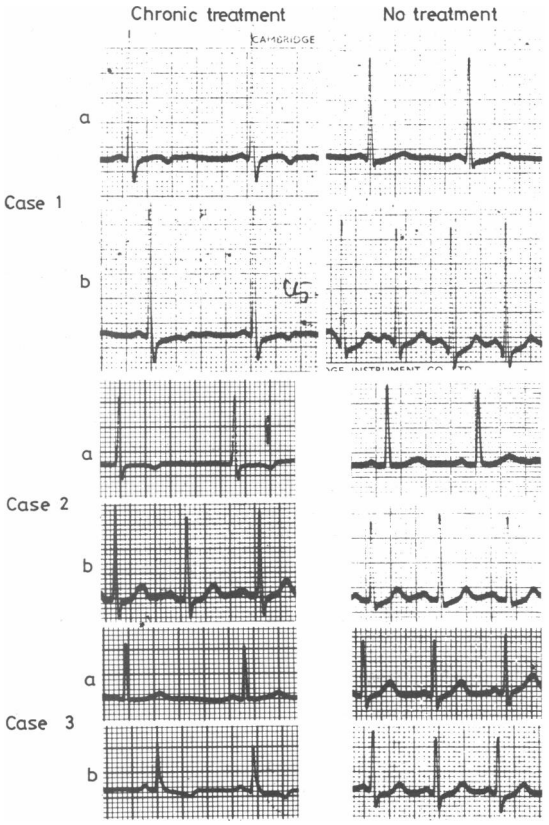
beta-blocker treatment (acebutolol 300 mg, atenolol 200 mg, and propranolol 160 mg daily, respectively). In each patient T-wave inversion was present in leads II, III, aVF, and V4-6: after exercise as well as at rest (supine and standing) in case 1, only at rest in case 2, and only after exercise in case 3. Two weeks after beta-blocker treatment was stopped the T waves became normally upright in each patient, though in case 1 they could again be inverted after the patient had been standing for 15 minutes.

Full cardiovascular investigation while the patients were not receiving any treatment included haemodynamic assessment, left ventricular and selective coronary angiography, arterial and coronary sinus lactate measurements, a pacing test, and provocation with ergometrine (500 μg intravenously). There was no evidence of coronary artery stenosis, coronary artery spasm, myocardial ischaemia, or other cardiovascular abnormality. A maximal treadmill test (Bruce protocol[2]) was normal in all the patients.

The effects on the electrocardiogram of acute treatment with acebutolol 800 mg by mouth over 12 hours (case 1) and propranolol 10 mg intravenously (cases 2 and 3) were studied. The T waves remained upright in each case both at rest (supine or standing) and on exercise testing, immediately and 20 minutes after exercise. A further course of chronic treatment with acebutolol 300 mg, atenolol 200 mg, and propranolol 320 mg respectively for three weeks reproduced the original T-wave inversion in cases 1 and 2 but not in case 3 (figure). After treatment was stopped again the T waves became upright



Electrocardiograms obtained in the three patients (supine, lead V5) before (a) and immediately after (b) exercise.

in all patients, though in case 1 they could again be inverted on standing. T waves were not inverted in any patient by hyperventilation, but in case 1 hyperventilation normalised the inversion induced by standing when the patient was not receiving treatment.

Comment

Beta-blocker treatment has been thought to be a useful test for restoring to normal "innocent" T-wave inversion.[3] Our observations indicate that chronic beta-blocker treatment may sometimes paradoxically be the cause of abnormal T-wave inversion. This is perhaps not surprising, given that the direction of the T wave is probably determined by slight regional differences in the relative duration of the action potential and that adrenergic activity influences their absolute duration and so may exert arbitrary effects on T-wave direction. Chronic and acute beta-blocker treatment have different effects on the duration of action potential,[4] which may also be relevant to our finding of T-wave inversion with chronic but not acute treatment. Patients with non-cardiac chest pain are often inadvertently treated with beta-blockers. Unrecognised iatrogenic T-wave inversion might add to the diagnostic difficulties in such patients.

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Insect-sting encephalopathy

Cerebral infarction after insect stings occurs rarely. Extrapyramidal disturbances are extremely unusual, however, only two cases having been reported in which necrosis of the basal ganglia occurred.[1 2] We describe two patients in whom extrapyramidal syndromes developed after insect stings.

