

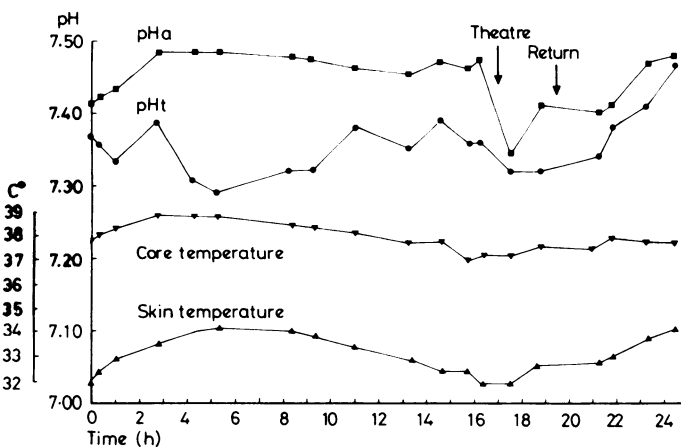
Continuous monitoring of tissue pH

Rapid changes in arterial pH are common in critically ill patients and may be observed only if frequent blood samples are taken. This has obvious disadvantages, and there has recently been increasing interest in developing continuous measuring techniques. Various studies have been published on the monitoring of skeletal muscle pH (pHm) and its relation to tissue perfusion.¹ Animal and human studies have shown that pHm varies directly with arterial blood pH (pHa), and that pHm decreases in states of diminished peripheral perfusion.² The pH probes that were used in this work were, however, cumbersome and difficult to position.

Stamm *et al*³ have recently designed a miniaturised glass probe for continuously measuring tissue pH (pHt),⁴ and it has been developed by Roche. Investigations into the relation between pHt and pHa have been carried out by several workers on animals and on neonates, but no information is available for adults. We therefore determined the relation between pHt and pHa in critically ill adults.

Patients, methods, and results

Twenty-two adults, aged 32 to 80, were studied, 14 of them during and after open heart surgery. Before use the electrode tip was sterilised in glutaraldehyde (Cidex). The probe was prepared with a reference solution and then calibrated with fresh buffer solutions (pH 7.0 and 7.40), and the shoulder or chest just below the clavicle was used for the monitoring site. The electrode was placed perpendicular to the skin with its tip penetrating about 4 mm into the subcutaneous tissue. A skin temperature electrode was placed about 2 cm away from the pH electrode, and a rectal probe was inserted to measure core temperature. The pHa measurements were made on a Corning 165 blood gas analyser from arterial blood.



Variation of tissue pH with arterial pH, core temperature, and skin temperature in one patient.

Positioning of the electrode took less than one minute and the recording quickly stabilised, with the drift in calibration of the system never exceeding 0.03 pH units. The electrode functioned satisfactorily in each case. One hundred and eighty-five observations were made on the 22 patients, and the correlation coefficient for all measurements was 0.8 ($P < 0.001$). The value varied greatly in different groups of patients, however, being higher than 0.9 in six patients, less than 0.7 in five patients, and indicating an extremely poor correlation ($r < 0.5$) in another five patients. In some of the patients pHt varied with pHa, although the former was generally 0.02 to 0.08 pH units lower than the latter. In other patients, who had poor peripheral perfusion and low skin temperatures, there was a wide discrepancy. The figure shows how pHt was consistently lower than pHa in a patient who was developing pericardial tamponade and how relief of the tamponade resulted in an increase in pHt.

Comment

A good correlation between tissue pH and arterial pH has been observed in neonates,⁵ but this should not lead us to suppose that they are one and the same. Tissue pH may reflect arterial pH very accurately but it is affected by the state of local tissue perfusion. We have shown how a poor correlation may be obtained in patients with poor tissue perfusion and how the difference between arterial pH and tissue

pH may provide an index of tissue perfusion. This is being studied further. These preliminary results are encouraging and suggest that the measurement of tissue pH may be of value in managing sick adults.

We wish to thank the surgeons and physicians who permitted us to study their patients, Dr Mindt for his kind co-operation, and Miss Julie Ray for her secretarial services.

