surgeons who work for the HMOs have the expertise to handle this. I do, however, know an excellent surgeon to whom I normally refer such cases. If I send the patient to this surgeon the plan won't pay. What do I do? Explain that the plan's surgeon is second rate and persuade the patient to pay to go outside the plan or keep quiet on the basis that you can't expect five star service on a bicycle premium?"

Perhaps, not surprisingly, HMOs find it difficult to draw up guidelines about which patients need referral and to whom. In Britain the NHS has had decades to consider the problem yet by no means has all the answers. For example, there have only recently been complaints about variable referral rates to hospital by general practitioners who seem unaware of the economic implications of their decision.¹ Nevertheless, a system whereby district general hospitals deal with straightforward cases and more complex problems get referred to regional centres that have the necessary skill does seem equitable.

Of course, this presupposes that people accept that their gall bladder won't be taken out by one of Britain's top general surgeons when and where they want, but in recompense they will get surgeons of the top calibre to operate promptly on their child with a congenital heart defect. The steady growth in the private sector in Britain does not suggest that all are satisfied with this approach. How much harder then for HMOs, with few years of experience, to please both their customers and the doctors. For their survival depends on competing with rival health plans on the basis of both quality—and cost.

Conclusion

A decline in clinical freedom may grudgingly be accepted as inevitable—it is evident in all spheres of medical practice in America now—but the lack of flexibility within HMOs is widely criticised. So too is the practice of awarding bonuses to doctors for, to put it crudely, "not doing things."

To suggest that life in an HMO consists of a continual battle with your conscience over whether to follow house rules or the dictates of clinical judgment is putting it a bit strongly—doctors in the fee for service sector are also under considerable pressure to contain costs and the quality of their work is not monitored. Nevertheless, the anti-HMO camp, which has a strong representation among senior medical staff, is extremely concerned that as competition between HMOs accelerates and more become "for profit," quality of care is, or will be, compromised.

Studies that have been done, albeit many are not that recent, do not back this view—indeed, most have suggested that care in HMOs is superior.² So, although anecdotal information abounds, the hard evidence is not there . . . yet.

References

- 1 Prentice T. Doctors criticised for sending too many patients to hospitals. *The Times* 1986; January 9:p 3 cols 1-3.
- 2 Cunningham FC, Williamson JW. How does the quality of health care in HMOs compare to that in other settings? *Group Health Journal* 1980 Winter.

Lesson of the Week

Alcoholic ketoacidosis: an underdiagnosed condition?

C J THOMPSON, D G JOHNSTON, P H BAYLIS, J ANDERSON

The syndrome of alcoholic ketoacidosis has not been reported in Britain, whereas in the United States it has been estimated to occur once for every four cases of diabetic ketoacidosis.¹ We describe two patients with alcoholic ketoacidosis who presented to this unit within one month and discuss the pathogenesis and features of the condition.

Case 1

A 41 year old known alcoholic man presented to the casualty department after collapsing in the street. He had been drinking two bottles of whisky daily for three months and for 10 days had eaten little and suffered increasingly severe nausea and vomiting. He had longstanding asthma treated with salbutamol inhaler and prednisolone 10 mg daily. He was confused, icteric, and tachypnoeic with a ketotic odour to his breath. Pulse

Alcoholic ketoacidosis must be considered in the differential diagnosis of any alcoholic patient with acidosis, irrespective of the blood glucose concentration

was 100 beats/min, blood pressure 90/40 mm Hg supine, and he had peripheral circulatory collapse. There was widespread expiratory wheeze and the peak expiratory flow rate was 160 l/min after inhaled salbutamol. He had mild epigastric tenderness and a smoothly enlarged non-tender liver.