Case reports

CASE 1

A few minutes after being stung on the arm a 36-year-old nurse had a convulsion, after which blood pressure of 90/60 mm Hg was recorded. She was given intravenous fluids, hydrocortisone, 10 mg chlorpheniramine, and 12·5 mg prochlorperazine intravenously. The next morning she complained of muscle aches; she had involuntary movements of the left leg, and her speech was soft and repetitive. She developed dystonia and her face became immobile. Increasing axial and limb rigidity with cogwheeling ensued. Tendon reflexes were brisk and plantar responses flexor. Cerebrospinal fluid was normal. A computed axial tomographic scan on the 12th day showed low attenuation in both posterior parietal regions.

Sequential treatment with dexamethasone, benzodiazepines, barbiturates, baclofen, dantrolene, benzhexol, and levodopa produced no benefit, and she developed generalised muscle spasms accompanied by rage, tachycardia, and sweating. After three months she had improved and could walk and feed herself.

CASE 2

Five minutes after being stung on the temple by a wasp a 38-year-old housewife lost consciousness and became cyanosed and her blood pressure became unrecordable. She was given parenteral adrenaline, hydrocortisone, and chlorpheniramine, and her blood pressure rose to 130/70 mm Hg. During the subsequent hours she became restless and resisted attempts to move her limbs. There were slow, conjugate, roving eye movements, and oculocephalic movements were absent. She developed akinetic mutism and plastic hypertonicity in the limbs, and held either arm in any position in which it was placed for a few seconds. Tendon reflexes were symmetrically brisk, abdominal reflexes were absent, and both plantar responses were flexor. Cerebrospinal fluid was normal, and electroencephalography showed alpha rhythm and excess theta.

She improved slowly with dexamethasone, but her plantar responses became extensor and ankle clonus developed. There was no apparent visual-field defect. She showed some improvement and regained speech but required care in hospital. She died four months later from pulmonary embolism, but no further information became available.

Comment

Both patients suffered anaphylactic reactions to insect stings. Drug-induced disturbances seem unlikely as, apart from a single dose of prochlorperazine administered to the first patient, neither received

phenothiazines. Although the first patient had no visual impairment or apraxia, computed tomographic appearances were compatible with parieto-occipital infarcts in arterial boundary zones and may have been due to hypotension.[3] The paroxysms of muscle spasms, tachycardia, sweating, and rage were probably due to brain-stem dysfunction analogous to the "rage reaction" produced experimentally in animals by diencephalic damage or stimulation.[4] The akinetic mutism, catatonic posturing, and disordered eye movements in the second patient indicated a lesion of the upper brain stem affecting the basal ganglia.[5]

Despite systemic hypotension the clinical features described above are not those expected from lesions in arterial boundary zones but are more in keeping with damage to basal ganglia and diencephalic structures, which are fairly resistant to hypotension. Asphyxic anoxia may affect basal ganglia, and hypoxia may have caused such damage in our cases. In addition, anaphylaxis may cause vasoconstriction or increased vascular permeability, and these mechanisms may have produced lesions in the well-vascularised structures of the brain stem and basal ganglia.

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Paracetamol-induced acute renal failure in the absence of fulminant liver damage

Acute renal failure has often been reported[1] with paracetamol poisoning but usually in association with fulminant hepatic failure. Nevertheless, renal failure may develop in the absence of liver failure. We identified 10 such cases and report here the clinical details.

Case reports

The case notes of all patients presenting with paracetamol overdose during 1974-81 were reviewed. Ten patients were identified who had manifested moderate or severe renal impairment (serum creatinine concentration >400 μmol/l (4·5 mg/100 ml)) in the absence of evidence of liver failure such as deep jaundice, encephalopathy, or severe bleeding diathesis (table). In these patients the renal failure could not be attributed to other factors such as septicaemia or ingestion of other potentially nephrotoxic drugs. All but one patient had a period of oliguria (24-hour urine <500 ml). In general, renal failure was most evident one week after ingestion compared with two to four days for the liver damage. Liver function, as indicated by the prothrombin time, usually recovered rapidly, and in no case did hepatic dysfunction cause problems in management, as may be seen from the following case report.

