the natural history of the underlying disease process are only partially effective or are controversial or experimental. However, many effective symptomatic therapies are available to the clinician. The action and uses of corticosteroids in multiple sclerosis are discussed, and approaches to the treatment of spasticity, paroxysmal disorders, bladder dysfunction, cerebellar ataxia, neurobehavioral manifestations, fatigue, and acute and chronic pain in patients with multiple sclerosis are examined


Abstract: In spite of the different uses of the term "spasticity", hyperactivity of skeletal muscle stretch reflexes is the one common factor and we therefore need to know how this is produced by lesions within the central nervous system and what are its consequences to the initiation and execution of voluntary movement, not only initially but also chronically. The alpha motoneurone is directly responsible for the initiation of skeletal muscle contraction and final integration of excitatory and inhibitory nervous input normally takes place on its surface. In spasticity there is not only loss of descending direct excitatory and inhibitory control of motoneurones, but also loss of the control of spinal interneurones which would normally regulate (principally by inhibition) segmental spinal reflexes, including the stretch reflexes, especially those concerned with antigravity muscles. Gamma motoneurones may also have a reduction inhibitory control with consequent increase of muscle spindle sensitivity to stretch, and this may be further exaggerated by changes in the physical properties of affected muscles. The peripheral disorders of function are more accessible to study and to pharmacological and physical treatment, but with the increasing knowledge of inhibitory mechanisms and their pharmacology there is hope that some degree of influence may be possible within the central nervous system, by therapy with drugs that mimic or prolong the action of inhibitory transmitters

Abstract: The protective effects of pentobarbitone, hydroxydione and diazepam against acute and chronic toxicity of high-pressure oxygen (HPO) were studied in
rats. During exposure to hyperbaric oxygen body temperature was measured and ECG as well as EMG tracings from the diaphragm were obtained. Long term observations of animals after the exposure to HPO were conducted. Pentobarbitone and hydroxydione reduced the manifestations of acute toxicity but increased those of chronic toxicity. Diazepam reduced the manifestations of acute toxicity and seemed to counteract those of chronic toxicity. Lowering of body temperature of the animals which occurred during exposure to HPO was probably connected with manifestations of chronic toxicity. Observation of the cardiorespiratory functions suggested a possible connection between their disturbances and an onset of seizures and development of oxygen-induced paralysis.

Abstract: Baclofen (Lioresal) is a derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). It is used to treat spasticity particularly for the relief of flexor spasms, pain, clonus, and muscular rigidity. There have been many rare neurologic side effects reported with its use. These side effects, in particular, hallucinations and seizures, have been observed predominantly following precipitous withdrawal of the drug. We present a case demonstrating a muscular dyskinetic side effect when baclofen treatment was first initiated. The mechanism by which baclofen affects spasticity and how the resulting side effect of dyskinesia developed in our patient is not known. They are, however, most probably related to dopamine receptor hypersensitivity and the resulting imbalance of the dopaminergic/cholinergic systems. Clinicians should be aware of this additional adverse effect of muscular dyskinesia, with the use of baclofen, and its reversibility when baclofen is discontinued.

Abstract: Topical anesthesia was applied to the skin of the leg and thigh of a hemiparesis patient resulting from embolic infarction in the middle cerebral artery. After application of the anesthesia, the angular displacement of the ankle and knee joints measured during a full gait cycle showed a substantial shift towards normal. This response indicated a reduction in muscle spasticity which was confirmed by clinical tests. Neurophysiologic studies performed on the patient suggested that the reduction in muscular hypertonicity was mediated by reduced cutaneous inputs on the alpha - gamma motoneuron interaction. This conjecture is supported by studies of other investigators performed on animals as well as humans.

Abstract: The continuous spinal administration of baclofen has been shown to have therapeutic benefit in the management of spasticity in humans with
neuraxial injuries. The present study systematically investigated the potential spinal neurotoxicity of continuous intrathecally-infused baclofen in dogs. Male beagle dogs were prepared with chronic lumbar intrathecal catheters connected to subcutaneously implanted infusion pumps. Three groups of dogs received 28 days of infusion of saline (vehicle: 1 ml/24 hrs; N = 10), 200 micrograms/ml/24 hrs baclofen (N = 10) or 2000 micrograms/ml/24 hrs baclofen (N = 10). A mild, dose-dependent anti-nociception and muscle weakness was observed. Independent assessment of spinal histopathology in dogs sacrificed and perfusion fixed at 28 days of treatment revealed a mild fibrotic reaction to the catheter, but there were no changes distinguishable from vehicle infused animals which could be ascribed to any dose of intrathecal baclofen. Cisternal CSF protein and cells in samples taken at sacrifice were also not different for the three groups. These findings with chronic intrathecally administered baclofen in this dog model jointly support the lack of toxicity of chronic intrathecal baclofen at concentrations up to 2000 micrograms/ml.


Abstract: A double-blind, five-week, multicenter trial was conducted to compare the effect of baclofen, a unique amino acid derivative, with that of placebo in the treatment of 106 patients with spasticity secondary to multiple sclerosis. A spasticity assessment method that included a neurological examination, physicians' clinical impressions of changes during treatment, and a patient's self-evaluation was used to determine efficacy. This method showed baclofen (70 to 80 mg daily maximum, titrated) is effective relative to placebo in relieving symptoms of spasticity, such as flexor spasms, pain and stiffness, resistance to passive joint movements, and tendon stretch reflexes. Patient self-evaluation results also showed a significant reduction in clonus. Side effects were generally mild and transient.


Abstract: Ten patients with severe spasticity were evaluated according to a standardized protocol in order to be treated by intraspinal baclofen. Entry criteria in the protocol were the following: 1) Stable central nervous system lesion, 2) Severe spasticity and/or flexo-extensor spasms not controllable by oral treatment, 3) Normal CSF circulation and 4) Informed consent. All patients received a test dose of twenty-five micrograms of baclofen injected intrathecally. At intervals of at least one day, doses were increased in 10-25 microgram steps until total abolition of spontaneous spasms was achieved in complete spinal cord lesions. In patients with residual motor function, doses were titrated until the
optimal dose was found that reduced spasms and enabled performance of maximum daily life activities according to the patient's neurological level. In nine patients a multidose reservoir was implanted to deliver intrathecal baclofen. Effective dosage was 60 +/- 31 micrograms in the entire group. Ashworth score was reduced from 4.6 +/- 0.7 to 1.2 +/- 0.4 (mean +/- SD) (p less than 0.0001) and spasms from 3.2 +/- 0.8 to 0.2 +/- 0.4 (p less than 0.0001). Follow-up of the nine patients in whom a reservoir was implanted has been 18 +/- 9 months. Initial dosage requirements and tolerance were significantly different in complete (Frankel's A grade) or incomplete lesions (Frankel's B, C and D grades). Complete spinal cord lesions required a greater initial dose (156 +/- 43) than incomplete lesions (44 +/- 24), these differences being statistically significant (Student's t-test, p less than 0.05). Tolerance was observed only in patients with complete motor and complete sensory lesions. In incomplete lesions, dose increase was insignificant

Abstract: Case report of a 48-year-old man with a severe tetanus managed with conventional treatment associated with subarachnoid administration of baclofen. An epidural catheter was placed in spinal fluid at level L3- L4. Two injections of 1 mg baclofen at an interval of 1 hour amended the spasticity. Thereafter the treatment was maintained with a continuous infusion of 2 mg.24 h-1 over 20 days which resulted in an efficient control of spasticity. The final outcome was favourable

Abstract: The pharmacokinetic parameters in the CSF of baclofen given to 4 patients as an intrathecal bolus are reported. Considerable inter- individual variability in the parameters was observed. The elimination half-life ranged from 0.9 to 5 h and the clearance from 0.013 to 0.08 l.h-1. In order to optimize treatment, it is suggested that CSF baclofen levels be matched to changes in Hoffman's monosynaptic reflex (H reflex)


Abstract: In 19 patients, who suffered from severe spinal spasticity of different etiologies and did not respond sufficiently to oral antispastic therapy, intrathecal Baclofen test bolus were administered. In 11 patients a DAD (Drug Administration Device) [SynchroMedR Model 8611 H, Medtronic Inc. Minneapolis, USA] was implanted. Catheter dislocation or torsion was the most common complication to be observed in these 11 patients. Long term intrathecal Baclofen application was effective in all patients, as reducing spasticity, flexor spasms and spasm induced pain. In some cases the motor performance ameliorated


Abstract: Baclofen, a derivate of gamma-amino butyric acid (GABA), is known to be a useful drug in spasticity treatment. To achieve a good therapeutic response higher oral dosages have to be administered related with central side effects. Intrathecal application of Baclofen in microgram range dosages is proved to be effective in spinal spasticity. The efficiency of intrathecal Baclofen in patients suffering from supraspinal spasticity is discussed controversially. We report on 9 patients with long-term intrathecal Baclofen treatment, all of them responding well presenting a marked reduced muscle tone. In most cases an improvement of motor performance and in two cases improved bladder function was observed. The therapeutical dosages administered to patients with supraspinal spasticity exceed those administered to patients with spinal spasticity by approximately 100% without provoking central side effects. Despite the risks connected with this method it has to be considered as treatment of choice in cases of severe supraspinal spasticity

Saltuari L. and Frischhut B. (1992) [Treatment concepts of tertiary damage of the locomotor system after craniocerebral trauma]. Orthopade 21, 339-345.

Abstract: Brain injuries are the most frequent cause of handicap in young adults. The success of rehabilitation depends mainly on the avoidance of tertiary lesions of the locomotor system. Between January 1989 and December 1991, 54 patients were treated at the neuro-rehabilitation unit of the Neurology Department of the University Hospital for severe brain injuries. On admission these patients were in different stages of recovery. All patients underwent physiotherapy adapted to their specific needs. The decision as to whether other kinds of treatment were indicated depended on the patients’ problems in the recovery phase reached and on the presence or absence of tertiary lesions. In 14 patients, contractures caused by spasticity were successfully treated with plaster casts, which were changed weekly. These contractures were corrected sufficiently. In 5 other patients contractures, also caused by spasticity, were treated with regional anaesthesia administered through an implanted catheter system. In 11 patients a system for continuous intrathecal administration of Baclofen was implanted. Central side effects could be avoided while a lasting decrease of spasticity and
hyper-reflexia was achieved. Persisting tertiary lesions, such as contractures, dislocations and spinal deformities, were corrected surgically.


Abstract: Intrathecal baclofen infusion (IBI) is being used with increasing frequency in children to treat spasticity and dystonia. In this report, we summarize the clinical course of a 9-year-old boy with quadriplegic cerebral palsy with mixed tonal abnormalities (spasticity and dystonia) experiencing withdrawal from intrathecal baclofen. His clinical course is compared to that of adults experiencing withdrawal from IBI and to neuroleptic malignant syndrome. If unrecognized, this disorder may have significant potential for morbidity and mortality. Clues to diagnosis, appropriate evaluation, and potential treatments are discussed. When a child treated with IBI presents with unexplained multiorgan system dysfunction, particularly if accompanied by evidence of rhabdomyolysis, the integrity of the IBI system must be evaluated. In some cases, evaluation might necessitate surgical exploration. Caregivers most commonly seek urgent evaluation and treatment from their primary care provider when their child experiences fever or acute illness. Primary care providers of children treated with IBI should be made aware of this clinical scenario to prevent delays in diagnosis.


Abstract: INTRODUCTION AND OBJECTIVES: Positive outcome of patients with spastic cerebral palsy treated with botulinum toxin reported in the last three years has led us to perform this study with the aim to show our experience in the management of spastic cerebral palsy with the toxin, determine its indications, analyze the results and propose new possible indications in the future.

MATERIAL AND METHODS: We include 10 hemiplegic and 17 diplegic patients with an average age of 6 years and 7 months, followed up between 5 and 17 months. Clinical improvement was monitored using the PRS and EVFEL scales and articular motion range was measured 6 months before and after the injection while continuing physiotherapy. The injected muscles were adductor, hamstrings, triceps and posterior tibialis, and the doses were 1-2 U/muscle/kg body weight.

RESULTS: The values on PRS improved an average of 24%, adductor angle 66% (p < 0.01), knee angle 40% (p = 0.05) and ankle angle 52% (p < 0.01); 96% of patients could get more physiological static or walking patterns because of the decrease of spasticity and those persisted after the effect of the toxin had worn off. It was maximum at 2 months, stabilized 4 to 6 months later and decreased during further 2 months. CONCLUSIONS: This experience leads us to propose higher starting dosage and to take into account the stability of postural pattern of
each patient to choice the muscle to be injected. Other therapeutic possibilities are also proposed in children with fixed shortening e.g. combining the toxin with stretching casts

Abstract: Treatment of 27-year-old Black man with writer’s cramp with a combination of sodium valproate (Epilim) and baclofen (Lioresal) resulted in dramatic improvement of symptoms and signs. The possible mechanism of action of these drugs is discussed. This combination should be tried in the initial management of this syndrome

Abstract: Spasticity and flexor spasms can be most incapacitating in SCI victims. Muscle relaxants, physiotherapy and elimination of triggering factors must be tried before opting for peripheral surgery or alcohol block. The choice of alcohol block or peripheral surgery depends in whether damage to the spinal cord is complete or incomplete. Results of both the procedures are satisfactory in rightly chosen patients. Alcohol block is a simple, safe and effective method of treating spasticity in the patients of complete paraplegia. The effect is immediate and almost permanent. However, alcohol block is contra-indicated in the patients of incomplete paraplegia where peripheral surgery is a better choice

Abstract: Baclofen (beta-p-chlorophenyl-GABA) has been used in humans to treat spasticity, as well as trigeminal neuralgia. Since GABA (gamma-aminobutyric acid) has been implicated in inhibitory and analgesic effects in the nervous system, it was of interest to study the effect of baclofen in experimental neuropathic pain. With this purpose, experiments were carried out in 17 neuropathic rats with constrictive sciatic injury, as described by Bennet and Xie (1988), taking as pain parameters scratching behaviour and the latency to the thermal nociceptive stimulus. The results showed that baclofen induces, in a dose-dependent manner, significant decrease (p < 0.05) of scratching behaviour and significant increase (p < 0.05) of the latency to the nociceptive thermal stimulus. The absence of antagonism of naloxone suggested a non-participation of an opioid-mediated mechanism in this analgesic effect of baclofen on experimental neuropathic pain

Abstract: Severe and disabling spasticity frequently occurs in people with multiple
sclerosis and spinal cord injury. Approximately 30% of these people are treated with oral antispasmodic medications that do not provide adequate relief from spasticity (Hattab, 1980). Clinical trials with spinal stimulation and ablative neurosurgical procedures have not been as uniformly successful for controlling spasticity as has intrathecal baclofen injection (Kasdon, 1986). Delivered by an implantable programmable drug pump, intrathecal baclofen injection has proven to be successful in treating individuals with intractable spasticity. Significant reduction in muscle tone and frequency of spasms have contributed to improved function with activities of daily living, bladder management, overall comfort, and quality of sleep (Penn et al., 1989; Parke, Penn, Savoy, & Corcos, 1989). This article introduces an innovative therapy for controlling spasticity and discusses the nurse’s role in patient selection and management.

Abstract: Baclofen was used in a double-blind crossover placebo-controlled trial to treat spasticity in patients with multiple sclerosis (MS). While on Baclofen, patients obtained a significant (p less than 0.001) reduction in spasticity compared to controls. The drug was particularly effective in alleviating flexor and extensors spasms, as well as their associated pain. Side effects were common in this study, but were usually well tolerated by the patients. The commonest side effects were sedation, nausea and vomiting. There were no changes in hepatic, renal, or hematological function in any patients. Increase weakness due to loss of spasticity for support was also a fairly common complaint. The drug seems best indicated in patients in whom spasticity is not required for support or other activities of daily living. Careful monitoring of the patient is essential for effective use of this drug.


Abstract: Renshaw cells, which mediate the recurrent inhibition of spinal a-motoneurones, are activated by acetylcholine, both through motoneurone collaterals and the reticulo-spinal system. Since it is known that L-acetylcarnitine (L-AC) has central cholinergic effects, we tested in ten normal subjects and three spastic patients the ability of L-AC to induce changes in excitability of the Renshaw cells. These were activated by a conditioning monosynaptic reflex of the soleus muscle, evoked by electrical stimulation of the tibial nerve, and the resulting recurrent inhibition of the motoneurones was assessed by a subsequent monosynaptic reflex (H'). Recurrent inhibition was tested prior to, during and after an intravenous administration of a solution containing 2000 mg of L-AC. L-AC
administration proved to be able to induce in all subjects a decrease in the H'-reflex. This effect ensued approximately 30 min after onset of L-AC administration, reached the peak after 40 min and vanished in about one hour. The extent of the decrease in H' varied among subjects, being on the average 22% of the control values. A relationship was found between duration of L-AC administration and time for reaching the maximal effect. These results show that L-AC is able to decrease a-motoneurone excitability by increasing Renshaw cell activity, both in normal and spastic subjects.


Abstract: PURPOSE: Total colectomy and mucosal protectomy with ileal reservoir and anal pull-through is used in the treatment of ulcerative colitis or familial polyposis, with one complication being frequent bowel movements. A simple radiographic test to predict frequency of bowel movements and measure spasticity was evaluated. METHODS: Fourteen patients underwent evaluation after ileal reservoir and anal pull-through J-pouch construction. Barium sulfate suspension was instilled into the pouch via the anus in the standing position until reflux flowed into the small intestine proximal to the pouch and patients felt the urge to defecate. Total volume infused (VOLtot), volume to reflux (VOLrflx), and volume voided (VOLvoid) were measured. RESULTS: VOLvoid and the "voiding efficiency" (VOLvoid/VOLtot) correlated significantly with stool frequency (R=-0.744, P<0.002 and R=-0.754, P<0.002, respectively). Time from operation was correlated with VOLvoid and stool frequency (R=-0.723, P<0.003 and RO.573, P<0.032, respectively). CONCLUSIONS: The addition of quantitative measurements to this radiographic test gives useful information about pouch performance. Furthermore, the data imply that spasticity, as measured by voiding quantum and efficiency, rather than actual pouch volume is a major determinant of bowel movement frequency.


Abstract: The effects of dantrolene sodium and diazepam were compared in a
A double crossover study of 42 patients with spasticity due to stable multiple sclerosis. Both drugs reduced the findings of spasticity, clonus, and hyperreflexia, and the complaints of muscle stiffness and cramping. Each drug had different side effects which suggest indications and contraindications for its use in spastic patients.


Abstract: Botulinum toxin is known as a relatively safe and efficacious agent for the treatment of various neurologic and ophthalmologic disorders. Since dysphagia and deglutition problems combined with aspiration are often caused by spasticity, hypertonus, or delayed relaxation of the upper esophageal sphincter (UES), conventional treatment including lateral cricopharyngotomy was replaced by localized injections of botulinum toxin into the cricopharyngeal muscle (CM) in a series of 7 patients. The study comprised patients with slight dysphagia caused by isolated hypertonus of the UES, as well as patients with severe deglutition disorders, complete inability to swallow, and aspiration problems. Preoperative diagnostic evaluation included careful history-taking, physical examination, cineradiography, and esophageal manometry to exclude other causes of dysphagia. For precise localization, injections were performed under general anesthesia after location of the CM by direct esophagoscopy and electromyographic guidance. Injections were administered into the dorsomedial part and on both sides into the ventrolateral parts of the muscle. Depending on the severity of symptoms and the intraluminal pressure of the UES, the dose varied between 80 and 120 units (botulinum toxin A from Dysport). The treatment outcome was evaluated by a disability rating score: patients' complaints were scored by subjective and objective parameters before and after injection. All but 2 patients experienced complete relief or marked improvement of their complaints. There were no severe side effects or postoperative complications. Local botulinum toxin injection proved to be an effective alternative treatment to invasive procedures for patients with isolated dysfunction of the UES, and also for patients with more complex deglutition problems combined with aspiration.


Abstract: After major head trauma, a 28-year-old male patient developed tetraparesis with marked left-sided contractions of the leg adductors. Spasticity was resistant to antispastic drugs and intensive physiotherapy. Therefore, we injected 12.5 ng botulinum A toxin (Dysport) in the left adductor longus and adductor magnus. Eight measurements of the post-micturition residual urine of the bladder before botulinum-A-toxin administration gave no evidence for urinary retention. Between day 5 and 14 after injection we measured pathologically increased urinary volumes up to 130 ml at five different points of time. This case
report indicates possible subclinical side effects on the autonomic nervous system of the urinary bladder

Abstract: Pseudocholinesterase (E.C. 3.1.1.8) activity was measured in plasma of whole blood, bank blood, and several commercially available blood protein solutions by means of a colorimetric assay technique at 25 degrees C, pH 7.7, and with butyrylthiocholine as substrate (Merckotest- R No. 3337). Activity of whole blood was 5.79 plus or minus 0.20 U x ml-1, of bank blood 4.53 plus or minus 0.27 U x ml-1, and of two human serum solutions (Biseko-R, Seretin-R) 3.05 plus or minus 0.13 and 3.04 plus or minus 0.22 U x ml-1, respectively (mean plus or minus S.E.M.). The other blood protein solutions contained no clinically significant esterase activity. Since transfusion of blood plasma has been suggested for treatment of cholinesterase deficiency and postoperative suxamethonium-induced muscle paralysis, an in-vitro attempt was carried out to correlate the amount of plasma necessary and the rise of pseudocholinesterase activity in the recipient's blood: A large amount of blood has to be transfused to yield a comparatively small increase in esterase activity. Thus, considering the potential hazards of blood transfusion, this treatment does not seem to be advisable.

