	No	Serum Magnesium Concentration					
		mmol/l.			mmol/100 g protein		
		Mean	S.D.	Significance of difference from normal mean	Mean	S.D.	Significance of difference from normal mean
Group A	151	0.77	0.05	P<0.001	1.04	0.08	P<0.001
Group B	16	0.79	0.05	N.S.	1.02	0.10	P<0.02
Group C	59	0.78	0.05	P<0.001	1.04	0.10	P<0.01
All epileptics	226	0.78	0.05	P<0.001	1.04	0.09	P<0.001
Control subjects	95	0.81	0.04		1.08	0.07	

Group A: Patients treated with phenytoin.

Group B: Patients treated with phenobarbitone or primidone.

Group C: Patients treated with phenytoin and phenobarbitone or phenytoin and primidone.

N.S. = Not significant (P>0.05).

tion, like calcium absorption, tends to increase after vitamin D administration;² and vitamin D deficiency is accompanied by impairment of both calcium and magnesium absorption.³ It is known that children with florid rickets often exhibit hypomagnesaemia in addition to hypocalcaemia.⁴ After completing our recently published article on anticonvulsant osteomalacia¹ we have investigated the possibility that epileptic patients on anticonvulsant therapy show hypomagnesaemia.

Serum magnesium was determined by atomic absorption spectrophotometry (Perkin-Elmer, model 403) and serum protein refractometrically in the 226 epileptics and 95 control subjects, details of whom have been given.¹ Mean duration of anticonvulsant treatment was seven years. The coefficient of variation of duplicate measurements of serum magnesium was 0.9% and of serum protein 0.3%. The results are given in the table. The epileptics had serum magnesium concentrations significantly lower than the control subjects, whether the concentrations were expressed as mmol/l. or as mmol/100 g serum protein. Fourteen and 12% of the patients had a serum magnesium concentration below the normal range (mean $\pm$ 2 S.D.) in terms of mmol/l. and mmol/100 g serum protein respectively. Accordingly, the lower serum magnesium concentration in the epileptics was not due to differences in serum protein concentrations and protein-bound magnesium. Serum magnesium was not correlated to serum calcium nor to the duration of anticonvulsant therapy.

Lowering of the magnesium concentration in extracellular fluid would tend to increase neuromuscular irritability and is therefore probably an undesirable side effect of anticonvulsant therapy. The clinical significance of such minor degrees of hypomagnesaemia in epileptic patients remains to be established.—We are, etc.,

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Department of Clinical Physiology,
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¹ Christiansen, C., Rodbro, P., and Lund M., *British Medical Journal*, 1973, 4, 695.

² Hanna, S., *Metabolism*, 1961, 10, 735.

³ Wasserman, R. H., *Journal of Nutrition*, 1962, 77, 69.

⁴ Hütter, W., *Monatsschrift für Kinderheilkunde*, 1964, 112, 16.

Adverse Reactions to Alclofenac

SIR,—The intent of Dr. D. Mansel Jones's letter (26 January, p. 160) is fully supported by this company, which has co-operated with his colleagues in the exchange of information on adverse reactions.

Our data sheet on alclofenac is currently

under revision, but present circumstances will produce a delay in the distribution of this to prescribers. May we, therefore, use your columns to point out that this company considers the role of alclofenac is in the treatment of the chronic arthritides, where it is being shown to be of particular value and safety in long-term treatment. To our knowledge, all adverse reactions have occurred in the first three weeks of treatment, while treatment over months and years has not been accompanied by any sign of toxicity. We would appreciate receiving any information that appears to contradict this statement.—I am, etc.,

J. F. HORT
Medical Director

Berk Pharmaceuticals Ltd.,
Godalming, Surrey

Fluoride and Osteoporosis

SIR,—We feel compelled to reply to the comments by Drs. J. Dequeker and A. Burssens (3 March 1973, p. 551). They make three main criticisms of our report on the treatment of osteoporosis with fluorides¹: they question the diagnosis in our cases, our choice of fluoride dosage, and the validity of our measurements. All of our 11 patients had the syndrome of postmenopausal osteoporosis as defined by Albright, and they did not have osteomalacia. We have previously reported² that osteoid borders are somewhat wider in osteoporotic persons than in control persons of the same age, but the width is still significantly less than that found in clinical osteomalacia.

One of the purposes of our study was to determine the optimum dose of sodium fluoride for effective treatment. The dose was chosen as 50 mg of sodium fluoride daily because this was approximately halfway between the ineffective dose, less than 45 mg, and the maximum, 60 mg, which may lead to an undesirable effect on mineralization of new bone. Monitoring serum fluoride values might be of value, particularly because the intestinal absorption of fluoride is variable, but this is both tedious and impracticable in a large group. As Drs. Dequeker and Burssens state, renal sclerosis decreases fluoride elimination. Our patients were noted to have normal renal function. Indeed, the use of sodium fluoride and, more particularly, the administration of large doses of vitamin D and calcium would be contraindicated if there were any evidence of impaired renal function.