Investigations (see table) showed a moderately severe metabolic acidosis with compensatory respiratory alkalosis. Serum glucose concentration was 3.5 mmol/l (63 mg/100 ml; normal fasting range ≤ 5.0 mmol/l (90 mg/100 ml)), serum ethanol concentration 8.5 mmol/l (39 mg/100 ml), and serum methanol undetectable. Semiquantitative measurement of blood ketone values using Acetest tablets showed a weakly positive reaction, but the plasma creatinine concentration could not be measured because of assay interference suggesting high values of ketone bodies²; plasma β -hydroxybutyrate concentration was in fact grossly raised and plasma acetoacetate concentration moderately so. Evaluation of liver function showed aspartate transaminase activity 300 IU/l (normal < 37), γ glutamyltransferase activity 1750 IU/l (normal < 60), and a large, poorly functioning liver on technetium-99m liver scan. IgG antinuclear antibodies were present in a dilution of 1/160 but hepatitis B surface antibodies were absent and α fetoprotein, α_1 antitrypsin, and iron values were within normal limits.

The patient was treated with intravenous dextrose and saline, parenteral vitamins, and an increased dose of steroid and by the next day his metabolic

Endocrine Unit, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP

C J THOMPSON, MB, MRCP, honorary research associate

D G JOHNSTON, PHD, MRCP, honorary consultant physician

P H BAYLIS, MD, FRCP, consultant physician and senior lecturer in medicine

J ANDERSON, FRCP, FRCOG, honorary consultant physician and senior lecturer in medicine

Correspondence to: Dr Thompson.

Blood gas values and intermediary metabolite estimations at presentation and one day after treatment with intravenous dextrose and saline

	pH	PO ₂ (kPa)	PCO ₂ (kPa)	Bicarbonate (mmol/l)	β-Hydroxybutyrate (mmol/l)	Acetoacetate (mmol/l)	Lactate (mmol/l)	Pyruvate (μmol/l)	Glycerol (mmol/l)	Alanine (mmol/l)	Glucose (mmol/l)	Aspartate transaminase (IU/l)
	7.35-7.42	12.0-14.0	4.5-6.1	21-25	Fasting 0.01-0.34	Normal ranges Fasting 0.01-0.15	Fasting 0.40-1.19	Fasting 30-160	Fasting 0.03-0.10	Fasting 0.18-0.48	Fasting 3.5-5.0	<37
						Case 1						
Day 1	7.21	18.1	2.0	6	7.13	0.52	1.34	54	0.38	0.18	3.5	300
Day 2	7.40	14.1	2.6	12	1.02	0.24	1.09	51	0.11	0.25	7.1	—
						Case 2						
Day 1	7.05	15.4	2.3	5	9.58	2.51	1.63	134	0.12	0.17	0.8	—
Day 2	7.42	9.0	3.5	17	1.19	0.58	0.83	117	0.07	0.26	13.2	189

Conversion: SI to traditional units—PO₂, PCO₂: 1 kPa≈7.5 mm Hg. Bicarbonate: 1 mmol/l=1 mEq/l. β-Hydroxybutyrate: 1 mmol/l≈104 μg/ml. Acetoacetate: 1 mmol/l≈102 μg/ml. Lactate: 1 mmol/l≈9.0 mg/100 ml. Pyruvate: 100 μmol/l≈0.9 mg/100 ml. Glycerol: 1 mmol/l≈92 μg/ml. Alanine: 1 mmol/l≈89 μg/ml. Glucose: 1 mmol/l≈18 mg/100 ml.

profile (table) and clinical state were much improved. He continued to improve but one week after admission he became suddenly very dyspnoeic and suffered a cardiac arrest from which he could not be resuscitated. Necropsy showed severe coronary artery atheroma with a tight stenotic lesion of the anterior descending coronary artery but no myocardial or pulmonary abnormality. Histologically the liver showed gross steatosis and focal centrilobular fibrosis but no other stigmata of alcoholic liver disease.

Case 2

A 55 year old man was admitted confused and drowsy to the casualty department. He had longstanding alcohol related manic depressive psychosis and, though he had abstained from alcohol for several years, had been drinking heavily and eating little solid food for one week. He had been vomiting for two days. His medication was lithium carbonate 400 mg daily and tranylcypromine sulphate 10 mg twice daily. He was sweating profusely and had Kussmaul's respiration with ketotic fetor. He was dehydrated with a heart rate of 110/min and blood pressure 90/60 mm Hg. There were no stigmata of chronic liver disease.

