dependent Cushing's disease but there was no recurrence after a short course of metyrapone and while totally abstaining from alcohol; although the possibility of cyclical true Cushing's syndrome remained, we think this unlikely. Alcohol abuse should always be considered in the differential diagnosis of Cushing's syndrome. Abstinence does not necessarily lead to rapid clinical improvement; in this case the signs and biochemical abnormalities persisted for over two months and closely mimicked pituitary-dependent Cushing's disease.

1 Rees LH, Besser GM, Jeffcoate WJ, et al. Alcohol-induced pseudo-Cushing's syndrome. Lancet 1977;i:726-8.
2 Smals AGH, Njo KT, Knober JM, Ruland CM, Kloffenburg PWE. Alcohol-induced Cushingoid syndrome. J R Coll Physicians Lond 1977; 12:36-41.
3 Paton A. Alcohol-induced Cushingoid syndrome. Br Med J 1976;iv:1504.
4 Lamberts SWJ, Klijn GM, De Jong FH, Birkenhager JC. Hormone secretion in alcohol-induced pseudo-Cushing's syndrome. JAMA 1979;242:1640-8.
5 Frijria R, Angelli A. Alcohol-induced pseudo-Cushing's syndrome. Lancet 1977;i:1050-1.

Selly Oak Hospital, Birmingham B29 6JD
R M JENKINS, MRCP, registrar in medicine
M McB PAGE, MD, MRCP, consultant physician

Remission of primary pulmonary hypertension during treatment with diazoxide

Until recently primary pulmonary hypertension was an untreatable illness characterised by steady deterioration and death about three years after diagnosis. Short-lived reductions in pulmonary vascular

months after starting diazoxide there were no clinical signs of pulmonary hypertension and the chest radiograph and electrocardiogram were normal. Pulmonary artery pressure after 15 months' treatment was 25/12 mm Hg and the patient was asymptomatic. Diazoxide was then stopped. The patient remained well for six months, when she noticed a return of the dyspnoea. Physical signs of pulmonary hypertension were again evident and the electrocardiogram showed right-sided changes. Cardiac catheterisation confirmed the relapse, the pulmonary artery pressure being 100/40 mm Hg. Since then she has been taking increasing doses of hydrallazine and is once more improving symptomatically. Haemodynamic data are summarised in the table.

Comment

In one patient with primary pulmonary hypertension we have shown how the effects of the disease may be completely ameliorated by treatment with the vasodilator drug diazoxide. We believe that all patients with this condition should be given a trial of treatment with drugs of this type. Our experience suggests that a successful response is more likely if the illness is treated at an early stage, when the pulmonary hypertension is still labile and before irreversible changes have occurred in the pulmonary arteries.

It is interesting that the pulmonary hypertension in our patient returned when diazoxide was stopped; this suggests that the underlying disease process responsible for the development of pulmonary hypertension is still active.

1 Shettigar UR, Hultgren HN, Specter M, Martin R, Davies DH. Primary pulmonary hypertension: favourable effect of isoproterenol. N Engl J Med 1976;295:1414-5.
2 Dresdale DT, Michtom RJ, Schultz M. Recent studies in primary pulmonary hypertension including pharmacodynamic observations on pulmonary vascular resistance. Bull NY Acad Med 1954;30:195-207.
3 Wang SWS, Pohl JEF, Rowlands DJ, Wade EG. Diazoxide in treatment of primary pulmonary hypertension. Br Heart J 1978;40:572-4.
4 Rubin LJ, Peter RH. Oral hydralazine therapy for primary pulmonary hypertension. N Engl J Med 1980;302:69-73.
5 Honey M, Cotter L, Davies N, Denison D. Clinical and haemodynamic effects of diazoxide in primary pulmonary hypertension. Thorax 1980; 35:269-76.

Haemodynamic data of patient with primary pulmonary hypertension

	Pulmonary artery pressure (mm Hg)			Pulmonary artery wedge pressure (mm Hg)	Cardiac output (l/min)	Pulmonary vascular resistance (units)
	Systolic	Diastolic	Mean	Mean		
Before treatment	65	35	42	4	5·4	7·0
After five months' treatment	37	20	25	9	6·8	2·4
After 15 months' treatment	25	12	17	3	6·0	2·3
Seven months after stopping diazoxide	100	40	60	8	3·8	13·7

resistance have been obtained by intravenous injections of isoprenaline and tolazoline,[1] [2] but not until 1978 was sustained improvement in the pulmonary hypertension described after treatment with oral diazoxide.[3] Of three patients treated two improved, one symptomatically and the other both symptomatically and haemodynamically for more than two years. Further studies have confirmed that pulmonary artery pressures may be reduced by diazoxide and hydrallazine[4] [5] but in no patient has a complete remission of the pulmonary hypertension been achieved. We describe a patient with primary pulmonary hypertension in whom pulmonary artery pressures returned to normal during treatment with diazoxide.

