over the two days. She was extremely anxious about being left alone, but once the analgesia was withdrawn all symptoms disappeared.

Case 3— A 58 year old woman underwent fusion of the posterior lumbar bodies with fusion of the alar transverse processes at L5-S1. On the third postoperative day the became convinced that her leg was black despite reassurances to the contrary. A total dose of buprenorphine of 1150 μg had been given. When the drug was withdrawn the symptoms disappeared.

Cases 4 and 5—Two further cases occurred (table). Symptoms did not develop until the third postoperative day.

Patients with psychotomimetic symptoms after epidural buprenorphine

Case No	Sex and age (years)	Operation	Presenting hallucinatory symptoms	Total dose of buprenorphine
1	F 40	Fusion of lumbar bodies posteriorly	Saw horrifying creatures in wall	900 μg
2	F 38	Fusion of spine between transverse processes posteriorly	Dreamt of frightening episode of her youth	750 μg
3	F 58	Fusion of lumbar bodies between alar transverse processes	Believed her leg to be black	1159 μg
4	M 42	Fusion of lumbar bodies posteriorly (L4-5)	Thought that there were people in room talking about him	1000 μg
5	M 55	Repair of pseudoarthrosis (L3-4)	Thought that objects in room were falling on top of him	1200 μg

Comment

Buprenorphine, with its high lipid solubility and avidity for opiate receptors, is a useful alternative to intramuscular morphine when injected into the epidural space after spinal reconstructive surgery.[2] The incidence of associated psychotomimetic symptoms, however, has not been reported. We examined the records of all cases of spinal reconstructive surgery in this hospital in 1987 and 1988. One hundred patients were operated on, of whom nine exhibited some form of hallucinatory behaviour. The epidural dose prescribed in the five cases reported here was 150 μg six to eight hourly as required, which is slightly less than the normal postoperative dose.

The high lipid solubility of the drug results in local action at the level of the spinal cord. The drug may act through attachment to β enkephalin receptors as well as through the systemic circulation via the epidural venous plexus. This latter effect was probably the aetiological mechanism in the cases reported here and is supported by a report of near fatal auditory hallucinations after sublingual administration of buprenorphine.[3] Though no firm evidence exists to implicate altered opiate systems in the aetiology of the affective psychoses,[4] our cases provide evidence of a possible excitatory or disinhibiting effect of buprenorphine on the limbic and extrapyramidal systems, which have a role in changes in behaviour and mood induced by opiates. Whether this is caused by a direct effect on specific opiate receptors which then stimulate other arousal pathways, whether buprenorphine causes an increase in β endorphin concentrations in the corpus striatum, or whether a hitherto unknown class of receptors that induce arousal could be a factor remains to be elucidated.

1 Harcus AH, Ward AE, Smith DW. Buprenorphine in postoperative pain: results in 7500 patients. *Anaesthesia* 1980;**33**:382-6.
2 Murphy DF, MacEvilly M. Pain relief with epidural buprenorphine after spinal fusion: a comparison with intramuscular morphine. *Acta Anaesthesiol Scand* 1984;**28**:144-5.
3 Paraskeviades EC. Near fatal auditory hallucinations after buprenorphine. *Br Med J* 1988;**296**:214.
4 Thompson JW. Opioid peptides. *Br Med J* 1984;**288**:259-60.

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Occupational asthma in nurses caused by chlorhexidine and alcohol aerosols

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Chlorhexidine is known to sensitise skin[1] and has been associated with severe allergic reactions.[2] We are not aware of any previous report of an association between asthma and the use of chlorhexidine and alcohol aerosols. We describe two cases.