Investigations showed a severe metabolic acidosis with pH 7.05 (see table) and pronounced hypoglycaemia (0.8 mmol/l; 14.4 mg/100 ml). Ethanol was undetectable in the serum, blood lactate concentration was 1.6 mmol/l (14.4 mg/100 ml), and salicylate concentration 52 mg/l. Blood taken before treatment of hypoglycaemia showed suppressed concentrations of insulin (2.0 mU/l; normal fasting range 2.8-13.5 mU/l) and C peptide (0.14 nmol/l (420 ng/l); normal fasting range 0.18-0.52 nmol/l (540-1560 ng/l)) but an increase of plasma cortisol (3960 nmol/l (143 μg/100 ml); 0900 reference range 190-720 nmol/l (6.9-26.1 μg/100 ml)). Growth hormone concentrations and thyroid function values were within normal limits. The acidosis was shown to be due almost entirely to ketone bodies, with plasma β-hydroxybutyrate concentration 9.6 mmol/l (997 μg/ml) and acetoacetate concentration 2.5 mmol/l (256 μg/ml). Lithium was undetectable in the blood.

After intravenous dextrose and saline the patient improved greatly overnight and his metabolic profile returned rapidly towards normal (table). A 75 g oral glucose tolerance test one week after admission gave a normal result. Two weeks after admission, when the aspartate transaminase activity had fallen to 41 IU/l, liver biopsy showed mild fatty change and abundant glycogen stores. There was a normal response of blood glucose to 1 mg glucagon given intravenously (fasting value 3.7 mmol/l (66.7 mg/100 ml) rising to 6.4 mmol/l (115.0 mg/100 ml) 30 minutes after injection). A 48 hour fast failed to produce clinical or biochemical hypoglycaemia and an intermediary metabolite profile remained normal (figure).

Nine months after presentation he remained well and free of hypoglycaemia and was following a regimen of lofepramine hydrochloride 210 mg daily, carbamazepine 200 mg twice daily, and complete abstinence from alcohol.

Discussion

Dillon *et al* first described alcohol ketoacidosis in 1940³ and a total of 67 patients with the syndrome have now been described in the English reports,^{1,3-13} almost entirely from the United States. The clinical syndrome has been well summarised^{14,15}; the patients—almost invariably alcoholics—undergo a period of binge drinking associated with a negligible intake of solid food. After the characteristic development of abdominal pain and severe vomiting—due to pancreatitis, gastritis, or acute hepatitis—the patient usually stops

drinking so that at presentation ethanol is frequently undetectable in blood. The patient's mental state may vary from completely

Response of plasma insulin, plasma β-hydroxybutyrate, and blood glucose values to 48 hour fast in case 2. LD=Lower limit of detection of insulin by assay used. Stippled area represents range of responses to 48 hour fast of six healthy volunteers studied by Johnston *et al*.¹⁹

Conversion: SI to traditional units—β-Hydroxybutyrate: 1 mmol/l≈104 μg/ml. Glucose: 1 mmol/l≈18 mg/100 ml.

normal to severe disorientation and he is dehydrated and tachypnoeic. Although mild epigastric tenderness is usual and dramatic signs are rare, presentation with an acute abdomen has been reported.¹³

The arterial pH is decreased—though not usually as low as in diabetic ketoacidosis, as the vomiting causes a metabolic alkalosis.¹⁶ The blood glucose concentration may be low, normal, or high and there is considerable variation in parameters of liver function, from normal serum transaminase activities and liver biopsy appearances to alcoholic cirrhosis. Plasma β -hydroxybutyrate concentrations are very high, with a moderate increase of plasma acetoacetate; as only the latter is measured by standard sodium nitroprusside agents such as Acetest and Ketostix, apparently insignificant ketosis may be indicated and the diagnosis may rest on direct measurement of plasma β -hydroxybutyrate and acetoacetate. The Acetest reaction showed only mild ketosis in both our patients, and the diagnosis was suspected because of the strong ketotic breath odour and the spurious increase of plasma creatinine, which has been shown to occur in the presence of high values of circulating ketone bodies.²

