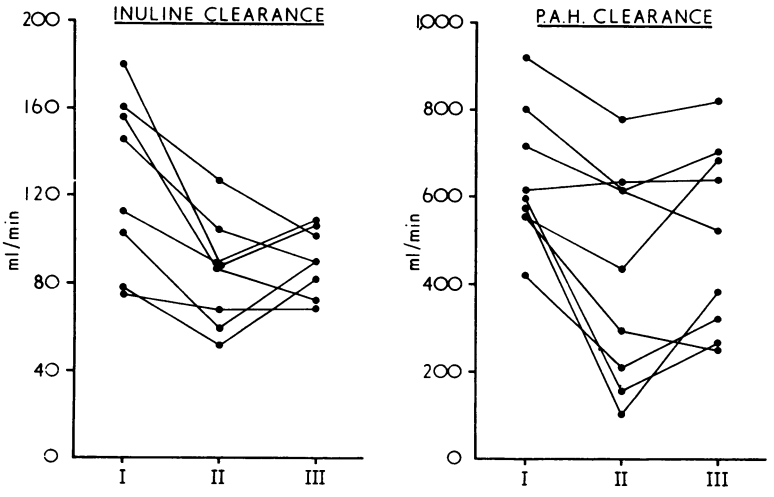

Fig. 2

The complete results are given in the Table.

m + Σ	Phase 1	Phase 2	Phase 3
Creatinine clearance ml/min	102·4 ±8·5	72·4 ±7·6	74·5 ±8·8
Inulin clearance ml/min	126·4 ±14·2	85·1 ±8·8	89·7 ±5·4
P.A.H. clearance ml/min	643·8 ±53·0	429·9 ±81·2	514·4 ±70·5

The average blood salicylic acid level was 10·8 ± 0·7 mg/100 ml in sample S_2 and 12·4 ± 0·13 mg/100 ml in sample S_3.

The exact mode of action of aspirin on renal function remains unknown. A vascular action with perhaps constriction of the afferent arterioles seems possible taking into account the reduction in glomerular filtration rate and renal plasma flow. In common with Beeley and Kendall[1] we found that the renal effects of acetylsalicylic acid were not constant: the glomerular filtration rate and P.A.H. clearance remained unaltered in one of our patients. This fact warrants further study using a greater number of cases. Indeed, it is possible to imagine that, at large, people have widely differing reactions, some being rapid inactivators of aspirin and others slow.[2]—We are, etc.,

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1 Beeley, L., and Kendall, M. J., *British Medical Journal*, 1971, **1**, 707.
2 Evans, D. A. P., *Pharmacogenetics, Annals of the New York Academy of Science*, 1963, **151**, No. 4, 723.

New Electronic Metal Locator

SIR,—George Bernard Shaw in *The Doctor's Dilemma* made one of the characters say that "all the best inventions are made regularly every 20 years." This appears to apply perfectly to the new electronic metal locator (15 April, p. 157).

In 1941 when in charge of the medical experimental laboratory set up by G.H.Q., Middle East Forces at the 63rd General Hospital in Cairo I discovered the existence of the highly secret mine detector project being developed by the Ordnance Corps. Eventually in collaboration with the late Lawrence Balls, F.R.S., director of the Cotton Research Board at Giza, a metal locator was developed with two pairs of search coils. A large pair of coils about 5 cm in diameter were used to search for a foreign body over the skin surface. A very small pair of coils were inserted in a test tube and could thus be used under sterile conditions to relocate the metallic foreign body in relation to the actual incision.

I still have the prototype as a treasured possession, but the "production prototype" made by the Ordnance Corps at Abbassia was taken to the South African Casualty Clearing Station at Mersa Matruh and had no sooner been brought into use than General Rommel captured both C.C.S. and foreign body locator.

