

tact with Monensin. Monensin (Lilley) is a commonly used veterinary feed additive with anti-protozoal, anti-bacterial, coccidiostatic and anti-fungal properties. No data were found on the ability of Monensin to penetrate human skin.

A 67 year old retired teacher rapidly developed tremor of the right hand. The tremor was especially bad when eating or driving and improved if he gripped the steering wheel more tightly. He had occasional brief shaking of his right leg. He did not have weakness or sensory symptoms. The patient's father had a tremor of his hands in the last year of his life before he died aged 75 years.

One month before the patient's tremor began, five of his horses died as a result of Monensin poisoning. After several days of accidental ingestion of Monensin, the horses became acutely incoordinated and ataxic and died within 24 hours. Necropsy of one animal showed cardiac changes. The brain was not examined.

The patient had excessive skin contact with the erroneously contaminated feed for several days before the horses died and one month before the onset of his tremor. On examination, he was intelligent without altered sensorium, speech or language. He had no head tremor and all cranial nerve functions were normal. There was no akinesia. Gait and balance were unimpaired but he had a mild tremor of the right hand at rest. There was no postural or kinetic tremor and none could be brought out by his gripping a steering wheel like object in front of him. There was no cogwheel rigidity and all tests of coordination were done smoothly. Tendon reflexes were symmetrical and he did not have Hoffmann's or Babinski's sign. He had mild vibratory sense reduction at the ankles. Benign essential tremor was not clinically evident.

Artane 4mg three times daily helped reduce the intensity of the tremor. Treatment with alcohol was not tried. Neurological follow up over the next 9 months showed no progression of symptoms either by the patient's observations or by neurological examination.

Monensin sodium is isolated from culture filtrates of *Streptomyces cinnamonensis*. This substance is effective in controlling coccidiosis in chickens and it is given to feedlot cattle to improve weight gain by attacking parasite infections. Horses are extremely sensitive to Monensin sodium and the known toxic effects are related to an inotropic effect on the heart. Monensin is cytotoxic to He La and murine clone NCTC-1742 cells in tissue culture. There are

no previous reports of human toxicity (personal communication from Stanley H Chernish, MD, Lilley Research Laboratories).

Development of the mild unilateral tremor in this patient one month after exposure to Monensin may have been coincidental, but the temporal relationship suggests Monensin might be a neurotoxin which merits further study.

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Parkinsonian syndrome caused by a tumour of the left supplementary motor area

Sir: Occasionally a brain tumour may cause a typical Parkinsonian syndrome by infiltration or compression of the corpus striatum or the substantia nigra.¹⁻³ We describe a patient with a probable low grade glioma involving the left supplementary motor area (SMA) with resting tremor, rigidity and akinesia as seen in Parkinson's disease

In 1983 the now 56 year old woman first noticed a disturbance of gait with a discrete weakness of the right leg and also difficulties in performing simultaneous bimanual skilled movements. One year later CT demon-

strated a lesion in the left fronto-central region. At the first examination (June 1986) we saw a typical Parkinsonian syndrome with discrete bradykinesia of all voluntary movements (also on the left side), a tremor at rest with a small amplitude and a frequency of 4-6 Hz, a rigidity of the extremities, pronounced on the left side, and micrographia. There was also a mild monoparesis of the right leg with hyperreflexia.

Electrophysiological studies with visual evoked potentials (50 checker board pattern reversal), somatosensory evoked potentials (tibial nerve stimulation) and also the electrically evoked long loop latencies (medial nerve stimulation with recording of the adductor pollicis brevis muscle response) were normal. The standard EEG showed an inconstant focal slowing over the left temporo-parietal region. CT demonstrated a 5 × 3 × 4 cm hypodense space occupying lesion without enhancement near to the corpus callosum and compressing the medial part of the left lateral ventricle. MRI disclosed the involvement of the left supplementary motor area more accurately (fig). A low grade astrocytoma (WHO 1-2) was assumed to be present. A biopsy of the tumour was refused by the patient.

The Parkinsonian syndrome was treated successfully with levodopa in combination with carbidopa (Sinemet (R)) and the direct dopamine agonist bromocriptine (Pravidel (R)). There has been a good response with 400 mg Sinemet and 12.5 mg Pravidel daily. There has been no progression of the monoparesis in the right leg so far.

There are several reports in the literature dealing with Parkinsonian syndrome in

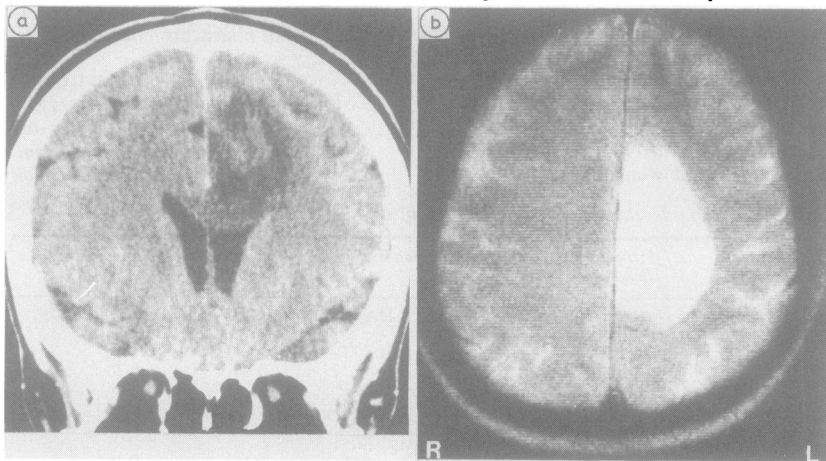


Fig Contrast-enhanced CT scan in the coronal plane (left) and T2 enhanced MRI in the transversal plane (right) demonstrate a tumour involving the left supplementary motor area.