Abstract: We report a case of acute oculogyric crisis due to prochlorperazine administration in a young black woman with a concomitant viral infection. Neuroleptic medications are the most common cause of drug- induced acute dystonic reactions such as oculogyric crisis. Prochlorperazine is an antiemetic agent with a phenothiazine-type chemical structure and is known to cause dystonic reactions. Drug- induced acute dystonic reactions are most common in young adults and in men. Viral infections may also predispose patients to these adverse reactions. Caution is warranted when this drug is used in patients who have other risk factors for an acute dystonic reaction.

Abstract: The goal of this study was to try to determine the effects of the Botulinum A Toxin on the spasticity of the rhabdosphincter in 9 men with spinal cord injury and detrusor-sphincter dyssynergia. The cystometrygraphy, before and after the endoscopic injection of 100 units of Botulinum A Toxin, consisted of recording the bladder, urethral and rectal pressures with microtip transducers the anatomical position of which was radiographically controlled. The subjective and objective results of that study allow us to conclude that the Botulinum A Toxin has a place in the treatment of spinal injuries with detrusor- sphincter dyssynergia. Due to his blocking effect on the release of acetylcholine in the
motor nerve endings, the Botulinum A Toxin suppresses or decreases the spasticity of the rhabdosphincter and improves voiding. Although its relatively short living action (2-3 months) may require renewed injections, it has the advantage to hold off a surgical treatment such as a sphincterotomy and to give the patient another chance to reach a balanced bladder function secondary to the postinjection changes of reflexes which may have taken place between the bladder and the rhabdosphincter and vice versa.


Abstract: The loss of benefit from intrathecal baclofen, with increased spasticity and a discrepancy between the residual and the calculated volume content (underinfusion), made us suspect dysfunction of the intrathecal baclofen infusion in a paraplegic patient. Although all possible usual checking methods were used, no failure in the drug administration device (DAD) could be found. Despite some benefit from increasing the daily dose of baclofen, it has not been possible to control the spastic symptoms. Surgery was therefore decided upon, and a small leak at the end of the catheter tip was discovered. Surgeons and physicians should be aware that checking methods of DAD cannot exclude failure of the system. Their errors and limitations are discussed.


Abstract: In a 75-year-old man acute intestinal pseudo-obstruction was observed during treatment with baclofen 20 mg daily. After discontinuation of the baclofen he recovered completely. No other cause of intestinal obstruction could be demonstrated. Baclofen is an agonist of spinal GABA receptors. It is used in the treatment of spasticity caused by multiple sclerosis or other diseases of the spinal cord, in particular traumatic lesions. Physicians should be aware of this possible adverse effect of baclofen.


Abstract: Diazepam (0.4-4 mg/kg i.p.) reduced the spontaneous tonic activity in the electromyogram (EMG) recorded from the gastrocnemius-soleus muscle of spastic mutant Han-Wistar rats in a dose-dependent manner. The muscle relaxant effect of diazepam was antagonized by the benzodiazepine antagonists Ro 15-1788 (5 mg/kg i.p.), beta-CCM (2 mg/kg i.p.) and CGS 8216 (5 mg/kg i.p.), but not by EMD 41717 (50 mg/kg i.p.). These results add further support to the hypothesis that Ro 15-1788, CGS 8216 and beta-CCM do antagonize all pharmacological effects of benzodiazepines while EMD 41717 displays more selectivity in antagonizing the different actions of benzodiazepines.

Abstract: The action of delta-aminovaleric acid (AVA) on the muscle relaxant properties of baclofen, a GABAB receptor agonist, was investigated in two experimental models: (1) the pathologically increased muscle tone of the gastrocnemius muscle in spastic mutant Han-Wistar rats and (2) the Hoffmann (H)-reflex recorded from plantar foot muscles after electrical stimulation of the tibial nerve in barbiturate (60 mg/kg) anaesthetized rats. In both paradigms coadministration of AVA (500 nmol/5 microliter) antagonized the muscle relaxant action of intrathecally applied baclofen (0.2-2 nmol), but failed to affect the muscle relaxant effects of intrathecally injected muscimol (2-20 nmol). In contrast, coadministration of bicuculline (1 nmol) did block the muscle relaxant action of muscimol, but failed to alter the effects of baclofen. When administered alone, bicuculline (1 nmol), or AVA (500 nmol-2 mumol) were without intrinsic action in both paradigms. In an additional series of experiments we investigated the action of AVA on a supraspinal effect of baclofen. Coadministration of AVA (12.5 nmol/0.5 microliter) in the ventromedial thalamic nucleus antagonized the catalepsy induced by baclofen (ED50 10 pmol/0.5 microliter), as indicated by an increase in ED50 of baclofen by a factor of 4.835 and a parallel shift of the probit-log dosage regression line to the right. The parallel shift seems to be consistent with a competitive mechanism of action of AVA. This study presents evidence that AVA antagonizes central pharmacological actions of baclofen at both spinal and supraspinal sites without affecting the actions of a GABAA agonist, muscimol.


Abstract: The present study examined in vivo whether memantine exerts muscle relaxant activity via an antagonistic action at N-methyl-D-aspartate (NMDA) receptors. Intraperitoneal (i.p.) administration of memantine, 50-100 mumol/kg, reduced the tonic activity in the electromyogram recorded from the gastrocnemius muscle of spastic mutant rats. This effect was prevented by coadministration of NMDA. Memantine, while not affecting monosynaptic Hoffmann (H)-reflexes, depressed polysynaptic flexor reflexes in anaesthetized rats following i.p. (6.25-100 mumol/kg) or intrathecal (i.t., 10-500 nmol) administration. The latter effect was prevented by i.t. coadministration of NMDA, but not of alpha- amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA). These observations suggest that NMDA receptors might be involved in the mediation of the muscle relaxant activity of memantine.


Abstract: Intractable lower extremity spasms after spinal cord injury is a significant source of morbidity. A case of refractory spasticity in paraplegia was successfully converted to flaccid paraplegia by intrathecal injection of phenol and glycerin in metrizamide. This chemical rhizolysis is simple and effective, and the presence of metrizamide allows both fluoroscopic guidance for accurate intrathecal phenol placement and good miscibility with cerebrospinal fluid. A brief comparative review of alternative therapeutic modalities is presented.

Abstract: Implantable drug-delivery pumps are being developed to provide the external control of delivery rate or to deliver volumes of drug that are beyond the capabilities of conventional controlled-release formulations. The delivery of insulin to diabetics and chemotherapeutic agents to cancer patients represents the two major applications of such devices, but other applications (chronic pain control, Alzheimer’s disease, spasticity, etc.) exist or have been proposed. The most popular device is the Infusaid which is driven by a fluorocarbon vapor-liquid mixture to provide a constant delivery rate. Implantable peristaltic pumps have recently been developed to deliver drugs at variable rates according to a physician-preprogrammed schedule which is actuated with the aid of transcutaneous telemetry. Other devices are available in the literature, if not yet in clinical application.

Abstract: STUDY OBJECTIVE: To determine the effects of the long-term administration of 4-aminopyridine (4-AP) on sensorimotor function in humans with long-standing spinal cord injury (SCI). DESIGN: Randomized, open-label, active-treatment control, dosage-blinded study. SETTING: University-affiliated, tertiary-level care, Department of Veterans Affairs Medical Center. PATIENTS: Twenty-one healthy men and women outpatients suffering from traumatic SCI (14 tetraplegic, 7 paraplegic) for 2 years or more. INTERVENTIONS: Dosages of an immediate-release formulation of 4-AP were titrated. At 3 months, 16 subjects were receiving 4-AP 30 mg/day (high dose); 5 subjects were receiving 4-AP 6 mg/day (low dose) and served as an active-treatment control group. MEASUREMENTS AND MAIN RESULTS: Composite motor and sensory scores had statistically significant increases at 3 months. Maximal expiratory pressure, maximal inspiratory pressure, forced vital capacity, and forced expiratory volume in 1 second showed clinically meaningful and/or statistically significant increases among patients receiving 4-AP 30 mg/day. These subjects also had significant decreases in spasticity (modified Ashworth Scale). Serial biochemical profiles and electroencephalographs were unchanged from baseline, and no clinically significant drug toxicity was encountered. CONCLUSIONS: Long-term oral administration of immediate-release 4-AP was associated with improvement in and recovery of sensory and motor function, enhanced pulmonary function, and
diminished spasticity in patients with long-standing SCI. 4-Aminopyridine appears to be safe and relatively free from toxicity when administered orally over 3 months. Each patient who received immediate-release 4-AP 30 mg/day showed a response in one or more of the outcome measures.

Abstract: Nine patients (7 with amyotrophic lateral sclerosis, 1 with progressive spinal amyotrophy and 1 with chronic anterior poliomyelitis) were treated by sequential intravenous administration of 240 mg of TRH over one hour every two weeks. Results were assessed by an analytical evaluation of muscle strength before and 24 h after each infusion and by objective and subjective evaluation of spasticity. Significant improvement, as shown by statistical analysis, was noted in muscle strength in the 9 patients by 5 infusions over a 4-week period and a subgroup of 5 patients treated by 8 infusions over 10 weeks. Continued use of this therapy is justified by the need to determine its long-term effects and the psychological improvement noted in some patients after an even transient improvement in motor performance. However this treatment is obviously not curative.


Abstract: The paper is concerned with a study into the mechanisms of central restructures in formation of a new motor stereotype using functional biomonitoring (FBM) after different pharmacological exposures. There were 117 patients aged 5 to 14 years with spastic forms of infantile cerebral paralysis. Biomonitoring sessions were carried out with the aid of portable indicators. Pharmacological correction was performed by midocalm or galanthamine or by combining the latter one with ganglerone++. The treatment course consisted of 15 training sessions. To study the EEG structure, use was made of the method of computing conditional probabilities of one wave of the EEG, provided it was preceded by any other one. Analysis of the dynamics of the biorhythmical structure of the EEG revealed the common mechanism of restructuring the central components of movements regulation for all the patients' groups using FBM. That mechanism lay in a highly significant increase of interrelated correlations of the main components of the EEG to the alpha-component together with formation or gain of the "alpha-nucleus". The patients' group who underwent biomonitoring sessions after galanthamine and ganglerone administration manifested, as compared to the other groups, a highly significant transformation of teta- and delta-components to the alpha-frequency range and
enhancement of interrelation of teta-components in the "working" hemisphere. This was coupled with the most beneficial data on the patients' status


Abstract: Recurrent inhibition via Renshaw cells provides a mechanism by which spinal and supraspinal centers exert control over movement. The conditioned H-reflex technique of Pierrot-Deseilligny and Bussel permits noninvasive assessment of recurrent inhibitory pathways. We employed this technique to investigate changes in Renshaw cell activity due to nicotine (a potent CNS cholinergic agonist that excites Renshaw cells in animals) contained in inhaled tobacco smoke. In 10 normal subjects, cigarette smoking caused a large, rapid drop in the conditioned H-response amplitude, implying increased activation of Renshaw cells. The time course of the change in conditioned H-response amplitude closely approximated the known pharmacokinetics of inhaled nicotine. Nicotine administered via chewing gum had a much slower and less dramatic effect, probably due to the slower rise in blood levels with this mode of administration. Increased activity in Renshaw cells may contribute to spasticity in spinal cord-injured patients, raising the possibility that cigarette smoking could cause further increases in tone in such patients


Abstract: Clinical trials with tizanidine when administered alone have shown that 5-chloro-4-(2-imidazolin-2-ylamino)-2,1,3-benzothiodiazole (tizanidine) is safe and effective for spasticity control. However, given its mechanism of action and requirement for titration, clinical experience suggests that tizanidine is likely to be used in combination with other antispastic agents with different mechanisms of action, such as baclofen. The objective of this study was to examine the pharmacokinetics of both tizanidine and baclofen under steady-state conditions when administered alone or concomitantly. This was a randomized, three-period, multiple-dose, Latin Square design study consisting of tizanidine HCl, 4 mg t.i.d. for seven consecutive doses; baclofen, 10 mg t.i.d. for seven consecutive doses; and both regimens simultaneously for seven consecutive doses. Drug administration was performed every 8 h, three times daily. Fifteen normal men served as study subjects. A priori, a clinically significant difference was set as 30%. Concentrations of tizanidine and baclofen were nearly identical during the single and concomitant dosing periods. All of the calculated steady-state pharmacokinetic parameter changes for baclofen, tizanidine, and its major
metabolites were within the 30% criterion. Small differences in renal clearance were observed when the two drugs were coadministered, but these changes are unlikely to be clinically important. Thus, it is unlikely that coadministration of tizanidine and baclofen during dose-titration of the former will result in a pharmacokinetic interaction.


Abstract: A 60-year-old female was admitted because of intermittent fever, arthralgia, itching of whole body, pretibial edema, urinary incontinence, pain of both legs and gait disturbance, after an insect bite. On admission, she had fever of 38 degrees C, and nuchal pain and stiffness. Neurological examination revealed spasticity of lower legs and increased deep tendon reflexes of all extremities. Hyperesthesia and hyperalgesia were noted on C2-4 and L5-S5 areas. Leukocyte count was 10,100/mm3 and CRP was 2+. CSF showed no pleocytosis (3/mm3, lymphocyte), but total protein (50 mg/dl) and IgG (10.5 mg/dl) were increased. On T2-weighted images of brain MRI, multiple small high signal areas were shown. The symptom improved markedly by prednisolone, but 3 months later left lateral gaze palsy appeared abruptly. A demyelinating lesion of the pons to the medulla oblongata including the left paramedian pontine reticular formation was suspected, and a corticosteroid pulse therapy was very effective. Serum titer of anti- Borrelia burgdorferi-IgG antibody by indirect immunoperoxidase method was 400 x at first and 1600 x after 3 months. Neuroborreliosis was diagnosed, but high doses of intravenous penicillin were not effective, and an immune-mediated demyelinating mechanism was probably thought to play a role in the pathogenesis of neuroborreliosis.


Abstract: Fifteen patients with human T-cell lymphotropic virus type-I (HTLV-I)-associated myelopathy (HAM) were treated in an uncontrolled preliminary trial by oral administration of pentoxifylline (PTX). Motor function, neurological evaluation, immunological markers and parameters were evaluated after four weeks. In 13 of the 15 patients, motor disability, especially spasticity, improved substantially. PTX suppressed spontaneous proliferation of peripheral blood mononuclear cells in 14 of the 15 patients at four weeks. No adverse effect was observed. We concluded that PTX may be a safe and beneficial agent for the treatment of HAM.

Abstract: At the autopsy of a man, aged 21 years, who had suffered from spastic tetraplegia for 10 years, the distal 25 cm of the Pudenz low-pressure ventriculoatrial shunt was found in the pulmonary artery, partly adherent to and partly covered with intima. The site of the detachment was the connection at the entrance to the facial vein. It is mentioned in the literature that the entrance of the venous system is, indeed, the most common site of detachment. An x-ray film of the chest, taken 3 1/2 years previously, retrospectively disclosed the catheter at the same location as demonstrated at the autopsy, but it had been overlooked at the time. On the non-intima-coated parts of the catheter, fresh thrombotic material was found, and there was cor pulmonale. The cause of detachment may have been the long-standing spastic tension in the neck muscles

Abstract: The overall efficacy and tolerance of a new skeletal muscle relaxant DS 103-282 was evaluated by treating 10 patients with chronic spinal spasticity. Other agents such as baclofen, dantrolene sodium or diazepam had been only minimally beneficial in these patients. Treatment was started with DS 103-282 at a mean dosage of 7.4 mg. per day which was adjusted according to response up to 14.5 mg. per day at the end of the 8-week trial period. Objective rating assessments showed improvement in spasticity, medullary automatism and clonus. No changes were recorded in the reflex pattern nor improvement in disability scores. Only a few mild side-effects were reported, there was a noticeable absence of sedation, but reduction in systolic and diastolic blood pressure was noted in most patients. DS 103-282 appears to have demonstrable myotonolytic action and in view of its good tolerance it deserves further investigation

Abstract: In 1983, approximately 40 000 patients in France and 5 760 patients in Switzerland suffered from cerebral palsy, representing more than 0.1% of their respective populations. The functional disability of these patients is particularly impressive and emphasizes the medical, social and economic importance of this problem. The term cerebral palsy is restricted to non-progressive disorders of motor function, already observed at an early age and due to cerebral lesions. These motor disorders can be of paretic, dystonic and dyskinetic nature. Their epidemiology, classification, etiology, pathology, early diagnosis and evolution are extensively reviewed by Th. Deonna. The difficulty in evaluation of treatment is the absence of a generally accepted rating scale. G. Broggi has proposed one on the basis of a large experience which could serve in the future for more objective evaluation. This monograph is devoted to the functional neurosurgical
treatment of cerebral palsy. Physiotherapy and rehabilitation are part of the basic
treatment of cerebral palsy, and must be continued after any neurosurgical
treatment. Various conservative methods of treatment and their
neurophysiological rationale are mentioned by P. Claverie. Some technical
devices which improve the neurological deficits and facilitate rehabilitation are
presented. Radiculotomies and neurotomies are probably the oldest
neurosurgical operations for the treatment of spasticity. The neurophysiological
and neuroanatomical basis of this therapeutic approach are treated in the review
of the material from the neurosurgical department of Montpellier. Sixty cases
were collected and the results analysed according to the type of operation
(posterior radiculotomy, anterior radiculotomy, mixed) performed. Stereotactic
thalmotomies and subthalmotomies are believed to be the best neurosurgical
method to treat the tremor and improve other dyskinesias and hyperkinesias. The
technique and a personal review of 49 cases of cerebral palsy are presented.
The long-term follow-up in this study demonstrates that this type of operation
markedly improves the functional disability of patients with moderate
hyperkinesias, moderately improves patients severely affected, but also
demonstrates that possible side effects cannot be ignored. Review of the
literature indicates the difficulty in interpretation of results due to a lack of
objective evaluation. Nevertheless, stereotactic thalamotomy can still be
recommended when tremor and rigidity are the most prominent symptoms.
Stereotactic dentatotomies in the treatment of spasticity were very popular 20
years ago, but have been largely forgotten for nearly a decade.(ABSTRACT
TRUNCATED AT 400 WORDS)

Siegfried J. and Rea G.L. (1987) Intrathecal application of baclofen in the
Abstract: Baclofen, a derivative of g-aminobutyric acid (GABA) has been known
for many years to be a useful drug in the treatment of spinal spasticity. However,
when the spasticity is severe, the systemic administration has to be increased,
often without therapeutic effects but frequently with central side-effects. Baclofen
given intrathecally however, in microgram doses has been previously reported to
be effective and safe. A personal experience is reported of 9 severely spastic
patients residing in chronic care facilities who were treated from July 1984 to
March 1986 with intrathecal baclofen. The spasticity was causing significant
nursing care problems, and 6 patients were reduced to a completely bedridden
state. Each patient initially received a percutaneous intrathecal drug injection of
0.2-0.7 mg of baclofen to test its efficacy. A subcutaneous intrathecal system for
further injections was placed in 6 patients. In 3 patients a decreased level of
consciousness was observed. In the 3 cases of multiple sclerosis, intrathecal
baclofen resulted in significant reduction of spasticity for 24 to 48 hours after
each injection. The spasticity was improved in only one of the 2 cases of
posttraumatic paraplegia. The effect was not convincing in the 2 cases of spinal
cord tumour, and in the case of cerebral palsy the effect was improvement in
spasticity, but also significant drowsiness. Baclofen, in comparison with some
other drugs such as morphine or midazolam, also tried intrathecally by the
authors, is the most effective in reducing spasticity. Its use however warrants caution, for it can cause decreased consciousness, and there is currently no antagonist.

Siegfried J. and Rea G.L. (1988) Intrathecal application of drugs for muscle hypertonia. Scand. J. Rehabil. Med. Suppl 17, 145-148. Abstract: The literature regarding the intrathecal use of morphine, baclofen, and midazolam to treat spasticity is reviewed. Nine patients with significant spasticity due to different etiologies were treated. Morphine and midazolam decreased spasticity but did not change the patient's functional status. Baclofen improved patient status, but was associated with significant CNS depression in two cases.