Finally, Drs. Dequeker and Burssens have made an error in questioning the validity of our quantitative values. Estimates of error are expressed as percentages of the absolute

values. In this case the absolute values of our measurements are also percentages (percentage of total surface). Thus the increase in bone formation that we reported, 4.4% in absolute terms, is approximately 100% in terms of the percentage differences. In addition, measurement errors are generally random and the P value of less than 0.001 indicates a highly significant, non-random difference between the before-treatment and after-treatment values for bone formation.—We are, etc.,

JENIFER JOWSEY
B. LAWRENCE RIGGS
PATRICK J. KELLY

Mayo Clinic and Mayo Foundation,
Rochester, Minnesota

¹ Jowsey, J., Riggs, B. L., Kelly, P. J., and Hoffman, D. L., *American Journal of Medicine*, 1972, 53, 43.

² Johnson, K. A., Riggs, B. L., Kelly, P. J., and Jowsey, J., *Journal of Clinical Endocrinology*, 1971, 33, 745.

New Constant Positive Pressure Respiration Apparatus

SIR,—Gregory *et al.*¹ described a method whereby constant positive pressure respiration is made possible for the newborn infant, making use of the simple apparatus described by them. There are, however, two major disadvantages in Gregory's method: (1) tracheal intubation in the neonate for an extended period of time is hazardous; and (2) the aneroid manometer is adversely affected by high humidity, and personal observation has shown that very often the pressures indicated are incorrect. The former pitfall may be avoided by the use of the Bennet face mask, and the latter by using a water manometer.

A simple and highly effective apparatus (see fig.) has been designed and has been in use in our department for more than a year. It consists of: a U-tube (a), with scale for reading off the positive pressures attained in the system; an escape valve (b) for regulating these pressures; connecting tubes (Bird) (c) from the above to the Bennet face mask; (d) and an anaesthetic bag and connecting gas line (e) from an air/O₂ blender.

The U-tube and escape valve are assembled on a plastic board fitted with a Gabler snaplock to fit a Gabler wall rail. The Bennet face mask is applied snugly to the patient's face. The constant positive pressure is adjusted according to the needs of the patient.

The apparatus has been used with success in our neonatal units and is a very effective, simple, and cheap method of treating the idiopathic respiratory distress syndrome of the neonate weighing more than 1,500 g. We

prefer treating smaller babies in the constant negative pressure respirator.—I am, etc.,

J. C. THOM

Department of Paediatrics,
University of Stellenbosch,
Tiervlei, C.P.,
South Africa

¹ Gregory, G. A., *et al.*, *New England Journal of Medicine*, 1971, **284**, 1333.

Solids and "Sleeping through"

SIR,—A survey into infant feeding habits has been carried out in South-east Monmouthshire on 100 mothers with babies between 6 weeks and 6 months of age. The major purpose of the survey was to ascertain whether there was a demonstrable link, as popularly believed, between introducing solids into the diet and giving up the 2 a.m. night feed. Only eight of the 100 mothers had not yet started solids (cereal in all but two cases) and all these had babies between 6 and 12 weeks old.

Of the 91 babies in whom the age of dropping the night feed was known, 49 had done so before, 18 during, and 14 after the introduction of cereal. Thus in only 32 cases could one even postulate a relationship between the introduction of cereal and sleeping through the night, and in 14 of these there was a delay of two or more weeks.

We are therefore unable to sustain the belief of many mothers (and others) that cereal feeding leads to babies sleeping through the night. If there were such a relationship it would be difficult to blame a mother who tried to ensure a good night's sleep for herself and the rest of the family. Perhaps these findings may help to counter some rather persuasive advertising and to avoid sowing some of the seeds of infant obesity.—I am, etc.,

R. M. ROBERTSON

Newport, Mon.

Time of Death

SIR,—In the course of a recent Horizon broadcast the statement was made that most deaths occur about three o'clock in the morning, and this is a widespread belief both in the profession and elsewhere. Among the distinguished authors who have perpetuated the myth was Robert Louis Stevenson.

Over the past two years I have kept a note of the time of death of every patient in this long-term and terminal care unit and, as the chart shows, these were distributed fairly

Distribution of times of death (corrected to nearest hour) of 363 patients.

evenly throughout the 24 hours with, if anything, a slight decrease in the small hours of the morning. Possibly being at a low ebb ourselves when called from a warm bed we feel that the patient should be at the point of death.—I am, etc.,

JOHN FLEETWOOD

Our Lady's Hospice,
Dublin

Intermittent Claudication and Vitamin E Therapy

SIR,—I was most interested in the finding by Mr. J. A. Dormandy and others (8 December, p. 576) of raised red cell malonyldialdehyde content in patients with intermittent claudication. I understand that this reflects the susceptibility of red cell lipids to auto-oxidation, malonyldialdehyde being a secondary breakdown product of lipid peroxides. Lipid peroxide is known to damage cell membranes and is known to be present in human atheromatous lesions.¹ Perhaps, as Mr. Dormandy and his colleagues suggest, the breakdown products of auto-oxidation have an effect on blood vessels and in pain causation.