Case 3—A 23-year-old woman was admitted 16 hours after taking 17 g paracetamol. She was initially drowsy, due to alcohol, but her level of consciousness was normal by 12 hours and remained so thereafter. At 48 hours her prothrombin time had fallen to 21% but two days later it was back to 100%. Creatinine clearance, however, had fallen below 10 1/24 h (6 ml/min) and peritoneal dialysis was started. Liver biopsy showed centrilobular collapse with some residual necrosis; renal biopsy on the sixth day showed distal tubular necrosis with regenerative changes.

Comment

To give a truly accurate estimate of the incidence of renal failure after paracetamol overdose is impossible. During the seven years covered by this study 1035 patients were admitted to this hospital after paracetamol overdose and 23 died from liver failure (2·2%). Perhaps half of these patients,[3] however, had taken small quantities of the drug, insufficient to produce any toxic effect. Ninety-two patients had been transferred from other hospitals for inclusion in a trial of paracetamol antidote treatment.[3] In the present series four patients had been referred from other hospitals, including one who was transferred to the renal unit because of renal failure. Thus the incidence of this complication appears to be about 1% overall or 0·6% for non-referred patients. When patients who did not develop any liver dysfunction are excluded the incidence is rather higher.

Wilkinson *et al*[1] found six patients with renal failure out of 90 who had liver damage without fulminant hepatic failure after paracetamol overdose, an incidence of 7%, but the severity of the renal failure was not fully described. One further case has been reported, with results of renal histology and electron microscopy,[4] and two of the present patients have been mentioned as part of a separate study.[5] The size of the present series confirms that this pattern of damage after paracetamol overdosage may not be uncommon and highlights the severity of the renal failure that may develop.

The pathogenesis of the renal failure remains uncertain. Interestingly, in four of the seven cases in which it was recorded urine osmolarity was surprisingly low. Increases in plasma renin activity have been reported[5] and an endotoxinaemic insult implicated.[1] These factors may act together to produce renal tubular damage. A direct

Clinical details of 10 patients who developed acute renal failure in absence of fulminant liver failure after paracetamol overdose

Case No	Age (years)	Paracetamol dose (g) (time before admission (hours))	Paracetamol concentration (mg/l)	Specific treatment (time after admission (hours))	Highest aspartate transaminase activity (IU/l) (day)	Lowest prothrombin time (%) (day)	Urine sodium; osmolarity (mmol/l) (day)	Highest serum creatinine (μmol/l)	Lowest creatinine clearance (1/24 h)	Period of oliguria (days)
1	45	12·5 + 12·5 (12) (24)	48	Acetylcysteine (14)	8280 (3)	17 (3)	33; 200 (5)	811	6	3–5
2*	18	50 (14)	124	Cysteamine (17)	732 (2)	41 (2)	43; NR (3)	1240 (PD 5 days)	1	3–12
3*	23	17 (16)	34	Placebo	>1000 (2)	29 (2)	22; NR (4)	1310 (PD 8 days)	2	3–14
4	20	25 (60)	NR		>2000 (3)	27 (4)	NR; NR	700	7	2–3
5	41	29 (48)	NR		8440 (2)	21 (2)	19; 292 (4)	1080 (PD 8 days)	2	3–11
6	26	10 (12)	NR		260 (3)	70 (3)	20; 294 (4)	1460 (PD 7 days)	1	4–12
7	38	50 (6)	390	Placebo	3980 (3)	28 (2)	46; 292 (5)	560	7	4–6
8	17	11 (6)	226	Placebo	>5000 (4)	33 (2)	19; 180 (4)	480	10	Not oliguric
9	19	30 (18)	NR		4200 (2)	24 (2)	70; 210 (7)	585	8	3–4
10	25	50 (8)	328	Acetylcysteine (11)	2150 (2)	12 (2)	66; 207 (5)	789	5	4–7

NR = Not recorded. PD = Peritoneal dialysis.
*Renal biopsy performed: histology showed distal tubular damage.
Conversion: SI to traditional units—Sodium: 1 mmol/l = 1 mEq/l. Osmolarity: 1 mmol/l = 1 mosmol/l. Creatinine: 1 μmol/l ≈ 11·3 μg/100 ml.