CORRESPONDENCE

Correspondents are asked to be brief

Maternal Phenylketonuria

SIR,—With reference to your leading article on this subject (24 October, p. 192), we have had in our care in recent years two pregnant phenylketonuric women.

The first patient made little of formal education (I.Q. 65), married, produced a phenylketonuric male child (phenylalanine-loading suggested that the father was indeed heterozygotic) and after a gap of years again became pregnant. Abortion was declined. She had never previously received diet, her urine was positive for phenylketones, and her serum phenylalanine was 17 mg/100 ml. She was admitted to hospital and our usual dietary combination of Albumaid and a restricted daily phenylalanine intake from natural foods and phenylalanine-free preparations was begun. Nausea prevented her from full co-operation, however, and within a week she aborted. The conceptus was not examined.

The second patient's phenylketonuria was recognized in later childhood and she was never treated with diet. Her I.Q. is 55. She concealed the pregnancy until, it was thought, the 20th week. Therapeutic abortion was declined. She still had a positive urine test for phenylketones. The initial blood specimen went missing but her serum phenylalanine level 3 months after delivery was 24 mg/100 ml. The same dietary principles were employed but Aminogran was substituted for Albumaid. She took both with some difficulty and expressed no preference but had neither nausea nor vomiting. The serum phenylalanine was maintained between 3 and 12 mg/100 ml (average 7) and she delivered herself spontaneously at what was judged to be term. The male infant weighed 2,380 g, appeared well, showed no congenital anomalies, and in particular no phenylketonuria and no abnormalities of skull or skeleton on radiological survey, or of eye or heart. He is now 17 weeks old, is responsive, vocal, and has no obvious evidence of brain damage, although it is still too early to be sure that he has escaped it.

Within a few years from now the oldest of the successfully treated female children in Edinburgh of normal intelligence approach puberty. If we have finally decided by that time that diet can be discontinued at some point in childhood without incurring brain damage, such women face a reimposition of diet in pregnancy when tolerance of strange tastes may be impaired. Diet is certainly more palatable than it was and further improvements can be anticipated. Nevertheless documentation of experience with such patients as the two described, whether the outcome is successful or unsuccessful, may provide guidelines for the future.

In the light of these events we are at last making a start on an experimental basis on testing all women attending an antenatal clinic. Since blood and urine are taken routinely, we shall use both the Guthrie and the Phenistix test. We are not so well informed about the effects of hyperphenylalaninaemia without phenylketonuria that we can feel confident about its benignity, and we are sufficiently informed about negative urine tests in phenylketonuria that we are unwilling to use them to exclude this disease in pregnancy.—We are, etc.,

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SIR,—I was interested to read your editorial (24 October, p. 192) on the occurrence of maternal phenylketonuria, but surprised that the writer showed so little foresight as to claim that: "The logical outcome of all these observations is that screening for phenylketonuria should become part of every antenatal examination." This kind of blanket statement on a screening procedure should never be made without carefully considering all the issues involved, a point which is cogently argued in a recent publication on screening.[1]

In the case of maternal phenylketonuria, I previously[2] drew attention to the fact that antenatal screening of a population originally screened as newborn would be expected to result in the detection, on average, of only one case of maternal phenylketonuria among total pregnancies (births) in the United Kingdom over a five-year period. If a previously unscreened population is to be considered, the number of pregnancies at risk will depend almost entirely upon the numbers of women with phenylketonuria *and* relatively normal intellect. The frequency of such persons[2] is probably between 1×10^{-5} and $2{\cdot}5 \times 10^{-6}$. Since the economic justification for screening neonates for phenylketonuria has been called in question,[3,4] screening for a condition between 10 and 100 times less frequent would be exceedingly difficult to support on economic grounds. It may be noted that the above frequency of cases of maternal phenylketonuria (unscreened population) is of the same order of magnitude as the frequency of "missed" cases of phenylketonuria in newborn using the single Guthrie test[5], a British study[6] has concluded that this frequency did not warrant the use of a second test in order to ascertain those cases missed by the first.