In an excellent survey of the therapeutic value of vitamin E Marks² reviews the evidence for its use in intermittent claudication and concludes that there is a very sound basis for its use on grounds of clinical improvement. Vitamin E is known to inhibit lipid peroxidation *in vitro*³ and is a known *in vivo* lipid antioxidant. These facts and the authors' findings in patients with intermittent claudication might add more weight and some theoretical basis for vitamin E therapy in this potentially crippling yet often unrelievable condition.—I am, etc.,

WILLIAM D. ALEXANDER

Bristol Royal Infirmary,
Bristol

¹ Glavind, J., Hartmann, S., Clemmesen, J., Jessen, K. E., and Dam, H., *Acta Pathologica et Microbiologica Scandinavica*, 1952, **30**, 1.

² Tappel, A. L., *Archives of Biochemistry and Biophysics*, 1959, **80**, 333.

³ Marks, J., *Vitamins and Hormones*, 1962, **20**, 573.

Doctors in South Africa

SIR,—In your leading article on the World Medical Association (3 November, p. 245) you state that "too little credit is sometimes given to the Medical Association of South Africa for what it does under difficult circumstances." This opinion is most unlikely to be shared by any of the Black doctors in South Africa. On numerous occasions Black doctors in Cape Province, Natal, and Transvaal have separately urged the M.A.S.A. to take up their grievances with the authorities. It is interesting to note that the Federal Council of the M.A.S.A. has never included an elected representative of Black doctors whenever they have met the authorities to discuss their grievances. Blacks in South Africa are naturally very suspicious when matters of vital importance to them are discussed by Whites in their absence.

Despite the fact that all English-speaking newspapers in South Africa now use "African" when referring to the indigenous population, the *South African Medical Journal* continues using "Bantu" irrespective of the wish of the authors. The Nationalist Government never uses the word "African" as

this would in a way acknowledge that they were the earliest inhabitants of South Africa. This is contrary to their version of South African history. The editor of the *S.A.M.J.* also does not allow the use of "Black" instead of "non-White." However, "Whites" have never been referred to as "non-Blacks" in the journal. We should all strive for the day when people are no longer referred by their colour. Anyway, Blacks and Whites are incorrect terms; we are all varying shades of brown, pink, and yellow.—I am, etc.,

F. DINDAR

Etobicoke, Ontario

Testing Factory Workers for Glycosuria

SIR,—Clinistix strips were placed, with suitable instructions, in the pay envelopes of 13,466 employees working in an aero engine factory in Bristol. This exercise was publicized on the works notice boards after the permission of the management and the co-operation of the unions had been obtained. Known cases of diabetes were excluded. A total of 7,169 strips were returned. When the result was positive the urine was re-tested, and in 67 cases was found to contain sugar in amounts varying from $\frac{1}{4}\%$ to 2% . All employees with more than 1% of sugar in their urine were referred to their own doctors for further investigation. In 38 of these cases the diagnosis of diabetes was confirmed after a glucose tolerance test. Of these 38 diabetics, 21 are now controlled by diet only and the rest, showing smaller amounts of sugar in the urine, are also sugar-free with carbohydrate restriction.

This exercise, the cost of which amounted to £147, was thought to be a useful preventive measure in a large works. We have now passed on to phase 2 of our preventive measures and are testing the blood pressure of all employees over the age of 40.—I am, etc.,

E. P. GRIFFITHS

Senior Medical Officer,
Rolls Royce (1971) Ltd.,
Bristol Engine Division

Bristol

Glucagon in Acute Pancreatitis

SIR,—I was interested to read your leading article "Glucagon Therapy in Acute Pancreatitis" (1 December, p. 503). Unfortunately, the trial of glucagon reported by Condon *et al.*,¹ to which you refer, has done little to establish the drug's usefulness since they had no controls and, like your article, used the figures of Efron² and of Trapnell³ who reported mortalities of 22% and 23% respectively. Of Trapnell's series only 63% were diagnosed clinically and only 95 of his 324 patients underwent laparotomy. Efron does not give his laparotomy figures. Trapnell considered diagnostic laparotomy to be a fairly safe procedure, a point which may be debatable, but interestingly enough 13 patients out of Condon's series of 30 underwent laparotomy. Corlett and Mishell,⁴ studying the disease in pregnancy, (admittedly a selected group) had no mortality. Unpublished figures for this area on a series of 45 patients give a mortality of 8.8% or, excluding postoperative deaths, 4.7%. My point is that statistics of mortality from acute