terns and of the 4th ventricle, secondary to posttraumatic atrophy in the bulbomesencephalic regions (fig).

The patient was conscious but easily fatigued and sleepy. He was aphonic and dysarthric and had an apparently preserved comprehension of surrounding events and speech. Soon after admission we noticed a dramatic improvement in the patient's phonatory ability during episodes of high fever. Pyrexia was almost always associated with signs of general excitation in this otherwise lethargic patient. Over 20 episodes of fever, reaching 39–40°C and lasting less than 24 hours, occurred during the first year at irregular intervals. The phenomenon occurred less often thereafter and disappeared altogether 18 months after injury. On three occasions fever was due to infection but in the other episodes no apparent cause could be found in spite of extensive laboratory investigations. The patient's speech was non-functional owing to severe dysarthrophonia. Although facial gesticulations as well as tongue and soft palate movements during articulation were impaired, the dysarthric component was mainly of a "suprasegmental" nature, that is, it was exhibited not so much in the production of individual speech sounds as in the production of longer units.¹ The major obstacle for communication was the phonatory impairment. Phonation length ("ah") was only 1–2 s. Loudness was inconsistent, the usual state being aphonia with occasional marked hypophonia. Phonation improvement with fever was as prominent during the infectious episodes as in the more than the 20 unexplained ones. We constructed a quantitative measure of speech intelligibility by submitting the patient to read from lists of monosyllabic and bisyllabic words in front of "judges" who tried to decipher what was said. This was done repeatedly during febrile and afebrile states. Basic pulmonary function tests were measured concomitantly as the patient suffered from a severe restrictive disturbance contributing to the phonatory problem. The improvement in speech intelligibility during fever was found to be statistically significant. There was also some change in respiratory parameters during fever. Respiratory rate increased from 20/min to 36/min, tidal volume from 0.31 to 0.42 l and forced vital capacity from 0.49 l to 0.61 l. Peak expiratory flow rate remained very low (95 l/min). Administration of moderate doses of methylphenidate, caffeine and epinephrine, in an attempt to reproduce the excitatory effect of fever, failed to improve phonation or to induce mental excitation although an improvement in lung functions did occur.

Transient mutism and aphonia are quite common in head injured patients, especially in those suffering from damage to the upper brainstem. Gradual recovery of speech functions, including the phonatory ability, is the rule in these patients.² On the basis of data derived from animal experimentation, in which the major role played by the periaqueductal grey and the lateral tegmental area was shown,^{3,4} it was speculated that lesions in these regions might be responsible for aphonia and perhaps other phenomena seen in posttraumatic mutism.² The persistence of aphonia in our patient suggests that apart from the damage to brainstem phonatory control systems, other factors operated to produce the phonatory problem. It is known that head injured patients may develop ventilatory disturbances of a restrictive nature.⁵ As gross alteration of the respiratory pattern takes place during speech production,⁶ the disturbances in ventilatory mechanics found in our patient could further aggravate his phonatory problem. A correlation was found between the improvement in speech intelligibility during fever and the occurrence of thermal hyper-ventilation and a general excitatory effect. The drugs used failed to induce such an excitation and although an increment of considerable magnitude in tidal volume was obtained, the patient's phonation remained unchanged. It seems therefore that simple ventilatory augmentation cannot in itself account for the entire effect of fever upon phonation. Efficient sound production demands a rapid and precise neuromuscular coordination of ventilatory and laryngeal musculature.^{6,7} Most probably this complex activity depends, as other motor activities do,⁸ on an optimal level of arousal for its proper execution. It is proposed that the elevation of body temperature, through its effect upon the level of arousal⁹ improved our patient's sleepy state and thereby his ability to coordinate respiratory, laryngeal and oral muscles functioning during vocalisation. Search for the possible existence of a relationship between body temperature and phonation in other aphonic brain damaged patients may shed further light on the exact mechanism and the clinical significance of this phenomenon.

The authors express their appreciation to Y Ben-Nun and to Y Shechter for help in constructing the speech intelligibility test.

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Accepted 11 February 1987

Unusual drug interactions between monoamine oxidase inhibitors and tricyclic antidepressants

Sir: Monoamine oxidase inhibitors and tricyclic antidepressants are both capable of producing severe side effects when taken in excess and these have been well documented in the past.¹ It is less well recognised that combining these two drugs, in either therapeutic or excessive dosages, may have potentially lethal side effects. The following case report is an unusual example of the dangerous side effects that may result from combining these two drugs.