Simon D.L., Carron H., and Rowlingson J.C. (1982) Treatment of bladder pain with transsacral nerve block. Anesth. Analg. 61, 46-48. Abstract: Fifteen patients with bladder spasticity and pain of three different etiologies were referred to the pain clinic by urologic specialists. These patients were refractory to all prior methods of treatment, excluding major surgical procedures. In a prospective study started in 1976, these patients were treated with transsacral nerve blocks using 0.25% bupivacaine and, in most cases, subsequent 6% aqueous phenol at the right S-3 ventral foramen. If indicated, transsacral nerve blocks were performed at other levels, as described in the text. Of the patients studied 53% have had significant or complete relief of pain for an average of 26.5 months. The associated morbidity was negligible and there was no mortality. This is in contrast to the morbidity and mortality associated with some major surgical “curative” procedures. The technique is proposed as a successful and economical approach to treatment that can be managed on an outpatient basis.

smooth muscle (SM) insufficiency are eliminated by serotonin, irrespective of whether it has been caused by the use of drugs or impaired smooth muscle innervation. The mechanism of vascular rhythmic oscillations in the microcirculatory bed, the so-called endogenous vasomotility (EV) has been decoded. The mechanism of EV regulation is due to the fact that platelets constantly (continuously) adsorb serotonin from the enterochromaffin cells of the gastrointestinal tract and constantly (continuously) release it into the microcirculatory bed, thereby providing the continuum of entry of the stimulant to the SM fibers which are able to contract at this time. The summation of these contractions of smooth muscle contractions in the microcirculatory bed maintains their vascular tone and yields the pattern of EV. The paper also describes the earlier unknown properties of hemoglobin and myoglobin to cause smooth muscle spasm and to accelerate platelet destruction. A correlation between the EV and vascular platelet hemostasis is described in terms of these properties. The continuous mechanism of EV is impaired and it transforms to intermittent (final) vascular platelet hemostasis.


Abstract: Spasticity is a disorder of excess muscle tone associated with CNS disease. We hypothesized that botulinum toxin, a neuromuscular blocking agent, would reduce tone in spastic muscles after stroke. This randomized, double-blind, placebo-controlled, multicenter clinical trial evaluated the safety and efficacy of botulinum toxin type A (BTXA) in the treatment of chronic upper limb spasticity after stroke. Thirty-nine patients received IM injections of a total dose of either 75, 150, or 300 units of BTXA or placebo into the biceps, flexor carpi radialis, and flexor carpi ulnaris muscles. At baseline, patients demonstrated a mean wrist flexor tone of 2.9 and elbow flexor tone of 2.6 on the Ashworth Scale (0 to 4). Treatment with the 300-unit BTXA dose resulted in a statistically and clinically significant mean decrease in wrist flexor tone of 1.2 (p = 0.028), 1.1 (p = 0.044), and 1.2 (p = 0.026) points and elbow flexor tone of 1.2 (p = 0.024), 1.2 (p = 0.028), and 1.1 (p = 0.199) at weeks 2, 4, and 6 postinjection. In the placebo group, tone reduction at the wrist was 0.3, 0.2, and 0.0 and at the elbow was 0.3, 0.3, and 0.6 at weeks 2, 4, and 6 postinjection. BTXA groups reported significant improvement on the physician and patient Global Assessment of Response to Treatment at weeks 4 and 6 postinjection. There were no serious adverse effects. In this 3-month study, BTXA safely reduced upper extremity muscle tone in patients with chronic spasticity after stroke.


Abstract: Botulinum toxin has been tested as a treatment for spasticity resulting from cerebral palsy, multiple sclerosis, traumatic brain injury, spinal cord injury, and stroke. The results of 18 studies are reviewed in this article. In both open
label and double-blind, placebo-controlled trials, botulinum toxin has proven to be an effective measure for reduction of focal spasticity. Improvements have been documented in tone reduction, range of motion, hygiene, autonomic dysreflexia, gait pattern, positioning, and other criteria, though not all criteria tested showed improvement in all studies. In none of the studies were there significant adverse effects. Future trials may be improved by refinement of several design parameters, including patient selection, treatment timing, and selection of dose and injection site.

Abstract: Suppression of increased muscle tone by epidural spinal cord stimulation, an invasive method for treating spasticity, increases segmental concentrations of inhibitory amino acid neurotransmitters, particularly glycine. The role of glycine in spasticity and spinal shock was explored further in rabbits with ischemic spinal cord injuries that produced spastic paraparesis or flaccid paraplegia. H- reflexes were monitored following posterior tibial nerve stimulation and plantar surface recording. Spasticity was quantified by using H/M ratios. Spastic animals were intrathecally infused with 100 mmol/l solutions of glycine and related compounds. Glycine agonists suppressed tone whereas glycine antagonists increased tone. In addition, microdialysis sampling from the cord was done in injured, non-infused animals and aspartate, GABA, glutamate, glycine and taurine were measured. Flaccid animals had glycine levels two-three times higher than spastic or control animals. High concentrations of glycine within spinal cord segments is associated with spinal shock. Glycine and related compounds may be useful as treatment for excessive tone.

Abstract: The authors report a series of 53 bedridden patients having harmful spasticity in one (6) or both (47) lower limb(s) and treated with selective posterior rhizotomy (SPR) in the dorsal root entry zone (DREZ). This severe spasticity was associated with irreducible flexion contracture in 49 cases and hyperextension in 3 others. 37 of these patients also had painful manifestations. The method was introduced in 1972 on the basis of anatomical studies of the DREZ in humans which showed a topographical segregation of the afferent roots according to their anatomico-functional destinations. The technique consists of a 2 mm deep DREZ microsurgical cut directed at a 45 degree angle into the posterior lateral sulcus just ventral to DREZ and Lissauer's tract of the spinal cord. The procedure was carried out at each sensory rootlet considered to be responsible for the harmful spasticity and pain. SPR interrupts selectively the lateral nociceptive and central myotactic afferent fibers curving toward Lissauer's tract and the anterior spinal cord, while sparing most of the medial lemniscal fibers curving toward the dorsal columns, as well as the fibers of the inhibitory circuitry of Lissauer's tract and dorsal horn. The results were evaluated after a 1 to 14 year follow-up. Mild to
severe complications occurred in 25 patients (47.1%) and were responsible for death in 5 (9.4%). Both spasticity and spasm were significantly decreased or completely eliminated in 75% and 88.2% respectively; when present, pain was relieved without a total suppression of sensation in 91.6%. These benefits—combined with complementary orthopedic surgery in 23 patients—resulted in either a complete resolution or marked reduction of the abnormal postures and articular limitations (85.2% complete and 96.75 marked reduction). Because of the extreme severity of the pre-operative neurological deficits in almost all the patients in this series, surgery improved voluntary movements with a significant functional benefit in only 5 cases and vesico-sphincter function in none. Thanks to its valuable effects on hyperspasticity and pain, SPR in the DREZ made it possible for these very disable patients to be more comfortable in bed and wheelchair and it allowed effective nursing and kinesitherapy to be resumed.


Abstract: INTRODUCTION: Botulinus toxin (BTX) is the most potent biological toxin yet known. It is produced by Clostridium botulinum, a Gram positive bacteria. DEVELOPMENT: Type A Botulinus toxin is the most widely used in human drug trials. It has become the treatment of choice for blepharospasm, hemifacial spasm, cervical dystonia and laryngeal dystonia. It may also be used in the treatment of patients with oromandibular dystonia and limb dystonia, especially writer's cramp, and has been used successfully in the treatment of spasticity and cerebral paralysis. There are many benefits from this treatment, including improved walking, improved posture of wheelchair patients, improvement of patients with spasms and easier extension of their arms and knees. The toxin also alleviates pain and may be used in therapeutic trials for prediction of the response to surgical elongation.


Abstract: The alpha 2-adrenergic agonist tizanidine was reported to be more efficient than baclofen in reducing muscle tone in some spastic patients. The aim of this study was to investigate if this might be due to more specific depressive actions of tizanidine on transmission from muscle afferents which contribute to muscle tone. This was done by comparing the effects of tizanidine and baclofen on amplitudes of monosynaptic spinal focal field potentials produced by stimulation of muscle nerves in the cat. Such field potentials were recorded in the intermediate zone of the fourth lumbar segment, where they display two distinct components, an early one from group I afferents and a later one from group II afferents. Both reflect EPSPs produced in interneurones in disynaptic pathways.
to motoneurones. Tizanidine strongly depressed potentials caused by group II afferents, while it had no effect or slightly facilitated potentials produced by group I afferents. In contrast, baclofen had inconsistent effects on the group II potentials; in some cases it caused a depression and in others it caused only an increase in the latency and time to peak, at doses that strongly and consistently depressed the group I potentials. These effects have been found after both local and systemic applications. The antispastic actions of tizanidine may therefore only be related to the depression of transmission from group II muscle afferents, while antispastic actions of baclofen may be secondary to the depression of any sensory fibres. Since tizanidine is as effective in depressing spasticity as baclofen, it is suggested that the enhancement in synaptic transmission from group II muscle afferents may play an important role in the development of exaggerated stretch reflexes in spastic patients.


Abstract: This multicenter, stratified, randomized, placebo-controlled, double-blind trial evaluated tizanidine for use in the United States for spasticity secondary to MS. The 15-week trial was divided into baseline (weeks 0 and 1), titration (2 mg to a maximum of 36 mg/d; weeks 2 to 4), and plateau (weeks 5 to 13) phases, followed by dose tapering (week 14) and a final visit (week 15). Primary efficacy parameters were scores on muscle tone (Ashworth Scale) and type and frequency of muscle spasms (patient diaries). All efficacy parameters were evaluated by the physician/assessor, and the physician/prescriber was responsible for all dosage adjustments. The patient, physician/assessor, and physician/prescriber made global evaluations of antispastic efficacy. Tizanidine produced a significantly greater reduction than placebo in spasms and clonus (patient diaries) but no significant differences in Ashworth scores. Patients and physician/prescribers, but not physician/assessors, gave significantly better scores in the overall assessment of efficacy and tolerability. No significant differences in other secondary efficacy parameters were noted. Adverse events were reported for 66 (61%) of the 109 placebo-treated patients and 101 (91%) of the 111 tizanidine-treated patients; 6 (6%) and 14 (13%) discontinued treatment, respectively. Patient and physician perception of improvement demonstrated more consistent differences between groups than did the Ashworth Scale, perhaps because of inexperience with this measure or failure to consider time between drug administration and assessment.

Abstract: We reviewed a 10% random sample of charts from an outpatient clinic for multiple sclerosis to determine the frequency with which baclofen was prescribed for spasticity in high doses (greater than 80 mg/d). About 20% of patients had taken high-dose baclofen, and 15% were still receiving a high dose. Taking a high dose was not associated with discontinuing treatment.


Abstract: Spasticity and other muscle symptoms in the palliative care patient can contribute to suffering, significantly detracting from overall quality of life. Current therapy primarily includes use of centrally acting muscle relaxants, which are beneficial in treating some symptoms, but frequently have extensive side effects, such as sedation and muscle weakness. Tizanidine, a central alpha 2 adrenergic agonist, has been shown in clinical studies to be as effective as other commonly used antispastic agents, but without debilitating muscle weakness. Tizanidine can cause sedation, which is minimized by dose titration. When taken at night, patients report improvement in getting to sleep and little drowsiness or "hangover sensation" upon waking. Tizanidine is potentially helpful to many palliative care patients with chronic muscle pain and sleep disturbances.


Abstract: Twelve female mongrel dogs were made paraplegic by midthoracic spinal cord transection. Beginning at 9 weeks posttransection, either glycine (50 mg/kg) or saline was injected intramuscularly each day and the signs of spinal spasticity were assessed clinically. After treating the dogs for 3 weeks, we removed the lumbar enlargement of each dog and microdissected it into gray and white areas which we assayed for glycine, glutamate, and aspartate content. Some of the clinical signs of spasticity improved in the animals injected with glycine compared to the saline-injected controls. The content of glycine was significantly elevated in the central gray matter and ventral medial white matter of the glycine-treated dogs. The levels of glutamate were also significantly elevated in the central, lateral ventral, and medial ventral gray matter and in the dorsal lateral and ventral medial white matter of the glycine-treated dogs. The possible role of these segmental putative neurotransmitters in spinal spasticity is discussed.


Abstract: Weakness has been reported by patients as one side effect of baclofen. We evaluated torque production as a measure of contractile strength in 30
subjects with clinically definite multiple sclerosis. Participants, with minimal to moderate spasticity, were titrated onto baclofen by 5mg increments every other day for seven days and maintained at 20mg for one week. Using a KinCom isokinetic unit set at 60 degrees per second, subjects performed maximal concentric quadriceps contractions; three consecutive trials were recorded. Results indicated no significant difference in maximum torque production between sessions. Although torque values remained unchanged, the angle at which peak torque production occurred moved closer to normal values. Subjective reports of weakness do not appear related to physiologic properties of contraction, but may be a subjective interpretation that less stiffness is weakness because of less resistance to muscle contraction.


Abstract: OBJECTIVE: To assess dose-response relationships to a single dose of botulinum toxin 'A' in upper limb spasticity associated with stroke or head injury. DESIGN: A double-blind placebo-controlled randomized dose ranging study. SETTING: A regional centre for neuroscience and a neurorehabilitation outpatient clinic. SUBJECTS: Twenty-one hemiplegic patients with troublesome upper limb spasticity. Nineteen with stroke and two with head injury. MAIN OUTCOME MEASURES: Spasticity (modified Ashworth), range of movement, posture (postural alignment and finger curl), disability (upper body dressing time and Frenchay Arm Test), patient-reported global assessment scale. RESULTS: Combining data from all doses of botulinum toxin there was a significant reduction in spasticity at the wrist and fingers associated with a greater range of passive movement at the wrist and less finger curl at rest. There was a tendency for a further reduction in spasticity at elbow and wrist to occur with increasing dose but not for finger spasticity or curl. Effects present at six weeks were lost by 12 weeks except for a small improvement in elbow range of movement at the 1,500 Mu dose. There was no change in upper limb disability but a significant increase in patients' global assessment of benefit. CONCLUSION: Botulinum toxin produced beneficial effects in spasticity and passive range of movement in the hemiplegic upper limb. Increasing the dose increased the magnitude of response for impairments in some muscle groups but had little effect on duration of response.


Abstract: We report an unusual case of an acute encephalopathy following injection of iohexol for myelographic study, which was reversible after a treatment with water restriction and glucocorticoids. The pathophysiologic mechanism appears to be related with hyponatremia. We conclude that drinking of large amounts of fluids must be not recommendable in order to avoid the developing of encephalopathy.

Abstract: Hoffmann’s reflex or H-reflex (HR) is an electrically elicited reflex that measures excitability of motoneurons and shares some physiologic properties with the deep tendon reflex. Children with tendon hyperreflexia due to cerebral palsy usually have higher amplitude HRs. Nitrous oxide (N2O) depresses the HR in patients with normal spinal reflexes, although the effect of N2O in conditions with hyperreflexia such as cerebral palsy is not known. We propose to determine the effect of N2O on the amplitude of the HR under general anesthesia in children with hyperreflexia due to cerebral palsy. We studied eight children undergoing selective dorsal rhizotomy (SDR) for the relief of spasticity. The maximum amplitudes of the HR (HRmax) and direct motor response (MRmax) were routinely evoked under the following anesthetic conditions: 1) sufentanil and 66% N2O/33% oxygen; and 2) sufentanil and 100% oxygen. The HRmax amplitude was significantly lower when N2O was part of the inspired gas mixture. The differences between the no N2O and the 66% N2O groups were significant. The MRmax did not change significantly. Abnormal spinal reflexes seen in spastic diplegia can be abolished by inhaled N2O. This finding also suggests that N2O-induced depression of spinal reflexes should be a consideration during physiologic monitoring of the spinal cord under general anesthesia.


Abstract: The authors present a case of methaemoglobinemia of acute onset, with an unusually protracted course. The long persistence of this disorder led to a search for the cause which was eventually traced to medication with dapsone. The latter was found to be inappropriately being taken by the patient instead of an antispasmodic that had been prescribed for a spinal condition; this was because the tablets had been incorrectly labelled and dispensed in a pharmacy. The patient took increasing doses of the presumed ‘antispasmodic’ tablets as they seemed to lack clinical effect, thus further exacerbating the toxic consequences. Moreover, the patient brought his wrongly labelled tablets into hospital and was allowed to use them there, contrary to normal hospital policy. As treatment for the methaemoglobinemia both bolus and continuous infusions of methylene blue were used, which probably contributed to the severe haemolysis which followed. Furthermore, the development of a rare side effect of dapsone toxicity, namely that of a sensorimotor neuropathy, is reported.


Abstract: Postoperative pain control can be a major problem after selective dorsal rhizotomy for the treatment of spasticity. We report the use of epidural
morphine delivered via a catheter placed at surgery for postoperative analgesia in 28 consecutive patients undergoing this procedure. Pain was well controlled using this technique, and no patients required concomitant parenteral analgesia. There were no instances of respiratory depression, wound infection, or central nervous system depression, and the patients were easily mobilized in the early postoperative period. Epidural morphine is concluded to be a safe and very efficacious method of analgesia after selective dorsal rhizotomy.


Stanko J.R. (1990) Review of oral skeletal muscle relaxants for the craniomandibular disorder (CMD) practitioner. Cranio. 8, 234-243. Abstract: The presence of acute or chronic muscle pain and muscle spasm is a common finding in the treatment of craniomandibular disorders. A review of the literature on the centrally acting oral skeletal muscle relaxants is presented to assist the practitioner in treating CMD. The pharmacology, pharmacokinetics, metabolism, adverse reactions and available dosage forms of the skeletal muscle relaxants are discussed. The agents reviewed are carisoprodol, methocarbamol, chlorphenesin carbamate, metaxalone, chloroxazone, orphenadrine citrate, diazepam, and cyclobenzaprine. Their mechanisms are not well defined. Most act via selective inhibition of polysynaptic pathways in the central nervous system. Most evidence for their efficacy is based on subjective responses and there is question as to the adequacy of the clinical studies to date. Based on the data all of the relaxants (possibly excepting diazepam) are better than placebo based on subjective analyses. Although combinations with analgesics provide better symptom relief, no superiority over analgesics exists. No skeletal relaxant has been shown to be superior over any other oral relaxant. Based on recent clinical suspicions, further study of multiple pharmacologic effects of newer agents is indicated.

Stark R.J. (1979) Spasticity due to phenytoin toxicity. Med. J. Aust. 1, 156. Abstract: A young epileptic presented with spasticity as well as ataxia, diplopia and nystagmus; his serum phenytoin level was very high. All the abnormal signs disappeared after withdrawal of phenytoin. Spasticity, hyperreflexia, and clonus are features of phenytoin intoxication, present in this case, which are not commonly seen, and which have rarely been mentioned previously in the literature.

Steers W.D., Meythaler J.M., Haworth C., Herrell D., and Park T.S. (1992) Effects of acute bolus and chronic continuous intrathecal baclofen on genitourinary dysfunction due to spinal cord pathology. J. Urol. 148, 1849-1855. Abstract: A prospective, blinded study was done to examine the effects of acute bolus and chronic continuous intrathecal baclofen on genitourinary function in 10 patients with severe spasticity due to spinal cord pathology. Genitourinary function was assessed by symptom questionnaires and urodynamic studies.
performed after a bolus dose of baclofen and 6 to 12 months after continuous intrathecal baclofen. Results were compared to placebo for acute bolus testing or to pre-continuous intrathecal baclofen values. In all patients with irritative voiding and urge incontinence uninhibited bladder contractions were eliminated. Of 3 patients with an indwelling urethral catheter for incontinence due to detrusor hyperreflexia 1 was converted to intermittent self-catheterization. Whereas bladder capacity, compliance, sensation and voiding pressures were not different after continuous intrathecal baclofen, when a mean of all patients was compiled, a 72% increase in capacity and 16% improvement in compliance were observed in subjects without cervical spinal cord pathology. Detrusor-sphincter dyssynergia was abolished in 40% of the patients. Continuous intrathecal baclofen may represent a novel approach to the management of patients with a neurogenic bladder who have decreased bladder compliance and detrusor hyperreflexia not controlled by oral medications.


Steinberg F.U. and Ferguson K.L. (1975) Effect of dantrolene sodium on spasticity associated with hemiplegia. J. Am. Geriatr. Soc. 23, 70-73. Abstract: The effects of dantrolene sodium (Dantrium) were studied in 23 patients with hemiplegic spasticity, 13 of whom were younger than 50, and 10 older than 50. The dosage of dantrolene ranged from 100 mg per day initially to 600 mg per day maximally. The drug was most effective in reducing or abolishing clonus and somewhat less efficacious in decreasing the resistance to stretch and the tendon reflexes. Functionally, gait was improved and the patients found it easier to take care of their personal needs. In general, motor performance was improved. The observation that patients in the 50+ age group responded less well remains unexplained. Dantrolene sodium is a valuable tool in the management of spasticity due to hemiplegia.

Steinbok P., Daneshvar H., Evans D., and Kestle J.R. (1995) Cost analysis of continuous intrathecal baclofen versus selective functional posterior rhizotomy in the treatment of spastic quadriplegia associated with cerebral palsy. Pediatr. Neurosurg. 22, 255-264. Abstract: The purpose of the study was to analyze the relative cost of selective functional posterior rhizotomy (SFPR) and continuous intrathecal baclofen in the treatment of children with severe spastic quadriplegia related to cerebral palsy. No attempt was made to analyze the efficacy of the two types of treatment. Nine children with spastic quadriplegia secondary to cerebral palsy in whom continuous intrathecal baclofen was attempted were matched as closely as
possible with a group of 10 patients with spastic quadriplegia out of a total of 100 children who had undergone SFPR in the same time period. Clinical care flow charts were created to identify the various points of contact with members of the health care team, so that cost points could be identified and costs calculated. The cost per patient up to 1 year after treatment CDN$ 64,163.10 for patients with implanted pumps for continuous intrathecal baclofen versus CDN$ 16,913.54 for SFPR. When adjustments were made to exclude costs and savings associated with research protocols, the average for the baclofen group decreased to approximately CDN$ 63,000, with minimal change for the SFPR group. The higher cost per patient on baclofen was related to the cost associated with screening patients who did not go on to have implantation of a continuous infusion pump, and to additional hospitalization for complications in the baclofen group. It is cautioned that this cost analysis was based on the experience at British Columbia’s Children’s Hospital, and the results may not be generalizable to other institutions or to other patient populations.


