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Diabetes Mellitus and Refined Carbohydrate

SIR,—Those of us who have worked in Africa when diabetes appeared to be uncommon must congratulate Dr. A. C. B. Wicks and Professor J. J. Jones (31 March, p. 733), who have extended the observations of other doctors¹ in Salisbury, Rhodesia. They are beginning to elucidate the role of refined carbohydrates as a factor in the pathogenesis of diabetes mellitus.

If one wishes to state the degree of refinement of any starchy carbohydrate, it is desirable to record the crude fibre content; thus maize meal, such as that consumed by Africans in Rhodesia, might vary in crude fibre content from 0.7 g/100 g if of 60% extraction to 1.5 g/100 g if of 96% extraction. That of wheat wholemeal 100% extraction is 2.0 g/100 g, while white flour 70% extraction has only a trace,² probably a crude fibre content of about 0.1 g/100 g. It would be helpful if investigators could state the degree of extraction of the maize meal consumed in Rhodesia. In South Africa a recent analysis reported that Bantu preferred maize meal 80% extraction (crude fibre 1.4 g/100 g), or 60% extraction (crude fibre 0.8 g/100 g).³

Reports of the experimental production of diabetes mellitus in small rodents seldom mention the crude fibre content of the food offered, though tables² can often supply these figures.

Interpretation has been that excessive calorie intakes encourage obesity and hyperglycaemia. This is correct, but a more comprehensive appraisal of the situation suggests that diets rich in undigested fibre have different satiety mechanisms because a larger proportion of the food remains undigested in the bowel; less is consumed.

When an animal feeds on its traditional food, fed *ad libitum*, it seldom becomes obese or develops diabetes. Perhaps man has a similar response, for refined starchy carbohydrates have not been his traditional food in Africa or in the Western World.—I am, etc.,

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² Platt, B. S., *Tables of Representative Values of Foods Commonly Used in Tropical Countries*. Medical Research Council Special Report Series, No. 302, p. 6. London, H.M.S.O., 1971.
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Insulin and Glucose in Treatment of Cardiogenic Shock

SIR,—Dr. S. P. Allison and his colleagues (16 September 1972, p. 675) reported the

value of daily infusions of insulin, glucose, and potassium in cases of severe congestive heart failure. Omitting the potassium, because hyperkalaemia was already present, we have been giving similar treatment to patients in cardiogenic shock after myocardial infarction.

The table shows typical findings in a case of cardiogenic shock before and during the course of one hour after the infusion of glucose 20 g and insulin 20 U over a period of five minutes. Apart from these results, we have seen diuresis begin after 30 minutes in oliguric cases. Our experience prompts us to recommend glucose and insulin infusions in cases of this kind when immediate lowering of serum potassium concentration and an improvement in cardiac efficiency is required.—We are, etc.,

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Prolonged Action of Pindolol

SIR,—Drs. P. D. Nigam and A. S. Malhotra (24 March, p. 742) reported that in a comparative clinical trial of pindolol and propranolol in angina pectoris they observed a prolonged action of pindolol (Visken, LB 46) for about one week after cessation of treatment. Slome¹ has suggested that a sudden withdrawal of beta-adrenoceptor blocking drugs might precipitate myocardial infarction in patients with angina pectoris. A prolonged action of pindolol could therefore offer some advantages.

Our studies in human volunteers² showed, in agreement with experiments in anaesthetized dogs,³ a significantly longer duration of action for pindolol than for propranolol: 5 mg of pindolol and 100 mg of propranolol were equipotent in reducing the increase in heart rate in response to exercise on the cycle ergometer two hours after oral administration. After eight hours pindolol still elicited 84% of its full effect and propranolol 67%. After 24 hours the figures were 36% and 16% respectively.

While the duration of action of pindolol is clearly longer than that of propranolol there is, however, no pharmacokinetic evidence that pindolol accumulates with prolonged administration. At the end of a 52-week toxicity study in monkeys given oral daily doses of 2.5 mg/kg and 25 mg/kg blood levels and urinary excretion data were comparable to those found after a single oral dose of the drug.⁴ Similar results were found in a pharmacokinetic study in man with an oral dose of 5 mg pindolol three times daily for eight days. Blood levels varied within the same range throughout the treatment period and they declined on the last day with the same half-life as after a single dose.⁵ There were therefore no measurable

amounts of pindolol released from the tissues when treatment was stopped.—We are, etc.,

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- ¹ Slome, R., *Lancet*, 1973, 1, 156.
² Aellig, W. H., *British Journal of Pharmacology*, 1973, 47, 621P.
³ Saameli, K., *Die therapeutische Anwendung β sympathikolytischer Stoffe*, ed. H. Dengler. Stuttgart, Schattauer, 1972.
⁴ Rentsch, G., unpublished results.
⁵ Aellig, W. H., and Pacha, W., unpublished results.