Mr. M. J. Roper-Hall[1] reinvented the device for use in ophthalmic surgery and now Dr. J. Watson and Mr. H. J. Hambury have invented it all over again. Major-General D. C. Monro, K.H.S., who encouraged the development of my original device, decided not to replace the captured one because he considered it was unwise to tempt surgeons in forward areas to remove foreign bodies. With the invention of antibiotics this still seems to be a sound attitude except within the eye, but there ultrasonic location is proving vastly more satisfactory and will detect non-metallic foreign bodies and pathological conditions as well.—I am, etc.,

DOUGLAS GORDON

Harrow, Middx

1 Gibson, R., *Journal of Laryngology and Otology*, 1965, **79**, 23.

Prevention of Deep Vein Thrombosis

SIR,—Many have been the concepts concerning disease patterns in Africa. And many times we have seen that so-called non-existent diseases in Africa were in fact quite common. Surgeon Captain T. L. Cleave states (4 March, p. 629) that deep thrombosis and other venous conditions are rare among tribal (a rather unfortunate word) Africans living on unrefined carbohydrates. I do not know the investigations to support this statement, but I know that I see a surprising number of cases of thrombosis and pulmonary embolism—after operations and deliveries—as well as admissions for the symptoms of thrombosis and embolism only.

This notion comes from an isolated area in Kenya where half of the patients are Maasai, living on milk only, and half are Kisii, living on unrefined carbohydrates only.

While arterial disease is rare indeed, venous disease is, in my experience, quite common, not least among those Africans living on unrefined carbohydrates.

It will be interesting to hear from other countries in Africa whether venous disease is as common there as it it here.—I am, etc.,

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Sotik, Kenya

SIR,—We are writing in reply to Dr. N. H. Hills and others (1 April, p. 49) about our letter (4 March, p. 628) concerning the use of intermittent calf compression as a prophylactic against deep vein thrombosis. As a matter of record, a preliminary report of our findings was formally presented at an international symposium on venous thromboembolism[1] which was held at King's College Hospital on 10 July 1971, one week before the Surgical Research Society meeting to which they refer.

We would agree that the statement in the report of our trial, that patients were "randomly selected" was misleading. All suitable patients (as defined in our trial report) were entered consecutively into the trial and the treated leg was selected by drawing a card from a pack. Dr. Hills's question on the technique we used for assessing postoperative thrombosis has already been answered in our paper (13 November 1971, p. 394).

The great advantage of our technique is that intermittent compression of the calf applied within the limits we have defined,[2] need only be applied during the operation. This is the most important finding of our four years' research into this problem.

At last we see hope of preventing a complication of surgery that kills many thousands of patients a year. Let us now stop splitting hairs and get on with conducting large multicentre trials to establish the value of the methods that are now available.—We are, etc.,

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London S E 5

1 Kakkar, V. V., and Jouhar, A. J., eds. *Thromboembolism: Diagnosis and Treatment*. London, Churchill-Livingstone, 1972.
2 Roberts, V. C., Sabri, S., Beeley, A. H., and Cotton, L. T., *British Journal of Surgery*, 1972, **59**, 223.

Parathyroid Hormone Production and Malignancy

SIR,—I read with interest Dr. R. A. Melick and others' Medical Memorandum (22 April, p. 204) on tissue assay for parathyroid hormone in hypercalcaemic states. May I add that the differentiation between hypercalcaemia due to malignant disease and that of hyperparathyroidism can be a difficult diagnostic problem, as is illustrated in the following case.

A housewife aged 46 presented with a fractured right neck of femur after a fall in August 1971. Three months before admission, she had back pain with generalized weakness. She also complained of anorexia, loss of weight, constipation, polydipsia, and poly-

uria. On clinical examination there was no evidence of a primary malignant condition. *X*-ray of the femur revealed a pathological fracture. The site was explored, plated, and a biopsy obtained. It consisted of organizing blood clot with no evidence of growth.

Biochemical investigations: serum calcium 16·2 mg/100 ml, serum phosphate 2·9 mg/100 ml, alkaline phosphatase 30 K.A. units, urine calcium 1,600 mg/24 hr, urine phosphate 940 mg/24 hr. There was no myeloma band on protein electrophoresis. Bone marrow biopsy was non-specific. Chest *x*-ray, intravenous pyelogram, and skeletal survey revealed no abnormalities. Urinary output averaged 5·0 l./24 hr and the patient became rapidly dehydrated.