Abstract: Selective dorsal rhizotomy (SDR) has been shown to be an effective treatment for the spasticity of cerebral palsy, but few studies have addressed specifically the side effects of the procedure. A retrospective study was performed to determine the frequency and nature of complications in 158 children who had undergone SDR at British Columbia’s Children’s Hospital from 1987 to 1996. Intraoperative, preoperative (immediate postoperative until discharge at approximately 7 days) and postdischarge complications occurred in 3.8, 43.6 and 30% of patients, respectively. The most common intraoperative complication was aspiration pneumonia, which was experienced by 2 patients (1.3%). Perioperatively, sensory changes were found in 8.9% of the children, and transient urinary retention in 4.4%. Complications after discharge included back pain starting more than 6 months after surgery in 10.8%, sensory changes in 13.9%, and neurogenic bladder or bowel problems in 12.7%. Persistent sensory changes occurred in 3.8%, were not important functionally, and tended to occur in patients with the largest amount of dorsal root tissue cut. In 8 patients (5.1%), bladder and/or bowel dysfunction attributed to the SDR was present at the latest follow-up, although in only 2 patients (1.3%) this dysfunction was a definite complication of the rhizotomy. The use of pudendal monitoring and/or cutting less than 50% of the S2 roots may have been associated with a lower incidence of long-term sphincter dysfunction. Data about the nature and frequency of complications may result in further modifications to the SDR procedure, and is critical for counseling about SDR and alternative options available for treatment of the child with spastic cerebral palsy.


Abstract: OBJECTIVE: To obtain information from continuous intrathecal baclofen infusion (CIBI) pump centers regarding specific clinical practices and experiences. METHODS: A total of 115 centers were surveyed by mail. RESULTS: Forty centers (35%) responded with information about 1,002 test doses and 936 pump placements. Patient diagnoses included cerebral palsy, spinal cord injury, traumatic brain injury, and others. The average test dose was 50 microg. A total of 87% of trials were successful. The most common test dose complications were nausea/vomiting (2.6%) and sedation (2.2%). Pump placement complications included cerebrospinal fluid (CSF) collection (3.3%), constipation (2.9%), headache (2.4%), and CSF leak (2.2%). The most common long-term complications were catheter kink or migration (4%) and infection (1.2%). Improved daily activities including easier diapering, dressing, transfers, orthotic wear and comfort, and sitting tolerance were reported in the majority (>90%) of patients. Mixed results were reported for oral motor function and head, bladder, and bowel control. CONCLUSIONS: CIBI is an effective treatment for severe spasticity, with dramatic quality-of-life improvements and a small number of significant complications. Long-term benefits and complications need to be monitored in this complex population.


Abstract: Lesch-Nyhan syndrome is a rare X-linked recessive disorder of purine metabolism associated with a virtually complete deficiency of the enzyme hypoxanthine-guanine phosphoribosyl-transferase (HPRT). The disease is characterized by hyperuricemia, self-multilation, choreoathetosis, spasticity, and mental retardation. The abnormalities of purine metabolism are present at birth and may lead to uric acid crystalluria and stone formation early in life. Radiographic findings described in Lesch-Nyhan syndrome include faintly radiopaque stones on abdominal radiographs or, if renal disease is present, small kidneys with poor function on intravenous urogram. Radiolucent stones are usually composed of uric acid; however, several cases of xanthine and hypoxanthine-containing calculi in Lesch-Nyhan patients receiving allopurinl therapy have also been described. Oxypurine is the collective name for the compounds hypoxanthine, xanthine, and uric acid, and all may be radiolucent. We report a case of Lesch-Nyhan syndrome with presumed renal parenchymal oxypurine deposition demonstrated readily by ultrasonography but not detected on standard radiographs or intravenous urogram.

Abstract: Severe spasticity is a major problem in the rehabilitation of patients with dysfunction of the spinal cord or cerebral hemispheres. Oral baclofen is often effective. However, in patients with severe spasticity adequate control may not be obtained from oral therapy with the drug. Over the past 5 years we have developed a program for the use of intrathecal baclofen for severe spasticity, and in relation to this discuss patient assessment, practical aspects of drug administration, complications of therapy and patient benefits. Continuous intrathecal baclofen is a safe and effective adjunct to physical therapy in the management of patients with severe spasticity.


Abstract: This double blind cross-over study, involving 9 chronic spinal cord injured (SCI) patients (6 paraplegic and 3 paretic), was a first attempt to investigate the effects of the noradrenergic agonist, clonidine, on the modulation of the locomotor pattern and spasticity in patients with spinal cord lesions. Electromyographic (EMG), footswitch and video recordings were made as the patients walked on a treadmill with the support of an overhead harness if needed. Overground locomotion was also assessed in the paretic patients. All 3 spastic paretic patients had kinematic deviations and abnormal EMG recruitment profiles during the premedication or placebo sessions. With clonidine therapy one patient demonstrated a marked improvement in locomotor function. This patient progressed from non-ambulation to limited independent ambulation as the extent of coactivation in antagonist muscles decreased. The other 2 paretics who presented limited spasticity showed minimal changes while on clonidine. In the paraplegic patients, clonidine did not elicit locomotor activity, although there were marked reductions in stretch reactions and clonus during assisted locomotion. They remained incapable of locomotion, either during the control period or during the clonidine therapy. These results indicate that clonidine may be a potentially useful medication for both locomotion and certain manifestations of spasticity in SCI patients but further investigation is warranted.


Abstract: Excessive accumulation of glutamate or other excitatory amino acids and the subsequent overactivity of NMDA receptors is currently thought to lead to neuronal injury in cerebral ischemia. Therefore, antagonists of the NMDA receptor may offer an approach for the treatment of ischemic brain injury. Dizocilpine (MK-801), an NMDA receptor-associated channel blocker, protects neurons in several rodent stroke models. However, this drug has numerous side
effects and causes apoptosis of neonatal neurons. Recently, another NMDA receptor-associated channel blocker, memantine, has been shown to ameliorate NMDA-receptor mediated neurotoxicity in neuronal cell cultures and in focal cerebral ischemia models in adult rats without substantial side effects. Memantine has been used clinically in the treatment of Parkinson's disease and spasticity for a number of years. Here we tested the effects of memantine on focal stroke caused by photochemical thrombosis in neonatal rats and demonstrated a neuroprotective effect of memantine in this model. We also found excellent correlation between infarct size determined by magnetic resonance imaging (MRI) and histopathological analysis in the same animals. A single pre-ischemic dose of memantine (20 mg/kg) given 15 min prior to induction of stroke reduced the infarct size by 36.3% when compared to control animals treated with normal saline (P < 0.0001). At this dosage, memantine manifests few, if any, neurobehavioral side effects. Thus memantine appears to be both safe and effective in neonatal as well as adult animal models of stroke.

Stien R., Nordal H.J., Oftedal S.I., and Slettebo M. (1987) The treatment of spasticity in multiple sclerosis: a double-blind clinical trial of a new anti-spastic drug tizanidine compared with baclofen. Acta Neurol. Scand. 75, 190-194. Abstract: The anti-spastic effect of a new drug, tizanidine, was compared with that of baclofen in a double-blind clinical trial; 40 seriously handicapped patients with multiple sclerosis (MS) were randomly allocated treatment with one or the other drug for a 6-week period. The antispastic effect was evaluated by clinical criteria. The optimal daily dose of both drugs varied considerably from patient to patient, and was on the average 23 mg for Tizanidin and 59 mg for baclofen. To the extent an antispastic effect was observed, the 2 drugs appeared to be equally effective when given at a 1:2 ratio (mg tizanidine: mg baclofen). Side effects of both drugs were sleepiness, muscular weakness and dry mouth. Tizanidine had a mild depressive effect on blood pressure. Sudden withdrawal of both drugs was accompanied by a transient relative increase of spasticity in approximately half the patients. There were no other changes suggesting physical or psychological dependence. The present study underscores that neither baclofen nor tizanidine are ideal antispastic drugs, and emphasize the need for further research.

Stolp-Smith K.A. and Wainberg M.C. (1999) Antidepressant exacerbation of spasticity. Arch. Phys. Med. Rehabil. 80, 339-342. Abstract: Patients with spinal cord injury (SCI) may develop depression. This may be related to adjustment to living with an SCI in addition to dealing with complications of the injury, such as spasticity. Pharmacologic treatment of depression can be difficult because of neurochemical and receptor changes that are associated with SCI. Newer antidepressant agents are purported to have selective activity by alteration of serotonergic neurotransmission. A case report is presented that illustrates exacerbation of spasticity by this family of antidepressant medications. Mechanisms possibly explaining this exacerbation of spasticity are the effects of serotonin on motor neuron and reflex activity, denervation supersensitivity, and the serotonin syndrome. Understanding the
relationship between serotonergic systems and spasticity can be important in treating depression in patients with spasticity


Abstract: N-Butyl benzenesulfonamide (NBBS), a plasticizer used commercially in the polymerization of polyamide compounds, is neurotoxic. Young adult New Zealand white rabbits, inoculated repeatedly with NBBS by the intracisternal or intraperitoneal routes, developed a dose-dependent motor dysfunction characterized by limb splaying, hyperreflexia, hypertonia, gait impairment, and abnormal righting reflexes. Histopathological changes consisted of intramedullary thickening of the ventral horn axons, random neuroaxonal spheroids confined to brain stem nuclei and spinal motor neurons, and swollen dendritic processes of spinal motor neurons. Immunoreactivity to a monoclonal antibody against microtubule-associated protein-2 (MAP-2) was markedly increased in the dendrites of spinal motor neurons following thrice weekly intraperitoneal inoculations of NBBS for 4 months, whereas after 12 monthly intracisternal inoculations, MAP-2 immunoreactivity was absent or strikingly reduced in the same neuronal populations. Ultrastructurally, postsynaptic zones contained vacuoles and multilamellar bodies. These findings raise questions about the safety of NBBS to humans

Abstract: Repeated monthly intracisternal inoculations of N-butyl benzenesulfonamide induced a chronic, slowly progressive myelopathy in young adult New Zealand white rabbits that was manifested by hyperreflexia, spasticity, hypertonia, gait impairment and altered tonic immobility responses. The neuropathological features consisted of scattered neuroaxonal spheroids, fusiform distention of the intramedullary portions of the spinal cord ventral roots and, as defined by microtubule-associated protein-2 (MAP 2) immunoreactivity, an initial distention and subsequent loss of dendritic processes in neurons of the nucleus motoris lateralis with the perikaryon of these cells remaining intact. A similar chronic progressive myelopathy was induced by repeated low dose intracisternal inoculations of aluminum chloride in New Zealand white rabbits. However, the neuropathological changes were more extensive and consisted of dendritic, axonal and perikaryal inclusions of phosphorylated and nonphosphorylated neurofilament localized to spinal motor neurons in the nucleus motoris medialis, substantia grisea intermedia and select brainstem nuclei with only minimal involvement of the nucleus motoris lateralis. The co-administration of these two neurotoxins over the course of 8 months induced
striking behavioral changes as well as a fulminant myelopathy. This was accompanied by a loss of neuronal perikarya in the nucleus motoris lateralis and topographically extensive neocortical neurofilamentous degeneration. These features suggest that potentiation occurs when the two toxins are co-administered, a view supported by an estimation of the co-neurotoxicity coefficient (CNC greater than 1). Our results have implications for understanding human neurodegenerative disorders in which potentiation of insults may occur, producing a clinical and neuropathological disease state not expected from either agent alone.


Abstract: The effect of epidural opioids on spinal spasticity is demonstrated in a patient suffering from multiple sclerosis. Flexor reflex spasms are abolished and muscle tone is markedly reduced by the epidural administration of morphine 3 mg or fentanyl 0.1 mg. In contrast, the oligosynaptic motor responses and voluntary movements were unaffected. This is documented by EMG-recordings. Sensory perception thresholds were elevated for pain, but unchanged for touch and vibration sense. Effects on enkephalinergic interneurons on the spinal level are discussed.


Abstract: The effect of intravenously administered Ginkgo biloba extract (EGB 761) on the vasospastic response to platelet activation has been assessed using a cutaneous flap preparation in anaesthetized mice. Arterioles of the axillary artery were observed by intravital microscopy, and platelets were activated by topical application of ADP under two steady state conditions: normothermia (37 degrees C) and hypothermia (24 degrees C). Responses of the cutaneous arterioles to stimulation by topical application of a thromboxane agonist (U46619) were also compared in animals treated intravenously with EGB 761 or with a thromboxane synthesis inhibitor (U63557). ADP induced a 34% constriction of the arterioles in control animals. However, no arteriolar constriction occurred in response to ADP in platelet-depleted animals (collagen-induced thrombocytopenia) or in animals treated with EGB 761 or with a thromboxane synthesis inhibitor (U63557). ADP induced a 34% constriction of the arterioles in control animals. However, no arteriolar constriction occurred in response to ADP in platelet-depleted animals (collagen-induced thrombocytopenia) or in animals treated with EGB 761 (60 mg/kg, i.v.). Exposure of the arterioles to hypothermia (24 degrees C) for 10 min induced constriction of 7-12% in all experimental groups of animals. Under these hypothermic conditions, either EGB 761 or thrombocytopenia abolished ADP-induced arteriolar constriction which was substituted by arteriolar dilation, indicating that EGB 761 can inhibit the vasospasm that is produced by platelet activation. As topically applied U46619 (10(-5) M) induced arterioles constriction (about 22%) that was abolished by intravenous treatment with EGB 761, the extract appears to act directly rather than as a thromboxane synthase inhibitor. Collectively, these
findings indicate that platelet factors can play a significant role in cutaneous
vasospasm, and that EGb 761, via an action on the thromboxane pathway, could
be useful in treating Raynaud's phenomenon and other vascular disorders which
involve increased thromboxane production

Su P.H. and Ma Z.S. (1989) Observation on 38 cases of drug-induced
myospasm treated with massage over the acupoints. J. Tradit. Chin Med. 9, 269-
271.

Susset V. and Bedoiseau M. (1976) [Therapy of spasticity by alcoholization of

Arch. Neurol. 48, 1285-1293.
Abstract: Aberrant iron metabolism in the brain is typified by Hallervorden-Spatz
syndrome. In this disorder, large amounts of iron are deposited in the globus
pallidus and the pars reticulata of the substantia nigra. It is characterized by
extrapyramidal dysfunction, as demonstrated by dystonia, rigidity, and
choreoathetosis; onset during the first two decades of life; and progression of
signs and symptoms. Corroborative findings include corticospinal tract
involvement, ie, spasticity and extensor toe signs, progressive intellectual
impairment, retinitis pigmentosa and optic atrophy (usually associated visual
evoked response and electroretinogram abnormalities), seizures, familial
occurrence, hypointense areas in the basal ganglia on magnetic resonance
imaging scans (particularly in the substantia nigra), abnormal cytosomes in
circulating lymphocytes, and sea-blue histiocytes in bone marrow. Iron function in
normal brain metabolism is manifold, but high concentrations of iron in the basal
ganglia area may signal a unique relationship. Data support the likelihood that
iron plays a role in the modulation of dopamine binding to postsynaptic receptors.
In addition, transferrin receptors and iron are also concentrated in
oligodendrocytes in normal brain and, thus, may have a function in myelination. A
role of iron also seems likely in oxidation and peroxidation reactions involving
membranes and DNA, a capability that becomes uncontrolled when protective
biologic mechanisms become inadequate

Baclofen suppresses hippocampal epileptiform activity at low concentrations
without suppressing synaptic transmission. J. Pharmacol. Exp. Ther. 237, 881-
887.
Abstract: Baclofen is used clinically to treat spasticity, but has received little
attention as a potential antiepileptic agent. To explore the antiepileptic potential
of baclofen further, we tested its effect on stimulus train-induced bursting, an in
vitro model of hippocampal epileptiform activity. In hippocampal slices prepared
from male rats, extracellular field potentials were recorded in stratum pyramidale
of CA3, and electrical stimuli were delivered to s. radiatum of CA3. After stable
responses to single stimuli were established, stimulus trains were delivered every
5 min until stable triggered and spontaneous population bursting were elicited. (+/-)-Baclofen was bath-applied to the slices at varying concentrations to study its ability to suppress synaptic transmission and epileptiform activity. EC50 values for suppression of orthodromic population spike amplitude, of triggered burst duration and of spontaneous burst frequency were 2300, 355 and 26.9 nM, respectively; all statistically significantly different. These findings suggest that baclofen suppresses epileptiform electrical activity in the hippocampus at concentrations well below those which suppress normal synaptic transmission, and support renewed consideration of baclofen as an antiepileptic agent.


Abstract: Baclofen is an analog of the inhibitory neurotransmitter, GABA, which is used clinically to control spasticity. Recent evidence has accumulated showing this compound to have profound inhibitory effects upon hippocampal neural activity at both the cellular and circuit levels, and to attenuate epileptiform bursting in the hippocampal slice. However, it does not appear as an anticonvulsant on most traditional drug screens. Baclofen can produce inhibition by increasing potassium conductance, and therefore may fail to appear efficacious in typical anticonvulsant screens due to techniques that cause rapid and massive increases in interstitial potassium. We tested the hypothesis that baclofen is less effective at attenuating epileptiform bursting in the hippocampal slice under conditions of elevated extracellular potassium. Male Sprague-Dawley rats were decapitated and hippocampal slices were prepared. Epileptiform bursting was induced by bathing the slices in an artificial cerebrospinal fluid solution which contained either 7.0 mM K+ or 30 microM bicuculline methiodide, or by stimulus train-induced bursting. In each of these media, baclofen was applied in a random presentation of concentration format. Baclofen attenuated epileptiform bursting in both bicuculline and elevated K+, although considerably higher concentrations were necessary to attenuate bursting in high K+ than in bicuculline or after stimulus train-induced bursting. These results further support the antiepileptic actions of baclofen and provide evidence that this drug may be of value for attenuating epileptiform activity when there is not a tonic elevation of interstitial brain potassium.


Abstract: Baclofen (Lioresal, Ciba-Geigy) is an analog of the inhibitory neurotransmitter GABA and is used clinically to control spasticity. Recent studies have demonstrated that this compound produces a marked inhibition of synaptically evoked responses in area CA3 of the hippocampal slice, suggesting that this drug could influence behavior mediated by the limbic system. In the present study, male rats of the Fischer-344 strain were trained on a one-trial passive avoidance task and tested for retention 1 week later. After the training
trial, separate groups of rats received either 5 or 10 mg/kg/4 ml IP of baclofen or the distilled H2O vehicle immediately, 10 min, or 60 min after training. One week later, the rats that received baclofen immediately after training reentered the test chamber with a significantly higher frequency than controls, although no differences in vacillatory responses were observed between groups. Similar effects were observed following posttrial administration of chlordiazepoxide. In a separate experiment rats were tested for locomotor activity after receiving the same doses of baclofen. Although baclofen decreased activity during a 30-min period after dosing, rats exposed to baclofen showed no significant change in activity relative to controls 1 week later. These data are consistent with the interpretation that baclofen may interfere with memory consolidation or retention.

Abstract: Electrical currents similar to those used for relief of pain and spasticity were applied to the spinal cord and cerebellum of monkeys and cats. Direct coupled monopolar pulses increased pH at the tissue surface near a negative electrode and correspondingly decreased the pH near a positive electrode. Cerebrospinal fluid (CSF) circulation around the electrodes neutralized these changes. Capacitively coupled currents up to a 10 mA peak and 2.5 m/coul per peak failed to change tissue pH measurably. Current levels with power densities of 100 mW per cm2 did not cause any change in tissue temperature.

Abstract: OBJECTIVE AND IMPORTANCE: We describe a unique presentation of a thoracic spinal Pantopaque cyst. Although Pantopaque is no longer used, sequelae of its long-term use may continue to surface. CLINICAL PRESENTATION: Our patient presented to the emergency room with 4 months of progressive lower extremity numbness, spasticity, and incontinence and a 2-day history of left upper extremity dysesthesias. Magnetic resonance imaging at admission revealed a C7-T10 syrinx and an intrathecal extramedullary mass to the right of the spinal cord at T10- T11. INTERVENTION: Radiographic evidence led to the initial diagnosis of hemangioblastoma. The results of a critical analysis of the preoperative studies caused us to suspect a Pantopaque cyst. This suspicion was confirmed at the time of surgery, when a cyst filled with contrast medium was revealed. T9-T11 laminectomies were performed, allowing for a 5-cm dural opening. The cyst was aspirated and excised, and then the syrinx was decompressed. CONCLUSION: Our patient experienced significant sensory and motor improvement postoperatively. We present a previously undescribed complication of one of the most commonly used contrast media, Pantopaque. Despite its replacement with newer agents, it may continue to play a significant role in the pathological presentation of patients in whom it was previously used.

