to 6.53 kPa (70.2 to 49.1 mm Hg). Despite this, individual values did not correlate well with the infant's condition, especially beforehand. This agrees with the view of Phelan *et al*⁵ that there is no absolute value of PCO_2 to indicate the need for intermittent positive-pressure ventilation.

Clinical improvement, though more difficult to assess objectively, was very obvious. The patients appeared more settled, sternal recession decreased, and cyanosis, when present, usually disappeared. The pulse and respiratory rates of the group had decreased significantly after two hours ($p < 0.01$). All patients were improved by CPAP, and in none was ventilation considered as an alternative. CPAP increases the functional residual capacity and thereby enlarges the diameter of all the airways. Raised intraluminal pressure also prevents poorly supported small airways from collapsing during increased expiratory effort.¹⁶ At first, applying a distending pressure to the already overdistended lungs of a baby with bronchiolitis seems to be a wrong principle; presumably CPAP widens the terminal airways enough to allow deflation to occur.

Quite probably some of these infants would have recovered without any intervention, but it is highly unlikely that they all would. The intervention rate during 1976-80 was 7.5%, compared with 6.9% during 1970-5, when all the patients treated had severe respiratory failure, including those subjected to bronchial lavage. Even allowing for possible differences in the nature of the disease, probably many of the infants managed with CPAP would have progressed to a critical state without early intervention.

Nasal CPAP is easy to apply, non-invasive, and relatively free from complications. The patient may need an endotracheal tube if secretions are excessive or nasal CPAP fails to maintain improvement but can usually be extubated early and CPAP continued by nasal cannula. This avoids prolonged intubation and reduces the incidence of secondary infection. In this series three of the intubated patients had bacterial colonisation of the airway compared with only one of the infants who were not intubated.

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SHORT REPORTS

Death due to overdose of nefopam

Nefopam is recommended for the relief of acute and chronic pain. Though chemically and pharmacologically distinct from both narcotic and anti-inflammatory analgesic agents, it is one-fifth to one-half as potent as morphine, and its mode of action is unknown.¹ It appears to have low toxicity and a low potential for addiction and abuse. We report the clinical and pathological features of a patient who died due to an acute overdose of this drug, together with details of nine patients who recovered after overdosage.

Case reports

A 30-year-old woman was found unconscious by the roadside, having apparently fallen from her moped. Apart from a suicide note in the basket of the moped there was no indication of what had occurred. Although conscious during transport to hospital, she developed generalised clonic convulsions occurring at 30-second intervals and respiratory arrest ensued. After intubation and resuscitative measures gastric lavage yielded a white sediment. In the intensive care unit she was sedated and ventilated; she was deeply unconscious with reacting pupils, absent conjugate eye movements, flaccid paralysis, and extensor plantar reflexes. Electrocardiography showed a rate of 150 with first-degree block and right bundle-branch block. After five hours she had a fever of 41.9°C. She subsequently developed gross haematuria and oliguria. Coagulation studies, initially slightly abnormal, later showed considerable prolongation of the prothrombin time (31 s v 13 s), partial thromboplastin time (90 s v 44 s), and thrombin time (15 s v 10 s). Platelet count was $101 \times 10^9/l$.

Her condition deteriorated with alternating nodal and ventricular tachycardia and anuria, which was unresponsive to fluid challenge or diuretics. She died 19 hours after admission after two cardiac arrests. At necropsy the

brain showed considerable oedema with early coning. Both lungs were acutely congested with focal areas of parenchymal haemorrhage, and there was moderate pulmonary oedema and small pleural effusions. The liver, spleen, and kidneys were acutely congested and there was diffuse eosinophilic swelling of the renal tubular epithelium. The gastric mucosa was intensely congested with patchy epithelial necrosis, and the stomach contained 340 ml of pink-stained white granular material.

Extensive toxicological investigations were carried out using thin-layer chromatography, ultraviolet spectrophotometry, gas-liquid chromatography, and mass spectrometry. No drug other than nefopam was detected, and a serum concentration of 11.9 mg/l was measured in a postmortem sample. Therapeutic doses of nefopam give rise to peak plasma concentrations of about 0.1 mg/l,¹ and it was concluded that death was due to a massive overdose of nefopam.

Nefopam was first marketed in the UK in 1978, since when seven cases of overdosage have been followed up through the National Poisons Information Service and a further two have been reported to the manufacturers. These are summarised in the table. Plasma concentrations were measured in one case (case 9). A concentration of 3.8 mg/l was found at three hours in this patient, who had distinct clinical evidence of toxicity.

Comment

Few data are available on the toxicology of nefopam in man. Dogs receiving 40-80 mg/kg/day show stimulation of the central nervous system characterised by excited behaviour and convulsions,² and the median lethal dose in dogs is about 20 mg/kg intravenously and 100-200 mg/kg by mouth.³ The present case is the first known death due to nefopam in man.

