SHORT REPORTS

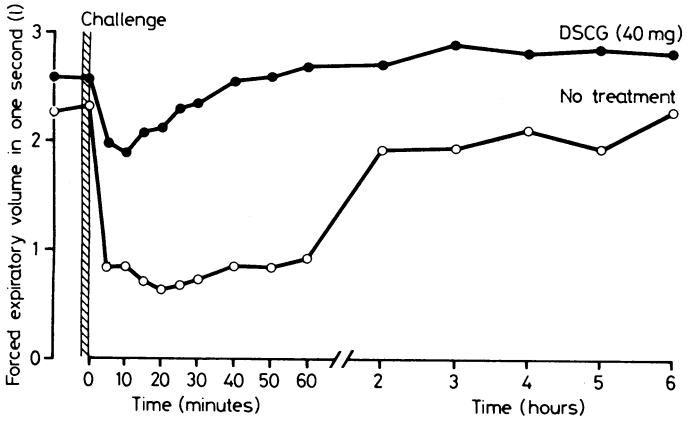
Occupational asthma caused by allergy to pigs' urine

We report a case of asthma due to occupational exposure to pigs. The cause of the symptoms was exposure to the urine of the animals. This was proved by provoking acute asthma with an inhalation challenge of an extract of pigs' urine at a concentration of 1 g/l. On a second occasion this asthmatic response was blocked by prior treatment with 40 mg sodium cromoglycate (Intal). The patient's serum contained specific IgE antibody to the urine extract which was not found in unexposed controls.

Case report

The patient, a 21-year-old eczematous woman who enjoyed a vigorous sporting life, playing squash and hockey to a high standard, had not suffered respiratory symptoms since the age of 3. During her second year at university studying agricultural sciences her class visited a pig house. Within two to three minutes she had to leave because she felt as if she was being "stifled with a plastic bag." She took about an hour to recover her breath and within a few minutes her eczema had begun to itch, and this took a further two hours to settle. One year later, within five minutes after starting to watch a laparotomy on a pig, she again became short of breath. Her only other exposure to these animals had been during a visit to the pig house in her first year, when she remained symptomless.

Skin-prick tests yielded positive reactions to grass, house-dust mite, horse, cat, dog, and pork extract. Pigs' urine (50 ml) was filtered, sterilised, and freeze dried as described[1] and reconstituted in Coca's solution at 0·1 and 1·0 g/l. Skin testing produced a 3 mm weal with the solution at 1·0 g/l. After inhaling a nebulised dose (0·0015 g) for one minute her forced expiratory volume in one second (Vitalograph) fell by 70% from 2·3 to 0·7 l. The same test was conducted one week later after 40 mg of sodium cromoglycate had been given by inhalation 10 minutes before the challenge. On this occasion her forced expiratory volume in one second fell by nearly 28% from 2·5 to 1·8 l. In each case recordings were made for a further five hours throughout



Results of two inhalation tests performed one week apart. On each occasion subject inhaled nebulised pigs' urine 1 g/l for 60 seconds. Asthmatic response was inhibited with sodium cromoglycate (DSCG) 40 mg given 10 minutes before test.

the day. No non-immediate reaction developed (figure). A radioallergosorbent test performed with the same urine extract showed her blood to contain specific IgE antibody, 23·9% of the counts added in the assay being bound, as compared with 0·73% with cord blood and a mean of 0·69% with six blood-bank controls.

Comment

Asthma has resulted from inhaling certain proteins in the urine of mice, rats, guinea-pigs, and rabbits in sensitised subjects but not from inhaling the animal serum.[1 2] Our patient's sensitivity to pigs' urine raises the possibility that urine of other mammals may also cause asthmatic symptoms. Previous studies have shown that atopic people are more at risk of developing asthma from exposure to environmental antigens than non-atopic persons.[3] Our patient was highly atopic and eczematous.

We thank Professor M Lessof for permission to investigate this patient and Dr D S Fernando for referring her.