Abstract: We administered local botulinum toxin injections on the leg adductors of 12 patients with spastic paraparesis (9 patients with HAM, 2 patients with spinal spastic paraparesis, 1 patient with an identified degenerative disease). Two of them were wheelchair-bound and the other patients could walk with or without help. The patients were assessed by the time to walk 10 m and the spasticity score which was derived from the degree of muscle tone and spasm frequency of leg adductors. After the initial injection, 7 of the 12 patients improved spasticity scores and 8 of the 10 patients could walk 10 m within a shorter time. The time to walk 10 m was markedly shortened in moderate cases. However, one patient complained of leg weakness and the time to walk 10 m was prolonged. Five of the 12 patients received injections 3 to 7 times, and were followed up for a mean of 16.2 months. In 4 of the 5 patients, repeated injections could maintain the improvement of spasticity score and time to walk 10 m. However, injection was discontinued in one patient because of leg weakness. The other side effects were pain and swelling at the injected site and dysarthria. However, these side effects were slight and transient and did not require treatment. No other systemic side effects were observed. In conclusion, the beneficial effects of botulinum injections to spastic paraparesis were (1) improvement of objective symptoms in mild cases, (2) improvement of ADL in moderate cases, and (3) improvement of objective symptoms and ease of nursing care in severe cases. Furthermore, we confirmed the long-term efficacy and safety of botulinum toxin.


Abstract: This paper discusses two cases of bilateral subcapital fracture of the proximal femur as a complication of myelography with Conray 60. The literature is reviewed.


Tardieu G., Tardieu C., and Hariga J. (1971) [Infiltrations with 45 degrees ethyl alcohol of the motor points, the roots by the epidural route, or of the posterior tibial nerve. Their indications and contra-indications in the various forms of spasticity (experience of 10 years)]. Rev. Neurol. (Paris) 125, 63-68.
Abstract: Structure, biological activity, mode and mechanism of action of botulinum toxin as well as its therapeutic use is described. Botulinum toxin type A, one of the most potent biologic toxins, has been found to be of therapeutic value in the treatment of several neurologic and ophthalmologic diseases. Its ability to produce chemical denervation of muscles makes it option for treatment of disorders in which traditional therapeutic procedures are of limited value (e.g. blepharospasm and other focal dystonias, strabismus, spasticity)

Abstract: OBJECTIVE: To review the pharmacology, therapeutics, adverse effects, and societal implications of the medical use of marijuana. DATA SOURCES: MEDLINE and manual searches of English-language marijuana literature, supplemented with interviews of scientists currently conducting cannabinoid research. Search terms included pain OR palliative care AND cannabis or ALL marijuana; cachexia OR appetite OR appetite stimulants; muscle spasticity OR spasm; immune system and cannabis; nausea and vomiting and cancer and cannabis. MEDLINE search terms: cannabis OR marijuana smoking OR marijuana abuse; all glaucoma; multiple sclerosis AND cannabis OR marijuana smoking OR marijuana abuse. STUDY SELECTION: Studies on pharmacology, risks, and medical potential of marijuana. DATA EXTRACTION: Not applicable. DATA SYNTHESIS: The most prominent effects of marijuana are mediated by receptors in the brain. Acute intoxication is characterized by euphoria, loss of short-term memory, stimulation of the senses, and impaired linear thinking. Depersonalization and panic attacks are adverse effects. Increased heart rate and reddened conjunctivae are common physical effects. Chronic, high doses may cause subtle impairment of cognitive abilities that are appear to be long-term, but of unknown duration. Marijuana may be a risk factor for individuals with underlying mental illness. It causes dependence, but compared with cocaine, alcohol, heroin, and nicotine, marijuana has little addictive power and produces only mild withdrawal symptoms. Marijuana shows clinical promise for glaucoma, nausea and vomiting, analgesia, spasticity, multiple sclerosis, and AIDS wasting syndrome. CONCLUSION: As a recreational drug, marijuana poses dangers, particularly to social and emotional development during adolescence and young adulthood. As a medical drug, marijuana should be available for patients who do not adequately respond to currently available therapies

Abstract: The histological changes produced in peripheral nerve by topical ethyl alcohol have been infrequently studied in spite of widespread use of this neurotoxic agent in the management of pain and spasticity. In the present study the sciatic nerves of a series of albino mice were exposed to ethanol in
concentrations of from 10% to 50% for from 15 to 60 seconds. An immediate physiochemical reaction took place, resulting in splitting of myelin sheaths and swelling of cellular organelles and cytoplasm. Nerves subsequently underwent Wallerian degeneration. A central core of fibers appeared to be normal. The longer exposure times or higher alcohol concentrations increased the extent to which the peripheral rim of altered tissue extended centrally into the nerve. Within altered tissue, all fiber types and sizes were found to be affected to an equal degree. To study the physical properties of alcohol in solution, absolute alcohol was slowly placed at the bottom of a cylinder filled with artificial or normal human spinal fluid and sequential levels of the solution were sampled 30 and 60 seconds after injection. Though hypobaric, alcohol dispersed rapidly so that specimens taken from the bottom of the cylinder were 65% as concentrated as specimens taken from the surface.


Abstract: The medical records of 46 consecutive patients who have had intrathecal Baclofen drug delivery systems implanted in the National Spinal Injuries Centre, the Paddocks Hospital Spinal Unit, Princes Risborough, Lodge Moor Hospital Spinal Unit, Sheffield, the Northern Regional Spinal Injuries Unit, Hexham and The Radcliffe Infirmary, Oxford, were reviewed. Patients were contacted to describe their views on the treatment. The complications of the treatment are described. Some, such as overdose and meningitis are particularly hazardous. Others, in particular pump tubing revisions, are more of an inconvenience and time consuming for the patient and physician. If the serious risks of this valuable treatment are to be minimized and the therapy applied most effectively than a well co-ordinated team is essential, involving in particular the physician responsible for the initial assessment and follow-up of the patient and an experienced surgeon. It is recommended that only a small number of centres in the UK undertake these implants.


Abstract: In carefully selected groups of patients, intrathecal baclofen therapy offers well-proven benefits in reducing spasticity, notably in cases of spinal injury and multiple sclerosis. The initial costs of implantation are high, and there must be a long-term commitment by both patient and medical personnel to careful and proper management. Nevertheless, in suitable cases, the techniques should generally be properly considered before proceeding to any irreversible destructive neurosurgical procedure.


Abstract: Application of heat generally increases metabolic activity, with resulting increase in circulation and exacerbation of inflammation, while cold in most cases has the opposite effect. Choice of treatment method in a given case is based on many factors, including the physical properties (ie, depth of penetration and
method of energy delivery) of the modality under consideration and knowledge of the contraindications. A thorough understanding of the physiologic bases for use of thermotherapy and cryotherapy as well as of the various methods for delivery of therapeutic heat and cold will allow the physician to make optimal use of the modalities available.

Abstract: A third case of hyperargininaemia occurring in one family was studied from birth. In cord blood serum arginine concentration was only slightly raised, but arginase activity in red blood cell haemolysates was very low. In the urine on day 2 a typical cystinuria pattern was present. Arginine concentration in serum increased to 158 mumol/100 ml on the 41st day of life. Later determinations of the arginase activity in peripheral blood showed values below the sensitivity of the method. Blood ammonia was consistently high, and cystinuria was present. The enzymatic defect was further displayed by intravenous loading tests with arginine. Serum urea values were predominantly normal or near the lower limit of normal, suggesting the presence of other metabolic pathways of urea synthesis. In urine there was no excretion of guanidinosuccinic acid, while the excretion of other monosubstituted guanidine derivatives was increased, pointing to a connexion with hyperargininaemia. Owing to parental attitude, a low protein diet (1-5 g/kg) was introduced only late. The infant developed severe mental retardation, athetosis, and spasticity.

Abstract: A 24-year-old black female presented for repeat elective Caesarean section. The procedure was performed under epidural anaesthesia. Sufentanil 25 micrograms, intended for postoperative analgesia, was inadvertently diluted to 10 ml with 15 per cent potassium chloride (KCl) instead of preservative-free normal saline (0.9 per cent NaCl). This solution was then injected via an epidural catheter into the epidural space at the conclusion of surgery. Two hours after injection of the sufentanil-KCl mixture, the patient had a level of sensory blockade to T1 and diaphoresis above this level. Painful muscle spasms had also developed below T1. One hour later she developed hypertension which required hydralazine 10 mg and labetalol 25 mg IV for treatment. The patient was treated supportively with oxygen. Dexamethasone 10 mg was administered intravenously to reduce spinal cord oedema. Intravenous diazepam 10 mg and meperidine 75 mg were given for sedation and analgesia. Complete recovery occurred within 12 hours.

Abstract: In this case study we describe a dual approach to the palliation of
difficult muscle spasms using intrathecal baclofen via a fully implanted system, together with the homeopathic approach to symptom control. The homeopathy is seen to complement rather than to replace conventional prescribing and using both approaches together appears to have avoided the necessity for increasing drug doses and to have minimized side-effects. As well as encouraging us to take on experience from other disciplines, this case study also suggests that palliative care could be a forum for evaluating the effectiveness of the homeopathic approach in symptom control in carefully designed studies.

Abstract: Vinblastine and erythromycin are among the most commonly used chemotherapeutic and antimicrobial agents, respectively. No interaction between the two has ever been reported. Towards the end of a phase I study of vinblastine plus oral cyclosporin (to reverse multidrug resistance), three patients also received erythromycin to raise their cyclosporin levels. All developed severe toxicity consistent with a much higher vinblastine dose than was actually given. This apparent potentiation of vinblastine toxicity has not been previously described.


Abstract: In a dose of 0.1 mg/kg clonidine, an alpha-2 receptor agonist, depressed the spontaneous EMG activity of the biceps and quadriceps femoris in chronically-spinalized rats. It also antagonized in a dose-dependent manner the stimulating effect of 5-hydroxytryptophan (5-HTP, 100 mg/kg). Doses of more than 0.1 mg/kg were less potent in antagonizing the effect of 5-HTP. Clonidine reduced the tonic activity of the hindlimb muscles but allowed walking movements. The depressant effect of clonidine in animals pretreated with 5-HTP was prevented by yohimbine (1.25 mg/kg), while the depressant action of the serotonin antagonist, cyproheptadine was not. In chronically-spinalized rats, clonidine (0.1 mg/kg) increased the threshold of electrically-induced flexor and extensor reflexes and decreased their amplitude. No significant modification of reflexes was seen with this dose 24 hr after spinalization. Thus, clonidine in doses of 0.1 mg/kg or less reduced directly or indirectly the excitability of motoneurons. Clonidine may prove to be a useful therapeutic adjunct in the treatment of spasticity.

Abstract: We investigated the influence of four substances on the excitability of lumbar motoneurons. These substances, three of which coexist in the same bulbospinal descending pathways that end, for the most part, around motoneurons (MNS), are: 5-hydroxytryptamine (5-HT), substance P (SP) and thyrotropin-releasing hormone (TRH). We also studied the effects of clonidine, an alpha 2 noradrenergic (NA) agonist. This study was carried out in rats spinalized at T5 and treated three weeks earlier with 5-7 dihydroxytryptamine (5-7 DHT). Under these conditions, the following responses were observed: 5-HTP (5-HT precursor) intraperitoneally (I.P.), 5-HT intrathecally (I.T.), TRH (I.P. or I.T.) and substance P (I.T.) all elicited strong excitation of MNS as measured by integrated EMG of the hindlimb muscles; substance P reduced by almost half the response to 5-HTP given one hour and 24 hours later; TRH given acutely did not modify the response to 5-HTP, but given chronically for 21 days markedly increased the response to this substance. Clonidine by itself decreased the excitability of MNS and antagonized the excitatory effects of 5-HTP and TRH. In two separate pilot trials, cyproheptadine, a 5-HTP antagonist, decreased the manifestations of spasticity in a patient with a partial spinal lesion. It would appear that clonidine may have potential use in the management of spasticity.


Abstract: The formation of tolerance to the hypothermic effect of ethanol was inhibited in rats after intraperitoneal injection of the neurotoxin DSP-4 50 mg/kg. The neurotoxin also significantly suppressed the ethanol withdrawal syndrome; hyperlocomotion, audiogenic seizures and spasticity. These behavioural changes were accompanied by a 52% decrease of the brain norepinephrine (NE) content, with no alterations in the dopamine or serotonin levels. The results indicate that intact NE neurons are necessary for the development of tolerance to ethanol-induced hypothermia and are involved in the expression of the ethanol withdrawal syndrome.


Abstract: The mechanical effect of acute decerebrate rigidity upon the ICP and the mechanisms underlying the relationship between them have been investigated with experiments performed on 26 cats. It has been shown that: a) Extreme rigidity of the peripheral musculature with or without partial activation of the trunkal muscles produces no change in ICP, b) the simultaneous elevation of the intra-thoracic and intra-abdominal pressures is the factor primarily operative in raising and maintaining the elevated ICP, c) when cerebrovascular homeostasis is already defective a subsidiary but not unimportant role is played
by the elevation of the systemic arterial pressure, d) under conditions of normal brain elastance mild and short-lasting spasms produce no effect on the ICP. In an animal, however, in which the brain elastance had been increased by inflating a small air-filled balloon, similar spasms produced a marked increase in ICP.

Abstract: Dystonic torticollis has been treated with local injections of botulinum toxin in a single blind study of 12 patients. A significant decrease of abnormal movements was recorded, and pain improved. Further studies are desirable to define the optimum dosage and site for injections, and the long term effects of repeated injections.

Abstract: In a double-blind trial in 21 patients with spasmodic torticollis botulinum-A toxin produced both subjective and objective improvement, including significant pain relief in 14 of the 16 patients presenting with pain. Side-effects were more frequently reported during placebo administration and no significant systemic adverse reactions were noted.


Abstract: Sarcoidosis is a multisystem granulomatous disorder that rarely involves the spinal cord. This report describes the presentation and rehabilitative course of a 31-yr-old man with quadriplegia secondary to spinal cord sarcoidosis. The patient had insidious, progressive weakness in his arms and legs for six weeks before evaluation. Examination revealed a C4 incomplete spinal cord injury. Computed tomography demonstrated an intrinsic cord lesion from the brainstem to approximately T8. Magnetic resonance imaging (MRI) suggested the lesion was granulomatous and cervical laminectomy confirmed noncaseating granulomas. The patient was started on high dose steroids, subsequently gained strength in the distal upper extremities, and was sent for spinal cord rehabilitation. Examination revealed 3 to 4+/5 strength in the upper extremities, 2- to 3-/5 in the lower extremities. The right side was slightly stronger than the left, with proximal musculature stronger than distal. Sensory examination was intact except in the C-8 to T-2 dermatomes. The patient was dependent in self-care and mobility except for feeding. Initial progress was inhibited by severe spasticity requiring medication, but by discharge he was independent at the wheelchair level with 4/5 strength in all four extremities except for his hands, which had 3/5 strength. Sensory exam did not change. Follow-up MRI studies revealed reduction of the lesion. Review of previous cases revealed that myelopathy is the most common presenting complaint and cervical
segments are most commonly involved. Survival averaged almost three years and significant gains were made in functional status. Rehabilitative course and special considerations, treatment and follow-up recommendations are discussed

Abstract: To define the risk of spinal deformity after selective dorsal rhizotomy (SDR) for the treatment of spasticity due to cerebral palsy, 43 patients were reviewed before and after the procedure. The average length of follow-up was 5.3 years with a range of 2-9 years. Scoliosis was present in three patients before rhizotomy. One patient had a thoracic hyperkyphosis, and another, a lumbar hyperlordosis deformity preoperatively. Wide laminectomies were performed in 46 patients, and none had laminoplasties. Twenty-eight significant spinal deformities developed in 19 patients; 15 cases of scoliosis, seven instances of lumbar hyperlordosis, five thoracic hyperkyphosis, and one L4-5 spondylolisthesis. Five patients were placed in braces, and three patients went on to have surgical stabilization of their deformities. For the entire group, the risk of developing a structural spinal deformity was 36%, with 6% requiring stabilization at an average of 4.9 years after SDR. Older age, more severe neurologic impairment, and preexisting spinal deformity seems to increase this risk

Abstract: The muscle relaxant (antispastic) effect of diazepam, alone or in combination with phenytoin, was studied in mutant Han-Wistar rats with progressive spastic paresis. Alone, phenytoin did not alter the spontaneous activity in the electromyogram (EMG) of the gastrocnemius soleus (GS) muscle of mutant rats, but strongly enhanced the depressant action of diazepam on the spontaneous EMG activity. Picrotoxin reduced the antispastic effect of diazepam alone and partially reversed the antispastic effect of combined treatment. Therefore, the antagonistic effect of picrotoxin on the reduction of the spontaneous activity in the EMG produced by the combination of both drugs hardly suggests an interaction of picrotoxin with phenytoin, but rather indicates an interaction with the effect of diazepam. Phenytoin enhancement of the depressant action of diazepam on the spontaneous EMG activity of mutant rats strongly suggests the potential therapeutic usefulness of the combined treatment with both drugs

Abstract: The effect of aminophylline on the muscle relaxant action of both diazepam and phenobarbitone was studied in genetically spastic rats of the Han-
Wistar strain which exhibit spontaneous tonic activity in the electromyogram of the gastrocnemius-soleus muscle. Both diazepam (0.8 and 4.0 mg/kg i.p.) and phenobarbitone (20 and 30 mg/kg i.p.) reduced the spontaneous activity measured in the electromyogram in a dose-related manner. Aminophylline (50 mg/kg i.p.), a methylxanthine with potent antagonistic activity of adenosine-mediated inhibition, partially reversed the muscle relaxant action of diazepam (4 mg/kg) but not that produced by phenobarbitone. The muscle relaxant effect of phenobarbitone (30 mg/kg) was antagonised by beta-carboline-3-carboxylic acid methylester (beta-CCM), 2 mg/kg i.p. The reversal of the muscle relaxant effect of phenobarbitone produced by beta-CCM was abolished by CGS 8216 (2-phenylpyrazolo-(4,3c)quinolin-3(5H)-one), 5 mg/kg i.p. Aminophylline altered neither the muscle relaxant effect of a low dose of diazepam (0.8 mg/kg) nor the reversal of the muscle relaxant effect of phenobarbitone produced by beta-CCM. These findings indicate that the interaction between diazepam and aminophylline does not involve competition for the benzodiazepine receptor and add further support to the suggestion that purinergic mechanisms may be engaged in the muscle relaxant action of diazepam.

Turski L., Schwarz M., Turski W.A., and Sontag K.H. (1985) Muscle relaxant action of 2-chloroadenosine in genetically spastic rats is independent of gamma-aminobutyric acid-mediated inhibition. Neurosci. Lett. 54, 369-374. Abstract: The role played by benzodiazepine (BDZ) receptors and GABAergic mechanisms in the muscle relaxant effect of the adenosine receptor agonist, 2-chloroadenosine (2-CLA) was evaluated in genetically spastic rats. 2-CLA reduced in a dose-related manner the spontaneous tonic activity in the electromyogram (EMG) of the gastrocnemius-soleus muscle. While the muscle relaxant effect produced by the adenosine analogue was abolished by aminophylline, a methylxanthine with potent antagonistic activity of adenosine-mediated inhibition, the two gamma-aminobutyric acid (GABA) antagonists bicuculline and picrotoxin did not reverse it. Neither Ro 15-1788 nor CGS 8216, specific BDZ receptor antagonists, nor beta-carboline-3-carboxylic acid methyl ester, an inverse agonist at BDZ receptors, affected the depressant effect of 2-CLA in the EMG. These results suggest that 2-CLA does not interact with GABA or BDZ receptor-mediated events in vivo to produce the muscle relaxant action. It is proposed that purinergic mechanisms may be involved in the muscle relaxant effects of a variety of drugs.