Acute Water Intoxication from Compulsive Drinking

SIR,—Dr. E. R. Alexander and others (13 January, p. 89) reported an interesting case of water intoxication in relation to acute psychogenic disorder. We have seen a very similar case of acute water intoxication from compulsive water drinking,¹ and we investigated the patient's water metabolism a week after his admission to hospital, when the intoxication had disappeared. An oral water loading test (15 ml/kg) was followed by a constant negative concentration of water (as with inappropriate antidiuretic hormone secretion), and this was hardly compatible with the profuse diuresis of low specific gravity observed after his admission to hospital.

To find the reason for this we tried to reproduce the water intoxication by infusing isotonic (5%) sorbitol at a rate of 1,000 ml/hr, and every half hour we checked the water concentration. The infusion produced a noticeable lowering of serum osmolality (260 mOsm/kg water). Initially the water concentration was negative, and it became positive only when the serum osmolality reached a value below 260 mOsm/kg water. A similar impairment of the water excreting mechanism was found by Hobson and English.²

Water intoxication therefore occurs only when there is impairment of water excretion as well as excessive water intake. Our findings, which differed from those in neurogenic hypernatraemia,³ made us think that the water intoxication in our case was due to excessive thirst and a lowered threshold for vasopressin release.—We are, etc.,

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Artificial Insemination by Donor

SIR,—May I, as a practitioner of A.I.D., be permitted to comment upon the conclusions of the panel on human artificial insemination chaired by Sir John Peel (*Supplement*, 7 April, p. 3)?

Selection of Donors.—Medical students, as a group, are not the best donors. The best donor is a man who has fathered two or three healthy children, which is the only

	Mean Arterial Pressure (mm Hg)	Central Venous Pressure (cm H ₂ O)	QRS (sec)	Serum Potassium (mEq/L)	Blood Sugar (mEq/L)
Before infusion	59	25.5	—	7.05	165
Immediately after	60	—	0.12	6.62	223
20 minutes after	67	—	0.10	5.75	218
30 minutes after	61	22.5	0.08	5.80	193
60 minutes after	71	23.5	0.08	5.05	193

way of knowing that sperms are normal. Without exception, when I inform prospective A.I.D. recipients that only proved donor semen will be used they are that much more reassured.

Frozen Semen.—The fact that good results are obtained in cows with semen frozen by liquid nitrogen has little bearing on human A.I.D. A farmer will have no second thoughts about killing a deformed calf. From my extensive reading of the American use of frozen semen I regard their apparently successful results—up to 70%—with great suspicion. No British doctor who practises A.I.D. has admitted a success rate of much greater than 50% using *fresh* semen. I have studied the method of using frozen CO₂ for freezing semen used by Dr. R. G. Bunge of Iowa (personal communication), who also claims excellent results, and found a considerable increase in immobility and fragmentation of sperms after defreezing. No one knows the effect on the genetic material in the frozen sperm, and there is no method of detecting any damage. The great majority of my patients who have been successfully inseminated by donor have resisted any type of follow-up. They want to forget the husband's infertility, and this reaction is understandable. Therefore I consider it extremely difficult for any organized scientific investigation to determine, with reasonable accuracy, the effects of using frozen semen over a sufficiently long period of time to produce statistically significant results proving or disproving the harmlessness of this method. In my view the demand for A.I.D. is insufficient to warrant the use of frozen semen, with all the hazards that this may entail.

Semen Banks.—It is difficult to see how anyone with personal experience of A.I.D. could suggest the setting up of semen banks. How could one confirm, in some way similar to the cross-matching of blood before transfusion, that the semen in tube XYZ was in fact the semen from a fair-haired white man (or dark-haired black man) before using it for insemination? As one cannot confirm whose semen is in the tube, whose responsibility will it be if a white-skinned mother gives birth to a black baby or a West Indian mother to a white baby?

Confidentiality.—What can happen in an N.H.S. hospital concerning confidentiality is illustrated by the experience of an unmarried woman of my acquaintance who was admitted for termination of pregnancy. She was assured by the gynaecologist that the abortion would be conducted under completely confidential conditions but when her mother arrived at reception and inquired which ward her daughter was in, she was told by the porter, "You'll find your lass in the abortion ward, darling."

Public Attitudes to A.I.D.—If the "climate of opinion" has changed towards A.I.D., then the extent of the change may be less than the panel is aware. Last year the editor of the *Daily Telegraph* would not allow my advertisement for a suitable Hindu-Sikh donor to be placed in the personal column. This month the editor of the *Jewish Chronicle* has refused a similar advertisement for a Jewish donor.