Our first patient presented with classical alcoholic ketoacidosis and his metabolic abnormalities disappeared rapidly with intravenous dextrose and saline. His sudden death one week after admission was unexplained, but sudden cardiac arrest well after correction of metabolic abnormalities has been reported in alcoholic ketoacidosis.⁶

The second patient was receiving tranlycypromine, a monoamine oxidase inhibitor, before presentation. These drugs have been reported to cause hypoglycaemia but this has been attributed to the hydrazine group which some monoamine oxidase inhibitors possess.¹⁷ Tranlycypromine is a non-hydrazine agent, and as the undetectable lithium concentration in this patient pointed to non-compliance we do not think that his medication contributed appreciably to his metabolic abnormalities. The appropriate rise in this patient's blood glucose to intravenous glucagon¹⁸ implies normal glycogenolysis, and the response of blood glucose to a 48 hour fast was entirely appropriate,¹⁹ suggesting adequate gluconeogenesis in the absence of alcohol.

For the development of alcoholic ketoacidosis in our patients and those reported on elsewhere a period of diminished dietary carbohydrate and excess alcohol intake preceded admission. In this clinical setting glycogen stores fall and, as the oxidation of ethanol causes a rise in the ratio of reduced nicotinamide adenine dinucleotide to nicotinamide adenine dinucleotide (reflected in the raised β -hydroxybutyrate to acetoacetate ratio in peripheral blood), hepatic gluconeogenesis is inhibited. Glucose production falls and the illness and volume depletion stimulate a catabolic response. Pancreatic insulin secretion falls and plasma concentrations of

cortisol, growth hormone, and probably glucagon and catecholamines rise, creating a hormonal milieu favourable to lipolysis, which was reflected in the raised glycerol concentrations in our patients (table). Ketogenesis is thus increased and as clearance of ketone bodies is impaired by the low plasma insulin and volume depletion, ketones—particularly β -hydroxybutyrate—rapidly accumulate to acidotic concentrations.

Treatment is simply intravenous replacement of fluid, dextrose, and electrolytes. Hypophosphataemia may occur during treatment even when values are raised initially⁹ and phosphate concentrations should be regularly monitored. Response to treatment is rapid and complete, though the patient is liable to further episodes if he continues to drink.^{4,9}

We believe this to be the first report of alcoholic ketoacidosis in Britain but think that increased awareness of the syndrome and the critical appraisal of a negative or weakly positive Acetest result will lead to an increase in the rate of diagnosis.

We thank Ann Potts for secretarial help.

References

- Cooperman MT, Davidoff F, Spark R, Pallota J. Clinical studies of alcoholic ketoacidosis. *Diabetes* 1974;23:433-9.
- White TF, Laker MF. Plasma creatinine levels in diabetic ketoacidosis: spurious elevation of levels using a kinetic reaction in a discrete analyser. *Med Lab Sci* 1984;41:185-7.
- Dillon ES, Dyer WW, Smelo LS. Ketone acidosis in non-diabetic adults. *Med Clin North Am* 1940;24:1813-22.
- Jenkins DW, Eckle RE, Craig JW. Alcoholic ketoacidosis. *JAMA* 1971;217:177-83.
- Weisberger CL, Hamilton W. Alcoholic ketoacidosis. *JAMA* 1971;217:1865-6.
- Levy LJ, Duga J, Girgis M, Gordon EE. Ketoacidosis associated with alcoholism in non-diabetic subjects. *Ann Intern Med* 1973;78:213-9.
- Petersen G. Alcoholism and ketoacidosis. *Ann Intern Med* 1973;78:983-4.
- Fulop M, Hoberman MD. Alcoholic ketosis. *Diabetes* 1975;24:785-90.
- Miller PD, Heinig RE, Waterhouse C. Treatment of alcoholic acidosis. *Arch Intern Med* 1978;138:67-72.
- Podratz KC. Alcoholic ketoacidosis in pregnancy. *Obstet Gynecol* 1978;52 (suppl):545-75.
- Lumpkin JR, Baker FJ, Franaszek JB. Alcoholic ketoacidosis in a pregnant woman. *Journal of the American College of Emergency Physicians* 1979;8:21-3.
- Platia EV, Hsu TH. Hypoglycemic coma with ketoacidosis in non-diabetic alcoholics. *West J Med* 1979;131:270-6.
- Hasselbach H, Selmer J, Kassis E. Alcoholic ketoacidosis presenting as an acute abdomen. *Dan Med Bull* 1981;28:218-9.
- Palmer J. Alcoholic ketoacidosis: clinical and laboratory presentation, pathophysiology and treatment. *J Clin Endocrinol Metab* 1983;12:381-9.
- Williams HE. Alcoholic hypoglycemia and ketoacidosis. *Med Clin North Am* 1984;68:33-8.
- Fulop M, Hoberman D. Diabetic ketoacidosis and alcoholic ketoacidosis. *Ann Intern Med* 1979;91:796-7.
- Potter WZ, Zaharko DS, Beck LV. Possible role of hydrazine group in hypoglycemia associated with the use of certain monoamine oxidase inhibitors. *Diabetes* 1969;18:538-41.
- Marks V, Rose FC. *Hypoglycaemia*. London: Blackwell Scientific, 1981:440-1.
- Johnston DG, Blesa-Malpica G, Burrin JM, et al. Dopamine blockade inhibits starvation ketosis in man. *Clin Endocrinol (Oxf)* 1983;19:389-96.