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Sustained ventricular fibrillation in deep accidental hypothermia

Cardiac arrhythmia is an important cause of death in deep accidental hypothermia (temperature $<30°C$) in otherwise healthy patients. Superficial or core rewarming is the most important treatment. I report a case in which the patient had continuous ventricular fibrillation for three hours 40 minutes and was rewarmed with simple and inexpensive equipment that is generally available in any hospital. To my knowledge this is the longest period of ventricular fibrillation in deep hypothermia in which resuscitation has been successful.

Case report

A 33-year-old previously healthy man had ingested 300 mg chlorprothixene hydrochloride and 6 mg flunitrazepam during an attack of acute depression. He had afterwards slept on an exposed hill and had been found unconscious 12 hours later. The air temperature had been approximately 4°C.

On admission to hospital his spontaneous respiration stopped, and an electrocardiogram recorded over two minutes showed asystole, which was converted to ventricular fibrillation after intravenous adrenaline. His pupils did not react to light, and there was general hyporeflexia. Rectal temperature was 24°C measured with a laboratory thermometer. Arterial blood pH and serum potassium, chloride, and sodium and blood glucose concentrations were normal. Packed cell volume was raised (55%).

External cardiac massage at a reduced rate and artificial ventilation were started. Arterial blood pH was kept alkaline at around 7·5-7·6 and serum potassium concentration monitored within normal limits. Sodium chloride 0·9% solution and plasma prewarmed to 37°C were given intravenously. The room temperature was kept at 30°C, and he was wrapped in layers of prewarmed wool carpets. His temperature fell 1°C during the first 10 minutes of resuscitation but then rose steadily to 28°C after a further three hours 30 minutes.

Electrocardiography showed continuous ventricular fibrillation throughout this period. DC defibrillation was tried at 24°C, 26°C, and 27°C, together with lignocaine 100 mg intravenously at 26°C and 27°C, both with no effect. When his temperature reached 28°C he was electroconverted to nodal rhythm and external cardiac massage was stopped. At 30°C there was spontaneous sinus rhythm. At 31°C the blood pressure became measurable with a sphygmomanometer and arm cuff. Spontaneous respiration started after 16 hours of treatment with a ventilator. Two days later he was alert; at discharge he had some soreness over the sternum but no other physical abnormality.

Comment

The amount of drugs ingested by this patient was far below the level at which cardiac and respiratory complications would be expected, and his condition was probably caused by hypothermia. The cerebrum can withstand an increasingly longer period of cardiac arrest with

decreasing temperature. Cardiac massage at a reduced rate is the usual treatment in such cases. In contrast, Niazi and Lewis[1] described one hour of asystole at 9°C in controlled hypothermia; their patient reattained spontaneous sinus rhythm during superficial rewarming.

Our patient was ventilated as if he were normothermic, thus generating alkalosis. This is controversial[2] but has been advocated by some clinical investigators.[3] He had asystole on arrival at hospital. It is not clear when this began, but serious arrhythmias may occur when hypothermic patients are handled—for example, when they are lifted on to or from stretchers.

The initial drop in temperature that occurred in our case is a well-known phenomenon when superficial rewarming is used and should not discourage staff from continuing the resuscitation. Core rewarming requires trained staff and more expensive and sophisticated equipment such as a heart-lung machine, peritoneal dialysis, and peritoneal lavage. This case supports previous suggestions[4 5] that in the treatment of accidental hypothermia successful results may be attained without resort to sophisticated equipment.

