chemist into the wards is to maintain the sometimes tenuous link between the patient and the laboratory—a link which often seems to be in danger of breaking down. It may be argued that there is nothing to stop any medical graduate from going on ward rounds, etc., but I feel that this clinical role must be “part of the job” and not an occasional exercise.

I realize that implementation of my suggestions would mean complete reappraisal of an area of medical establishment, involving other specialties as well as clinical chemists. However, one could point out that this reappraisal appears to be taking place in haematology, and there seems no particular reason why it should not take place in clinical chemistry. If it did recruitment of doctors into this fascinating branch of medicine would greatly increase, to the mutual benefit of patient and clinical chemistry alike.—I am, etc.,

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¹ Mitchell, F. L., *Annals of Clinical Biochemistry*, 1974, 11, Part 5, 149.

Chronic Diuretic Therapy and Potassium

SIR,—Though there are a number of clinical conditions—cirrhosis of the liver and nephrotic syndrome, for example—in which potassium supplements are important when diuretics are given the common problem is to decide how necessary supplements are in patients given diuretics as part of therapy for hypertension. Dr. H. J. Dargie and others (9 November, p. 316) rightly emphasize that potassium supplements need not always be given during chronic diuretic therapy. It is important, however, that a false extrapolation should not be made from a restricted study. Their patients with essential hypertension and normal renal function took only a single dose of frusemide daily. Such a regimen would be less likely to produce much potassium loss than one using a longer-acting thiazide diuretic. Incidentally it is also less effective in hypertension therapy.¹ Frusemide has a rapid, short action so that with a single dose it would not be acting over much of the 24 hours, so allowing possible retention of potassium to compensate for the excess lost. Not surprisingly, therefore, the reduction in plasma potassium values they observed were small, the mean values were within the normal range, and total body potassium (T.B.K.) remained normal.

Our experience, gathered from the study of patients receiving thiazide diuretics over some years at University College Hospital, London, is in general agreement in that when plasma potassium is maintained within the normal range then, in the absence of significant acid-base disturbances, T.B.K. remains normal. Here potassium supplements are obviously unnecessary. In a considerable proportion (more than 60% in our current studies) of younger patients, well apart from mild or moderate hypertension, plasma potassium has remained within the normal range without potassium supplement. Some patients, however, have developed persistent hypokalaemia (plasma potassium <3.4 mEq/l); these patients tend to be older and to have more severe hypertension, but there is

unfortunately no certain way of prediction. In our first report of T.B.K. changes measured by ⁴⁰K-counting² we were particularly interested in this type of response and we found that persistent hypokalaemia was usually associated with some reduction, usually modest, of T.B.K. In the patients of Dr. Dargie and his colleagues hypokalaemia was infrequent but in two with plasma potassium of 3.2 mEq/l (shown in table IV of their paper) T.B.K. appeared to be reduced by about 10%, which is the sort of change we have observed.

The control of intracellular potassium is complex, dependent on the activity of ionic pumps and not simply on extracellular potassium concentration. It is not really surprising, therefore, that mild hypokalaemia is not necessarily associated with reduction of T.B.K. It is important not to think of potassium deficiency in terms of T.B.K. alone. The plasma potassium level itself may be of more clinical significance, since the cellular transmembrane potentials depend on the ratio of extracellular to intracellular potassium.

In practice, plasma potassium is usually all that is available and so has to be the basis of monitoring. We suggested² that patients on chronic thiazide diuretics should begin with a potassium supplement (20–30 mEq/day) with plasma monitoring at one- to two-monthly intervals at first and the supplement stopped if plasma potassium remained in the normal range. It is probably better to start with a supplement to reduce the initial, often transient, potassium deficiency that often occurs on starting diuretics. Plasma potassium should be monitored for a further few months after stopping the potassium supplement but subsequently only infrequent monitoring (4–6 monthly) is needed. What level of hypokalaemia should be treated is more difficult to say for certain. With a plasma potassium of 3.0–3.4 mEq/l E.C.G. abnormalities are infrequent and T.B.K. reduction is small. There is, however, a case to be made for correcting even this deficiency by giving potassium supplements or, if these fail, a potassium-sparing diuretic, especially to older patients. It is most important that the work of Dr. Dargie and his associates should not be generalized to imply that potassium supplements (or potassium-sparing diuretics) are unnecessary in prolonged diuretic therapy except in certain particular conditions such as cirrhosis of the liver. The need for potassium correction must in all cases be decided by monitoring of the individual patient.—I am, etc.,

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¹ Anderson, J., et al., *Quarterly Journal of Medicine*, 1971, 40, 541.

² Edmonds, C. J., and Jasani, B., *Lancet*, 1972, 2, 8.

Maternal HL-A Antibodies and Fetal Sex

SIR,—With reference to the report by Mr. K. Johansen and Dr. H. Festenstein (26 October, p. 202) some unpublished data from a survey of cytotoxic antibodies in first pregnancies are of interest. In each instance the pregnancy was the first term pregnancy. A sample of serum was obtained when the patient booked in and a second sample was

taken at delivery. The sera were tested for cytotoxic antibodies against a pool of 20 random lymphocytes.

Of the 279 pregnancies studied in this way the infant was male in 126 and female in 153. Forty-five women had cytotoxic antibodies at some time in the pregnancy and in 23 instances the infant was male and in 22 female. In 34 pregnancies the first sample of serum was negative and the delivery sample positive for antibodies. Of these, 15 produced a male and 19 a female infant. There was thus no evidence from this study that a first pregnancy in which the fetus was male was more likely to be associated with antibodies in the mother than one in which the fetus was female. Though these data do not support those of the above report they are not statistically different from them (uncorr. $\chi^2=1.75$). The HL-A specificities of the antibodies were not determined.

The reason for giving attention to the sex of the fetus in this survey was the evidence that where an Rh-positive fetus is male the Rh-negative mother is more likely to produce anti-D than where it is female. It has previously been shown in retrospective studies¹ that the male:female ratios of immunized fetuses in two different series were 1.44:1 and 1.74:1 respectively. In a prospective survey of Rh antibody formation in the months subsequent to delivery of first Rh-positive ABO-compatible infants in Rh-negative mothers, of 72 instances where anti-D appeared the infant was male in 37 and female in 25—a ratio of 1.5:1.² Though this figure was not significantly different from that for pregnancies not associated with the appearance of anti-D, the data supported the findings of the previous report. Studies of the count of fetal cells after delivery in these mothers showed no evidence that a greater volume of cells entered the mother's circulation when the fetus was male.

If there are unidentified sex-specific histocompatibility systems influencing the antibody responses to HL-A antigens they are most probably also involved in the response to red cell antigens.—I am, etc.,

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¹ Renkonen, K. O., and Timonen, S., *Journal of Medical Genetics*, 1967, 4, 166.

² Woodrow, J. C., and Donohoe, W. T. A., *British Medical Journal*, 1968, 4, 139.

New Causes of Malignant Hyperpyrexia

SIR,—I was disturbed to find that in your leading article (30 November, p. 488) you accept the conclusions of Ellis *et al.*¹ without further question.

The most obvious question is—what precautions had these workers taken to eliminate halothane from the anaesthetic machine used? Titel and Lowe² found the rubber-gas partition coefficient for halothane to be 120, which means that a single rubber breathing tube in equilibrium with 1% halothane will hold about 700 ml of vapour. Assuming half of this to diffuse inwards (the other half diffusing to the outside air)—this is the equivalent of giving the patient 1% halothane in 5 litres gas flow for seven minutes. If a circle absorber has been used the time is nearly 20 minutes. Neither flushing the system with oxygen nor washing