(Accepted 30 October 1985)

Is there any scientific evidence for the theory that chlorination of water—especially soft water—is a likely factor in the aetiology of vascular disease and is perhaps more important than saturated fats in the diet or even smoking?

There is no scientific evidence that the chlorination of water, soft or hard, is a likely factor in the aetiology of vascular disease. There is certainly nothing to suggest that it is as important or more important than smoking or saturated fats in the diet. In a study of water quality and cardiovascular mortality, which included assessment of chlorine (total) chloride and chloride/carbonate ratios in the water supply, none of these factors emerged from analysis as having any relation to cardiovascular mortality in Britain.—A G SHAPER, professor of clinical epidemiology, London.

Pocock SJ, Shaper AG, Cook DG, et al. British regional heart study: geographic variations in cardiovascular mortality, and the role of water quality. *Br Med J* 1980;280:1243-9.

For what period should replacement hormonal therapy be given to a 44 year old woman who had both ovaries surgically removed 10 years previously? What biochemical and cytological monitoring should be done?

Women undergoing an early surgical menopause are particularly susceptible to symptoms of oestrogen withdrawal, and are more liable to osteoporosis than women undergoing a natural menopause.¹ It has been recommended

that in these women oestrogen replacement should be continued at least until the age of the natural menopause—that is, age 50—provided that there is no contraindication such as oestrogen dependent neoplasia.² Whether or not treatment should be continued any longer is uncertain, since the optimum duration of treatment for the prevention of osteoporosis is unknown.³ Normally women having hormone replacement therapy are monitored by six monthly checks of weight and blood pressure, annual clinical examination of the breast, annual pelvic examination, and endometrial biopsy if indicated.³ Routine endometrial sampling is done every two years, though some gynaecologists now think that this is unnecessary,³ and regular cervical smears are taken until the age of 65, after which they may be stopped if they have been normal until then.⁴ If this woman has had a total hysterectomy, however, the question of sampling the endometrium or cervical smears does not arise, and hormone treatment may be given with oestrogen alone.³ Lipid profiles should also be checked every two to three years during long term therapy.⁵—JAMES OWEN DRIFE, senior lecturer in obstetrics and gynaecology, Leicester.

- Hammond CB, Ory SJ. Endocrine problems in the menopause. *Clin Obstet Gynecol* 1982;25:19-38.
- Carr BR, MacDonald PC. Estrogen treatment of postmenopausal women. *Adv Int Med* 1983;28:491-508.
- Craig GM. Guidelines for community menopausal clinics. *Br Med J* 1983;286:2033-6.
- Draper GJ. Screening for cervical cancer: revised policy. The recommendations of the DHSS committee on gynaecological cytology. *Health Trends* 1982;14:37-40.
- Whitehead MI. The climacteric and postmenopause. *Medicine International* 1981;1:302-4.