Case report

A 31-year-old housewife complained of fainting attacks since her last pregnancy 21 months earlier and exertional breathlessness for 12 months. Physical examination showed signs of severe pulmonary arterial hypertension for which investigation revealed no cause. Pulmonary artery pressure was 65/35 mm Hg and pulmonary wedge pressure was normal. The patient was treated with warfarin for anticoagulation and started on oral diazoxide, the dose being slowly increased to 600 mg a day. Side effects included fluid retention, hyperglycaemia, and hypertrichosis. After three months' treatment the patient's symptoms had improved, radiographs showed a reduction in heart size, and the electrocardiographic changes of right heart strain were less evident. Repeat cardiac catheterisation showed a pulmonary artery pressure of 37/20 mm Hg and normal pulmonary vascular resistance. Nine

The Ipswich Hospital, Heath Road Wing, Ipswich, Suffolk IP4 5PD
D RUSSELL HALL, MD, MRCP, consultant physician

Papworth Hospital, Papworth Everard, Cambridge CB3 8RE
MICHAEL C PETCH, MD, MRCP, consultant cardiologist

Transposons and trimethoprim resistance

The release of trimethoprim for use alone has led to speculation on possible effects on the incidence of trimethoprim-resistant bacteria.[1] The incidence of trimethoprim resistance has been increasing among hospital bacteria but is still low in strains causing urinary infections in the community outside hospital.[1] Nearly all trimethoprim-resistant bacteria isolated from clinical material are also sulphonamide-resistant.

Plasmids are DNA molecules that replicate autonomously in bacteria and may be transferred from one bacterium to another, a replica remaining in the original cell. R plasmids encode antibiotic resistance genes and disseminate resistance among bacteria. Transpo-

sons are specific DNA sequences that can jump from one DNA molecule to another. They do not replicate autonomously but only as inserts in a plasmid or other replicating molecule; again, a replica remains in the original molecule. Transposons can carry resistance genes, which are thus disseminated among the plasmids and chromosomes of bacteria. Plasmid-borne trimethoprim resistance may be increasing.[1] Two transposons encoding trimethoprim resistance are known—namely, Tn7 and Tn402; neither carries sulphonamide resistance. These transposable DNA sequences have been found in various naturally occurring plasmids, and Tn7 has also been found in the chromosomes of bacteria from clinical isolates.[1] [2] Possibly, with the use of plain trimethoprim, greater spread of trimethoprim-resistance transposons will occur. Trimethoprim without sulphonamide has been used for several years in Finland, but reports do not show whether trimethoprim-resistant, sulphonamide-sensitive strains of Escherichia coli have appeared as might result from the spread of trimethoprim-resistance transposons.[1]

We studied strains of E coli from urinary infections, looking for trimethoprim-resistance plasmids and transposons.

Sources of strains, methods, and results

We tested three sets of urinary isolates of E coli: 93 from schoolgirls taking part in a long-term study of bacteriuria, 1979-80[3]; 187 from specimens sent by general practitioners to the diagnostic laboratory at the department of bacteriology at this hospital, January-August 1980; and 269 from inpatients in this hospital, July and August 1980.

Methods for identifying and testing the sensitivity of bacteria and for characterising plasmids and transposons were as described.[4]

The table shows the incidence of resistance to trimethoprim, sulphonamide, and ampicillin in E coli from the different groups. Most of the trimethoprim-

Resistance to trimethoprim (Tp), sulphonamide (Su), and ampicillin (Ap) in urinary isolates of E coli. (Figures are numbers (%) of isolates)

	Schoolgirls (Cardiff) (n = 93)	General practice (Hammersmith) (n = 187)	Inpatients (Hammersmith) (n = 269)
Resistant to:			
Tp		3 (1·6)	27 (10·0)
Su	12 (12·9)	42 (22·5)	81 (30·1)
Ap	16 (17·2)	47 (25·1)	73 (27·1)
Sensitive to TpSuAp	75 (80·6)	122 (65·2)	157 (58·4)
Combinations of resistance:			
Tp		1 (0·5)	2 (0·7)
Su	2 (2·2)	17 (9·1)	31 (11·5)
Ap	6 (6·5)	22 (11·8)	25 (9·3)
SuTp			6 (2·2)
ApTpSu		2 (1·1)	15 (5·6)
ApTp			4 (1·5)
ApSu	10 (10·8)	23 (12·3)	29 (10·8)

All Tp-resistant strains, but not all Tp-sensitive ones, were tested for sensitivity to a wide range of antibacterial drugs, not shown here.

resistant strains (2/3 from general practice, 24/27 from hospital) would grow on media containing high concentrations (>500 mg/l) of the drug, which is characteristic of plasmid- or transposon-determined resistance. In most of them (2/2 from general practice, 18/24 from hospital) we found genetic or physical evidence for a Tn7-like transposon.

