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.,

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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 Kuschinsky¹ "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 isoniazid 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.,

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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 $\mu\text{l}/\text{animal}/\text{min}$ (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 $\mu\text{l}/100\text{ g liver}/\text{min}$. 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 Klaassen, 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 solutions¹ and their content of salts and glucose² 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

TABLE I—Mean Concentrations of Total Protein and Amino-Acids in Aspirates of Peritoneal Fluids

Kind of Dialysate	Immediate Specimens		30-Minute Specimens	
	Proteins (mg/100 ml)	Amino Acids (μM/ml)	Proteins (mg/100 ml)	Amino Acids (μM/ml)
Acetate	8.9	0.16	32.3*	0.57*
Lactate	9.3†	0.14†	23.3*†	0.55*†

*Significantly higher than respective immediate specimens (P < 0.01).

†Not significantly different from acetate solution.

TABLE II—Mean Numbers of Viable Bacteria per ml of Dialysate after Inoculation with Viable Organisms

Organism Added	After 18-Hour Incubation					
	Control Dialysate		Immediate Specimen		30-Min Specimen	
	Acetate	Lactate	Acetate	Lactate	Acetate	Lactate
<i>Staphylococcus aureus</i>						
6.1 × 10 ⁵	5.3 × 10 ⁵ *	3.0 × 10 ⁵	1.5 × 10 ⁵ †	1.9 × 10 ⁵ †	2.3 × 10 ⁵ †‡	1.7 × 10 ⁵ †
<i>Escherichia coli</i>						
1.5 × 10 ⁶	2.7 × 10 ⁶ *	3.4 × 10 ⁶	1.1 × 10 ⁶ †	3.8 × 10 ⁶ †	1.3 × 10 ⁶ †‡	6.3 × 10 ⁶
<i>Pseudomonas species</i>						
1.4 × 10 ⁶	5.5 × 10 ⁶	1.0 × 10 ⁷	2.2 × 10 ⁶ †	6.9 × 10 ⁶ †	7.5 × 10 ⁶ †‡	8.0 × 10 ⁶ †‡

*Significant decrease from original inoculum (P < 0.01).

†Significant increase over control specimen in same solution.

‡Significant increase over immediate specimen in same solution.

§Significant decrease from original inoculum (P < 0.05).

in the solutions were measured by a system of quantitative cultures.³

In both kinds of peritoneal solution, the mean concentration of amino-acids and total proteins increased by approximately three-fold during the 30-minute still period (Table I). No antibacterial effect (Table II) was apparent in the fluids withdrawn immediately after each change of acetate dialysate, nor was any such effect apparent after a 30-minute "still period." These results dispel the hope that the acetate solutions exert an intermittent antibacterial effect within the peritoneal space. The only protective effect against peritonitis, then, resides in their greater

capacity to kill organisms inadvertently introduced into fluids during preparation or storage. This advantage is of especial value to those who must manufacture solutions for peritoneal dialysis in hospital rather than purchase the proprietary fluids.—We are, etc.,

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- 1 Richardson, J. A., and Borchardt, K. A., *British Medical Journal*, 1969, 3, 749.
- 2 Borchardt, K. A., and Richardson, J. A., *British Medical Journal*, 1971, 1, 205.
- 3 Richardson, J. A., Philbin, P. E., and Herron, G. R., *British Medical Journal*, 1968, 4, 757.

Sir Paul Chambers's Inquiry

SIR,—While agreeing with much of Sir Paul's logic (*Supplement*, 6 May, p. 45), especially that regarding the duplicated lines of communication towards, and in, the higher echelons of the Association, I feel I must disagree with his conclusions regarding geographic representation.

I believe he is falling into the Orwellian trap of thinking that, while all members are equal, some should be more equal than others. This seems to be particularly so with regard to junior representation. Taking his line between senior and junior at age 35, and assuming that doctors qualify at 25 and work till 65, then there will be three seniors for every junior. The number of juniors is of course inflated by overseas doctors who come here for training. These overseas doctors have as much right to be heard on the subject of pay and conditions as their colleagues, but I do not think they should be consulted on the broader aspects of policy. Furthermore, junior members are peripatetic and are concerned primarily, and rightly, with consolidating their career and raising a family. In this area there are very few who expect to stay more than a year, never mind three. This situation is not

peculiar to the medical profession; all professional men expect to move around.

Nor do I think that there should be two electoral rolls for electing Representatives to the Representative Body. I accept Sir Paul's concept of an area council. I very much prefer the use of the older terminology and would call it a branch council. The new branches ought to be co-terminous with the area health boards. Nevertheless, I think that election to the R.B. should be on the same basis as at present, using the new branches as individual constituencies. So long as the Representatives are ex-officio members of the branch council, and serve for three years at a time, they will be au fait with current problems.

At the top level Sir Paul has reduced his central executive to too small a number. The chairmen of standing committees will become a very bureaucratic group unless they are able to discuss their problems with non-executive members of the new Council. Furthermore, the Council has to represent changes of policy to the membership as a whole. I think the non-executive members of the Council should be elected by Representatives on a regional basis.

Sir Paul is to be congratulated on his work. Many members will disagree with his suggestions, either in part or in whole. Nevertheless, the clarity of his work must make us all think.—I am, etc.,

M. J. ILLINGWORTH

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SIR,—There are reasons why Sir Paul Chambers's report of his inquiry into the Association's constitution and organization (*Supplement*, 6 May, p. 45) might meet less challenge than it deserves. Sir Paul's generosity in providing his services is inhibiting, as good manners alone make it difficult to criticize what is given free.

The report is a powerful and authoritative one appealing to logic and recommending ruthless solutions. It is, however, the logic of many of its conclusions which are most open to criticism. The General Medical Services Committee and the Central Committee for Hospital Medical Services are both praised for being well informed committees yet they are both recommended for extinction. Is it logical to destroy what is most valuable?

The Association has been criticized for not adapting to its changing relationship with the Government. It is suggested that as now 95% of doctors have the Government as their employer the Association should have a unified and single voice. As no collective action could be taken by the profession, why is this so essential? Should not a broadly based profession have an equally broadly based means of communication?

I distrust the reasoning that junior doctors should have proportional representation within the Association. Firstly, I distrust the anticipated division of our profession into the young and the old; professional life is a continuing process and at no stage should it be necessary to have representation because of one's age. Secondly, great institutions are great because of their past achievements, and this is their legacy given to the future to be used for good or to be dissipated and destroyed. It is the life style of many of today's younger generation to dissipate and destroy what has been valued in the past. Young doctors are no different from their lay contemporaries in this matter.

My main challenge to Sir Paul's report is that he has not got the "feel" of doctors. We are not characterized by political wisdom and administrative ability, nor are we over-impressed with such talents. Our organization should reflect the kind of persons we are. I feel the Association as envisaged by Sir Paul would be appreciated by the Government but would be alien to the doctors it attempts to represent. It would be tailored to the Government's needs, not to ours.

Finally, it is ironical that the main reason for an inquiry into our Association's constitution was the possible need to exclude the proviso to Clause 3 to enable us to function on the Special Register. We are assured by Sir Paul that no such alteration is necessary. The price of getting this information has been the opening of Pandora's box.—I am, etc.,

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SIR,—Congratulations to Sir Paul Chambers on his excellent report (*Supplement*, 6 May,