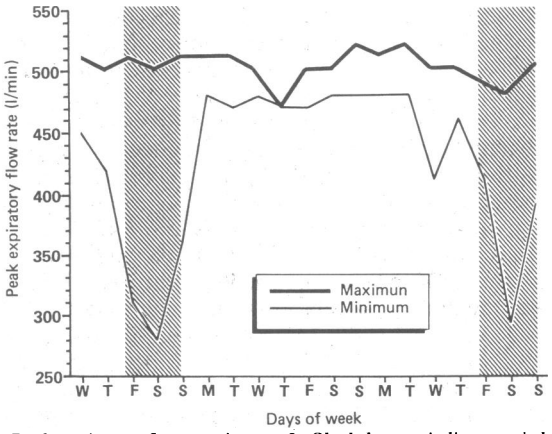
Case reports

Case 1—A 54 year old nursing auxiliary presented with a three month history of increasingly frequent attacks of cough and wheezing. These episodes occurred within minutes after she used a chlorhexidine and alcohol aerosol (Dispray 2 Hard Surface Disinfectant, Stuart Pharmaceuticals, Wilmslow, Cheshire) to disinfect incubators. She had been a cigarette smoker previously but did not have a history of asthma and was not receiving treatment for asthma. Spirometric testing gave normal results, with the ratio of forced expiratory volume in one second to forced vital capacity being 3·4:4·2 litres (81%). The concentration of histamine causing a 20% fall in the forced expiratory volume in one second was 9·2 g/l, indicating borderline hyperresponsiveness of the airways.[3] A bronchial provocation test that mimicked the woman's normal use of the aerosol was performed, during which she cleaned the work surfaces in a small ventilated laboratory with this agent for 30 minutes. Spirometric values were recorded over the next eight hours and compared with those taken over eight hours on a control day. The forced expiratory volume in one second fell by 13% 10 minutes after the challenge, and this was associated with cough and chest tightness. No late response was observed.

Case 2—A 43 year old midwife presented with a six month history of chest tightness after exposure to a chlorhexidine and alcohol aerosol (Dispray 2). She was a non-smoker and did not have a history of asthma, but she had recently been prescribed a salbutamol inhaler. Spirometric tests gave normal results, with the ratio of forced expiratory volume in one second to forced vital capacity being 3·49:4·05 litres (86%). A histamine challenge test indicated normal airways responsiveness, the concentration of histamine causing a 20% fall in the forced expiratory volume in one second being >16 g/l.[3] The patient recorded peak expiratory flow rates five times daily. At work there was a 43-48% variation between maximum and minimum values compared with less than 10% variation away from work (figure). A bronchial provocation test with the aerosol showed a maximum fall in forced expiratory volume in one second of 22% two minutes after exposure to the spray. No late response was observed.

Comment

Neither of our patients had a history of asthma or increased airways responsiveness to histamine when



Peak expiratory flow rate in case 2. Shaded areas indicate periods when patient was at work

investigated, and thus the bronchoconstriction is unlikely to have been a non-specific irritant reaction. The absence of airway hyperresponsiveness may have been because the measurements were taken some weeks after the last exposure to the spray, but hyperresponsiveness is not invariably present in patients with occupational asthma.[4,5] Challenge with the disinfectant spray produced an asthmatic response in both patients and supported the clinical diagnosis of occupational asthma due to this agent. The use of chlorhexidine-alcohol aerosols was stopped in the departments where these nurses worked, and they remained free of symptoms.

As this form of disinfection is widely used within the health service a large number of employees could be exposed to it. We have highlighted the risk within this health board and have notified both the manufacturers and the Committee on Safety of Medicines.

1 Ljunnggren B, Moller H. Eczematous contact allergy to chlorhexidine. *Acta Derm Venereol (Stock)* 1972;**52**:308-10.
2 Cheung J, O'Leary JJ. Allergic reaction to chlorhexidine in an anaesthetised patient. *Anaesth Intensive Care* 1985;**13**:429-30.
3 Hargreave FE, Ryan G, Thomson NC, *et al*. Bronchial responsiveness to histamine or methacholine in asthma: measurement and clinical significance. *J Allergy Clin Immunol* 1981;**68**:347-55.
4 Burge PS. Occupational asthma in electronics workers caused by colophony fumes: follow-up of affected workers. *Thorax* 1982;**37**:348-55.
5 Lozewicz S, Assoufi BK, Hawkins R, Newman-Taylor AJ. Outcome of asthma induced by isocyanates. *Br J Dis Chest* 1987;**81**:14-22.

