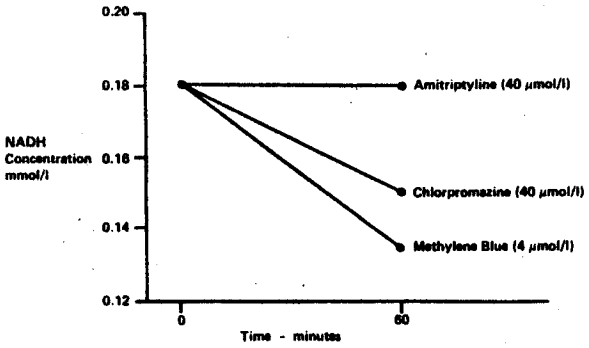

Fig. 1—The oxidation of NADH by vanadate in presence of drugs and FAD.

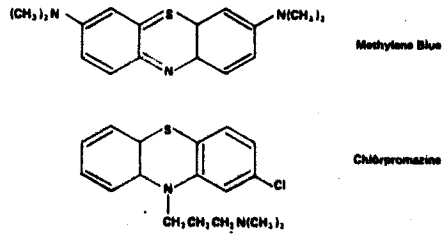

Fig. 2—Formulae of chlorpromazine and methylene-blue.

as sedation. Presumably reduction of vanadate to vanadyl would diminish the binding and would therefore increase the excretion of vanadium—again a slow effect but one which would not be immediately reversed on discontinuation of the drug. However, the drugs must also have other separate pharmacological effects—e.g., sedation and dopamine receptor blockade—which may also be of therapeutic benefit in this disorder.

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INTRAVENOUS IMMUNOGLOBULIN IN ANTIBODY DEFICIENCY SYNDROMES

SIR,—Patients with hypogammaglobulinaemia syndromes have to have regular doses of immunoglobulin by injection. Side-effects are common and the discomfort of large intramuscular injections has often endangered effective prophylaxis. Among 26 hypogammaglobulinaemic Swedish patients reviewed[1] 12 had not been given adequate prophylaxis, resulting in impaired lung function and decreased weight and height if the disease had started before the age of 15.[1]

Patients can be protected, with few side-effects, by intravenous injections of specially prepared immunoglobulin preparations.[1-4] Many preparations have been modified by enzymic degradation, reduction and alkylation, exposure to low pH, or S-sulphonation.[2] Native unmodified antibodies retaining all biological activities would be advantageous.[5] We are using such a preparation composed of ≥90% 7S IgG and with only traces of the IgG-fragments and dimers often seen in larger amounts in immunoglobulin preparations in addition to IgG polymers.[1] The preparation is a Cohn fraction II from pooled plasma purified by 'DEAE-Sephadex' and stabilised with 5% albumin and 2·5% glucose. It has been given in doses of 5–10 g in 142 intravenous infusions 1 ml/min (more slowly at first) every second or third week to eight patients with common variable immunodeficiency and one with IgA, IgG2, and IgG3 deficiency. The preparation ('Gammonativ'; KabiVitrum, Stockholm) has very little IgA. A similar preparation has been given uneventfully to other IgA deficient patients who lack IgG2 and profit from immunoglobulin prophylaxis.[6]

Seven of the nine patients had previously reacted, usually strongly, to i.m. and/or i.v. injections of other preparations. During the 142 infusions with gammonativ there were two occasions when the temperature rose by 1·1°C (one patient had a cold). One patient had temporary anuria, but this was in a patient on assisted ventilation after cardiac arrest, with respiratory failure, and several simultaneous infusions. After recovery this patient has received 15 gammonativ injections without side-effects. The nine patients have had few infections during the 6–8 months of this prophylaxis.

Gammonativ is an unmodified IgG preparation for intravenous use that seems to be safe. Therapy must be sufficient if chronic and ultimately lethal lung changes are to be prevented. The prevalence of common variable hypogammaglobulinaemia in Sweden is 2–3 per 100 000; if we add the cases, now being found more often, of IgG2-deficiency,[1,6] the number of patients requiring immunoglobulin prophylaxis is not inconsiderable.

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HALLUCINOGENIC FUNGI

SIR,—Dr Young and colleagues (Jan. 23, p. 213) describe an "epidemic" of abuse of hallucinogenic fungi in Glasgow. A similar epidemic occurred in Dundee between Sept. 13 and Oct. 17, 1981. 44 patients (mean age 18 years), chiefly schoolchildren and unemployed youths, were seen in the admissions and emergency department of Ninewells Hospital after ingestion of liberty caps (*Psilocybe semilanceata*). Large numbers of young people were eating these mushrooms and those presenting did so because of a dysphoric reaction to the experience, and 4 patients thought they were about to die.

The 44 patients seen were assessed according to a proforma prepared in the light of our previous experience with this condition.[7] All but 4 patients had dilated pupils. Other evidence of sympathetic stimulation was less frequent, a heart rate above 100/min being noted in 10 patients, diastolic blood pressure of 100 mm Hg or more in 17 patients, and hyperreflexia in 16 patients. Flushing of the upper trunk, neck, and face was noted in 8 patients; 23 patients were nauseated or had vomited, while 9 complained of upper abdominal pain, and in 2 cases this was severe enough to be the cause of presentation. Distortions of perception were very common and were usually visual although only 4 patients were frankly hallucinating. Paraesthesiae affecting the limbs and face occurred in 16 patients and 2 were ataxic.

