Effects of heparin administration on free fatty acids (FFA).

lipase activity and hence circulating free fatty acid levels the administration of even small quantities of heparin (figure) can result in significant reduction in the plasma protein binding of a number of drugs.¹⁻⁴ As it is the free, or non-protein bound, fraction of the total drug in plasma which is responsible for a drug's effect, an increase in the free concentration will result in increased pharmacological effect with possible deleterious results for the patient. Without in any way detracting from the interest of Mr Bailey's findings we think it is important to alert clinicians to the possibility that the administration of even small quantities of heparin may result in a sudden increase in the pharmacological effects of concurrent therapy.

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³ Wood, A J J, *et al*, *Circulation*. In press.

⁴ Desmond, P V, *et al*, *British Journal of Clinical Pharmacology*. In press.

The Budd-Chiari syndrome

SIR,—Having just received the *BMJ*, I would like to comment on your leading article on the Budd-Chiari Syndrome (19 May, p 1302). It is stated that clinical diagnosis is often difficult: percutaneous needle biopsy specimens of the liver will show hepatic venous congestion with areas of centrilobular necrosis and haemorrhage.

This may be the case in some patients but in others the liver biopsy may perhaps be suggestive of the diagnosis. We have seen two cases of hepatic vein occlusion disease in children in the northern savanna of Nigeria, one of which has been reported.¹

The liver biopsies certainly showed centrilobular congestion but the centrilobular and sublobular veins were dilated and empty and compressed sinusoids containing few red blood cells were present. Towards the periphery of the lobules the sinusoids were widely dilated and trabeculae packed with red blood cells could be easily distinguished. This type of lesion was described in adults suffering from hepatic venous outflow block by Leopold *et al*,² who considered that this was a collateral extrasinusoidal circulation whereby the blood cells leave the central

sinusoids and enter Disse's space, becoming intermingled with the cells of the liver plates.

This note is prompted by the fact that this lesion would not appear to be widely known overseas and can be mistaken for the classical "nutmeg" liver. Indeed, I had some difficulty in convincing some of my colleagues in pathology of the genuineness of this histopathological picture.

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¹ Edington, G M, and Haggie, M H K, *Nigerian Journal of Paediatrics*, 1977, **4**, 6.

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Medicine and scientific method

SIR,—“General practice is not a scientific discipline. It cannot . . . take its place beside the other major medical specialties, whose foundation rests on a corpus of definable knowledge scientifically tested and proved,” writes Dr K B Thomas (7 July, p 39).

This assertion is incorrect. Medical practice, general or specialised, is founded on anatomy, physiology, pathology, and pharmacology, to name the basic scientific grounding. Daily we are encountering problems requiring knowledge of these sciences and it is hard to see what else Dr Thomas would require to make general practice what he would call “scientific.”

It would further seem that Dr Thomas is not familiar with the Karl Popper view of the nature of the scientific. Falsifiability is the criterion of the scientific, and actually clinical medicine, whether general practice or specialised, is a neat example of the scientific method. We are presented with problems for which we generate falsifiable hypotheses (or diagnoses); our decisions regarding treatment are likewise falsifiable. Doubtless the greater precision in the specialties leads to less falsification but there is obviously even less exactness in medicine than in areas such as physics, where Popper developed his ideas. Philosophy of science should be generally applicable and clinical medicine is entirely compatible with the Popperian scientific method.

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Rickets in Asian immigrants

SIR,—In your leading article (30 June, p 1744) you stress the importance of a reduced dietary vitamin D intake in the aetiology of rickets and osteomalacia in the Asian immigrant population. Probably at least as important, however, is their high dietary fibre and phytate intake, which reduces the intestinal absorption of bile acids, calcium, and vitamin D.¹⁻³ In addition, a high fibre intake may reduce the absorption of 25-hydroxy vitamin D undergoing enterohepatic circulation, so that normal exposure to sunlight will not necessarily prevent the development of vitamin D deficiency; in support of this, we have seen severe histological osteomalacia in several young Asian women who wear Western-style clothes, go outdoors daily, and even sunbathe on occasions.

Thus the consumption of large amounts of fibre and phytate may considerably increase vitamin D requirements, and it is conceivable

that fortification of chappati flour with vitamin D might possess its own built-in safety device against the danger of vitamin D intoxication.

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¹ Wills, M R, *et al*, *Lancet*, 1972, **1**, 771.

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Reversible renal failure during treatment with captopril

SIR,—The paper by Drs P R Farrow and R Wilkinson (23 June, p 1680) described a case of reversible failure of a transplanted kidney with a significant stenosis of the renal artery during treatment with captopril (Squibb, SQ 14225) for resistant hypertension. It was concluded from the clinical course that the probable cause was the nephrotoxic effect of captopril rather than ischaemia from the fall in blood pressure. We have observed a similar case and have concluded, however, that the dramatic fall in blood pressure after captopril, as well as after minoxidil, was the primary reason for the reversible renal failure.

A female patient, born 1949, had had an operation in childhood for a myelomeningocele and suffered from dysfunction of the urinary bladder. She developed bilateral hydronephrosis and chronic pyelonephritis and became uraemic. She consequently had bilateral nephrectomy and chronic haemodialysis was initiated. After two years of haemodialysis, in December 1976, she underwent a transplantation with a cadaver kidney. A cutaneous ureterostomy was performed. The immediate clinical course was uncomplicated and the graft functioned well. Slight hypertension (160/100 mm Hg) developed four months later. After hepatitis in November 1978 her blood pressure increased to 235/135 mm Hg. Arteriography did not disclose any stenosis of the renal artery and medication of the hypertension was initiated. Despite combined treatment with α -methyl dopa 1 g, propranolol 520 mg, hydralazine 200 mg, prazosin 20 mg, and clonidine 125 μ g daily, the blood pressure remained high, with values up to 215/145 mm Hg. On 9 February 1979 minoxidil 10 mg daily was introduced. The blood pressure successively declined from 240/130 to 140/90 mm Hg. Simultaneously her kidney function deteriorated from normal values of serum creatinine up to 270 μ mol/l (3.1 mg/100 ml) on 2 March. The minoxidil treatment was discontinued. A kidney biopsy at that time showed no evidence of toxic damage or tubular necrosis. The blood pressure increased during the following few days to 220/120 mm Hg and during the same time the serum creatinine values returned to normal.

Captopril treatment was initiated on 19 April at a dose of 25 mg thrice daily. The blood pressure dropped dramatically during the first hour from 200/125 to 110/80 mm Hg. The captopril dose was reduced to 12.5 mg twice daily on 20 April. During this day the patient became anuric and developed uraemia. Captopril was withheld and peritoneal dialysis was initiated. Arteriography at this time revealed significant stenosis of the renal artery, with a reduction in the lumen to about 50%. During subsequent surgery the renal artery was successfully reconstructed with an autologous vein patch graft. During the following few days the blood pressure became completely normal, falling to 120/80 mm Hg, and has remained so until the present time.

The plasma renin activity in peripheral venous blood was analysed once before captopril treatment was initiated. It was 14.9 nmol/l/h (19.4 ng/ml/h), an extremely high value.

This patient was very sensitive to captopril, which could be anticipated from the high plasma renin activity. This was so despite