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Idiopathic hypoparathyroidism: a cause of fits in the elderly

Idiopathic hypoparathyroidism is rare and occurs characteristically in young people. It presents with the manifestations of hypocalcaemia; there are associations with other endocrine diseases,¹ and antibodies to several tissues have been reported.² Cases are either familial or sporadic, and it is the second form that is particularly associated with other endocrine abnormalities.³

We report two cases in elderly patients who presented with convulsions.

Case reports

Case 1—An 85-year-old widow was admitted to hospital after a fall at home. She had had cataract extraction 11 years before. On admission she was tremulous and confused, and the initial diagnosis was acute myocardial infarction. Two weeks later she had four epileptiform seizures. Serum calcium concentration was 1.4 mmol/l (5.6 mg/100 ml) corrected to a serum albumin value of 40 g/l, serum phosphate concentration was 1.5 mmol/l (4.6 mg/100 ml), and serum alkaline phosphatase activity was 74 IU/l. Liver function tests were normal. Creatinine clearance was 76 ml/min and urinary phosphate excretion 35 mmol/24 h (1.1 g/24 h). Assay for serum parathyroid hormone showed it to be almost undetectable. Screening for associated conditions and for autoantibodies yielded negative results. Treatment with oral 1 α -hydroxycholecalciferol and daily calcium supplements increased the serum calcium value to normal within 10 days and her clinical condition greatly improved. She had no further seizures, her mental state improved, and she became largely independent and fit for discharge.

Case 2—A 77-year-old man was seen at home after a grand-mal convulsion with subsequent confusion. There was no history of convulsions but there had been periods of confusion, apathy, and withdrawal from social contact for two years. After admission several further tonic convulsions occurred with no lateralising signs but with equivocal plantar responses, and, finally, Trousseau's sign was elicited. Serum calcium concentration was 0.95 mmol/l (3.8 mg/100 ml) corrected to a serum albumin value of 40 g/l, serum phosphate concentration was 2.0 mmol/l (6.2 mg/100 ml), and serum alkaline phosphatase activity was 105 IU/l. Liver function tests were normal. Creatinine clearance was 119 ml/min and urinary phosphate excretion 25 mmol/24 h (0.8 g/24 h). Serum parathyroid hormone concentration was below 0.22 μ g/l, consistent with the hypoparathyroid state. Screening for associated abnormalities was negative. Initial treatment with calcium gluconate and continuing treatment with calcium supplements and 1 α -hydroxycholecalciferol rapidly restored the serum calcium value to normal and prevented further convulsions. There was a definite improvement in mental state, and the patient returned to independent living at home.

Comment

The diagnosis of idiopathic hypoparathyroidism in these two patients rests on the presence of hypocalcaemia, hyperphosphataemia, and low serum parathyroid hormone values in the absence of severe renal impairment, steatorrhoea, osteomalacia, chronic diarrhoea,

iron-storage disease, malignant disease, and a history of neck surgery or irradiation. Bone biopsy was not performed in either case because of the absence of any biochemical or radiological evidence of osteomalacia. Our first case is the oldest known patient to present with this disorder, the oldest described elsewhere being an 80-year-old man who presented with confusion.⁴

Little is known about parathyroid function in the elderly, but we suggest that these cases might represent extreme examples of an age-related decline in parathyroid function. The clinical features of hypocalcaemia are less dramatic in the elderly⁵ and may easily be ascribed to irremediable causes, such as cerebrovascular disease. We therefore recommend that hypocalcaemia, which is disabling but remediable, should be more often sought in elderly patients, particularly those presenting with confusional states or epilepsy.

