is usually appointed. I should be grateful if any of your readers with such qualifications would inform me, adding a note of their present occupation.

T D WHITTET

Department of Health and Social Security,
Alexander Fleming House,
Elephant and Castle,
London SE1 6BY

Arsine toxicity aboard the Asiafreighter

SIR,—We are the managing agents to the owners of the above vessel, on whose behalf I now write, and have read with interest the article by Dr S P Wilkinson and others (6 September, p 559). In relation to the section headed "The incident and initial symptoms" the following should be pointed out in order to keep the record straight.

(1) It might be understood from the wording of the article that the double bottom tanks were examined as a result of heavy weather. The examination was in fact of a routine nature.

(2) The cylinders of arsine were stowed in the second tier from the top and not in the second from the bottom.

(3) The cause of the escape of the gas from the cylinder is open to some doubt and to attribute it to a previous storm can be little more than supposition.

P J F HENDERSON
Manager-Insurance,
Denholm Ship Management Ltd

Glasgow

Serum creatine phosphokinase and malignant hyperpyrexia

SIR,—I was interested in the paper by Dr F Richard Ellis and others (30 August, p 511) in which they concluded that serum creatine phosphokinase (CPK) estimations were of no value in screening for susceptibility to malignant hyperpyrexia. This conclusion was based on the assumption that halothane-induced muscle contracture in vitro was a specific test for susceptibility to malignant hyperpyrexia. Unfortunately this assumption is invalid, as we have already pointed out that halothane-induced contracture can occur in normal individuals.¹ More recently we have found that among 54 normal persons 30% had muscle fibres that responded to halothane treatment with contracture.

Individuals susceptible to malignant hyperpyrexia have muscle with heightened sensitivity not only to halothane but also to caffeine, succinylcholine, potassium chloride, and temperature change. Increased sensitivity to all these pharmacological agents must be shown in order to be certain that a patient is affected by the myopathy predisposing to malignant hyperpyrexia.

Using this more detailed in-vitro muscle test we have found that serum CPK levels are usually reliable in screening relatives of patients who have suffered from malignant hyperpyrexia for the presence of the predisposing myopathy. In particular, we have yet to find a relative with a normal serum CPK level who gave an abnormal muscle contracture response in vitro. If the serum CPK result is equivocal affected individuals must be identified by testing their skeletal

muscle for increased pharmacological sensitivity to caffeine, succinylcholine, and potassium chloride as well as halothane. Halothane-induced muscle contracture alone is a less reliable index of susceptibility to malignant hyperpyrexia than is the serum CPK.

M A DENBOROUGH

Department of Clinical Science,
John Curtin School of Medical Research,
Australian National University,
Canberra

¹ Moulds, R F W, and Denborough, M A, *British Medical Journal*, 1974, 2, 245.

Oral contraceptives and premenstrual tension

SIR,—I am writing to protest at the advice given in "Any Questions" (27 September, p 761) for the most suitable oral contraceptive for a woman suffering from premenstrual tension and irritability.

The general advice given by your expert over assessing the woman's own hormone balance/imbalance and choosing a suitable combination pill to alter it as required is sound, although, as the writer of the article referred to, my advice would be the opposite in such a case—that is, to give a pill which is on balance progestational rather than oestrogenic. However, there is a more major error. The articles to which the reader is referred classified all available oral contraceptives according to hormone balance, but your expert, quoting products from this list, has taken no account of the important findings and guidance since then over the amount of oestrogen in the pill—and all those named by your expert except one contain more than the recommended amount of oestrogen and some of them are rightly discontinued. This is quite unnecessary. The hormone balance of the pill does not depend on the dose of oestrogen or progestogen but on the balance of both. It is perfectly possible using newer low-dose oral contraceptives containing not more than 50 µg of mestranol or ethinyl oestradiol to attain the same effect on hormone balance without the added risks associated with the use of more than this amount of oestrogen.

ELEANOR MEARS

Grimsby, South Humberside

Transport of infants for intensive care

SIR,—In table I of their paper Miss A M Blake and her colleagues (4 October, p 13) seemed to show that the best chance is offered to seriously ill babies if they are born in a hospital with an intensive care baby unit. Much as we have appreciated the help that Dr Reynolds and his colleagues have given us on many occasions, their figures are incomplete unless they include the number of babies they have had to refuse from our and other district general hospitals. We have no foreknowledge on any one occasion when—with our inadequate staff—we will have to provide the only intensive care available to a particular infant. Up to the time of writing, since 1 January this year, University College Hospital has been able to accept only three of the 12 infants we have thought justified referral; seven of the remaining nine were

also refused admission at the other designated intensive care unit in our region.

Could Dr Reynolds and his colleagues publish details of the numbers of cases they have had to refuse over the period reviewed, so that the DHSS may begin to realise that No 127 of their Reports on Public Health and Medical Subjects remains a hollow mockery and that no provision is yet made for many of these babies either in the hospital where they are born or at designated centres?

SHEILA LEWIS
MARY ROSSITER

North Middlesex Hospital,
London N18

** We showed this letter to Miss Blake and Dr Reynolds, whose reply is printed below.

SIR,—We agree with Dr Lewis and Dr Rossiter that it is a matter for great regret that insufficient facilities are available in the UK for the intensive care of sick newborn infants. Our own unit always runs at more than 100% bed occupancy and we have to operate on a first-come first-served basis. Our data for the number of babies refused admission in 1972-4 are incomplete. During the past 12 months, however, more were refused than admitted, as implied in Dr Lewis and Dr Rossiter's letter.

ANTHEA M BLAKE
E O R REYNOLDS

Paediatric Unit,
University College Hospital,
London WC1

Clonidine overdose

SIR,—We read with interest the report by Dr S N Hunyor and others (4 October, p 23) describing two cases of clonidine overdose associated with severe hypertension.

The mechanism which they propose for the observed paradoxical hypertension in these cases is a dominance of the peripheral alpha-agonist action of the drug over its central hypotensive effect in the presence of high serum levels of the drug. In preliminary studies of clonidine pharmacokinetics and concentration-effect relationships in man, using a specific and sensitive mass fragmentographic assay for clonidine developed in our laboratory,¹ we have demonstrated an unusual relationship between plasma clonidine concentration and the effect on blood pressure. At low plasma concentrations the fall in arterial pressure is related to the plasma level. With high plasma concentrations, however, there is considerable reduction in the expected hypotensive effect. We think that this represents a predominance of the peripheral alpha-agonist effect of the drug at higher plasma concentrations and is probably seen only clinically immediately following intravenous bolus injection, when transient hypertension occurs. Our finding would support the proposed mechanism for the hypertension observed in Dr Hunyor and his colleagues' cases.

It was surprising to read that diazoxide and not alpha-adrenoceptor blocking agents had been used to lower blood pressure in these patients, as alpha-adrenoceptor blocking agents block the peripheral hypertensive action of clonidine.² We would suggest that