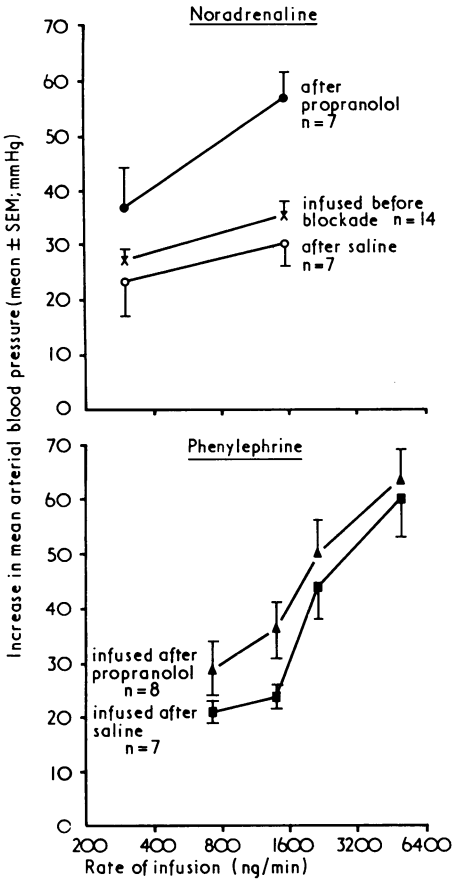

Dose-response curves for pressor agents infused intravenously into anaesthetised rats.

Noradrenaline infused into pentobarbitone-anaesthetised rats at 310 and 1480 ng/min caused marked increases in arterial blood pressure (see fig). These responses were augmented[1] when the noradrenaline infusions were repeated after an intravenous injection of propranolol (1 mg/kg body weight), but they were not augmented by a control "blockade" with saline. Furthermore, pressor responses to a more specific α-adrenoceptor stimulant, phenylephrine, were not significantly enhanced by propranolol.

F J IMMS

MRC Environmental Physiology Unit,
London School of Hygiene and Tropical Medicine,
London WC1

R L B NEAME
D A POWIS

Department of Physiology,
St Bartholomew's Hospital, Medical College,
London EC1

1 Imms, F J, Neame, R L B, and Powis, D A, *Journal of Physiology*, 1974, **241**, 47P.

SIR,—The report by Dr I Blum and others (13 December, p 623) serves only to emphasise that one should not increase the dose of a hypotensive drug too rapidly. The pressor effect they describe is not seen only when using propranolol: I have accidently induced it using each of guanethidine, acebutolol, and sotalol. None of these patients had a phaeochromocytoma. In a case of suicidal overdose practolol substantially increased blood pressure.[1]

It is not clear whether the pressor response is due to increased α-tone as suggested. I have controlled my paradoxically hypertensive patients with parenteral diazoxide or hydrallazine. It may be that the pressor effect of propranolol in the circumstances reported from Israel would not have been seen if the same high dose level had been reached over a longer time. The experiment should be repeated over an extended period to show that the hypertension is an induced artefact and not a feature per se of the valuable drug propranolol.

ROGER GABRIEL

Renal Unit,
Royal Infirmary,
Hull

1 Karhunen, P, and Hartel, G, *British Medical Journal*, 1973, **2**, 178.

Effect of junior doctors' action on self-poisoning

SIR,—Admission rates to this department have not shown the recent dramatic changes reported by Dr G S Crockett (10 January, p 92). The number of female admissions due to self-poisoning in November and December 1975 was 93 compared with 85 for the same two months in 1974 and 72 in 1973.

Junior doctors have been working normally in accident and emergency services in this city. This fact may explain the difference in admission rates between Bristol and Kettering, thus supporting Dr Crockett's conclusions.

A D BROOKMAN

Accident and Emergency Department,
Royal Infirmary, Bristol

Treatment of whooping cough

SIR,—I was interested to see the letter from Professor J A Davis (27 December, p 757) advocating the use of phenobarbitone as a very effective symptomatic treatment of whooping cough in young infants. Unfortunately I have never been impressed by this treatment and I suspect that this could be due to my failure to use the "relatively high dosage" recommended.