It is worth pointing out that the number of maternal phenylketonuria cases which might be detected in such a screening programme would be even less if one had previously screened from the population the known high-risk individuals, such as female sibs of known phenylketonuria patients, and mothers of one or more children with severe non-specific mental retardation—also suggested in your leading article, and with far greater justification. An additional point of great importance[2] is the action to be taken upon discovering a pregnant woman apparently homozygous for phenylketonuria, but your leading article did not discuss this issue.

I submit, Sir, that an antenatal screening programme of a general population has nothing to recommend it at this time, and that to advocate such a programme in the absence of a full discussion of the relevant issues, some of which I have touched upon here, is little short of irresponsible.—I am, etc.,

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1 *Screening in Medical Care*, London, Oxford, University Press (for Nuffield Provincial Hospitals Trust), 1968.
2 Welch, J. P., *Lancet*, 1970, **1**, 722.
3 Wilson, J. M. G., in *Screening in Medical Care* p. 97, London, Oxford University Press (for Nuffield Provincial Hospitals Trust), 1968.
4 Gerald, P. S., *Pediatrics*, 1967, **39**, 325.
5 Cunningham, G. C., *California Medicine*, 1966, **105**, 1.
6 Report by the Consultant Paediatricians and Medical Officers of Health of the South-east Scotland Hospital Region, *British Medical Journal*, 1968, **1**, 674.

Near Drowning

SIR,—Three days before the article "Drowning. Its Clinical Sequelae and Management" (18 April, p. 157) appeared, a severe case of near drowning was admitted to the Royal Air Force Hospital Ely. Some points in the management of our case may be of general interest, since despite the high national incidence of actual drowning—up to 1,500 per year—only few of our hospital staff have previously been involved with the treatment of severe near drowning.

The patient, a 7-year-old boy, fell from the bank of a gravel pit. He was found floating face down by his father who instituted mouth to mouth ventilation and external cardiac massage while his companion ran to alert the emergency ambulance service. Approximately 15 minutes later the patient arrived at the casualty department.

On arrival the patient was unconscious, deeply cyanosed, had inactive dilated pupils, occasional gasping respiration, and an irregular bradycardia about 40/min. The skin was extremely cold and pale. Shivering and intense muscle spasm, which produced opisthotonos and trismus, were present. Blood pressure was unrecordable. The upper airway was cleared and the patient ventilated with 100% oxygen. The suxamethonium used to facilitate intubation made management much easier as opisthotonos stopped. On the assumption that the muscle spasm was due to cerebral oedema resulting from cardiac arrest it was decided to give 100 ml of Urevert intravenously. While this was being given ampicillin 500 mg and cloxacillin 500 mg were given intramuscularly and hydrocortisone 100 mg intravenously. Dextran-40 was given to counteract the profound shock.

The following investigations were then undertaken from femoral arterial puncture. Astrup results 45 minutes after near drowning were:

pH	6·9
Actual P_{CO_2}	120 mm Hg
Base excess	−21 mEq/l. blood
Buffer base	30 mEq/l. blood
Standard bicarbonate	11·0 mEq/l. plasma
Actual bicarbonate	23·0 mEq/l. plasma
Total CO_2	26·6 mEq/l. plasma

(Ventilated on 100% O_2) P_{O_2} 175 mm Hg = 99·1% saturated.

Electrolytes: Sodium 114 mEq/l. Potassium 7·4 mEq/l. Chloride 82 mEq/l.

While awaiting these results an infusion of sodium bicarbonate was started and over the next four hours a total of 250 ml of 4·2% sodium bicarbonate and 350 ml of Ringer-lactate together with 500 ml of rectal Resonium "A" were given; this achieved correction to:

pH	7·22
Actual P_{CO_2}	105 mm Hg
Base excess	+7 mEq/l. blood
Buffer base	56 mEq/l. blood
Standard bicarbonate	30 mEq/l. plasma
Actual bicarbonate	41·5 m/Eq/l. plasma
Total CO_2	44·6 mEq/l. plasma

During this time the patient became restless and intolerant of his endotrachial tube, which was removed. Diazepam 4 mg intravenously had excellent effect in quietening the patient. Consciousness was regained for the first time six and a half hours after the accident; during this time his mean axillary temperature was 97° F (36·1° C).