Comment

Our findings indicate that, although trimethoprim resistance is rare in E coli causing infections in the community, when it is found it is likely to be transposon-determined. In the past decade the TEM β-lactamase transposon, carrying resistance to penicillins including ampicillin,[2] has spread world wide. This is an important cause of the present high incidence of ampicillin resistance in E coli (table) and is also found in unrelated species including Pseudomonas, Haemophilus, and Neisseria gonorrhoeae.[2] Ampicillin has been heavily used in the community, and increasing use of trimethoprin may result in analagous spread of transposable genes for trimethoprim resistance. A veterinary example is the intensive use of trimethoprim-sulphonamide combinations in pigs, both for treatment and prophylactically. A high proportion of healthy pigs sent to two separate markets now carry E coli strains with trimethoprim resistance plasmids,[5] and we have identified the Tn7 transposon in these plasmids (unpublished results).

Single courses of co-trimoxazole or trimethoprim in man do not, at present, select trimethoprim-resistant enterobacteria,[1] as would be the case if resistance was readily acquired by mutation. The incidence of

resistance acquired by gene transfer depends on the extent of the reservoir of transmissible or transposable resistance genes. With the use of trimethoprim alone, we should look for changes in this reservoir.

[1] Anonymous. Bacterial resistance to trimethoprim. Br Med J 1980;281: 571-2.
[2] Datta N, Nugent M, Richards H. Transposons encoding trimethoprim or gentamicin resistance in medically important bacteria. Cold Spring Harbor Symp Quart Biol (in press).
[3] Asscher AW, Verrier-Jones ER, Verrier-Jones K, Mackenzie R, Williams LA. Bacteriologic follow-up of schoolgirls with untreated covert bacteriuria. Kidney Int 1979;16:92.
[4] Datta N, Dacey S, Hughes V, et al. Distribution of genes for trimethoprim and gentamicin resistance in bacteria and their plasmids in a general hospital. J Gen Microbiol 1980;118:495-508.
[5] Smith HW. Antibiotic-resistant Escherichia coli in market pigs in 1956-1979: the emergence of organisms with plasmid-borne trimethoprim resistance. J Hyg (Camb) 1980;84:467-77.

Department of Bacteriology, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS

HILARY RICHARDS, PHD, senior research officer
NAOMI DATTA, MD, FRCPATH, professor of microbial genetics

Reversible myoclonus with uraemia

Myoclonus is an uncommon complication of uraemia,[1] but it may dominate the clinical presentation. The differential diagnosis of myoclonus[2] includes many uncommon conditions in which the underlying disease is generally irreversible—for example, myoclonic epilepsy, subacute sclerosing panencephalitis, Jakob-Creutzfeldt disease, and postanoxic action myoclonus. I report a case of uraemic myoclonus in which treatment of renal failure reversed the involuntary movements and their electroencephalographic concomitants.

Case report

A 64-year-old man presented to his local hospital with lethargy. He had taken large doses of Distalgesic (dextropropoxyphene and paracetamol) for many years for osteoarthritis of the hip. Investigations disclosed normocytic anaemia and a raised blood urea concentration of 35 mmol/l (210 mg/100 ml), and a chest x-ray film showed pulmonary infiltrates. He was treated symptomatically, and with improved hydration his urea concentration began to fall. Two months later he returned, incapacitated by myoclonus, which had been present for two days, and was transferred within 24 hours to this hospital.

There was striking myoclonus, which occurred simultaneously in all four limbs and also the truncal and bulbar muscles. The jerking occurred irregularly at a rate of 1-3 Hz at rest but was increased in amplitude and frequency by any attempt at movement of the limbs or trunk or even by attempts to speak. Passive movements and attempts to elicit tendon jerks also exacerbated the myoclonus but less so than active movement. The patient was aware of his surroundings but was unable to communicate because myoclonus made his speech unintelligible. There were no focal neurological deficits; the fundi were normal. Blood urea and serum sodium and potassium concentrations were 76 mmol/l (456 mg/100 ml), 136 mmol (mEq)/l, and 8·2 mmol (mEq)/l respectively. Peritoneal dialysis was begun. Diazepam was given several times to facilitate the insertion of intravenous lines and on each occasion reduced the myoclonus considerably for a few minutes. Within three days the myoclonus had disappeared and a neurological examination was normal. Intravenous pyelography showed changes of renal papillary necrosis, which was presumed to be related to the patient's excessive use of analgesics. Pulmonary tuberculosis was also diagnosed and treated. Electroencephalographic findings are shown in the figure.

Comment

Of all the causes of myoclonus, uraemia should probably be diagnosed most promptly because it may be associated with life-threatening electrolyte disturbances. Uraemic myoclonus is potentially rapidly reversible, as shown by the clinical and electroencephalographic findings in our patient. The electroencephalographic findings in this case have important physiological implications. The pathophysiology of myoclonus is incompletely understood. The disorder may arise at several different levels in the nervous system, from the cerebral cortex to the spinal cord.[2]