I wonder if Professor Davis could be asked to detail the doses he has in mind.

G MOSES

London W12

***We showed this letter to Professor Davis, whose reply is printed below.—ED, *BMJ*.

SIR,—The dose of phenobarbitone that we have been using in babies with whooping cough is 5-10 mg twice daily depending on weight, with two-thirds of the dose given in the evening and one-third in the morning. Babies will in fact tolerate larger doses without this interfering with feeding or affecting respiration.

JOHN A DAVIS

University Department of Child Health,
St. Mary's Hospital, Manchester

"Corrected" calcium concept

SIR,—Dr R W Pain and his colleagues (13 December, p 617) suggest that the regression coefficients for serum calcium on albumin differ so widely between individuals that use of an average population regression coefficient to correct serum calcium is invalid. They may prove correct, but the information presented in their paper does not allow this conclusion to be drawn.

The following example illustrates our principal concern. The relationship of serum calcium and albumin was studied in six subjects, inducing changes in serum albumin by altering the extracellular fluid volume and obtaining 10 measurements of calcium and albumin for each subject. The overall correlation of calcium on albumin was highly significant ($P<0.001$) and the average regression coefficient was 0·017 mmol/g. Individual regression coefficients for the six subjects ranged from 0·006 to 0·043 mmol/g, a sevenfold variation similar to that reported by Dr Pain and his colleagues. However, the six regression coefficients did not differ significantly ($P>0.1$). The error of the method was such that the results could easily be obtained by chance *if the regression coefficients for the six subjects were in fact identical*. Dr Pain and his co-workers reported individual regression coefficients between 0·018 and 0·080 mmol/g in 25 hospital inpatients and stated that the regression lines "were not always parallel," implying that they differed significantly. Unfortunately they had excluded data from nine patients in whom they could not fit a "satisfactory" regression line. When testing for significant non-parallelism of the regression coefficients there is no justification for excluding these nine patients, who contributed (probably considerably) to the error of the experiment. From the example we have given above it is quite possible that the range of coefficients observed by Dr Pain and his colleagues merely reflects the error of their experiment and not true inter-subject variation. While uncertainty exists on this point the frightening calcium "corrections" shown in their table I are not really valid.

In the preliminary information given in table II of the original paper it is clear that the regression coefficients for two of the three individuals studied using a tourniquet method did not differ significantly from the average population regression coefficient. The mean coefficient for the third subject was 33% higher than the population coefficient, a difference which, even if significant, is much less worrying than the 700% variation highlighted earlier in their paper. Before abandoning the current method for calcium correction it needs to be shown that individuals deviate *significantly* from the population regression, and also that the *magnitude* of any deviation is sufficient to justify the trouble of obtaining individual regression coefficients.

LAWRENCE E RAMSAY

Gardiner Institute,
Western Infirmary,
Glasgow

JOHN R SHELTON

G D Searle and Co,
High Wycombe, Bucks

SIR,—Dr R W Pain and his colleagues (13 December, p 617) "question the validity of 'correcting' an individual's measured serum calcium concentration by an average correction factor." They propose individual determination of binding coefficient by a four-point cuffing study as an alternative.

They believe this to be necessary because there is a "wide individual variation in the number of millimoles of calcium bound per gram of albumin in the serum." This belief cannot be soundly based on the two-point cuffing[1] or postural[2] experiments that they cite nor on their own determinations of regression coefficients from 3 to 17 (mean 8) serial determinations of calcium and albumin in individual patients, for there are no analyses to show that the variations found are any greater than those to be expected from the potentially gross sampling errors alone. Their case must rely on their triple determinations of binding coefficient in three subjects using the four-point cuffing method. Average binding

Br Med J: first published as 10.1136/bmj.1.6003.219-d on 24 January 1976. Downloaded from http://www.bmj.com/ on 21 May 2019 by guest. Protected by copyright.