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Oral contraception in patients with hyperprolactinaemia

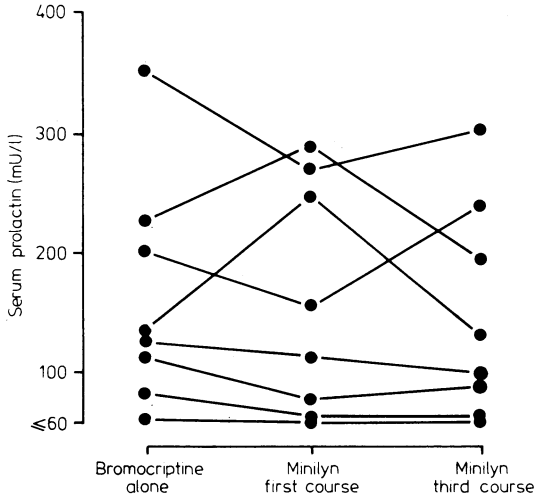
Prolactin-secreting pituitary tumours have oestrogen receptors[1] and may enlarge rapidly during pregnancy[2] or oestrogen administration.[3] Hence oestrogen-containing oral contraceptives are usually contraindicated in hyperprolactinaemia. Bromocriptine, however, inhibits the increase in animal pituitary weight and mitotic activity induced by oestrogens.[4] We have therefore tried to determine whether the medical control of hyperprolactinaemia could be maintained after introducing oral contraceptive treatment.

Patients, methods, and results

We studied 10 women aged 23 to 36 years; five had radiological evidence of pituitary tumour. In each patient at least three pretreatment prolactin concentrations exceeded 800 mU/l (MRC 75/504). All had taken bromocriptine for 11 to 58 months (mean 25 months) before starting oestrogen treatment. Doses (5-25 mg daily) were adjusted individually until prolactin concentrations were no longer raised and then maintained unchanged throughout the study. Blood samples were taken on days 12, 19, and 26 of the menstrual cycle immediately preceeding oral contraceptive treatment. Minilyn (ethinyloestradiol 50 μg, lynoestrenol 2·5 mg) was started on the fifth day of menstruation, being taken as one tablet daily for 22 days followed by six days without treatment to complete each course. Further blood samples were taken after 7, 14, and 21 days in the first and third courses. Sera were stored at −20°C and the prolactin concentration measured by radioimmunoassay against MRC standard 75/504, the nine samples from each subject being measured together and in triplicate. Mean intra-assay coefficient of variation was 7·9%. Right lateral and posteroanterior skull *x*-ray pictures were taken before Minilyn and repeated at intervals of six to 12 months.

One of the 10 subjects took bromocriptine only intermittently. Another had headaches and stopped the Minilyn after only one week. These two patients were therefore excluded from the analysis of prolactin results. The figure shows the serum prolactin concentrations in the remaining eight patients. When taking bromocriptine alone the serum prolactin concentration was below the limits of assay sensitivity in one subject but normal in the others. There was no overall change in prolactin concentrations during Minilyn, and comparison of concentrations at 7, 14, and 21 days showed no short-term trend within each cycle. Three patients complained of nausea or breast enlargement while taking Minilyn.

Eight of the 10 patients continued with Minilyn after the three-month sampling period and when last seen had completed six to 19 months of treatment (mean 13 months). Further prolactin concentrations remained within the normal range. Follow-up skull radiographs were obtained in nine patients after two to 19 months (mean 11 months), and in none was there any evidence of progressive pituitary enlargement. In one patient with gross unilateral expansion of the pituitary fossa there was diminution in the size of the fossa during 11 months of treatment with bromocriptine plus Minilyn.



Serum prolactin concentrations in eight patients taking Minilyn showing no overall change during first three months. Each point represents mean of three observations taken at weekly intervals. Normal range for serum prolactin 60-360 mU/l.

Comment

Oestrogen-related side effects were noted in three patients but there was no overall change in serum prolactin concentrations, and medical control of hyperprolactinaemia was well maintained. One patient had headaches during the first week of taking the contraception, but the relevance of this could not be assessed. In no other subject was there any evidence of progressive pituitary enlargement, and in one patient the pituitary fossa actually became smaller while taking oestrogens.

We conclude that oestrogen-containing oral contraceptives may be used in patients with hyperprolactinaemia and pituitary tumours, provided that serum prolactin concentrations are first restored to normal with bromocriptine and that bromocriptine is continued. Close supervision is required. In patients who cannot use other forms of contraception oestrogen-containing contraceptives with bromocriptine may be safer than an unplanned pregnancy.

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