As there was no evidence of primary or secondary malignant disease, the neck was explored. All four parathyroid glands appeared normal. Two were removed for histology, which proved normal. Postoperatively, the patient's condition deteriorated very rapidly and she died. Necropsy revealed secondary deposits in the spine and right femur but the primary was not found.

In the 73 cases of Omenn *et al.*[1] nine underwent neck exploration without abnormal parathyroid glands being found, including one patient in whom three operations were necessary before a parathyroid lesion could be ruled out.—I am, etc.,

M. W. SALAH

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Epping, Essex

1 Omenn, G. S., Roth, S. I., and Baker, W. H., *Cancer*, 1969, **24**, 1004.

Tuberculosis Chemotherapy

SIR,—In his excellent article on tuberculosis chemotherapy (12 February, p. 426) Dr. K. M. Citron states "Pyridoxine, 10 mg, is given with each dose to prevent isoniazid toxicity." According to Kuschinsky[1] "Pyridoxine abolishes the tuberculostatic effect of isoniazid." As far as toxicity is concerned only the toxic effect on the peripheral nervous system is balanced, not the toxic effect isoniazed exercises on the central nervous system.

Judging it a matter of general interest I should appreciate a comment from Dr. Citron on this question.—I am, etc.,

PETER VAITL

Berlin

1 Kuschinsky, G., *Kurzes Lehrbuch der Pharmakologie*, p. 239. Stuttgart, Georg Thieme, 1964.

*** We have shown Dr. Vaitl's letter to Dr. Citron, who offers the following reply: "Laboratory investigations support the view that pyridoxine may under some circumstances inhibit the antimycobacterial effects of isoniazid. There is no evidence, however, that when pyridoxine is given in small doses in man for the prevention of isoniazid toxicity it inhibits chemotherapeutic efficacy. Thus when pyridoxine 6 mg was given twice weekly with streptomycin and high dosage isoniazid in a continuation regimen in 232 patients 99% had become culture-negative by one year.[1] Pyridoxine 6 mg was the dose used in previous studies by the Tuberculosis Chemotherapy Centre in Madras and had been shown to be effective in preventing both peripheral neuropathy and the cerebral effects due to high dosage isoniazid.[2] The incidence of toxicity associated with isoniazid 15 mg/kg twice weekly is very low, occurring in only 2 of 78 patients in one study.[3] A small dose of pyridoxine given with the twice weekly regimen prevents toxicity and has no adverse effect on the high efficacy of the regimen. Pyridoxine 10 mg was recommended in the article because this is the smallest dose conveniently available in tablet form in Britain."—ED., *B.M.J.*

1 *Bulletin of the World Health Organization*, 1971, **45**, 573.
2 *Bulletin of the World Health Organization*, 1963, **29**, 457.
3 *Bulletin of the World Health Organization*, 1964, **31**, 247.

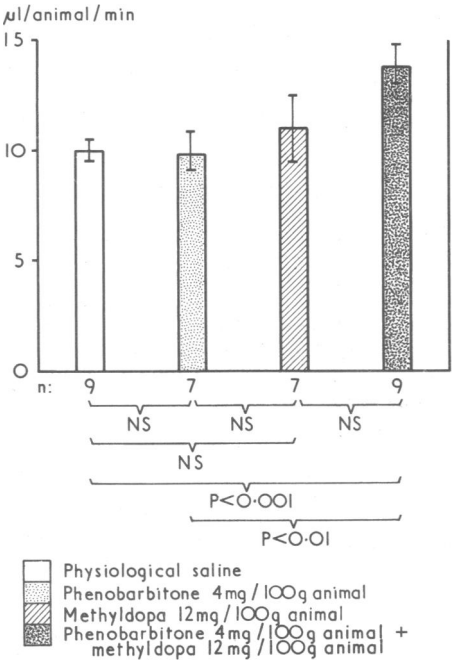
Methyldopa Metabolism and Barbiturates

SIR,—We have shown (28 August 1971, p. 518) that the spurious increase in serum catecholamine levels associated with methyldopa treatment can be reduced by the simultaneous administration of phenobarbitone, and we suggested that methyldopa metabolism may be accelerated by barbiturates through enzyme induction.

