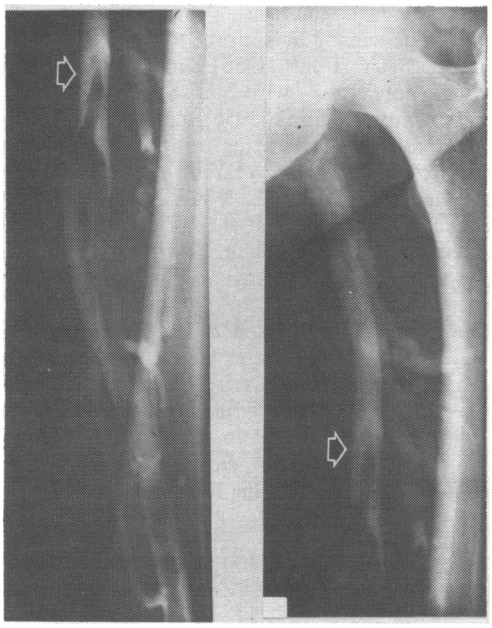
procedure she complained of the sudden onset of pain in the chest, shortness of breath, and haemoptysis. A lung scan showed large areas of impaired perfusion in both lung fields typical of pulmonary embolism. There were no physical signs in her legs but testing with the ultrasound flow detector showed an impairment of venous flow in the left popliteal and lower femoral vein. Peripheral ascending phlebography was carried out as an emergency procedure and showed extensive recent, non-adherent thrombus in most of the calf veins, the popliteral vein, and lower femoral vein of the left side (see Fig.).

It was considered advisable to protect her against a further and perhaps fatal pulmonary embolism by ligating the superficial femoral vein in the groin, so "locking in" the dangerous loose thrombus.

It took one hour to make the necessary arrangements, so that the femoral vein was opened just over an hour after taking the phlebogram. We were, therefore, most surprised to find that in the course of this hour, between phlebography and operation, the thrombus had extended from the lower femoral vein to a point 1 in (2·5 cm) above the inguinal ligament in the exernal iliac vein, a distance of 12 in (30·5 cm). This loose propagating thrombus was safely removed with a Fogarty thrombectomy catheter, and the superficial femoral vein was ligated below the profunda femoris vein to lock in the remaining thrombus in the thigh and calf.

The patient recovered completely and had no further episodes of pulmonary embolism.



Ascending phlebogram of left leg showing loose thrombus in the upper popliteal and lower half of the superficial femoral vein. The proximal end of the thrombus (arrowed) is 12 in (30·5 cm) from the inguinal ligament (right-hand panel).

Comment

This case shows that thrombus can propagate along a vein very quickly. Within an hour the risk to this patient of developing a massive, as opposed to a minor, pulmonary embolus was seriously increased, because the potential embolus had doubled in size. Anticoagulants had not been given because of the recent episode of haemorrhage from the cerebral artery aneurysm and it may be that they would have prevented the growth of the thrombus. Normally we find at operation that the thrombus fits the phlebogram perfectly, but most of these patients are already anticoagulated with heparin as the first line of treatment of their pulmonary embolus.

If thrombus can grow so quickly then the value of any routine screening procedure, such as ultrasound flow detection or the labelled fibrinogen uptake test, in the prophylaxis of sudden massive embolism is open to doubt.

This case emphasises the urgency with which any procedure must be carried out when attempting to prevent recurrent pulmonary embolism.

We would like to thank Dr. R. W. Ross Russell, National Hospital, Queen Square, London W.C.1, for permission to publish details of this case admitted under his care and referred to us.

Lactic Acidosis Complicating Liver Failure after Intravenous Fructose

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Lactic acidosis has been a recognized complication of liver failure for some 40 years (Alder and Lange, 1927) but further knowledge of the aetiology is needed so that a rational therapeutic approach to treatment can be made. We report the rapid development of lactic acidosis after intravenous fructose in a patient with liver failure.