From the nine non-fatal cases reported a clinical pattern of nefopam toxicity may be discerned. Convulsions, hallucinations, and agitation appear to be the neurological features of overdosage, and tachycardia

Cases of nefopam overdose followed up by National Poisons Information Service or reported to manufacturer. All patients were discharged within 24 hours or remained longer in hospital for psychiatric or social reasons

Case No	Age (years)	Sex	No of 30 mg nefopam tablets taken	Other drugs taken	Clinical features	Treatment
1	17	F	25-50	None	Conscious and orientated. Tachycardia 140 beats/min. Hyperreflexia	Stomach washout at two hours
2	24	M	Over 30	Nitrazepam	Conscious. Pupils dilated and unreactive	Stomach washout
3	19	F	35	None	Alert. Tachycardia 120 beats/min	Observation
4	32	F	50-60	Hyoscine, alcohol	Asymptomatic. Tachycardia 120 beats/min	Nil
5	16	M	20	Cephalexin (3 tablets)	Headache. Blurred vision. Tachycardia	Stomach washout
6	34	F	60	None	Grand-mal seizure. Extensor plantar reflexes. Hyporeflexia. Constricted pupils. Distorted colour vision. Tachycardia 104 beats/min. Blood pressure 120/60 mm Hg	Syrup of ipecacuanha
7	33	F	30	Alcohol	Alert, orientated. Tachycardia 108 beats/min. Blood pressure 150/100 mm Hg	Stomach washout at two hours
8	15	M	40-60	None	Excited, hallucinations. Pulse 120/min, blood pressure 140/80 mm Hg on admission; these reached maximum of 170 beats/min (sinus tachycardia) and 200/130 mm Hg	Salt-water emesis attempted at two hours. Intravenous diazepam (total 30 mg) and chlorpromazine (100 mg)
9	44	F	60	None	Sweaty, drowsy, hyperreflexic. Tachycardia 150 beats/min. Four grand-mal convulsions. Plasma nefopam: 3.8 mg/l at 3 h, 0.9 mg/l at 19 h	Stomach washout. Intravenous diazepam

with a hyperdynamic circulation are the principal cardiovascular complications. In case 4 hyoscine may have contributed to the tachycardia, and in case 8 a salt-water emesis may have contributed to hypertension; the dangers of this procedure are known.⁴

All patients recovered uneventfully with routine supportive treatment, which suggests that nefopam is fairly safe when taken in overdose. Since there is no specific antidote for nefopam poisoning, treatment should be directed primarily to the prompt removal of ingested drug by gastric lavage together with control of convulsions and hallucinations; diazepam would appear to be effective for this purpose, and beta-adrenergic blockade might help to control the cardiovascular complications.

We thank Dr T W G Kinnear, Hull Royal Infirmary, and Dr Philip Science, HM Coroner for North Humberside, for permission to report this case; Mrs H Court for compiling data; and Dr H E Lewis, Carnegie Medical, for helpful discussions. Mass spectrometry was carried out by Dr M Whitehouse of the Metropolitan Police Forensic Science Laboratory.

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Re-emergence of bullous impetigo

In common with other maternity departments, neonatal bullous impetigo (pemphigus neonatorum) has been seen only sporadically at this hospital over the past 10 years. Recently, however, 10 cases were seen in term infants on several postnatal wards. Rather than an outbreak originating from a single source, this appeared to have been a cluster of separate cases, as several different phage types were identified.

Patients, methods, and results

During the seven months from October 1979 to April 1980 10 babies developed bullous impetigo. All were full-term infants who had been nursed on the four postnatal wards at this hospital. The lesions developed when the infants were 3 to 8 days old, and in two infants were first noted shortly after discharge from hospital. The lesions were found in a wide variety of sites, particularly the axilla, groin, and neck (figure). In most babies several sites were affected but in no case did the lesions become generalised. Only one baby, who had several large bullae under the axilla, was systemically ill with fever and reluctance to feed.

Cultures, mostly of bullous fluid but otherwise of surface swabs, all grew *Staphylococcus aureus*, which was resistant to penicillin and sensitive to cloxacillin. Phage types of the strains in nine of the babies were obtained. Six of these belonged to group II. The same phage type was found in three babies, but they had been on two different wards and at different times: the second developed the condition three weeks after the first, and the third four and a half months after the second. The phage types in the remaining six infants were all different. In all, seven different phage types were identified. High vaginal swabs were obtained from eight mothers still resident at the time of diagnosis, and *Staph aureus* was not cultured from any. No further cases of bullous impetigo have been seen.

Routine care of babies on the postnatal wards includes the daily application of a powder containing 0.33% hexachlorophane (Sterzac powder) to the umbilicus, and the babies are first bathed with soap on their fifth day. There had been no change in nursing technique in the maternity department before this outbreak.

Bullous impetigo on arm of neonate.

After the first four cases had been diagnosed nose swabs were obtained from all the staff. On the sixth day one mother developed a *Staph aureus* breast abscess and on the eighth day her baby developed bullae infected with the same phage type. The strain in this baby was of the same phage type as that in another born three weeks later but nursed on a different ward. A member of the paediatric staff who had been present at the delivery of the former baby and examined the latter was subsequently found to be a nasal carrier of the same phage type of *Staph aureus*. Both babies' mothers were