Diabetogenic Effect of Oral Diuretics

SIR,—The study by Drs. O. O. Andersen and I. Persson (29 June, p. 798) does not claim to help resolve the problem of the mechanism of the diabetogenic effect of certain oral diuretics. It does present, however, a comparative study of two drugs, ethacrynic acid and chlorthalidone. The conclusion reached is that "Increased values in this test [the two-hour value in the glucose tolerance test] indicate a necessity for caution in the use of diuretics, particularly chlorthalidone."

In a comparative study it is essential that drugs should be evaluated in circumstances as similar as possible. Though the difference in duration of treatment between the two groups in this study (ethacrynic acid—90 days, chlorthalidone—114 days) does not quite reach the accepted 5% level of statistical significance ($t=1.8030$, $P<0.1$), the relative average daily dosages, calculated from Tables I and II, show a marked discrepancy. The usual and recommended dosage for chlorthalidone is of 50 mg. daily in the maintenance treatment of hypertension. This dose corresponds also to the average daily dose used in long-term diuretic therapy. The most commonly used daily dose of ethacrynic acid is one lying between 50 and 150 mg. daily. It is surprising, therefore, that the average daily doses used in this study were chlorthalidone—128 mg., and ethacrynic acid—65 mg. The difference here is significant at the 0.001 level ($t=7.3048$). Furthermore, no information is given as to the therapeutic efficacy of the two treatments and the need for administration of other antihypertensive therapy. Other hypotensive compounds may not have a deleterious effect on carbohydrate metabolism, but they might beneficially affect it when adequately lowering a raised blood pressure.

That chlorthalidone may, under certain circumstances, adversely affect glucose tolerance is a fact which we have long recognized, and all literature relating to Hygroton (chlorthalidone) has contained a note to this effect since January 1964.—I am, etc.,

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Geigy (U.K.) Ltd.

Macclesfield,
Cheshire.

Morphine for Accidents

SIR,—At a recent inquest held in a rural area of north Northumberland the coroner expressed concern that the police were not able, or entitled, to give a sedative such as morphine to the injured person before he died following the accident. It is obvious that with the increasing traffic on our roads and the number of serious accidents which are occurring daily the time has come when patrol cars should be furnished with sedative drugs, such as "Tubonic" ampoules of morphine, kept in a locked receptacle and used at the discretion of the police officers.

For many years now masters of sea-going vessels have had the authority granted by the Home Office to administer such drugs, and I see no reason why the police force should not have this authority extended to them, especially in rural areas, where an ambulance or a doctor may take a considerable time to reach the scene of an accident.—I am, etc.,

Ainsdale,
Southport.

R. ROSS HAIR.

Nasal Cancer in Woodworkers

SIR,—In your issue of 8 June (p. 572) there is a leading article, "Nasal Cancer in Woodworkers," which was stimulated by a paper in the same issue by Dr. E. D. Acheson and others (p. 587).

The leading article lists isopropyl alcohol among chemical agents known to cause nasopharyngeal cancer in man. In our view there is no evidence that isopropyl alcohol is carcinogenic to man. The paper of Weil, Smyth, and Nale¹ quoted by Dr. Acheson was concerned with an early process in the manufacture of isopropyl alcohol, and the authors showed that this chemical was non-carcinogenic to mice, but believed that isopropyl oil formed during the process was the actual carcinogen. As mentioned by Dr. Acheson and his colleagues, "... the risk has been abated by changing or enclosing the process." To the best of our knowledge nothing has occurred since to give rise to any doubt as to the safety of the process workers or to the non-carcinogenicity of isopropyl alcohol.

We feel it is important to bring this to your attention in view of the wide use of isopropyl alcohol as a chemical solvent, chemical intermediate, cosmetic ingredient, and skin antiseptic, etc.—I am, etc.,

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Division,
Shell International Chemical
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REFERENCE

- ¹ Weil, C. S., Smyth, H. F., and Nale, T. W., *Arch. industr. Hyg.*, 1952, 5, 535.