To summarize, it would appear that the panel was very poorly informed as to the problems associated with A.I.D.—I am, etc.,

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Achilles Tendon Reflex in Hypothermia and Myxoedema

SIR,—During the relaxation phase of a tendon reflex the muscle is electrically silent. "Brisk relaxation" of a muscle therefore cannot be caused by a lesion of the central nervous system as suggested by Dr. D. Maclean and others (14 April, p. 87). A more reasonable conclusion would be that hypothermia and hypothyroidism do not invariably delay muscle relaxation.—I am, etc.,

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Malignant Hyperpyrexia

SIR,—It is interesting to see in the letter from Dr. M. A. Denborough and others (24 March, p. 738) that their earliest recorded case of death from malignant hyperpyrexia occurred in 1921. Britt and Kalow mentioned another fatal case of malignant hyperpyrexia occurring in 1922. Both cases, of course, occurred well before the introduction of succinylcholine and halothane. These agents cannot therefore be specifically incriminated, as suggested by Dr. C. Langton Hewer (24 March, p. 738). Ether, cyclopropane, trichloroethylene, and methoxyflurane have probably also been responsible for inducing the syndrome,¹ though it is rarely possible to be absolutely sure of this because of the multiplicity of drugs commonly used during anaesthetic procedures. Ether may well be less potent in this respect than halothane; it is less potent in uncoupling oxidative phosphorylation in liver mitochondria, the relative potencies being related to the partition coefficient of the agents between lipids and water.²

Dr. Hewer is, I am sure, quite correct in maintaining the separation of malignant hyperpyrexia from the syndrome of late ether convulsions. In fact he made an early contribution to the discussion of the aetiology of ether convulsions.³ It is, however, unlikely that ether convulsions had a single cause. The earlier literature on operative and post-operative hyperpyrexia and fits contained much uncertainty about the possible roles of pre-existing hyperpyrexia, hot operating theatres, excessive draping of the patient, and atropine premedication. Agents other than ether were at times responsible for identical convulsions and hyperpyrexia.⁴

The major contribution of Dr. Denborough and his colleagues⁵ was the recognition of a family of patients developing fatal hyperpyrexia with anaesthesia.⁵ Sporadic cases, however, do occur,⁶ and I agree with the suggestion that some of the cases recorded in the earlier literature as late ether convulsions may well have been suffering from malignant hyperpyrexia. If ether is a less potent agent, which induces malignant hyperpyrexia less quickly than halothane and succinylcholine, then one may perhaps accept the six cases reported by Guedel⁷ as coming into the category of malignant hyperpyrexia. Certainly it is not easy to see from what they suffered if not malignant hyperpyrexia, and Britt and Kalow,¹ who have extensively reviewed the literature, accepted these as cases of malignant hyperpyrexia. Nevertheless, I agree that it is impossible to be certain of the diagnosis without the confirmation of a positive family history.

More important than this discussion, however, is the elucidation of the mechanism underlying the malignant hyperpyrexia reaction. As mentioned previously,^{8,9} contrary to the findings of Ellis *et al.*¹⁰ and of Dr. Denborough and his colleagues (3 February, p. 272), we found no histological abnormality in muscle biopsy specimens from six individuals, all of whom had raised serum creatine kinase levels and were relatives of patients who had suffered from malignant hyperpyrexia. In particular "moth-eaten fibres," cores, and pseudo-cores were not present. We did not find that halothane and succinylcholine invariably induced contraction in vitro in susceptible muscle, which again differed from the findings of Ellis *et al.*¹⁰ Our physiological⁸ and biochemical¹¹ studies failed to elucidate the underlying pathogenetic mechanism. Further studies of the muscle biochemistry and of the part played by thyroid hormones¹² are therefore awaited with great interest.—I am, etc.,

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Treatment of Depression in General Practice

SIR,—The paper by Dr. D. A. W. Johnson (7 April, p. 18) requires comment because it shows two serious deficiencies. In the first place the validity of many of his data is questionable owing to inadequacies of method. In the second place, even if accepted at face value, his results fail to justify his harsh criticism of his general practitioner colleagues.

Dr. Johnson fails to emphasize the accuracy of the G.P.'s diagnosis of depression. That 73 patients out of 91 interviewed by him satisfied his criteria is remarkable in view of the frequently repeated assertion that the G.P. does not recognize depression.

Dr. Johnson then criticized G.P. treatment in terms of drug therapy, psychotherapy, and the involvement of the social agencies. Seven days after the initial interview with the G.P. 72% of the patients were on the right drug in the right dosage, and of the remaining 28% the vast majority were on the right drug in what he considered to be inadequate dosage. Dr. Johnson's criticism is that this is not the best treatment, but he has no controls and cannot demonstrate better treatment apart from an assumption that he could provide it. Drug defaulting is a major problem, but in the absence of controls we would suggest that it could be an even larger