were aged 10 to 83 years (mean 37 ± 5) and four were newly diagnosed. Four had moderately impaired consciousness and three severely impaired consciousness. Thirteen had clinical evidence of precipitating infection. The initial plasma concentrations were as follows: glucose ranged from 17.5 to 65.0 mmol/l (315–1171 mg/100 ml) (mean 39.0 ± 2.9 mmol/l (702 ± 52 mg/100 ml)); plasma bicarbonate 2.0–13.0 mmol (mEq) l (7.1 ± 0.6 mmol/l); blood urea 3.5–25.9 mmol/l (127–156 mg/100 ml) (13.3 ± 1.5 mmol/l (80.1 ± 9 mg/100 ml)); plasma potassium 3.2–7.2 mmol (mEq) l (5.0 ± 0.2 mmol/l); and plasma sodium 113–142 mmol (mEq) l (130.4 ± 1.7 mmol/l). The arterial H⁺ concentration measured in eight patients was 69 to 118 nmol (mEq) l (95.3 ± 6.2 mmol/l).

The regimen—A loading dose of 2 units of soluble insulin was given intravenously. Soluble insulin was added direct to the drip bottle (or polyethylene container) to achieve an infusion rate of six units/h. Initial fluid replacement was given as saline (0.154 mol/l), the infusion rate of 1.0 l or 0.5 l per hour depending on the degree of dehydration. This continued until the plasma glucose concentration had fallen to an arbitrary correction level less than 15 mmol/l (270 mg/100 ml). Dextrose (50 g/l) was then substituted and the rate of insulin infusion halved to three units/h to prevent any further fall. Potassium chloride replacement was started immediately unless the initial plasma potassium was greater than 5.0 mmol/l. No patient needed treatment with sodium bicarbonate. Plasma insulin was measured in three of the newly diagnosed diabetics by specific radioimmunoassay.

The mean hourly plasma glucose concentration fall ($\pm$ SE of mean) was 5.8 ± 0.6 mmol/l (105 ± 11 mg/100 ml). It took an average of 5.2 ± 0.6 hours for the concentration to reach less than 15 mmol/l. The mean insulin dose given over this period was 32 ± 4 units (range 8–71). The mean time for correcting plasma bicarbonate (18 mmol/l or greater) was 15.2 ± 1.2 hours. The amounts of intravenous fluid given during correction of the plasma glucose and bicarbonate in the ketoacidotic patients were 3.7 ± 0.4 l and 5.8 ± 0.4 l respectively. The plasma potassium concentration was well maintained during treatment and the infusion concentration did not have to be increased above 20 mmol per 0.5 l. The cumulative amounts of potassium given at 6, 12, and 24 hours were 60 ± 5 , 85 ± 5 , and 114 ± 7 mmol, respectively. Plasma insulin in the three patients not previously treated with insulin showed an initial concentration of 10 ± 4 mU/l (range 6 to 18) with a rise to 76 ± 24 mU/l (range 45 to 124) at 2 hours and 59 ± 8 mU/l (range 46 to 72) after 4 hours. No complications occurred during treatment and all patients survived.

Comment

For several years we have treated diabetic ketoacidosis by adding insulin direct to the intravenous infusion drip bottle.² The technique has been discouraged by reports that insulin is variably adsorbed to glass or polyethylene surfaces, although this effect is offset if albumin or other protein carrier is added.³ These additives are considered unnecessary if excessively dilute insulin solution—such as results when small amounts are added to the drip bottle—are avoided and the insulin is used in concentrated solution as with a syringe pump.¹ We have shown, however, that when low-dose insulin was administered in dilute solution without the addition of albumin it was effective and insulin adsorption was not clinically important.

The rate of fall in plasma glucose concentration, the time to achieve correction of the plasma glucose, and the total amount of insulin given with our method were comparable with those with more elaborate techniques of low-dose insulin administration. In the three patients not previously treated with insulin the plasma insulin concentrations achieved were within the accepted physiological range⁴

and comparable with those obtained with the other techniques (see table).

Requests for reprints should be addressed to Dr B F Clarke.

¹ *British Medical Journal*, 1977, **1**, 405.

² Duncan, L J P, in *Textbook of Medical Treatment*, 13th edn, ed S Alstead and R H Girdwood, p 363. Edinburgh and London, Churchill Livingstone, 1971.

³ Kraggen, E W, et al, *British Medical Journal*, 1975, **3**, 464.

⁴ Sönksen, P H, et al, *Clinical Science and Molecular Medicine*, 1973, **45**, 633.