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Impaired filterability of white cells in acute cerebral infarction

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The outcome of cerebral infarction after thromboembolism depends on the extent of residual microvascular perfusion. Whole blood filterability is reduced in acute stroke,[1] but whether this reflects changes in plasma viscosity, fibrinogen concentration, packed cell volume, or the filterability of erythrocytes or leucocytes is not known. We therefore measured these variables in patients with acute stroke and in controls.

Subjects, methods, and results

We studied 39 patients with acute hemiparetic cerebral infarction, which had been confirmed by computed tomography in 24 and by the Guy's clinical score[2] in 15, on the morning after admission. We also studied 11 patients of similar age with radiological evidence of acute chest infection (acute phase controls) and 61 asymptomatic controls, who were hospital staff or patients without vascular, infective, inflammatory, or malignant disease. Venous blood was anticoagulated with edetic acid (1·5 g/l) for measurement of the packed cell volume, plasma viscosity (Coulter-Harkness capillary viscometer; 37°C), and fibrinogen concentration (by heat precipitation). Suspensions of blood cells in phosphate buffered saline (pH 7·4, 290 mmol/kg) were filtered at 25 (±1)°C through filters with pores of diameter 5 μm (Nuclepore, Pleasanton, California) after filtration of buffer. Flow variables were calculated relative to the values obtained with buffer. Erythrocytes were suspended at a packed cell volume of 0·10 and filtered (Carri-Med Filtrometer, Dorking) at constant pressure (3 cm water), the relative initial flow rate being measured.[3] Polymorphonuclear and mononuclear leucocytes were separated by Ficoll-Hypaque density gradient centrifugation, suspended at 10^5/ml, and filtered at constant flow (1·5 ml/min), the relative pressure at six minutes being measured.[4]

The table shows that there were no significant differences among the groups in the packed cell volume or filterability of erythrocytes. Plasma viscosity and fibrinogen concentration increased with age in the asymptomatic controls and were further increased in the patients with cerebral infarction. The most striking findings, however, were impaired filterability of leucocytes (increased relative pressure) in those controls aged 40 and over (mean difference from value in controls under 40=0·54 (95% confidence interval 0·02 to 1·06) for polymorphonuclear leucocytes and 1·69 (0·80 to 2·58) for mononuclear leucocytes). Further impairment was seen in the patients with cerebral infarction compared with controls matched for age (mean difference 1·17 (0·63 to 1·71) for polymorphonuclear leucocytes and 2·75 (1·69 to 3·81) for mononuclear leucocytes). Filterability of leucocytes was unrelated to sex, smoking habit, or death in hospital (n=15), but in the patients with stroke fibrinogen concentration correlated with the filterability of polymorphonuclear leucocytes (Spearman's rank test, r=0·43, p=0·01) and of mononuclear leucocytes (r=0·30, p=0·08). Filterability of leucocytes in the patients with stroke was similar to that in the patients with chest infection, who also showed similar acute phase increases in fibrinogen concentration and viscosity.

Results in four groups studied, expressed as means (SD)

	Controls		Patients with cerebral infarction	Patients with chest infection
	<40 Years	≥40 Years		
No in group	30	31	39	11
No of men	15	15	17	6
Age (years)	28 (4)	68 (11)	71 (11)	73 (11)
Packed cell volume	0·42 (0·03)	0·42 (0·04)	0·44 (0·05)	0·41 (0·05)
Viscosity (mPa.s)	1·41 (0·10)***	1·46 (0·10)***	1·59 (0·12)	1·54 (0·20)
Fibrinogen (ml/l)	26·8 (6·9)***	34·2 (7·1)***	49·3 (11·6)	47·3 (13·6)
Filtration variables†:				
Erythrocytes	0·496 (0·036)	0·498 (0·041)	0·497 (0·053)	0·486 (0·041)
Polymorphonuclear leucocytes	3·66 (1·10)***	4·20 (0·90)***	5·37 (1·23)	4·83 (1·95)
Mononuclear leucocytes	5·88 (1·62)***	7·57 (1·84)***	10·32 (2·44)	9·58 (2·38)

***p<0·001. Compared with values obtained in patients with cerebral infarction (unpaired Wilcoxon test).
†See text for definitions.

Comment

We showed that reduced filterability of blood in patients with acute cerebral infarction[1] is not due to changes in packed cell volume or the filterability of