A 34 year old depressive woman took an overdose of monoamine oxidase inhibitors (MAOI) and tricyclic antidepressants (TCA). The medications taken were tranylcypromine (40 mg), clomipramine (150 mg) and trazadone (400 mg). Cyclizine (150 mg) and oxazepam (60 mg) were also taken. Four hours after taking the drugs, the patient had a grand mal seizure, went into respiratory failure and was intubated and ventilated. On examination the patient was

conscious but appeared unable to move or co-ordinate her limbs. Severe rigidity and increased muscle tone was observed in all four limbs, predominantly the extensor muscle groups. Myoclonic jerks, twitching of all muscle groups and profound diaphoresis were observed. The patient was hyperpyrexial (40.6°C) and had a tachycardia (110 to 130 beats per minute). The rest of the examination was entirely normal. Specifically, the blood pressure was recorded as 100/70 mm Hg throughout the examination and there was no evidence of cardiac failure. Laboratory investigations, chest radiograph, electrocardiography and blood tests (full blood count, glucose, hepatic enzymes, urea, electrolytes, calcium and magnesium levels) were all within normal limits. A toxicology screen confirmed the presence of tricyclic antidepressants (TCA) and benzodiazepines in the blood.

The patient was paralysed with 4 mg pancuronium and was sedated with 10 mg diazepam both administered intravenously. Immediately following relaxation of the musculature the temperature decreased. Dantrolene sodium, at a dosage of 20 mg was administered 15 minutes later but by this time the temperature had already decreased to 39°C and became normal within 2 hours. Within 3 hours the patient was able to move all limbs and the following morning she was extubated. She had no residual neurological deficits after 16 hours.

The clinical presentation in this case report was not typical of the neuroleptic malignant syndrome which develops over 24–72 hours and resolves only 5 to 7 days after discontinuing the offending neuroleptic agents.¹ In addition, hyperthermia, hyper-tonicity and fluctuating levels of consciousness are invariably accompanied by instability of the autonomic nervous system, specifically blood pressure fluctuations. The rapid onset and recovery of symptoms in our patient and the stable blood pressure that she manifested made this diagnosis unlikely.

The more commonly recognised side effects of MAOI include severe hypertension, orthostatic hypotension, mania, anxiety and convulsions in patients with epileptic foci.^{1,2} Increased neuromuscular activity, muscle twitching and gross involuntary movements can occur when large doses of MAOI are administered.² Other symptoms which may take up to 12 hours to develop consist of agitation, rigidity and hyperpyrexia.^{1–3} Less well known are the rare hyperthermic reactions occasionally seen when synthetic narcotic drugs or tricyclic antidepressants are given with MAOI.² Guzé and Baxter¹ also described

drug interactions with MAOI inhibitors as causing a syndrome with some similarities to the neuroleptic malignant syndrome. The administration of tricyclic antidepressants in therapeutic doses in combination with MAOI in therapeutic doses may cause seizures, hyperpyrexia and death. These severe reactions including death are usually associated with drug overdoses but have been described when MAOI and small doses of imipramine,^{4–6} clomipramine,⁷ desipramine,⁸ or amitriptyline⁸ have been combined.

Our patient may have manifested her symptoms as a result of the MAOI tranylcypromine alone. However, only a small dose (40 mg) of tranylcypromine was ingested. The symptoms are more likely to have been caused by drug interactions. The hyperpyrexia in this patient appeared to be caused by muscle hyperactivity and responded promptly to paralysis and ventilation. It is obviously difficult to be certain which drug interacted with the MAOI but it appears most likely to have been clomipramine (a tricyclic antidepressant) or possibly trazadone.

When drug combinations of MAOI and tricyclic antidepressants are required for refractory depressions, it appears preferable to limit these combinations to those tricyclic antidepressants which have not been associated with adverse reactions. These drug combinations have been employed with very good results⁵ but, because of the potentially lethal side effects, they should only be used in exceptional circumstances when all else has failed.

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Accepted 24 February 1987

Carbamazepine induced vasculitis

Sir: Adverse effects due to carbamazepine occur in up to 25% of treated patients.^{1,2} Hypersensitivity reaction comprise about 5% and include skin rashes, agranulocytosis, fever and abnormal liver function tests.³ Skin involvement complicating carbamazepine therapy is usually manifested by a variety of dermatoses including maculopapular, urticarial, erythematous and pruritic rashes.¹ Lupus erythematosus-like diseases,⁴ exfoliative dermatitis⁵ and Stevens-Johnson syndrome⁶ have been reported rarely. Carbamazepine, as a cause of cutaneous vasculitis, is extremely uncommon.⁷ We describe a patient who developed hypersensitivity leukocytoclastic vasculitis, following the administration of carbamazepine.

A 66 year old man had suffered from trigeminal neuralgia for several months. Carbamazepine, 200 mg three times daily, was prescribed. Three weeks after initiation of therapy, he noticed a pruritic rash over the left leg which spread rapidly and was associated with a high grade fever. The patient had mild hypertension, treated by α -methyl dopa 250 mg bd for the previous 5 years.

On admission he appeared very ill and had peripheral cyanosis. The temperature was 39.8°C, pulse rate 104 min, blood pressure 140/90 mm Hg. A confluent purpuric rash was observed on the trunk and limbs without involvement of the mucous membranes (fig 1). The heart and lungs were normal. The liver was not palpable and the spleen was palpable 1 cm below the costal margin. Relevant laboratory findings were: erythrocyte sedimentation rate 38 mm after one hour (Westergren), urinalysis 2+ protein and 20–25 red blood cells per high power