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Lithium intoxication induced by dieting and saunas

Lithium is being increasingly used for long periods in the prophylaxis of recurrent affective illnesses. It has only a small margin of safety. Serum lithium concentrations between 0.7 and 1.2 mmol/l are aimed at, yet neurological toxic effects occur with concentrations around 2 mmol/l.¹ Irreversible neurological damage has been reported after serum concentrations of 2.3 mmol/l,² and with concentrations of 4 mmol/l patients are comatose and very ill.³

Lithium may cause weight gain of 5 kg or more.¹ This is often worsened by concurrent antidepressant drugs, which also cause weight gain. When this occurs patients may be tempted to diet drastically. This may be dangerous as fluid and salt restriction cause increases in serum lithium concentrations.³ The following case illustrates this danger.

Case report

A 60-year-old man was being maintained on phenelzine, 15 mg three times daily; tryptophan, 500 mg at night; nitrazepam, 10 mg at night; and a delayed release preparation of lithium carbonate, 1 g a day. The results of serum lithium estimations seemed stable around 1.1 mmol/l. He was psychiatrically well but mildly obese.

He asked his psychiatrist if he could have treatment at a health farm for one week to lose weight. He was advised not to diet too vigorously and to

Comparison of previous low-dose insulin techniques 1973–76 with that of present study

Author ¹	Low-dose insulin technique ²	No of ketoacidotic patients	No of non-ketotic hyperglycaemic patients	Mean plasma glucose (mmol/l)	Insulin loading dose (U)	Insulin hourly dose (U)	Criterion for plasma glucose correction (<mmol/l)	Mean plasma glucose fall (mmol/l/h)	Mean time for plasma glucose correction (h)	Mean insulin dose for plasma glucose correction (U)	Plasma insulin (mU/l)
Alberti et al 1973	1	14		34.8 ± 2.8	16	5–10	16.6	5.1	6.5	43	33–92
Moseley 1975*	1	12		35.0 ± 4.1	8	3–5	11.1	5.3†	5.3†	23	§
Kitabachi et al 1976	1	24		40.2 ± 3.4	13.5	5	13.8	4.0†	6.7	45 ± 5	82 ± 13
Kidson et al 1974	2,3	7	4	28.6 ± 3.7	0.5	2.4	11.0	4.2	4.0†	10†	36–143
Page et al 1974	2	31	7	44.9 ± 3.2	0	7.2	13.8	§	§	§	50–100
Semple et al 1974	2	13		40.3 ± 4.4	6.5	6.5	16.6	5.6	6.5†	39 ± 7	75 ± 8
Soler et al 1975	2	18		37.8	0	8	13.8	§	5.9	54 ± 19	§
Campbell et al 1976	3	46	8	37.2 ± 16.1	0	2.4	11.1	3.4	8.1	§	§
Clumbeck et al 1976	4	19	4	44.5 ± 4.4	0	5	13.8	4.3	§	§	0–>600
Malleson 1976*	4	4		35.4 ± 7.5	10	4	16.6	3.4†	8.3†	35 ± 6†	68–188
Present study	5	20	1	39.0 ± 2.9	2	6	15.0	5.8	5.2	32 ± 4	45–124

*Studies in children.

†1 = Intermittent intramuscular injection. 2 = Continuous intravenous infusion with syringe pump. 3 = Continuous intravenous infusion with paediatric set. 4 = Intermittent intravenous boluses. 5 = Direct addition to infusion bottle.

†Calculated from authors' data.

§No data.

Conversion: SI to traditional units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

take extra salt, and warned that dehydration in saunas might be dangerous. He went to a health farm, where his diet consisted solely of grapefruit juice (supplemented with celery salt). He had a 10- to 15-minute sauna each morning. During the first three days he lost 4.5 kg. On the fourth day he became confused, ataxic, and tremulous; his diet was immediately increased and saunas were stopped. Next day, after no further lithium, he was still obviously ill and his GP was called. His serum lithium concentration was 1.6 mmol/l. The patient's wife then restarted the lithium at the reduced dosage of 800 mg a day.

I saw him five days later. Although improving, he had slurred speech, mild ataxia, and mild impairment of memory. The serum lithium concentration was now 1.1 mmol/l. One week later he still had difficulty standing unaided on one leg but this minimal impairment went a few days later.