Intramuscular Injections and Gas Gangrene

SIR,—I suggest an alternate explanation for the fatal case of gas gangrene associated with intramuscular injection described by Drs. P. W. Harvey and G. V. Purnell (23 March, p. 744).

If phenobarbitone sodium has propylene glycol as its solvent vehicle the histotoxic action of this substance would create a

localized zone of tissue necrosis, totally deprived of circulation, an ideal culture medium for anaerobic organisms.

While the warning about intragluteal injections is a timely one, I wonder again whether the accusing finger has been pointed at the wrong agent. Firstly, probably all antibiotics produce upon intramuscular injection considerable areas of tissue necrosis. Secondly, several injectable agents are dispensed with propylene glycol as the solvent agent, some containing as high as 67.8 w/v of this substance. Experimentally it has been demonstrated that propylene glycol retains its histotoxicity in concentrations as low as 10%. It would be a service if a list of injectable agents in propylene glycol were made known in the *B.M.J.*¹—I am, etc.,

GEORGE MARGOLIS.

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Hanover,
New Hampshire, U.S.A.

REFERENCES

- ¹ Stephen, C. R., Nouril, W. K., Hall, H., Martin, R., and Margolis, G., *Anaesthesiology*, 1954, 15, No. 6.
² Margolis, G., Hall, Helen E., and Nouril, W. K., *A.M.A. Arch. Surg.*, 1953, 67, 715.

* * Drs. Harvey and Purnell inform us that at this distance of time it is impossible to ascertain (1) whether the phenobarbitone sodium was dissolved in propylene glycol, (2) whether it was injected into the buttock. Professor Margolis has shown that propylene glycol causes muscle necrosis: we agree that this effect should be recognized, and that the use of this substance as a vehicle for injected barbiturates, antihistamines and vitamins might with advantage be reconsidered. On the other hand, to sustain his thesis it would have to be shown experimentally that propylene glycol greatly reduces the infective dose of *Cl. welchii* spores, as do calcium salts or adrenaline. The fact that glycols have some antibacterial activity might operate against such an effect. In the absence of such evidence, and of clinical reports of gas gangrene following injections containing propylene glycol, the overwhelming probability remains that adrenaline was responsible in this patient.—Ed., *B.M.J.*

Hospital Career Structure

SIR,—Unlike our colleagues in other hospitals, we have not all resigned from the British Medical Association, for we believe that through it our views should be made known to the Minister of Health and his Ministry.

We, the junior medical staff of this hospital, in common with colleagues in other hospitals are becoming increasingly concerned at recent developments in the hospital services. We are particularly alarmed by the recommendation to expand the medical assistant grade.

This grade was originally created in an attempt to overcome staffing shortages by attracting general practitioners and married women into hospital practice. The Ministry of Health now appears to have departed from this concept and intends to enlarge the grade by encouraging doctors who are not suitably trained or qualified to remain in hospital practice. Into this grade they will also force fully trained specialists who have not yet attained consultant status. A situation will then arise where untrained staff will be called

on to do work beyond the limits of their ability and highly trained staff will be doing consultant work without consultant status.

Already we have evidence that medical assistant posts are being created at an increasing rate where consultant posts have been requested, despite assurances to the contrary. This should stop forthwith. In our opinion, if it continues it will be at the expense of the expansion in the consultant establishment which is required to provide a modern medical service in this country. Hospital doctors wish to provide the highest possible standard of specialized medical care, and if this is not possible in this country they will be forced to seek a more progressive environment.

It appears that despite the fact that it is now official B.M.A. policy to stop medical assistant appointments, the B.M.A. has taken no positive action in this matter. We note with despair that these posts are still being advertised in the *British Medical Journal*; no less than 17 having appeared on 6 July. We consider that the matter is one of considerable urgency and we appeal to those in