Case Report

A 69-year-old woman with no history of contact with hepatitis or of injections or ingestion of hepatotoxic drugs was admitted to hospital after four weeks of anorexia, vomiting, and increasing jaundice. She was drowsy and deeply jaundiced, with fetor hepaticus, but neither liver nor spleen was palpable and there was no ascites, oedema, or bruising; her blood pressure was 140/60 mm Hg. The serum bilirubin was 29 mg/100 ml, SGOT 1,800 units and SGPT 1,100 units/ml, alkaline phosphatase 15 K.A. units/100 ml, and serum albumin 2·6 g and globulin 5·4 g/100 ml. The blood urea was 73 mg and creatinine 2·6 mg/100 ml, and serum Na^+ 134 mEq and K^+ 3·9 mEq/l.

She received potassium supplements, vitamin K, neomycin by mouth, and frequent enemas. Intravenous saline and dextrose (equivalent to 120 g of dextrose daily) were given for two days, but then because of slight ketonuria the carbohydrate intake was increased to 400 g daily, given intravenously as 40% fructose. Immediately before fructose administration the pH of capillary blood was 7·43, P_{CO_2} 34 mm Hg, and standard bicarbonate 23·1 mEq/l., but 16 hours later, after 1 l. of 40% fructose, the pH was 7·24, P_{CO_2} 33 mm Hg, and standard bicarbonate 15 mEq/l. (see Chart), and the patient was comatose but normotensive. Fructose was continued for four days, during which 400 mEq of sodium bicarbonate was given without improvement in acid-base state. She became oedematous and oliguric, with a serum creatinine of 7·3 mg and blood urea of 89 mg/100 ml. A total of 80 mEq of magnesium sulphate given intravenously over eight hours restored the serum magnesium from 0·9 to 2·0 mEq/l. When the blood lactate result of 6·50 mmol/l. (normal less than 1·5) became available fructose was discontinued and 5% dextrose resumed; the blood lactate at this stage was 8·75 mmol and serum pyruvate 0·325 mmol/l. (normal less than 0·1 mmol/l.), giving a lactate/pyruvate ratio of 27:1 (normal 15:1).

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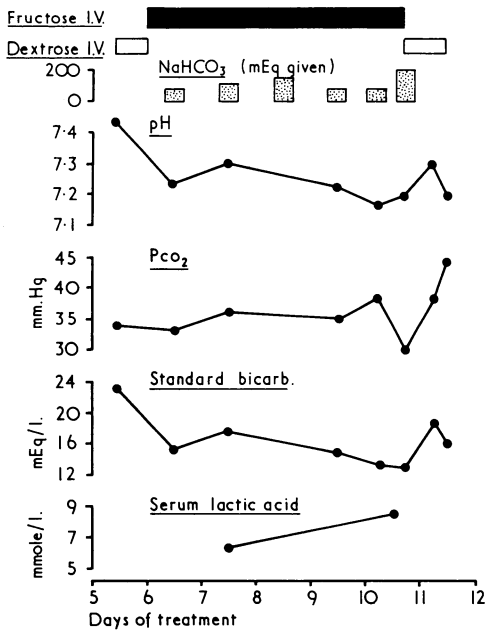

Time relationship between acid-base changes and treatment.

During the terminal 16 hours there was some improvement in acid-base status in spite of anuria. Terminal hypotension and death were due to bleeding from acute gastric erosions. At necropsy the liver was small (weight 870 g), yellow, and necrotic, with no signs of regeneration. The liver necrosis was thought to be due to fulminating infectious hepatitis.

Comment

Since the liver has a major role in removing lactic acid from the circulation defective hepatic metabolism of lactate is likely to be a major cause of lactic acidosis in liver failure. Nevertheless, hypocapnia and hypoxia may contribute. Hypocapnia causes a rise in lactate and pyruvate in proportion to the fall in P_{CO_2} (Mulhausen *et al.*, 1967) and may stimulate lactate production by erythrocytes and muscle. In the presence of hypoxia hepatic anaerobic glycolysis may occur, resulting in lactate production rather than removal (Berry and Scheuer, 1967). Leppla *et al.* (1964) showed that the lactate/pyruvate ratio may be influenced by changes in intracellular H^+ concentration as well as by the proportion of NADH to NAD according to the relationship Lactate + NAD $\rightleftarrows$ pyruvate + NADH + H^+.