Comment

This episode shows that precipitating lithium intoxication by dieting and salt depletion is not only a theoretical possibility but a practical danger. The dehydration and extra salt depletion resulting from sauna bathing¹ probably exacerbated the effects of the diet. The serum lithium concentration of 1.6 mmol/l some 36 hours after the last dose suggest that at one stage the concentration was probably around 3.2 mmol/l as the serum half life of lithium is one to two days.¹

Neurological signs continued for two weeks after serum lithium concentrations were within the therapeutic range. Equilibration of lithium is much slower within the central nervous system than in serum.³

This case also shows once again that patients may not heed or even hear the warnings of their doctors. It would seem sensible to give all patients taking lithium written instructions, such as those of Shaw,² that warn them against having special diets without consulting their doctor. This patient was also asked at the health farm if he was taking drugs. He said "no" because he felt that mentioning psychiatric medication would brand him. Perhaps it would be better if the staff at such establishments specifically mentioned lithium as a contra-indication to the regimen.

¹ Schou, M, et al, *British Journal of Psychiatry*, 1970, **116**, 615.

² von Hartitzsch, B, et al, *British Medical Journal*, 1972, **4**, 757.

³ Schou, M, Amdisen, A, and Bastrup, P C, *British Journal of Hospital Medicine*, 1971, **6**, 53.

⁴ Dean, S, Green, D J, and Melnick, S C, *British Medical Journal*, 1977, **1**, 1449.

⁵ Shaw, D M, *British Journal of Psychiatry*, 1977, **130**, 432.

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Chronic myeloid leukaemia of adult type in 5-month-old infant

Of the two types of chronic myeloid leukaemia (CML) that occur in children,^{1,2} juvenile CML is found in children aged under 2 while adult CML occurs in children mainly between the ages of 7 and 16. We report here a case of adult type CML in a 5-month-old infant.

Case report

A 5-month-old boy of Kenyan Asian parents presented in January 1975 with a four-day history of crying and abdominal distension. He had previously had persistent rhinitis and some feeding problems. Apart from a right hydrocele the routine examination at 3 months had shown nothing abnormal.

On admission he was anaemic. The liver was enlarged 3 cm and the spleen 7 cm in the midclavicular line. Haemoglobin was 4.5 g/dl; 12.1%, was Hb F; white cell count was $501 \times 10^9/l$ ($501\,000/mm^3$) with 47% polymorphs, 33% immature granulocytes, 4% blasts, 12% eosinophils, and 3% lymphocytes. Platelets were $64 \times 10^9/l$. The leucocyte alkaline phosphatase score was 1. Marrow aspirate was hypocellular. Erythropoiesis was normoblastic but depressed. Myelopoiesis was hyperplastic with normal maturation but an excess of myelocytes. Megakaryocytes were reduced. Marrow culture was positive for the Philadelphia chromosome in all of the 10 cells examined. The cerebrospinal fluid contained 20 lymphocytes. The serum urate was

0.52 $\mu\text{mol/l}$ (8.7 $\mu\text{g}/100\text{ ml}$). Scattered lytic lesions were seen on skeletal survey.

In view of the prognosis we decided not to treat him aggressively and this was explained to the parents. Busulphan treatment (0.4–1.5 mg/day) was started. He was supported by blood transfusions as required. Throughout the initial illness his blood count was relatively stable (see chart) but he had intercurrent infections of the ears and respiratory tract. Abdominal discomfort was troublesome. Latterly arthralgia and bleeding into the mucous membrane and skin were problems.

A marrow aspirate taken in the ninth month of the illness showed 50% replacement of the marrow by myeloblasts, with depression of the other cell lines. This was subsequently reflected peripherally as a relative pancytopenia. He was treated with mercaptopurine (25 mg/day) and prednisolone (20 mg/day). His condition rapidly deteriorated, however, and he died at home as planned, aged 16 months.

Haematological findings and treatment.

Comment

Chronic myeloid leukaemia (CML) comprises 2–5% of childhood leukaemia.³ There are two types.^{1,2} Juvenile CML, which is found in children under 2 years, is characterised by anaemia, recurrent infections, lymphadenopathy, purpura, and eczematoid facial rash. Classically the white cell count is $20\text{--}80 \times 10^9/l$ with profound thrombocytopenia and raised Hb F. The Philadelphia chromosome is absent. In contrast, the adult type is of insidious onset, with anaemia and hepatosplenomegaly, and its greatest incidence in children is between the ages of 7 and 16 years. The white cell count is considerably higher at $150\text{--}400 \times 10^9/l$. The Philadelphia chromosome is present.

Because of the presence of the Philadelphia chromosome, an extremely high white cell count, and gross splenomegaly in the absence of lymphadenopathy, facial rash, and purpura, we considered this case to be a classic example of the adult type of CML. A search of published reports⁴ has shown no other reported case of the adult type in a 5-month-old infant.

Requests for reprints should be addressed to Dr R G Wilson.

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³ Lascari, A D, *Leukemia in Children*. Springfield, Illinois, Thomas, 1973.

⁴ Bloom, G E, et al, *Pediatrics*, 1966, **38**, 295.

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