patients with frontal, temporal, parietal, thalamic or mesencephalic brain tumours.¹⁻³ Extraaxial masses with compression of the basal ganglia appeared to be more common than infiltrating lesions,¹ whereby frontal tumours may create Parkinsonism by impairment of the tissue perfusion in the striatopallidal region by the tumour oedema.³ The signs caused by the various tumour locations are not significantly different; bradykinesia and rigidity are the most common,¹ rarely also rest tremor. Compression or infiltration of the midbrain or the corpus striatum as a possible reason of the syndrome were revealed in our patient by CT and MRI; compression of the callosal connection can not be excluded in our case but CT and MRI did not support this explanation. The incidence of a Parkinsonian syndrome in the population is 0.1-0.5% and the incidence of low grade glioma is 0.05-0.2%, therefore the changes of both diseases occurring at the same time is smaller than 0.005-0.1%. The response to medication does not contradict this and has been reported by other studies.⁴ We therefore favour another explanation.

In 1955 Travis demonstrated that a unilateral lesion of the SMA caused by a transient contralateral grasp reflex and a moderate bilateral hypertonia in the monkey.⁵ Schell *et al*⁶ showed the connections of the basal ganglia to the SMA. Investigations of the "Bereitschaftspotential" in patients with unilateral lesions of the SMA supported the idea that the SMA is involved in the initiation of voluntary movements and in the temporal organisation of sequential tasks.⁷ Recently Benecke *et al* and Dick *et al*^{8,9} suggested that some motor disturbances in patients with Parkinsonian's disease are possibly caused by an impairment of this basal ganglia output to the SMA. Furthermore Dick described a patient with infarction of the right SMA showing a deficit in programming simultaneous and sequential movements in both arms with a preponderance of the contralateral extremities. These findings are similar to those in patients with "idiopathic" Parkinson's disease and could be found also in our patient at the beginning of the illness. Therefore we believe that in rare instances lesions of one SMA may lead to a Parkinsonian syndrome which may itself be due to an impairment of the basal ganglia output to the SMA.

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Extrapyramidal reactions to anti-inflammatory drugs

Sir: The association between the recognised dopamine receptor blocking agents such as the phenothiazines and acute dystonic reactions is well known and these reactions are readily recognised and treated by most physicians. A review of the published literature shows that non-steroidal anti-inflammatory drugs (NSAIDs) have only rarely been implicated in causing extrapyramidal reactions.¹⁻⁴ We present evidence suggesting that such reactions occur more commonly than is generally appreciated.

A 51 year old man who took indomethacin 200 mg/day for intermittent acute gout was also prescribed azapropazone 1.2 g/day when an attack failed to respond to the indomethacin alone. He did not take any other medication. Two days after starting the azapropazone he suffered an oculogyric crisis, complaining of retrocollis with upward deviation of his eyes. This lasted about an hour and was witnessed and described by his general practitioner. The following day he suffered another oculogyric crisis after taking another dose of his medication. Both drugs were discontinued and there was no

recurrence of the neurological symptoms although the gout worsened temporarily. Currently, neurological examination is normal. Investigations including measurement of serum caeruloplasmin and copper concentrations are normal.

NSAIDs frequently cause adverse effects on the central nervous system. These include, for instance, "confusion" and ataxia with indomethacin. However, extrapyramidal reactions are only reported infrequently. Mefenamic acid has been implicated in causing an acute dystonic reaction¹ and a generalised dyskinesia with dystonic features.² A schizophrenic patient was reported to develop bilateral ballistic movements after starting ibuprofen; these resolved on withdrawal of the drug.³ Sulindac has been claimed to exacerbate the extrapyramidal features of Parkinson's disease in a patient who was receiving a levodopa/carbidopa preparation⁴ but another NSAID, diflunisal was said to improve Parkinsonian disability in six patients.⁵ We have been unable to find any published reports of indomethacin- or azapropazone-related extrapyramidal reactions. However, a review of reports of indomethacin-related adverse reactions to the Committee on Safety of Medicines (CSM) shows nine listings under various headings encompassing extrapyramidal disorders quite separately from nine more than were listed under the heading, "tremor" (personal communication—CSM). Adverse extrapyramidal reactions to azapropazone have not previously been reported to the CSM.

The close temporal association between starting the azapropazone and the onset of the dystonic reaction suggests that this drug was responsible for precipitating the reaction. In view of the reports to the CSM linking indomethacin with extrapyramidal reactions, it seems possible that the azapropazone interfered with the protein-binding of indomethacin, allowing more of it to cross the blood-brain barrier. Prostaglandin synthetase inhibitors, such as NSAIDs have been shown to alter catecholamine turnover within nervous tissue.⁶ The mechanism by which NSAIDs effect their extrapyramidal side-effects is not known but, by analogy with the phenothiazines and butyrophenones, an action on dopaminergic function may be important.

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