The results are summarized in the Table.

Summary of Findings on Experimental Animals

Splenectomized:	Monkey No. 1 At time of infection	Monkey No. 2 2 months after infection	Monkey No. 3 Not
Infection	*P. malariae*	*P. malariae*	Control
Course of infection	Severe	Mild	—
Clinical appearance at time of biopsy	Oedematous	Normal	Normal
Urinary protein	700 mg/100 ml	30 mg/100 ml	<10 mg/100 ml
Streptolysin O titre	<200 units	<200 units	<200 units
Renal histology	Membrano-proliferative glomerulone-phritis	Mild mesangial changes only	Normal
Immunofluorescence staining of kidney sections for:			
IgM	++	–	–
IgG	–	–	–
Complement	–	–	–
P. malariae antigen	–	–	–
Serum malarial antibody titres:			
IgM	80	320	<20
IgG	320	1,280	<20

Discussion

Previous workers have shown that rhesus monkeys infected with *P. cynomolgi* develop transient complexes of immunoglobulins and complement in their kidneys but that these resolve spontaneously and do not lead to the classical nephrotic syndrome (Ward and Conran, 1969). However, *P. cynomolgi* infections are more analogous to vivax malaria in man, and the latter has not been found to be associated with nephrosis. In the only other studies of this type rodent malarias have been used in N.Z.B. mice, which develop late renal disease spontaneously. Such mice when infected with *P. berghei* developed transient proteinuria a month after infection but the onset of their late renal disease was delayed (Greenwood and Voller, 1970).

Deposits of immunoglobulin and of complement were heavier in the malaria-infected mice than in the control mice, and the time course suggested a malarial aetiology rather than a later onset of the usual N.Z.B. renal disease.

Though a non-malarial aetiology cannot be excluded, the nephrosis observed in the splenectomized aotus monkey infected with *P. malariae* resembles the nephrotic syndrome of human quartan malaria. The results of the streptolysin-O assays seem to rule out the possibility that intercurrent streptococcal infections played any part as a cause of the nephrosis.

We have not observed oedema in any normal aotus monkeys nor in over 50 animals infected with *P. falciparum*. Many of these animals have received antimalarial regimens identical with that given to the affected monkey (No. 1) described here.

The clinical, histological, and immunofluorescent observations are all consistent with the hypothesis that the kidney lesion was caused by the deposition of immune complexes in the glomeruli. In many human cases of quartan nephrosis IgG, IgM, complement, or all three have been detected in the glomeruli (Allison *et al.*, 1969; Ward and Kibukamusoke, 1969; Houba *et al.*, 1971). The granular appearance of the IgM deposit in the kidneys of the aotus monkey corresponds with that of IgM deposits in the human kidney. The apparent absence of detectable *P. malariae* antigen is not particularly surprising; it has been found in only a minority of the human cases (Houba *et al.*, 1971).

We did not observe any of the tubular fluorescence reported by Houba *et al.* (1971) but this may reflect the state of the disease at the time we obtained the kidney material.

In view of the relative infrequency of the appearance of nephrotic syndrome in areas where *P. malariae* is very common it seems unlikely that nephrosis will be a regular feature of induced infections in normal aotus monkeys. However, it may be that the nephrotic syndrome reflects a peculiar immunological status of the affected individual, and that the quartan malaria infection acts as a "catalyst."

The occurrence of the syndrome in a splenectomized aotus monkey suggests that it may be possible, using this model, to determine the immunological conditions that give rise to the nephrotic syndrome in human *P. malariae* infections.

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MEDICAL MEMORANDA

Rapid Propagation of Thrombus in Deep Vein Thrombosis

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It is known that when a thrombus begins in the soleal venous sinuses or femoral vein it may propagate up the iliofemoral segment. Such a thrombus is large enough to produce severe pulmonary embolism if it breaks free. Though it is accepted that there is a certain degree of urgency in treating these cases in order to prevent pulmonary embolism, there is little information about how rapidly thrombus can propagate up the femoral vein in man.

This case report shows that thrombus propagation may occur at a rapid rate, for within one hour a thrombus spread from the lower third of the femoral vein to above the inguinal ligament, putting the patient in imminent danger of a massive, possibly fatal, pulmonary embolism.

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Case History

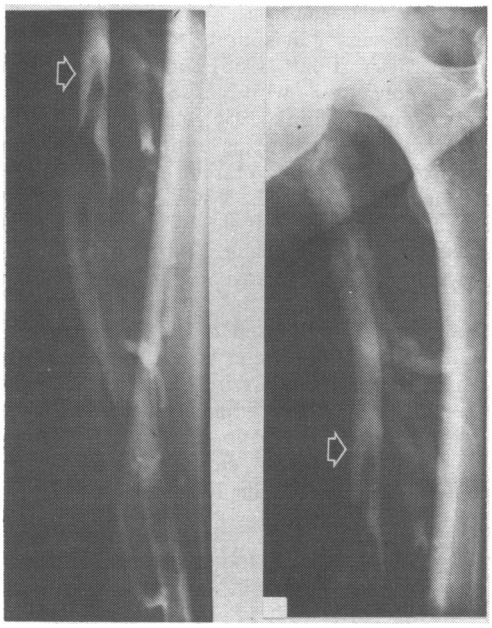
The patient, a woman aged 69, was undergoing routine investigations for a cerebral artery aneurysm and had had a carotid arteriogram taken under general anaesthesia. Five days after this

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

GILLIAN M. CRAIG, C. W. CRANE

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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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