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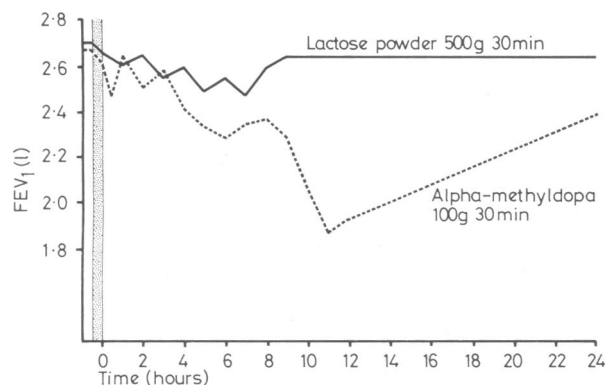
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Bronchial asthma due to alpha-methyldopa

Asthma from inhaling alpha-methyldopa powder was demonstrated by occupational type bronchial provocation testing in a woman who was handling the powder in a drug factory.

Case report

A 27-year-old woman started work in 1973 as an analytical chemist in a factory making methyldopa tablets. Two to three months later she developed blockage of the nose and repeated sneezing at work, which improved after three weeks. Her symptoms appeared intermittently with increasing frequency. She noted that they seemed to occur when methyldopa powder was present in the room. Six months before her referral to hospital she developed exercise-induced asthma. This was better when away from work on holiday.



Non-immediate asthmatic reaction resulting from 30 minutes' exposure to alpha-methyldopa dust, maximal at 11 hours. Recovery incomplete 22 hours later.

She was non-atopic and a prick test for sensitivity to alpha-methyldopa was negative. She had no serum precipitins to the drug and both direct and indirect Coombs tests were negative. She was admitted to hospital in May 1978.

Provocation tests were done in a ventilated sealed chamber measuring 6 cubic metres. She was exposed to methyldopa by pouring 100 g of powder between two trays for 30 minutes. After this challenge FEV₁ and FVC were measured with a dry wedge spirometer (Vitalograph) every five minutes for 30 minutes, then every 10 minutes for 30 minutes, and thereafter every hour for 12 hours. Control readings were made in the same way on a separate day after tipping dried lactose powder for 30 minutes. A fall in FEV₁ of 15% or more after challenge compared with lactose control was regarded as a significant bronchial reaction. Bronchial reactivity to histamine acid phosphate nebulised for 30 seconds up to a final concentration of 32 mg/ml was also measured on a separate day. Nine hours after exposure to alpha-methyldopa powder the patient complained of nasal stuffiness and sneezing, and 11 hours after she complained of tightness in the chest and wheezing. Her FEV₁ fell by 30% from 2.66 l to 1.85 l maximal at 11 hours (figure). There was no such asthmatic reaction to lactose control or to histamine.

Comment

Similar asthmatic reactions have been described in other pharmaceutical industry workers after inhaling the powders of piperazine dihydrochloride¹; ampicillin, benzyl penicillin, and 6-aminopenicillanic acid²; spiramycin³; glycol compounds; fenfluramine⁴; and clam's liver extract used in cancer chemotherapy.⁵ Asthma has also resulted from the ingestion of tetracycline in a sensitive subject. We were unable to demonstrate antibodies to alpha methyldopa in our patient, but she alone of those working with the drug developed rhinitis and asthma. These started after several months' exposure without symptoms, suggesting that they were allergic reactions. Since the diagnosis was made she has avoided exposure to alpha-methyldopa, with complete remission of symptoms.

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Reversible haemolytic anaemia after levodopa-carbidopa

A positive direct Coombs test and rarely autoimmune haemolytic anaemia (AIHA) are well-known complications of methyldopa treatment, particularly when given at higher dosage.¹ Patients taking levodopa may also have a positive Coombs test, and a few have developed AIHA.² The positive Coombs test is due to a warm-reacting IgG autoantibody with rhesus specificity indistinguishable from that seen in idiopathic AIHA but becoming weak or negative within a few weeks after stopping the drug. In one case of AIHA³ Parkinsonian disability became so severe after stopping levodopa that after two weeks it was reinstated, though at one-sixth the previous dose by using the dopa-decarboxylase inhibitor combination levodopa-benserazide (Madopar). The Coombs test remained positive but haemolysis did not recur. The following case, however, which was originally described by Barat *et al*,⁴ shows for the first time that severe AIHA may develop with combination chemotherapy.

Case report

In 1969 a 65-year-old Frenchman developed Parkinson's disease. Levodopa was prescribed in 1974, the dose gradually being increased to 6 g daily. The