Turski L., Schwarz M., Turski W.A., Klockgether T., Sontag K.H., and Collins J.F. (1985) Muscle relaxant action of excitatory amino acid antagonists. Neurosci. Lett. 53, 321-326. Abstract: Antagonists of neuronal excitation induced by dicarboxylic amino acids were tested in genetically spastic rats of the Han-Wistar strain. These animals exhibit an increased muscle tone which can be measured as a spontaneous tonic activity in the electromyogram of the gastrocnemius-soleus muscle. Compounds that block excitation due to N-methyl-D-aspartic acid reduced the spontaneous activity measured in the electromyogram in a dose-related manner. The most
potent compounds, 2- amino-7-phosphonoheptanoic and kynurenic acids were
effective muscle relaxants when given either intraperitoneally or
intracerebroventricularly. 2-Amino-5-phosphonopentanoic acid possessed much
weaker muscle relaxant activity, while L-glutamic acid diethylester was inactive
by either route. The results suggest that blockade of N-methyl-D-aspartic acid
receptors results in a myorelaxant effect. Specific antagonists of excitation at N-
methyl-D-aspartic acid receptors may provide a new class of muscle relaxants

Unusual interactions of excitatory amino acid receptor agonists: alpha- and beta-
kainate antagonize motor responses to N-methyl-D-aspartate in rodents.
Neuroscience 20, 285-292.
Abstract: The alpha- and beta-stereoisomers of kainate correspond sterically to
the L- and D-isomers of glutamate. Alpha-Kainate is a potent excitant at a
specific membrane receptor site (kainate receptor). Beta-Kainate has been
proposed as a functional N-methyl-D-aspartate antagonist in vivo. Because of the
structural similarities between the alpha- and beta-stereoisomers of kainate we
have investigated the interactions of both compounds with N-methyl-D-aspartate-
mediated excitation in two well established animal models for assessing the
action of excitatory amino acids and their antagonists in vivo: determination of
CD50 (convulsant dose) for myoclonic seizures in mice and electromyographic
measurement of muscle tone in genetically spastic rats. We find that alpha-
kainate and beta-kainate produce myoclonic seizures in mice when given
intracerebroventricularly and increase the muscle tone in genetically spastic rats
when given intrathecally. Alpha-Kainate is about 5000 times more potent than
beta-kainate as a convulsant and about 1000 times more active than beta-
kainate in increasing the muscle tone. The excitatory actions of alpha-kainate
and of beta-kainate are blocked by gamma-D-glutamylaminomethylsulphonate, a
preferential kainate/quisqualate antagonist, but not by (+/-)-2-amino-7-
phosphonoheptanoate, a specific N-methyl-D-aspartate antagonist. Surprisingly,
alpha-kainate and beta-kainate antagonize the myoclonic seizures and the
increase in muscle tone produced by N-methyl-D- aspartate, and potentiate both
the anticonvulsant and myorelaxant actions of (+/-)2-amino-7-
phosphonoheptanoate. Quisqualate induces myoclonic seizures in mice after
intracerebroventricular application and increases muscle tone in genetically
spastic rats following intrathecal injection.(ABSTRACT TRUNCATED AT 250
WORDS)

Substantia nigra: a site of action of muscle relaxant drugs. Ann. Neurol. 28, 341-
348.
Abstract: Sites of action of centrally active muscle relaxant drugs are not well
defined. Clinical experience with such drugs suggests that the spinal cord may
be one of the important regions from which pathologically increased muscle tone
may be relieved. Supraspinal centers that may also be involved in the expression
of muscle relaxant action have not yet been defined. We report here that
microinjections of therapeutically relevant muscle relaxants into the midbrain tegmentum of genetically spastic rats decrease muscle tone. The substantia nigra is the region from which midazolam, baclofen, and tizanidine (drugs used clinically in the treatment of spasticity), or gamma-vinyl-GABA, (−)-2-amino-7-phosphonoheptanoate, and [D-pro2-D-phe7-D-trp9]-substance P (experimental drugs active in animal models of spasticity), reduce muscle tone in genetically spastic rats and Hoffmann reflexes in normal rats. The effects of muscle relaxant drugs are topographically restricted to the substantia nigra pars reticulata and are receptor specific. These observations disclose a previously unknown function of the substantia nigra in mediating muscle relaxation.

Turski L., Klockgether T., Turski W.A., Schwartz M., and Sontag K.H. (1990) The entopeduncular nucleus regulates muscle tone in genetically spastic rats: role of substance P and gamma-aminobutyric acid. Brain Res. 509, 347-350. Abstract: Microinjections of the substance P (SP) antagonist (D-pro2,D-phe7,D-trp9)-SP, or the gamma-aminobutyric acid (GABA) agonist, muscimol, into the entopeduncular nucleus reduced muscle tone in genetically spastic rats in a dose- and time-dependent manner. Similar injections into the ventral thalamus, zona incerta or amygdala had no effect on muscle tone. The muscle relaxant effect of (D-pro2,D-phe7,D-trp9)-SP injected into the entopeduncular nucleus was blocked by co-injections of SP, and that of muscimol by the GABAA antagonist, bicuculline methiodide. These results suggest that SP- and GABA-dependent mechanisms in the entopeduncular nucleus mediate regulation of the muscle tone.

Turski L., Jacobsen P., Honore T., and Stephens D.N. (1992) Relief of experimental spasticity and anxiolytic/anticonvulsant actions of the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate antagonist 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline. J. Pharmacol. Exp. Ther. 260, 742-747. Abstract: Spasticity is characterized by pathological overactivity in spinal stretch reflex circuits and may be associated with disturbances in excitatory amino acid-mediated transmission in the cord. A genetically determined syndrome of spasticity in the rat permits the quantitative evaluation of the antispastic effects of drugs by recording activity in the electromyogram (EMG) from a hind limb extensor muscle. In genetically spastic rats, systemic administration of the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA) antagonist, 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F) quinoxaline (NBQX), normalized pathologically increased EMG activity, whereas the AMPA agonist, alpha-amino-3-hydroxy-5-tertbutyl-4-isoxazolepropionate (ATPA), exacerbated the EMG measures of spasticity. The reflex mechanisms in the spinal cord can be studied in mice using EMG recordings from the tibial muscle (Hoffmann reflex) or from the plantar foot muscle (flexor reflex) after electrical stimulation of the tibial nerve. Systemic and i.t. administration of NBQX blocked Hoffmann reflexes in mice, leaving flexor reflexes unchanged. ATPA enhanced Hoffmann, and had no effect on flexor reflexes. The effects of NBQX on spinal reflexes were seen in doses which do not affect locomotor activity, but show anxiolytic and some antiepileptic
activity in rodents. These data suggest that the design of novel muscle relaxant drugs acting at the AMPA subtype of glutamate receptors may be feasible.

Abstract: Abecarnil is a beta-carboline agonist at benzodiazepine receptors with potent anxiolytic activity but no muscle relaxant side effects in rodents. Clinical experience suggests that changes in the muscle tone induced by benzodiazepines are related to their effects on spinal reflexes. The authors therefore analyzed the effect of treatment with abecarnil on spinal monosynaptic (Hoffmann reflexes) and polysynaptic (flexor) reflexes in mice and the influence of abecarnil on muscle tone in genetically spastic rats. The i.v. administration of abecarnil in mice (dose range, 0.02-1 mg/kg) depressed flexor reflexes in a dose-dependent manner; Hoffmann reflexes remained unchanged. Administration of diazepam i.v. (0.01-1 mg/kg) also reduced flexor reflexes and had little or no effect on Hoffmann reflexes. In genetically spastic rats, i.v. administration of abecarnil (10-30 mg/kg) decreased the muscle tone in a dose-dependent manner. A similar muscle relaxant effect was observed in such rats after i.v. administration of diazepam (0.1-0.8 mg/kg). By contrast, i.p. administration of abecarnil in mice did not influence spinal reflexes up to the dose of 1 mg/kg and, in genetically spastic rats, did not affect muscle tone up to the dose of 100 mg/kg. Administration of diazepam i.p. (1 mg/kg) depressed flexor reflexes in mice and over the range 0.2 to 5 mg/kg produced a dose- and time-dependent decrease of muscle tone in genetically spastic rats. The muscle relaxant effect of i.p. diazepam could be antagonized by i.p. administered abecarnil. These studies thus demonstrate that i.v. but not i.p. administration of abecarnil may result in muscle relaxant action in mice and in genetically spastic rats.

Abstract: The recognition that all minor tranquillizers carry the risk of dependence has had a significant impact in their prescription over the years. But it has only recently had the same impact on the prescribing of benzodiazepines because their dependence risks were not recognized until late. Approximately one third of all patients prescribed a benzodiazepine regularly for six weeks or longer will experience withdrawal symptoms if the drug is withdrawn suddenly after this time. Even if the drug is withdrawn gradually withdrawal symptoms may still lead to demands for further prescription. The major change in prescribing has been towards shorter and intermittent treatment so that tolerance is reduced and withdrawal symptoms avoided. This is appropriate for acute anxiety reactions but more difficult for longer term anxious and depressive neurotic disorders, which have a much longer natural history. Continuing evidence that other drugs not specifically marketed for the relief of anxiety, particularly the antidepressants, are effective in relieving this anxiety has led to increased prescription of...
antidepressants. Some patients may also be helped by treatment with beta-blocking drugs and new agents such as buspirone which have no significant dependence potential. There has also been a move away from drug treatment to psychological treatments for anxiety as a consequence of concern over dependence. For some conditions, particularly medical ones such as spasticity and epilepsy, benzodiazepines may be considered for long-term treatment. They may also be regarded as necessary for more severe psychiatric disorders, usually as an adjunct to other therapy. In such instances the dependence risk is acknowledged but the benefits of treatment are considered to outweigh them. There may also be patients who are dependent on benzodiazepines but the alternative of withdrawing the drug may lead to dependence on a more dangerous drug such as alcohol. In such cases it is reasonable to regard continued prescription of the benzodiazepine as the least dangerous course of action. It is important to maintain a perspective of dependence on minor tranquillizers, particularly as attitudes are in danger of being distorted by excessive media attention. To date there is no evidence that dependence on benzodiazepines leads to any dangerous long term sequela although there is concern over their effects on higher cognitive function. Nevertheless, the dangers of barbiturates, alcohol and nicotine are so much greater that it would be unfortunate if public concern led to excessive restrictions on the use of benzodiazepines. (ABSTRACT TRUNCATED AT 400 WORDS)

Abstract: Dysport (Clostridium botulinum type A toxin-haemagglutin complex) has had its licence extended to include treatment of children aged 2 years and over with dynamic equinus foot deformity, caused by spasticity associated with cerebral palsy. Dysport reduces muscle tone, thus improving function, relieving pain, and facilitating physiotherapy, application and tolerability of splints.

Abstract: BACKGROUND: Cerebral palsy is the commonest cause of severe physical disability in childhood. For many years treatment has centred on the use of physiotherapy and orthotics to overcome the problems of leg spasticity, which interferes with walking and can lead to limb deformity. Intramuscular botulinum toxin (BT-A) offers a targeted form of therapy to reduce spasticity in specific muscle groups. AIMS: To determine whether intramuscular BT-A can improve walking in children with cerebral palsy. DESIGN: Randomised, double blind, placebo controlled trial. METHODS: Forty patients with spastic diplegia or hemiplegia were enrolled. Twenty two received botulinum toxin and 18 received placebo. The primary outcome measure was video gait analysis and secondary outcome measures were gross motor function measure (GMFM), physiological cost index (PCI), and passive ankle dorsiflexion. RESULTS: Video gait analysis showed clinically and statistically significant improvement in initial foot contact.
following BT-A at six weeks and 12 weeks compared to placebo. Forty eight per cent of BT-A treated children showed clinical improvement in VGA compared to 17% of placebo treated children. The GMFM (walking dimension) showed a statistically significant improvement in favour of the botulinum toxin treated group. Changes in PCI and passive ankle dorsiflexion were not statistically significant. CONCLUSION: The study gives further support to the use of intramuscular botulinum toxin type A as an adjunct to conventional physiotherapy and orthoses to reduce spasticity and improve functional mobility in children with spastic diplegic or hemiplegic cerebral palsy.

Abstract: One patient who underwent radiation therapy for laryngeal cancer two years earlier developed chronic progressive radiation myelopathy and exhibited localized swelling of the cervical spinal cord at the C4 level and resultant blocking of the subarachnoid space on myelography and CT myelography. The condition responded markedly to the administration of corticosteroid except for persisting mild spasticity and sensory disturbances. On myelography and CT myelography half a year later, the cervical spinal cord showed no swelling. The corticosteroid therapy is considered to be useful for radiation myelopathy.

Abstract: OBJECTIVE: To evaluate changes in coronary artery spasticity in patients with vasospastic angina who had been stable for years under continuous drug treatment. METHODS: Follow up coronary angiography was performed under intracoronary ergonovine provocation in 27 well controlled patients with vasospastic angina and no organic stenosis; the tests were done > 24 months after the initial coronary angiography, in which occlusive spasm had been induced by the same regimen of ergonovine provocation. RESULTS: The mean (SD) follow up period was 47.2 (21.6) months. All patients had been free from angina attack for more than 24 months under treatment with antianginal drugs. During this follow up period, organic stenosis developed in only one case. Occlusive spasm was observed during follow up coronary angiography in 23 patients. Spasm with 90% narrowing was observed in three other patients, and diffuse significant narrowing was seen in the final patient. No significant difference was found in spasticity (p = 0.75) between the initial and the follow up tests. CONCLUSIONS: Repeated ergonovine provocation during coronary angiography after a controlled period of several years showed that coronary spasm remains inducible in most patients. Discontinuance of drug treatment during the remission from anginal attacks achieved by medication may put the patient at high risk.

Abstract: This article summarizes current knowledge about the medicinal value of cannabis and its principal psychoactive ingredient, delta 9-tetrahydrocannabinol (THC), particularly in the control of nausea and vomiting, in glaucoma, and in reduction of spasticity in multiple sclerosis. The major issues in the controversy about marijuana and medicine, primarily moral and ethical, are discussed.


Abstract: Till forty years ago infants and children with hydrocephalus had a bleak future. Most of them used to die. Those who survived lived with mental retardation, spasticity and blindness. With the advent of an effective shunting device in 1957, a new era was ushered in the history of hydrocephalus. Today an infant with hydrocephalus has a good chance of symptom-free survival into adulthood. This landmark achievement divides the past from the present. Although CSF shunts bring about a dramatic improvement in symptoms, the long term results reveal a high incidence of shunt related problems and therefore, the search for a competent and long lasting surgical treatment continues. The purpose of this communication is to review the contributions of the past, to critically evaluate the achievements of the present and to predict the advances expected to come through in the future.


Abstract: This report describes a case of metrizamide encephalopathy with persistent disturbance of consciousness and extrapyramidal symptoms. These two conditions have rarely been reported among the various adverse effects of metrizamide. An 11-year-old girl had been in almost good health until she was ten years old, at which time she received a ventriculo-peritoneal shunt operation, suffering from hydrocephalus of unknown etiology. At the age of eleven, she was admitted to our hospital due to hydrocephalus recurrence. She was examined by metrizamide shunt-gram (1200 mg iodide/4 ml). On the next day, she became drowsy. The CT scan disclosed the periventricular penetration of metrizamide into the medial part of the thalamus and the caudate nucleus. Thirteen days later, disturbance of consciousness continued, and extrapyramidal symptoms, that is, rigo-spasticity and postural tremor, were observed. Oral administration of L-threo-DOPS, the direct precursor of noradrenaline, was effective against the persistent disturbance of consciousness and L-DOPA was effective against the extrapyramidal symptoms. She soon recovered almost to normal and no neurological deficit remained. We thus conclude that the CT scan findings and effects of L-threo-DOPS and L-DOPA suggest that metrizamide encephalopathy in this case were respectively due to its periventricular penetration into the medial part of the thalamus and the caudate nucleus, and the resultant deficiency of the ascending noradrenergic reticular activating system and the nigrostriatal dopaminergic system.

Abstract: Medical histories for 105 consecutive children who underwent selective posterior rhizotomy (SPR) were reviewed to determine the incidence and clinical significance of adverse events related to anaesthesia and surgery. No intraoperative or postoperative events with potential for lasting morbidity, nor life threatening events, were identified. Intraoperatively, the most common adverse events were moderate elevation of body temperature (13/105) and transient dysrhythmias (8/105). The most frequent postoperative complications were fever, marginal oxygen saturation in the absence of supplemental oxygen, and postcatheterization cystitis. Early surgical complications, such as wound infection, cerebrospinal fluid leak, haemorrhage, and bowel or bladder disturbance were absent in this series. Surgical technique and anaesthetic management are described


Abstract: A growing amount of evidence suggests that a disturbance of immunological function is of importance in the pathogenesis of multiple sclerosis. This is reflected in the drugs used to slow progression and to treat relapses. Immunosuppressive drugs such as azathioprine, cyclophosphamide and cyclosporin might have some potential to slow down progression of multiple sclerosis, but their use is limited by potentially serious adverse effects. Recently, it was shown that interferon-beta-1b can diminish the exacerbation rate in multiple sclerosis without leading to unacceptable adverse effects. Nevertheless, symptomatic treatment remains of crucial importance in the management of multiple sclerosis patients. Spasticity, depression, fatigue and urinary, paroxysmal and sensory symptoms can all be alleviated to some extent with pharmacological interventions, although rehabilitation procedures and psychosocial consultations are no less important. Further therapeutic approaches to multiple sclerosis will be directed at either the specificity of the immune response or the grade of activation of the immune response. Magnetic resonance imaging techniques will play an important role in the evaluation of efficacy of new therapeutic agents

Abstract: OBJECTIVE: To conduct a placebo-controlled prospective study of the effectiveness of intrathecal bolus injections and continuous administration of baclofen on functional parameters in patients with severe spasticity of cerebral origin. To compare this functional evaluation with spasticity scores in different muscle groups. METHODS: In 11 patients with spasticity of cerebral origin (mainly cerebral palsy), double-blind scoring of spasticity (Ashworth scale score and visual analog score), spasms, pain, and functional abilities was performed during tests with bolus injections including a placebo control. Eight patients were considered good responders and received a subcutaneous device for intrathecal drug delivery. Six of these patients were followed up for 2 years, during which they underwent the same scoring procedures as after their bolus injections. These patients were subjected to a blinded dose reduction test. RESULTS: There was a noticeable placebo effect on spasticity scores during tests with bolus injections. Eight patients demonstrated a significant beneficial effect of intrathecal bolus injections compared with this placebo effect. Functional improvements were noted in most patients. During continuous infusion, Ashworth scale scores were less favorable but still significantly lower than at baseline. Subjective evaluation (visual analog scores) remained positive, functional improvements were maintained, and patient comfort was invariably and significantly improved. CONCLUSION: Intrathecal administration of baclofen is a safe and effective treatment for spasticity of cerebral origin. Functional improvement was demonstrated. The presence of a placebo effect on the spasticity scores suggests the need for double-blind screening in each patient.


Abstract: The authors report their recent experience with 14 meningomyelocele patients with the Arnold-Chiari II malformation. Three major types of fourth ventricle anomalies seen in the Arnold-Chiari II malformation are defined, based on preoperative magnetic resonance imaging and intraoperative ultrasound studies. The Type A deformity is defined as no cystic dilatation of the fourth ventricle. In the Type B anomaly, there is intracranial dilatation of the fourth ventricle. The Type C deformity involves intraspinal dilatation of the fourth ventricle, either dorsal to the cord or within the substance of the cord. The Type A deformity was most common in infants, and in two cases progression from a Type A to Type B deformity was documented. Recognition of the type of Arnold-Chiari II malformation aids in designing an operative approach more specific to that structural abnormality. Intraoperative ultrasound is a valuable adjunct in localization of the underlying anomalies and permits safe decompression of the
fourth ventricle. The authors’ indications for surgery now include failure to thrive due to either early respiratory and swallowing dysfunction, progressive spasticity, or upper-extremity weakness. Nine patients significantly improved following surgery and three patients with a progressively deteriorating course were stabilized by surgery. Decompression of the fourth ventricle by fenestration and internal shunting appears to be well tolerated, even in young infants, and is recommended in the treatment of the Arnold-Chiari II deformity.

Vernant J.C., Maurs L., Gout O., Buisson G., Plumelle Y., Neisson-Vernant C., Monplaisir N., and Roman G.C. (1988) HTLV-I-associated tropical spastic paraparesis in Martinique: a reappraisal. Ann. Neurol. 23 Suppl, S133-S135. Abstract: Human T-lymphotropic virus type I (HTLV-I)-associated tropical spastic paraparesis in Martinique has been identified in 54 patients, 49 women and 5 men. This myelopathy represents an endemic problem on this island and the earliest documented case dates from 1952. A blood transfusion history was obtained in 7 of the 54 patients (13%). There was a preponderance of cases from the northern Atlantic coast of Martinique, the most humid region on the island. The prevalence in this region reached 49.5 per 100,000, compared with the global prevalence of 11.9 cases per 100,000 for the island. An immune-mediated mechanism may be important in the pathogenesis of HTLV-I-associated tropical spastic paraparesis.

Verrier M., Ashby P., and MacLeod S. (1976) Effect of diazepam on muscle contraction in spasticity. Am. J. Phys. Med. 55, 184-191. Abstract: The direct effect of diazepam on skeletal muscle has been examined in 15 patients with neurological lesions resulting in spasticity. Diazepam 15-30 mg. IV reduced the amplitude of the compound action potential of the direct muscle response (M response) and the isometric twitch tension. It is postulated that diazepam may affect the contractile properties of muscle and, possibly, the electrical properties of the muscle membrane. These peripheral effects may contribute to the reported clinical benefits of the drug in patients with spasticity including those patients with complete spinal lesions.