Increase of bile flow after treating rats with barbiturates has been reported by several authors and this was attributed by some to enzyme induction, but not by others.[1 2]

Our purpose was to find out whether this increase of bile flow could be influenced by the simultaneous administration of methyldopa.

Female albino rats weighing 180-230 g were used. They were of the same stock and fed on a standard diet with water. One group was given 0·1 ml/100 g physiological saline twice daily intraperitoneally for three days. For the same period of time, a second group was given 20 mg/kg phenobarbitone intraperitoneally twice daily, and the third group received 60 mg/kg methyldopa twice and 20 mg/kg phenobarbitone intraperitoneally twice daily. About 16 hours after the last injection under urethane anaesthesia the common bile duct was cannulated with polyethylene tubing just below the bifurcation. Body temperature was maintained by an electric bulb. The bile was collected over 30 and 60 minute periods every five minutes. The results were calculated as µl/animal/min (Fig.).



Our results indicate that phenobarbitone in the given dose did not change bile flow. When phenobarbitone was given simultaneously with methyldopa a marked increase of the bile flow was observed in a 30-minute period when compared with the control group and with the group receiving phenobarbitone only. For the 60-minute period the increase was significant only compared with the group receiving phenobarbitone. Similar results were obtained calculating in µl/100 g liver/min. Methyldopa alone in the given dose did not increase bile flow.

These results of methyldopa with phenobarbitone producing increased bile flow appear to indicate the presence of enzyme induction.—We are, etc.,

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1 Berthelot, P., Erlinger, S., Dhumeaux, D., and Preaux, A. M., *American Journal of Physiology*, 1970, **219**, 809.
2 Klaasen, C. D., *Journal of Pharmacology and Experimental Therapeutics*, 1969, **168**, 218.

Antibacterial Effect of Different Dialysates

SIR,—In an earlier experiment, we found that incubation of pathogenic *Staphylococcus aureus, Escherichia coli, and Pseudomonas* species in dialysis solutions which contained acetate resulted in greater reductions of viable organisms than incubation in solutions which contained lactate.[1] These results gave hope that acetate solutions for peritoneal dialysis might confer greater protection from peritonitis than the commonly used lactate solutions. In a later experiment,[2] the addition of 1 g/l. of human plasma protein abolished the greater antibacterial effect of the acetate solutions. During peritoneal dialysis, however, introduction of each new batch of solution dilutes the substances which have diffused into the peritoneal space during the preceding exchange. The possibility remained that the greater antibacterial effect of acetate existed in the more dilute fluids immediately after each change of dialysate.

We tested this possibility with eight pairs of dialyses on six 20-kg female dogs. For one dialysis of a pair, the solution contained 41 mEq/l. of acetate; for the other, a like concentration of lactate.

The methods of making and dispensing the sterile solutions[1] and their content of salts and glucose[2] have been described. Three preliminary one litre exchanges, totalling one hour each, preceded the experimental exchange. Immediately after the inflow of the fourth exchange ceased, we aspirated 50 ml of peritoneal fluid through the peritoneal catheter into a syringe. At the end of the 30-minute still period, this process was repeated.

Total proteins and amino acids were measured in portions of the aspirates. The remainder, as well as samples of unused dialysate, were used in the tests of bacterial growth. Thirty, new clinical isolates each of *Staph. aureus*, *E. coli*, and *Pseudomonas* sp. were used. Equal and known numbers of viable organisms from each isolate were inoculated into aliquots of the six different solutions (two control, two immediate, two 30-minute specimens) from each pair of experiments. After incubation for 18 hours at 35°C, the numbers of viable organisms