Chest *x*-ray showed widespread patchy shadowing more marked on the right than left. All urine passed in the first twelve hours was examined for haemoglobin and none found. The following morning, sixteen hours after the accident, the patient ate his normal breakfast and was playing with toys. He was discharged from hospital on the fourth day by which time chest *x*-ray showed considerable improvement in the shadowing.

It is interesting to note the patient's white blood count when seen in the outpatient department five weeks later. Total W.B.C.'s 8300/mm³ with 16% polymorph and 84% lymphocytes.

A case such as this at an inland hospital may take a casualty department by surprise and calls for enthusiastic resuscitation by a team, which in our case included surgeon, anaesthetist, and physician.—We are, etc.,

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Clonidine in Treatment of Hypertension

SIR,—We would like to comment on the work of Dr. A. I. Macdougall and others (22 August, p. 440) and that of Dr. A. Amery and others (14 November, p. 392) and to compare it with our work on clonidine. Since our preliminary communication[1] a detailed report has been published.[2] Our work on methyldopa and clonidine extended over a period of six months each, and we were able to study in 30 patients the side-effects, effectiveness, and tolerance of the two drugs. Unlike the experience with clonidine of Dr. Macdougall and colleagues who found that "side-effects from the drug were not disabling and were often transient" two of our patients developed such marked drowsiness that they refused to continue with clonidine. We feel that the greater number of side-effects from clonidine compared with methyldopa which has been observed by Dr. Amery and colleagues and by us, should make the clinician prefer methyldopa to clonidine, as one of the main factors dissuading a hypertensive patient from continuing with his therapy is unwanted side-effects. Tolerance occurred in six of our patients on methyldopa and in seven patients on clonidine. Our average dosage was 916 mg daily of methyldopa and 0·86 mg daily of clonidine.

It seems a pity that Dr. Amery and colleagues used chlorthalidone in combination with both clonidine and methyldopa, as thiazides themselves may be effective hypotensive agents.—We are, etc.,

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1 Seedat, Y. K., Vawda, E. I., Mitha, S., and Ramasar, R., *Lancet*, 1969, **2**, 591.
2 Seedat, Y. K., Vawda, E. I., Mitha, S., and Ramasar, R., *South African Medical Journal*, 1970, **44**, 300.

Idiopathic Hypercalciuria

SIR,—I read with interest the paper by Dr. Peter Adams and others (5 December, p. 582). I should like to know whether the plasma potassium was estimated in the five patients who had a low serum inorganic phosphate during the control period. Hypokalaemia may be causally related to hypophosphataemia,[1] and a fall in plasma phosphate can follow thiazide therapy, in some cases uninfluenced by potassium supplements.[2]

I note that five patients had hypercalcaemia after phosphate deprivation, and a further three after the addition of chlorothiazide. How many, if any, of the initial five hypophosphataemic patients appeared in this hypercalcaemic group?—I am, etc.,

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1 Anderson, D. C., Peters, T. J., and Stewart, W. K., *British Medical Journal* 1969, **4**, 402.
2 Condon, J. R., and Nassim, R., *British Medical Journal*, 1970, **1**, 110.

Lactic Acidosis

SIR,—We have recently seen a patient with biochemical findings similar to those reported by Dr. D. E. Barnardo and others (7 November, p. 348). However, our patient had diabetes mellitus and cirrhosis of the liver, and she was taking phenformin—all of which have been implicated as precipitating factors for lactic acidosis.

A 42-year-old female was admitted to hospital with a one-week history of malaise and a 24-hour history of progressive deterioration of conscious level. She had had diabetes mellitus for 18 years, treated recently with 20 units soluble insulin and 20 units P.Z.I. She was also receiving 50 mg phenformin per day because of the unstable nature of her diabetes. One week prior to admission she had reduced her dose of insulin to six units P.Z.I. and four units of soluble because of hypoglycaemic reactions. She also had a three-year history of hepatosplenomegaly with biopsy evidence of mild cirrhosis. On