Verrier M., Ashby P., and MacLeod S. (1977) Diazepam effect on reflex activity in patients with complete spinal lesions and in those with other causes of spasticity. Arch. Phys. Med. Rehabil. 58, 148-153. Abstract: The effects of diazepam on reflex pathways in patients having complete spinal lesions and in patients having incomplete lesions of the spinal cord or multiple sclerosis are compared to determine whether diazepam has an action at spinal level. The drug produced no significant alteration in the excitability of the monosynaptic arc in the patients with complete spinal lesions. In contrast, in the group with incomplete spinal lesions or multiple sclerosis, diazepam reduced the excitability of the monosynaptic arc. This action did not appear to result from a reduction in fusimotor drive. Diazepam also reduced the tonic vibration reflex in this group. It is postulated that these effects may be due to a supraspinal action of the drug.
Abstract: Children with cerebral palsy have tight, spastic muscles that often interfere with function, care, and, ultimately, quality of life. Until recently, treatment usually focused on the effects of the spasticity rather than the spasticity itself. Intrathecal Baclofen Therapy (ITB) administers a muscle-relaxing agent directly into the intrathecal space; thereby decreasing the amount of spasticity the child exhibits. This article discusses cerebral palsy and a new treatment for spasticity, ITB, and the development of an ITB program

Abstract: The authors evaluate the efficiency of the surgical technique of split anterior tibialis transfer, describe the long term functional results of the operation, and discuss the indications of this method of treatment. The results were very satisfactory: after surgery, 46 of 53 patients had normal shoes, 33 patients had improvement of their level of autonomy. The morbidity was very low, no patient had aggravation of the neurologic disease or general complications. The authors conclude that this operation should be employed more frequently in these disabled patients who can find definite improvement

Abstract: Intrathecal administration of baclofen has proved to be an effective treatment of spasticity related to CNS damage. Especially patients with spinal spasticity due to traumatic spinal cord injury or transverse myelitis showed a dramatic reduction of spasticity and improvement of their Ashworth scores. The results are, however, often disappointing in patients with muscular hypertension of the extensor muscles, which is frequently found in patients with multiple sclerosis or cerebral hypoxia. In the latter, using intrathecal baclofen may be restricted by serious side effects. Botulinumtoxin A is widely used in patients with various forms of dystonia. It has also been studied in spastic disorders, where local injections were valuable in relieving focal spasticity in hemiparetic patients and in infantile cerebral palsy. It is used only cautiously in severe paraspasticity. The case reports of 4 patients with incomplete and complete paraparesis due to spinal cord injury, neurodegenerative pyramidal disorder, and cerebral hypoxia demonstrate that a combination of intrathecal baclofen and botulinumtoxin A can improve clinical benefits and reduce side effects

Abstract: In acute experiments on cats anaesthetized with ketamine (25 mg/kg,
i.m.) and immobilized with myorelaxine (2 mg/kg, i.v.) the activity of two groups of motor thalamic (nucleus ventralis anterior thalami - nucleus ventralis lateralis thalami) relay neurons was studied. The neurons (n = 7) receiving afferents from deep cerebellar nuclei and projecting to the motor area 4 gamma were included in the first group, and those (n = 12) receiving afferents from nucleus entopeduncularis and projecting to the supplementary motor area 6 were included in the second one. All changes in the background activity and reactions to cerebellothalamic or nucleus entopeduncularis stimulation developing under the influence of D2 receptor antagonist haloperidol (1.5-1.7 mg/kg, i.v.) have been studied in the same cell. Under haloperidol influence both groups of neurons showed a reliable decrease of background activity and generation of high frequency discharges accompanied by a shift in the mode of interspike interval histograms. A regular decrease of probability and increase of response latencies after stimulation of afferent input were observed in neurons receiving afferents from the cerebellum. In nucleus ventralis anterior thalami - nucleus ventralis lateralis thalami neurons with an inhibitory input from nucleus entopeduncularis, a shortening of inhibition from 17.5 +/- 3.6 to 9.1 +/- 1.8 ms (P < 0.05) under the haloperidol influence was evident. If the inhibition evoked by nucleus entopeduncularis stimulation consisted of two phases separated by a period of excitation (n = 4), the duration of the second phase of inhibition after haloperidol injection regularly increased and the excitation separating the phase of inhibition after haloperidol injection regularly increased and the excitation separating the phases of inhibition became more prominent. Observation on the spontaneous activity and reactions of the same neuron for 2 h or more showed a gradual moderation of the changes evoked by haloperidol. On the basis of data obtained it is concluded that the blockade of D2 receptors is followed by the increase of inhibitory processes in the relay neurons of motor thalamic nuclei.

The suggestion is discussed that during the blockade of D2 receptors afferent impulsion to the motor cortex is being restricted and its influence on segmental apparatus of the spinal cord decreases. These conditions are beneficial for the development of spasticity (rigidity). At the same time, hyperpolarization of the relay neurons promotes the development of oscillatory processes at least in part of them and creates conditions for forming of tremor generators.


Abstract: The use of crude marijuana for herbal medicinal applications is now being widely discussed in both the medical and lay literature. Ballot initiatives in California and Arizona have recently made crude marijuana accessible to patients under certain circumstances. As medicinal applications of pure forms of delta-9-tetrahydrocannabinol (THC) and crude marijuana are being considered, the most promising uses of any form of THC are to counteract the nausea associated with cancer chemotherapy and to stimulate appetite. We evaluated the relevant research published between 1975 and 1996 on the medical applications, physical complications, and legal precedents for the use of pure THC or crude marijuana. Our review focused on the medical use of THC.
derivatives for nausea associated with cancer chemotherapy, glaucoma, stimulation of appetite, and spinal cord spasticity. Despite the toxicity of THC delivered in any form, evidence supports the selective use of pure THC preparations to treat nausea associated with cancer chemotherapy and to stimulate appetite. The evidence does not support the reclassification of crude marijuana as a prescribable medicine.


Abstract: Clioquinol is still consumed in India in considerable amounts but no new case reports have appeared since 1977. A review is made for a regional neurotoxicology group of an enquiry that we conducted in Bombay to gather information regarding SMON, spanning the period of 1967 to 1976. Nine patients were diagnosed with a variable degree of confidence as suffering from SMON, two from a retrospective search and seven after a prospective watch for the disease. Myelopathy with predominant more distal dysesthesia was seen more often than the full-blown picture of SMON. The peripheral neuropathy component (N) diagnosed clinically or electrophysiologically was seen only once. Pyramidal tract disturbances and resulting spasticity was as striking as posterior column disorder and sensory ataxia. Subacute myelopathy was seen in six patients, optico-myelopathy in two, and myeloneuropathy only once. It was clear that clioquinol has potential neurotoxicity, but no definitive explanation was forthcoming about the vast difference in the prevalence of SMON as reported from Japan and seen by us in Bombay.

Abstract: The central alpha 2 adrenoceptor agonist tizanidine is a myotonolytic agent used in the treatment of spasticity in patients with cerebral or spinal injury. Wide interpatient variability in the effective plasma concentrations of tizanidine means that the optimal dosage must be titrated over 2 to 4 weeks for each patient (dosages of 2 to 36 mg/day have been used in clinical trials). Maximum effects occur within 2 hours of administration. Antispastic efficacy has been demonstrated for tizanidine in placebo-controlled trials, with reduction in mean muscle tone scores of 21 to 37% versus 4 to 9% for patients receiving placebo. Improvement in muscle tone occurred in 60 to 82% of tizanidine recipients, compared with 60 to 65% of baclofen and 60 to 83% of diazepam recipients. Spasm frequency and clonus are also reduced by tizanidine. The most common adverse effects associated with tizanidine are dry mouth and somnolence/drowsiness. Muscle strength, as assessed by objective means, appears not to be adversely affected by tizanidine and subjective muscle...
weakness is reported less often by tizanidine recipients than by those receiving baclofen or diazepam. Global tolerability was assessed as good to excellent in 44 to 100% of patients receiving tizanidine, compared with 38 to 90% of baclofen and 20 to 54% of diazepam recipients. In conclusion, tizanidine is an antispastic agent with similar efficacy to that of baclofen and a more favourable tolerability profile. While drowsiness is a frequently reported adverse effect with both agents, subjective muscle weakness appears to be less of a problem with tizanidine than with baclofen. Tizanidine, therefore, appears to be an attractive therapeutic alternative for patients with spasticity associated with cerebral or spinal damage.


Abstract: We present the case of a spastic quadriplegic who developed mental symptoms which resolved when his Baclofen was discontinued. Of interest was the presence of EEG abnormalities similar to those described in cats receiving this drug. These abnormalities, previously unreported in humans, resolved upon discontinuing Baclofen therapy.


Abstract: The effects of cyproheptadine, a serotonergic antagonist, were studied in seven patients with spastic paresis of spinal origin. Six patients were included in a double blind crossover trial (maximal dose 24 mg/day). The patients were evaluated on both their spasticity and locomotor function. Four of the patients also participated in an open trial in which cyproheptadine was administered for a minimum of six months at optimal dose. Patients walked on a treadmill at full weight bearing when possible, or with 40% of their body weight externally supported, as required, by an overhead harness system. Cyproheptadine considerably decreased the sustained ankle clonus and episodes of spontaneous spasms observed in all the patients who previously presented these manifestations of spasticity. Two patients who required body weight support (BWS) during locomotion could walk at full weight bearing during cyproheptadine therapy. A more normal timing of EMG patterns in these patients during cyproheptadine therapy was associated with temporal distance changes and marked improvement of joint angular displacement. In contrast, the other patients showed marginal changes in the EMG and the kinematic pattern but eventually managed to walk at a higher speed. These preliminary results suggest that cyproheptadine can reduce spasticity and enhance locomotor function in spinal cord injured patients.


Abstract: A review of available studies supports a role for muscle relaxants in the treatment of painful musculoskeletal disorders. The utility of these drugs is limited.
by sedation and other side effects, as well as by the potential for abuse and dependency. Other drugs can also be used in the treatment of muscle spasm, specifically diazepam, baclofen, dantrolene sodium, and quinine sulfate. The pharmacology of the muscle relaxants and these other agents is discussed and practical suggestions for use are offered.


Abstract: Data from three placebo-controlled and 11 active-controlled studies of tizanidine were combined to permit analysis of the subsets, which were too small to evaluate within the individual studies. Overall analysis of placebo-controlled data confirms the effectiveness of tizanidine in reducing muscle tone in patients with spasticity of spinal cord origin. Subset analyses suggest that patients with more severe spasticity are more likely to respond, but age, sex, and race were not predictive of response. Comparisons of tizanidine with active controls showed no differences in efficacy compared with baclofen or diazepam. However, when compared with controls, patients treated with tizanidine did not experience increased weakness. Furthermore, patients tolerated tizanidine better than the control medications. More patients experienced adverse events during tizanidine treatment than did patients receiving placebo. The most common adverse events reported were dry mouth, somnolence, asthenia, and dizziness. Mild elevations in liver function tests were noted occasionally, but improved in all patients with dose reduction or withdrawal. Three patients from the double-blind database reported formed visual hallucinations. All three cleared; two continued tizanidine, and one discontinued.

Abstract: Mitochondrial diseases, or encephalomyopathies, are an uncommon, heterogeneous group of disorders with variable clinical course and presentation. Many of these patients present for surgery, or undergo anaesthesia in the course of investigation of their illness. Unfortunately, little information exists on their management in anaesthetic texts and the literature. We report on the anaesthetic management of a paediatric patient with mitochondrial disease, and briefly discuss the pathophysiology and anaesthetic implications of these disorders.

Abstract: Article abstract-Interferon beta (IFNbeta) reduces the relapse rate, disease activity as measured by serial MRI scanning, and disease progression of MS. Therapy with IFNbeta may be associated with a number of adverse reactions. Relatively frequent side effects include flu-like symptoms, transient laboratory abnormalities, menstrual disorders, and increased spasticity. Dermal injection site reactions occur after subcutaneous application of IFNbeta-1b and
IFNbeta-1a. Possible side effects of IFNbeta include various autoimmune reactions, capillary leak syndrome, anaphylactic shock, thrombotic-thrombocytopenic purpura, insomnia, headache, alopecia, and depression. We discuss the mechanisms and management of the different side effects of IFNbeta.

Waltz J.M., Reynolds L.O., and Riklan M. (1981) Multi-lead spinal cord stimulation for control of motor disorders. Appl. Neurophysiol. 44, 244-257. Abstract: This report presents observations in 160 patients undergoing chronic spinal cord stimulation for various disorders of the motor system and compares the results obtained using older conventional two-electrode bipolar stimulation with a newly developed four-electrode multiple level system. Improvement was noted in 84% of the 75 patients with cerebral palsy, 67% of the 42 patients with dystonia, 62% of the 21 patients with torticollis and 73% of the 22 patients with post-traumatic neurologic loss. Significant improvements were noted when comparing the two-electrode system with the new multiple level electrode. Marked to moderately improved patients increased from 57 to 84% in cerebral palsy, from 44 to 82% in dystonia, from 53 to 75% in torticollis and from 53 to 80% in dystonia, from 53 to 75% in torticollis and from 53 to 80% in posttraumatic neurologic conditions. There was a corresponding marked drop in unimproved patients in each condition.


Ward A., Chaffman M.O., and Sorkin E.M. (1986) Dantrolene. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic use in malignant hyperthermia, the neuroleptic malignant syndrome and an update of its use in muscle spasticity. Drugs 32, 130-168. Abstract: Dantrolene sodium acts primarily by affecting calcium flux across the sarcoplasmic reticulum of skeletal muscle. Recently, dantrolene has been used very successfully in the treatment of several rare hypercatabolic syndromes which have previously been associated with high mortality rates. In malignant hyperthermia, where early diagnosis and treatment usually with intravenous dantrolene in association with other supportive measures (and often subsequent dantrolene therapy) is performed, recovery is seen in virtually 100% of patients. There is a rapid resolution of hyperthermia, dysrhythmias, muscle rigidity, tachycardia, hypercapnia, mottled or cyanotic skin, and metabolic acidosis, and a slower normalisation of myoglobinuria and elevated serum creatine phosphokinase levels. In patients with family history or previous episodes of malignant hyperthermia, prophylactic treatment with dantrolene prior to anaesthesia prevents the syndrome occurring in most cases. Where malignant hyperthermia has developed patients have been successfully treated with further dantrolene therapy. Dantrolene has also been used successfully in the treatment
of a few cases of heat stroke and the neuroleptic malignant syndrome—both of which have many similarities to malignant hyperthermia. Dantrolene is well established in the treatment of patients with muscle spasticity where it generally improves at least some of the components of spasticity (i.e. hyper/hypotonia, clonus, muscle cramps and spasms, resistance to stretch and flexor reflexes, articular movement, neurological and motor functions and urinary control). However, in some patients, particularly those with multiple sclerosis, dantrolene may not be effective, and in many cases muscular strength may diminish. Long term dantrolene therapy has been associated with hepatic toxicity and may cause problems in patients treated for disorders of muscle spasticity. Thus, dantrolene offers a unique advance in the therapy available for the treatment of hypercatabolic disorders and is also useful in the treatment of muscle spasticity of various aetiology.


Abstract: Clonidine tablets have been used in the past for treatment of spasticity with some success. The use of clonidine, however, has been limited by adverse effects, mainly hypotension. Over a two-year period, 17 patients were started on clonidine transdermal delivery system. They were followed for up to 18 months. Twelve of the 17 patients had a beneficial response and have continued on the patch. In ten of these 12 patients, other antispasticity drugs were either reduced or discontinued. In another three of the 17 patients, the response was good, but the patch was discontinued. No patient demonstrated persistent problematic hypotension. Clonidine Transdermal Patch appears to be an effective treatment for spasticity after a spinal cord injury. Adverse effects appear to be minimized using this mode of delivery.


Abstract: The triad of rigidity, fever, and elevation of serum creatine phosphokinase (CPK) levels, labeled 'neuroleptic malignant syndrome' (NMS), is a dangerous complication of neuroleptic drug treatment. Amantadine was introduced for the pharmacological management of NMS because of its beneficial effects in Parkinson's disease which were attributed to direct or indirect dopaminomimetic properties of amantadine. While the dopaminomimetic effects of amantadine are weak under experimental conditions, recent studies have confirmed that amantadine is an antagonist at the N-methyl-D-aspartate (NMDA) type of glutamate receptor. Two lines of evidence suggest that amantadine or other NMDA receptor antagonists could be effective drugs for the reversal of NMS symptoms. First, glutamate antagonists restore the balance between
glutamatergic and dopaminergic systems when dopaminergic transmission has been antagonized by neuroleptic drugs. Second, by virtue of their effects against rigor and spasticity, NMDA antagonists may reduce increased muscle tone and prevent rhabdomyolysis. In conclusion, NMS may be considered an iatrogenic excitatory aminoacid syndrome which is amenable to NMDA receptor antagonist therapy.


Abstract: The adamantane derivative memantine (1-amino-3,5-dimethylaminoadamantane, D-145, Akatinol) is clinically used as well in the therapy of neurogenic motor diseases (e.g. spasticity) as in the treatment of cerebral disorders like coma, cerebrovascular and geronto-psychiatric disturbances. The aim of the paper is to summarize experimental evidences that may help to explain the clinical observations. Biochemical, pharmacological, and electrophysiological studies show that memantine interferes with the metabolism of the transmitters dopamine, noradrenaline (norepinephrine), and serotonin and modulates synaptic transmission. In order to explain the antispastic activity of memantine, a spinal action must be assumed in addition to the supraspinal effect on transmitter systems. Since memantine reduces the membrane resistance as well as the membrane conductance of sodium, potassium, and chloride ions, it is very likely that memantine is directly involved in the generation of action potentials.


Abstract: Botulinum toxin injections have been used to treat 31 patients with adductor spasmodic dysphonia. Injections of 3.00-3.75 units of botulinum toxin were performed bilaterally into the thyroarytenoid muscle. This treatment significantly decreased the standard deviation of the fundamental frequency of the speech sample, indicating a reduction in the variability of pitch amongst patients. A total of 96% of patients’ subjective diary reports showed an improvement with a median of 7 days to peak effect and a 5 week duration of peak effect.


Abstract: The administration of baclofen by intrathecal pump is a new technique used to reduce spasticity for individuals with upper motor neuron system injuries. Children with cerebral palsy often have difficulty in mobility because of this form of spasticity. The purpose of this study was to assess the functional outcomes of
intrathecal baclofen pump therapy with spasticity in children with cerebral palsy. A retrospective review of medical records for pediatric cerebral palsy patients receiving intrathecal baclofen for intractable spasticity was performed. Of 23 sequential medical records meeting requirements for inclusion in the study, 17 subjects had sufficient recorded data to be included in the study. Data from the medical records included Ashworth scores, therapy complications, and changes in mobility and independence. Although no significant changes in the upper extremities with intrathecal baclofen occurred at one and three months, the trial bolus showed statistically significant changes in mean Ashworth scores. The pre- and posttrial bolus Ashworth scores for the lower extremities showed statistically significant decreases in the posttrial scores and at one and three months when compared with the pretrial scores (p < .001). Complications were resolved with conservative management without long-term sequelae. No infections, respiratory depressions, or deaths occurred as a result of intrathecal baclofen therapy in this study. Although intrathecal baclofen had a significant effect in reducing lower extremity spasticity in children with cerebral palsy, further prospective studies are needed to determine the effects of intrathecal baclofen on such indicators as activities of daily living

Wiersbitzky S., Abel J., and Schroder C. (1993) [Spastic hemiparesis after apoplexy in renal hypertension due to mesangioproliferative glomerulonephritis (with immunosuppressive treatment) and primary hypothyroidism--which vaccinations are permitted?]. Kinderarztl. Prax. 61, 298-299.


Abstract: A one-year-old boy suffering from intermittent lactic acidosis, muscular hypotonia, horizontal gaze paralysis and spasticity in both legs had low activity of the pyruvate dehydrogenase complex associated with low amounts of immunoreactive E 1 alpha and E 1 beta. Leigh syndrome was diagnosed on the basis of the clinical and biochemical abnormalities and the typical lesions observed on MRI of the brain. Treatment with a ketogenic diet was associated with clinical and biochemical amelioration. A striking improvement of the cerebral lesions was observed by neuro-imaging


Abstract: The Clostridium botulinum neurotoxins (BoNTs) A and C1 cleave specific proteins required for neuroexocytosis. We demonstrated that, in intact neurons, BoNT A cleaves 25-kDa synaptosomal-associated protein (SNAP-25), and BoNT C1 cleaves both syntaxin and SNAP-25 (Williamson et al.: Mol Biol Cell 6:61a, 1995; J Biol Chem 271:7694-7699, 1996). Here, we compare the actions of BoNT A and BoNT C1 on mature and developing mouse spinal cord
neurons in cell culture and demonstrate that BoNT C1 is severely neurotoxic. In mature cultures, synaptic terminals become enlarged shortly after BoNT C1 exposure, and, subsequently, axons, dendrites, and cell bodies degenerate. Electron microscopy confirms that early degenerative changes occur in synaptic terminals when the somatic cytoplasm appears normal. In newly plated cultures, few neurons survive exposure to BoNT C1. Whereas both BoNT A and BoNT C1 cleave SNAP-25, BoNT A has no adverse effect on neurite outgrowth, synaptogenesis, or neuron survival. This cytotoxicity is unique to BoNT C1, is specific to neurons, and is initiated at the synaptic terminal, suggesting either a novel role for syntaxin or additional actions of BoNT C1. The neurodegeneration induced by BoNT C1 may be significant in terms of its efficacy for the clinical treatment of dystonia and spasticity.