Thus if lactate removal is impaired—for example, in diabetes, infection, or alcohol intoxication—minor changes in pH might initiate a severe lactic acidosis. The normal liver metabolizes fructose more rapidly than glucose for two reasons. Firstly, the activity in the liver of fructokinase, an enzyme which initiates fructose breakdown, is four times greater than that of glucokinase, one of the enzymes that initiate glucose metabolism (Heinz *et al.*, 1968), and, secondly, the subsequent steps in fructose utilization are largely independent of phosphofructokinase, whereas this enzyme regulates the rate of glucose metabolism after initial phosphorylation. As a result of rapid fructose breakdown the end products of glycolysis, lactate and pyruvate, accumulate in the blood (Bergström *et al.*, 1968) and the liver may be depleted of enough ATP and inorganic phosphate to reduce protein synthesis to an important extent, thereby impairing the integrity of enzyme systems concerned with lactate removal (Mäenpää *et al.*, 1968).

Magnesium deficiency has been reported in chronic alcoholism and cirrhosis (Flink, 1956) and in hepatic coma. Since many factors concerned with carbohydrate metabolism—in particular coenzyme A (Flink, 1956)—are magnesium dependent magnesium depletion may impair utilization of lactate, but the accumulation of lactate in the present case suggests that it does not impede lactate formation.

We believe that in this patient lactate formation resulting from fructose breakdown initiated the lactic acidosis, since this coincided with fructose therapy and improved slightly when glucose was substituted and the serum magnesium was corrected. The data of Mulhausen *et al.* (1967) show that once established in liver failure lactic acidosis is often irreversible. We feel that fructose is contraindicated in the treatment of liver failure and suggest that ethanol-fructose mixtures should be used with caution if hepatic function is disturbed, since ethanol can also induce lactic acidosis by altering the proportion of NADH to NAD in the liver cell.

We wish to thank Dr. J. Whitfield, of the renal unit, Queen Elizabeth Hospital, for kindly carrying out the lactate analyses.

References

Alder, A., and Lange, H. (1927). *Deutsches Archiv für klinische Medizin*, **157**, 129.
Bergström, J., Haltman, E., and Roch-Norlund, A. E. (1968). *Acta Medica Scandinavica*, **184**, 359.
Berry, M. N., and Scheuer, J. (1967). *Metabolism*, **16**, 537.
Flink, E. B. (1956). *Journal of the American Medical Association*, **160**, 1406.
Heinz, F., Lamprecht, W., and Kirsch, J. (1968). *Journal of Clinical Investigation*, **47**, 1826.
Leppla, W., Kumposcht, H., and Keller, H. E. (1964). *Verhandlungen der Deutschen Gesellschaft für innere Medizin*, **70**, 446.
Mäenpää, P. H., Raivio, K. O., and Kekomäki, M. P. (1968). *Science*, **161**, 1253.
Mulhausen, R., Eichenholz, A., and Blumentals, A. (1967). *Medicine*, **46**, 185.

Jakob-Creutzfeldt Disease: Treatment by Amantadine

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The subacute spongiform encephalopathy variety of Jakob-Creutzfeldt disease was described in detail by Jones and Nevin (1954). The disorder is characterized by progressive dementia accompanied by pyramidal and extrapyramidal signs, rigidity, and myoclonus, with terminal coma and death usually within a period of weeks or months. Typical E.E.G. changes with repetitive sharp waves appear during the course of the illness, and together with the clinical features constitute a syndrome which may be confidently diagnosed during life (Goldhammer *et al.*, 1971). The discovery by Gibbs *et al.* (1968) that the disease is caused by a transmissible virus has raised hopes that it may prove to be amenable to some specific form of therapy. Idoxuridine, apparently effective in herpes simplex encephalitis, has been tried in one patient in this department (Goldhammer *et al.*, 1971) without benefit. In the case here described the administration of amantadine was followed by encouraging clinical and electroencephalographic improvement.

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Case History

A 65-year-old man was admitted to hospital on 30 March 1971 with a three-month history of increasing mental confusion and