Wissel J., Heinen F., Schenkel A., Doll B., Ebersbach G., Muller J., and Poewe W. (1999) Botulinum toxin A in the management of spastic gait disorders in children and young adults with cerebral palsy: a randomized, double-blind study of "high-dose" versus "low-dose" treatment. Neuropediatrics 30, 120-124. Abstract: The present study was performed to assess dose-response relationships of local botulinum toxin A (BtxA) treatment in children and teenagers with spastic gait due to cerebral palsy (CP) in a randomized, double-blind study employing a "high-dose" (200 units Botox per leg) and a "low-dose" (100 units Botox per leg) treatment arm in 33 patients with CP. Response parameters included changes in muscle tone assessed by the Ashworth scale at knee joint, range-of-motion (ROM) measurements at knee and ankle joint, objective analysis of longitudinal gait parameters as well as subjective assessments of improvement. Patients in the "high-dose" arm received 40-80 units Botox/muscle versus 20-40 units Botox/muscle in the "low-dose" group. Patients in both treatment arms showed significant improvement of Ashworth score (p<0.001) and ROM (p<0.01), while gait analysis revealed significant increase in gait velocity (p<0.01) and stride-length (p<0.001) over baseline. Subjects in the "high-dose" group showed significantly greater improvement on objective response measurements compared to "low-dose" patients. Also, children aged 7 years or less had greater functional benefit compared to the subgroup of patients older than 7 years. Incidence and severity of side-effects were similar in both treatment groups. The present study demonstrated dose-dependent functional improvement of dynamic deformities and spastic gait pattern in children and young adults with CP treated with local injections of botulinum toxin. A dose of 200 units Botox per leg distributed to 4 or 5 muscle bellies per leg is superior compared to 100 units Botox per leg without significantly affecting the risk of side-effects.


Abstract: High dose oral anti-spastic medication is effective in the treatment of spasticity but has the disadvantage of frequent systemic side effects such as drowsiness and general weakness. Therefore, neurolytic and chemodenervation procedures are further therapeutic options, especially in cases of local spasticity. Apart from phenol blocks with the risk of persisting painful dysesthesia, botulinum toxin type A (BtxA) appears to be a safe and effective treatment. In 204 patients (mean age, 41.5 years [range 3-91 years]) with acute (n = 29, mean duration of disease 2.9 months [range, 1-6 months]) and chronic (n = 175, mean duration of disease 111 months [range, 7-500 months]) spasticity due to stroke, traumatic brain and spinal injury and other lesions of the upper motor neuron, the effects of single-dose BtxA treatment were studied. An overall dose of 181.2 units [range, 15-600 units] of BtxA (Botox) was injected in a mean of 3.3 [1-14] muscles per patient. Results were assessed using a modified Rating of Response to BtxA (RRB, Brin et al. 1995). The RRB includes a pre- and post BtxA assessment of the severity of spasticity-associated problems (patient’s self-assessment), a rating of the current percentage of normal function in the region of the body selected for BtxA and a global rating of changes induced by BtxA. 191 (93.6%) patients demonstrated improvement over a mean of 7.7 weeks [1- 36]; no deterioration was observed. Mean overall severity and function improved significantly (p < 0.001). No systemic or severe side effects were registered. Only in 5.9% of the patients were mild (n = 10) or moderate (n = 2) reversible adverse events reported. We conclude that BtxA injections are safe and effective in the treatment of local spasticity.


Abstract: Lesions of the central nervous system often result in an upper motor neuron syndrome including spasticity, paresis with pyramidal signs, and painful spasms. Pharmacological treatment with oral antispasticity drugs is frequently associated with systemic side effects which limit their clinical use. Botulinum Toxin A (BtxA) injected in spastic muscles has been shown to be effective in reducing muscle tone, but only few studies have reported pain relief as additional benefit. Therefore, we investigated the effects of local BtxA injections in 60 patients with acute (< 12 months) and chronic spasticity and pain in a prospective multicenter study. Target muscles for BtxA were selected on the basis of clinical examination. Intramuscular BtxA injections were placed in muscles exhibiting increased muscle tone in combination with pain during passive joint movement. Patients received a mean total dose of 165.7 +/ - 108.2 [30-400] units BOTOX((R)) per treatment session in a mean 3.4 +/- 1.5 muscles. Baseline and follow-up (mean 5.9 weeks) measures included a patient self-assessment of pain and function on a five-level scale, a physician’s evaluation of function, and a global rating of response to BtxA. Fifty-four of sixty patients experienced
improvement in pain without subjective functional improvement. The effects were comparable in acute (n = 17) and chronic (n = 43) spasticity. Physician's assessment of gain in function increased significantly (p < 0.05) only in patients with chronic spasticity. No serious adverse event was observed. Mild reversible side effects (local pain, hematoma, edema, mild weakness) were observed in four patients. In conclusion, we found that intramuscular BtxA injections are a potent, well-tolerated treatment modality to significantly reduce spasticity-related local pain. This problem may be a main indication, especially in patients with poor response or intolerable side effects to oral medication.


Abstract: This study determined whether the Achilles tendon reflex, H-reflex, and ankle range of motion (ROM) during ambulation undergo significant changes after application of benzocaine spray applied to the triceps surae skin area of eight stroke patients displaying spasticity in ankle plantar flexor muscles. The H-reflex amplitude increased significantly (p less than 0.05) at 30 minutes after both the benzocaine (0.346 +/- 0.101V) and the placebo (air spray, 0.324 +/- 0.078V) when the placebo was given first; however, there was no significant difference between the two interventions. A significant decrease in ankle ROM occurred during midswing at 20 (placebo administered first) and 30 (benzocaine administered first) minutes after the placebo, but this decrease was not significantly greater than the change after the benzocaine. Benzocaine spray did not change motor neuron excitability level or improve the subject's ability to perform a functional task.


Abstract: Spasmodic dysphonia (SD), a neurologic disorder characterized by involuntary vocal spasms during speech, has been effectively treated by injections of botulinum toxin (BT) into the laryngeal muscles. The aim of the present study was to determine if the therapeutic response to BT is enhanced by immediate and continuous activation of the injected muscles. Twenty SD patients were randomized into two groups following bilateral injections: vocal rest for 30 minutes and continuous vocalization for 30 minutes. Evaluations consisted of voice ratings by expert observers, acoustic measurements using computer analyses, and laryngeal aerodynamic measurements. The findings suggest that vocal rest, rather than vocalization, produces a superior and longer lasting response in SD patients receiving BT injections. It is recommended that SD patients refrain from post-injection vocalization to maximize the therapeutic effects of BT.

Abstract: Baclofen, a centrally acting muscle relaxant, is used in the treatment of spasticity. Its pharmacokinetics has been derived from plasma and urine data in four healthy subjects, whose renal function was simultaneously measured. After oral administration of a single 40 mg dose, baclofen was mainly excreted unchanged by the kidney, 69 (14)%. The half-life, calculated from extended least squares modelling (ELSMOS) both of plasma and urine data was 6.80 (0.68) h, which is longer than reported in most studies based solely on plasma data. The renal excretion rate constant had the high mean value of 0.35 (0.24) h⁻¹, and the apparent renal clearance of baclofen equalled the creatinine clearance. Passive tubular reabsorption is relatively unimportant, since no dependence was observed on variables urine flow or pH. Although active tubular secretion may contribute to its renal clearance, as shown by the effect of co-administration of probenecid, glomerular filtration appears to be the dominant transport mechanism.

Abstract: Dantrolene, a direct acting muscle relaxant used orally for spasticity, has appeared to be effective in the prevention and treatment of malignant hyperthermia in man and animals when administered intravenously. Its pharmacokinetics following intravenous administration have been studied in dogs. Concentrations of dantrolene and its metabolites in plasma, urine, and bile were determined by high-performance liquid chromatography. Recovery of unchanged drug and reduced metabolites was negligible; of the hydroxy metabolite 2% was found in the urine and about 25% in the bile. The half-life of 5- hydroxydantrolene was shorter than that of the parent drug as demonstrated by administration of the metabolite. The apparent renal clearance of 5- hydroxydantrolene was independent of creatinine clearance, urine flow and pH, and appeared to be reduced in the presence of probenecid. Bile to plasma ratios of the hydroxy metabolite were high with biliary concentrations far exceeding the maximum solubility in water. The results of this pilot study indicate that hydroxylation is primarily responsible for the excretion of the dantrolene molecule from the body.

Abstract: The pharmacokinetics of racemic baclofen as determined from plasma and urine data in six spastic patients treated with individualized oral doses, 30-80 mg daily, are presented. Peak plasma concentrations were achieved 1.9 h (+/- 0.7) after a dose. The fluctuation in the plasma concentration was great, ranging from 188 to 439%. The total body clearance averaged 175 ml.min⁻¹ (+/- 44),
plasma protein binding 35% (+/- 6). Baclofen was for the greater part excreted unchanged by the kidney, 65% (+/- 16). Its apparent renal equalled the creatinine clearance. The contribution of the renal clearance to the total body clearance can explain the previously described toxicity when renal impairment is present. The results agree with earlier reports on single doses in healthy subjects.

Abstract: Clonidine, a centrally acting alpha 2 receptor adrenergic agonist, has been successfully used as adjunctive therapy in patients with spinal cord injury with problematic spasticity not adequately controlled by recognized spasmolytic agents. A transdermal system providing approximately constant and continuous systemic delivery of clonidine has been recently introduced to enhance patient compliance. However, experience with transdermal clonidine in the management of spasticity is limited. Three cases are presented of patients with spasticity as the result of cervical spinal cord injury, inadequately managed by oral baclofen, in whom transdermal clonidine was administered. Significant improvement in spastic hypertonia was observed in all three cases. Transdermally delivered clonidine was well tolerated, with reported side effects limited to dryness of the mouth.

Abstract: Several opiate receptor systems have been identified in the spinal cord. They produce a powerful analgesia when opioid agonists are administered intrathecally in the intact, unanesthetized animal. These effects appear mediated by an action on opioid receptors which are located presynaptically, in the terminals of primary afferents, and postsynaptically on certain dorsal horn neurons. Based on structure-activity relationships in different tests, quantitative studies of naloxone antagonism and selective cross tolerance, it appears that, in the spinal cord, there are three distinguishable populations of opioid receptors: mu, delta and kappa. Aside from the effects on nociception, these receptors are also associated with a variety of spinal mechanisms related to other aspects of sensory, autonomic and motor functions. Though in some cases these represent important side-effects (e.g. inhibition of the micturition reflex), in others, the subtle effects may have important therapeutic benefits (e.g. relieving spasticity in spinal injured patients).

Abstract: Generalized komuragaeri disease (Satoyoshi disease) is a rare disorder of unknown etiology, characterized by painful muscle spasms, alopecia, diarrhea and various endocrine disorders. We administered glucocorticoid to a girl with this disease, resulting in a marked improvement of all clinical features. The patient was a 15-year-old girl. Since the age of 13 years, she had had...
intermittent painful muscle spasms, which affected any skeletal muscles 5 to 15 times a day at exercise and at rest and lasted for a few minutes. At the age of 14 years, she had idiopathic thrombocytopenic purpura which responded to the glucocorticoid treatment. Amenorrhea and orthostatic hypotension developed at the age of 14 years. Then the loss of body and head hair was noticed and progressed slowly. She had not experienced severe diarrhea. On admission, her physical and neurological examinations showed no abnormalities except for the thin hair and frequent muscle spasms. Laboratory examinations showed elevated levels of serum creatine kinase and aldolase, positive antinuclear antibody of speckled pattern and a mild disturbance in carbohydrate absorption. Endocrinological tests suggested the dysfunction of hypothalamus as a cause of amenorrhea. Electromyogram showed large action potentials on spasms. She was treated with glucocorticoid, 2 mg/kg on alternate days. The muscle spasms decreased gradually in frequency and duration in 1 month of treatment, and disappeared in 4 months. The growth of her hair was noticed and orthostatic hypotension disappeared in 4 months. Menstruation became regular in 7 months. The muscle spasms worsened when the dosage of glucocorticoid was reduced, and they improved on the increased dosage. She was free of symptoms at 6 months after the successful diminution of glucocorticoid. The etiology of this disease has not been revealed. The association of autoimmune disorders and the responsiveness of all clinical features to glucocorticoid suggest that an autoimmune process is involved in the pathogenesis of generalized komuragaeri disease.


Abstract: The results of the present electrophysiological investigation have shed some light on the mechanisms underlying many clinical signs, at least, in patients with capsular hemiplegia. A tentative interpretation of them is given below. Cerebral lesions due to haemorrhage or infarction in the area of the middle cerebral artery interrupt an extensive part of the corticospinal tract and disturb many other descending pathways involved in voluntary performance. In consequence, a marked reduction in the ability to drive the spinal motor apparatus occurs, resulting in weakness of motor power. Here, we refer only to muscle power but not to performance. For example, the disturbance of voluntary contraction by clonus is disregarded (cf. fig. 8). On the other hand, the same lesions also release the spinal reflexes from inhibition by the higher levels of the brain and cause increased excitability in flexors and extensors. In the lower extremity, this is much more marked in extensors and extensor spasticity becomes a dominant sign clinically. Any release effect on the flexor system is largely cancelled by the high activity of the reciprocal Ia inhibitory pathway from extensors and only a fragment of it is occasionally revealed in some patients as an H-reflex in pre-tibial muscles or as weak Ia inhibition of the triceps surae. Reduced driving power of the brain may be compensated by raised excitability in the spinal cord and spastic extensors are thus naturally in a better condition to preserve motor power. Flexor muscles are doubly crippled by reduced
descending impulses and strong reciprocal inhibition by the Ia impulses from the spindles of the extensor muscles

Yatsuzuka H., Kitajima T., Taguchi Y., Sakai H., and Nakamura N. (1986) [A case of ossified yellow ligaments (ossified ligamenta flava) of the thoraco-lumbar region and magnetic resonance imaging]. No Shinkei Geka 14, 1121-1125. Abstract: A Case of ossified yellow ligaments in thoraco-lumbar region is reported. A 47-year-old-male complained low back pain with suddenness in August, 1984. One month later, he noticed dyesthesia on his right lower extremity and gait disturbance. These symptoms progressed slowly. In June, 1985, he admitted to The Jikei University Hospital. On neurological examinations, he was noticed an intermittent claudication, spastic paraparesis and stocking type sensory loss in his lower extremities. Plain lumbar X-ray films showed ossified yellow ligaments (OYL) in the posterior half of the spinal canal from the level of 10th thoracic to second lumbar vertebrae. Magnetic resonance imaging disclosed marked indentations of the spinal cord at the same level. The wide laminectomy was carried out and OYL were removed totally in gentle manner. Postoperative course was uneventful. His sensory disorders improved remarkably and he gained good muscle strength in his lower extremities, but a considerable spasticity remained still. OYL is closely related to the developmental canal stenosis, the spondylosis and the other degenerative disorders such as ossification of posterior longitudinal ligaments. This allows more complicated neurological signs and symptoms in the case of OYL. When OYL is suggested, it is recommended to performed whole spinal radiological survey. The surgical consideration should be done. From this point of view, MRI would be a most useful weapon

Yeh J., Zheng S., and Howard B.D. (1998) Impaired differentiation of HPRT-deficient dopaminergic neurons: a possible mechanism underlying neuronal dysfunction in Lesch-Nyhan syndrome. J. Neurosci. Res. 53, 78-85. Abstract: Lesch-Nyhan syndrome is a hereditary disorder of purine metabolism causing overproduction of uric acid and neurological problems including spasticity, choreoathetosis, mental retardation, and compulsive self-mutilation. The syndrome is caused by a defect in the enzyme hypoxanthine-guanine phosphoribosyltransferase (HPRT), which converts guanine and hypoxanthine to the nucleotides GMP and IMP. There is evidence that the neurological problems are due to an adverse effect of the HPRT deficiency on the survival and/or development of dopaminergic neurons, specifically. Here we report that HPRT-deficient PC12 mutants that have a normal or near normal dopamine content (55-97% of that of wild-type cells) fail to undergo neuronal differentiation induced by nerve growth factor (NGF) when the de novo pathway of purine synthesis is partially inhibited. However, nerve growth factor-induced differentiation is near normal under these conditions in PC12 HPRT-deficient mutants containing much lower dopamine levels (<8% of that of wild type cells), indicating a neurotoxic effect of the endogenous dopamine in the mutants. The degree of inhibition of the de novo pathway of purine synthesis was the same in both classes of HPRT-
deficient mutants. Expression of BCl-2 in a PC12 mutant that has a normal dopamine content allowed partial NGF-induced differentiation suggesting that the apoptotic pathway might be involved in the failure of differentiation when the de novo pathway of purine synthesis is partially inhibited


Abstract: The term spasticity is used to describe many relatively unrelated syndromes and, because they share few common pathophysiologic mechanisms, it is not possible to define the physiology or pharmacology of spasticity. In patients with spastic paresis, it is the latter negative symptom (rather than the spasticity) that accounts for almost all the functional disability. Clinical neurophysiologic techniques are useful for categorization of patients with clinically identical syndromes into subgroups which respond to different therapies. Fusimotor or spindle primary afferent hyperactivity have not been demonstrated in spastic patients; reduction in central inhibitory mechanisms probably accounts for spastic hyper-reflexia. Increased passive muscle stiffness may also be clinically significant. Therapies for spasticity include elimination of causative or enhancing factors, frequent muscle stretching, surgical approaches and chemotherapy. The latter includes dantrolene (which weakens muscles), baclofen (particularly useful for reduction of flexor spasms and flexor dystonia in patients with spinal lesions) and diazepam


Abstract: A microcomputer-based system has been used to apply the technique of excitability testing to the study of the actions of a range of pharmacological agents on the excitability of single primary afferent terminals in the mouse spinal cord in vitro. GABAA analogues all evoked increases in excitability that were bicuculline sensitive. GABA itself also evoked biphasic changes in excitability, or occasionally only suppressed terminal excitability. This latter effect was often enhanced in the presence of bicuculline, and resembled the action of the GABAB
agonist, baclofen. The GABAA action could be enhanced by concurrent application of either benzodiazepine, midazolam or flurazepam. Bicuculline alone frequently decreased excitability. This action could be abolished by blocking synaptic activity with a low Ca2+ high Mg2+ superfusate, and was therefore considered to be due to reduction of the tonic action of GABA released at synaptic connections. Comparison of the action of these agents on terminals in the spastic mutant mouse showed an increased sensitivity of the GABA response to the benzodiazepines in mutant animals.


Abstract: Intrathecal baclofen administered by means of an implantable pump is being increasingly used for successful treatment of spasticity. Meningitis following intrathecally administered baclofen is a rare but serious complication that is difficult to treat without removal of the pump. Because success rates with intravenously administered antibiotic drugs for the treatment of meningitis have been low, intrathecal administration of antibiotic agents is often required to eradicate the pathogen. The authors report the case of a patient in whom Staphylococcus epidermidis meningitis developed after insertion of an intrathecal baclofen pump. The patient was successfully treated by intrathecal coadministration of vancomycin and baclofen.


Abstract: Ninety-six children aged 3 to 14 years with cerebral paralysis in the form of spastic diplegia of medium and grave intensity were examined. The majority of the children showed disorders of zinc metabolism and of other types of metabolism. To correct metabolic abnormalities, 20 children received zinc sulfate in biological doses per os in addition to the main complex of treatment measures. 38 children suffering from cerebral paralysis made up the control group and were given a complex of routine rehabilitation treatment measures. It has been established that introduction of the biotic doses of zinc sulfate into the complex of therapeutic measures for children with cerebral paralysis in the form of spastic diplegia favoured the improvement of metabolic processes, the clinical health status of the children, and enhancement of the body defence properties.
Abstract: In about one third of patients with violent spasticity due to spinal trauma, multiple sclerosis, and diffuse brain injury adequate control with oral antispastic medication cannot be achieved and successful rehabilitation is severely handicapped. In the past these patients were subjected to destructive chemical procedures or extensive surgery. The authors present the results of management of uncontrollable spasticity by means of continuous intrathecal administration of baclofen with a totally implantable gas driven pump system (Infusaid). 30 patients were treated between June 1985 and January 1987. The main indication was incapacitating spasticity resistant to oral treatment with baclofen and caused by spinal cord injury or lesion (11 patients), multiple sclerosis (11 patients), infantile cerebral palsy (3 patients) and cerebral injury, hypoxia or ischaemia (5 patients). Clinical assessment included spasticity scores, integrated electromyography (Iemg) and motography. Effective control for spasticity with mean reduction of Iemg by 55%, decrease of Ashworth's score from 3 to 0 and improvement of life quality was obtained in all patients with daily dose of 10-800 micrograms of Baclofen. Voluntary resting motoricity was not impaired and there were no untoward central side effects. The excellent effect of intrathecal baclofen in comparison with oral therapy is explained by local, spinal GABAergic inhibitory action of the drug which is delivered directly into spinal subarachnoid space. Dose finding and dose adjustment is performed prior to pump implantation by intermittent injections into a subcutaneous port. The complications of the procedure were minor (catheter displacement, disconnection) and easily correctable. (ABSTRACT TRUNCATED AT 250 WORDS)

Abstract: Total laryngectomy patients, after undergoing a tracheoesophageal puncture (TEP), may have poor TEP speech because of hypertonicity or spasm of the pharyngoesophageal segment (PES). Conventional treatment options include speech therapy, PES dilation, pharyngeal neurectomy, and myotomy. Botulinum toxin injection into the PES has recently been reported to be effective for this disorder. However, data accumulated were based primarily on subjective analyses. This prospective investigation used both qualitative and quantitative measures to assess the effects of videofluoroscopy-guided botulinum toxin injection on TEP voice quality in laryngectomees with PES dysfunction. Patients underwent voice analyses, tracheal air pressure measures, and barium swallows before and after botulinum toxin injection. Seven of 8 patients had significant voice quality improvement, and tracheal air pressures normalized in 6 of 8 patients after injection. Videofluoroscopic botulinum toxin injection into the PES is efficacious, safe, and cost-effective and should be considered as a first-line therapy for the treatment of laryngectomees with poor quality TEP speech caused by PES dysfunction.