Patients presented to the department an average of 3·8 h (range 1–8 h) after ingesting the mushrooms, and after a short period of observation 26 were sufficiently well to be discharged from the accident department in the care of a responsible adult. 18 patients were admitted to hospital and all had fully recovered within 12 h. In most patients therefore the effects of the hallucinogen are shortlived.

We have found that gastric intubation can be difficult in these young patients who are often already distressed and not infrequently aggressive. Furthermore the mushrooms may block

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the standard lavage tubes for drug overdose cases. There has therefore been a tendency for ipecacuanha emetic draught to be administered to these patients by doctors seeing them in the accident department (29 of the cases in the present series). We have not, however, found any difference between patients given ipecacuanha and those not given ipecacuanha in the rate of recovery from the effect of the mushrooms, and we remain to be convinced that gastric lavage or induced emesis is necessary unless there is other evidence to suggest that they have ingested potentially more toxic fungi. Indeed we have recovered large quantities of more or less intact mushrooms from the stomachs of patients already substantially recovered from the episode, suggesting that tolerance had developed to what was, presumably, a large dose of hallucinogen.

Given the large numbers of young people who have been collecting and ingesting these mushrooms from at least eight local parks and two golf courses and the gatherers' fairly primitive mycological knowledge it is perhaps surprising that no serious case of mushroom or "toadstool" poisoning has occurred in the Tayside area in recent years. This may be because potentially more toxic fungi are usually larger and appear very different from the small liberty cap with its characteristic nipple.

Part of the reason for the major problem encountered in this past Autumn was the very wet weather which produced a bumper harvest of the mushrooms for a population primed for their appearance. We would agree with our Glasgow colleagues that doctors ought to be more widely aware of "magic mushroom' ingestion since it is likely to become more frequent and since once diagnosed it is often possible with appropriate management to allow the patient home in the charge of a responsible adult.

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EFFECT OF STRICT DIABETIC CONTROL ON EYE AND KIDNEY FUNCTION

SIR,—A provisional report on work in progress is always welcome when its aim is as important as that of the Steno Study Group (Jan. 16, p. 121). However, I have some comments on the statistical analysis of their results and on the study design.

Nothing is said of the likely variation with time of the measures of ophthalmic or renal function. How reproducible are these measurements, with both technical and biological variability inevitable from week to week? If this variability is substantial in comparison with the observed changes over six months, several of the reported differences in "six-month change" may be an example of regression towards the mean, or, in sporting terms, "The bigger they are, the harder they fall". Except for albuminuria, the reported changes have served merely to bring the two groups closer together, and in none of these four instances does the CSII (continuous subcutaneous insulin infusion) group seem to end up after six months at a different functional level than the UCT (unchanged conventional treatment) group. The crucial question is whether, for all the subjects, there is a correlation between the initial value of a measurement and its change over six months in particular subjects. If such a correlation exists, then the changes observed in the two groups can only be fruitfully compared after allowing for this correlation. This is far more important than whether there is a significant difference between the initial means.

Unfortunately, it is not easy to estimate quantitatively the reproducibility of, for instance, macular recovery time or oscillatory potential. In non-diabetics the value may have increased (3 eyes) or decreased (7 eyes, with 6 eyes approximately unchanged) on retesting after one to two years, and differences of up to 30 μV in the added amplitudes are described as "very small".[1] No data are given for the diabetics who are said also to show "highly consistent" reproducibility. With nyctometric assessment of macular recovery time, it is even harder to judge, because the reference given[2] lists results entirely qualitatively as "reduced", "normal" or "hypernormal", and neither the arbitrary units of the Steno paper nor their reproducibility are discussed.

In the one exception, where the group means diverged after the 6-month study, there is a conflict between the text and table II; is the second largest urinary albumin excretion rate 840 or 320 μg/min?

If this study was indeed designed as a comparison between near-normal and moderate levels of glycaemic control, as stated in the last paragraph, why were not the two diabetics randomised to UCT whose median blood glucose during the six months fell within the enviably narrow range of the CSII group analysed along with them as a "near-normal" glycaemic group to compare with now just 13 diabetics in a "moderate" glycaemic group? The randomisation step was between two different methods of insulin injection and could not have been between two separate targets of glucose control, as the defined target for CSII falls within that for UCT.

The findings are indeed compatible with a conclusion that the combination of CSII and greatly improved metabolic control beneficially alters the course of microvascular phenomena associated with diabetes, but the same might be said for many other conceivable sets of results. To test the conclusion more rigorously, an analysis of variance would have been more impressive, to relate change in the measured factor against its initial value, against the median glucose (or the HbA_{1c}) and against the method of insulin delivery (let alone other possible influencing factors, such as age or sex).

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KIDNEY TRANSPLANTATION

SIR,—I was interested in your Jan. 9 editorial based on the 1981 review of the U.K. Transplant Service. The Service is to be congratulated on so efficiently and promptly disseminating this information. The data can easily be compared with data from other European countries with comparable populations thanks to the table provided annually by the European Dialysis and Transplant Association.

Northern California and Northern Nevada are in a zone which is designated as network no. 3 in the National Network of End Stage Renal Disease (ESRD) programme. The population is about 10 million. The incidence of ESRD (all figures relate to 1980) was 90·01 per million and the prevalence was 244·9 per million. The number of patients on dialysis was 2257 (1159 males and 1098 females). The total deaths in 1980 was 437 (19·3%). New patients who began dialysis in 1980 numbered 824.

Of the 2257 patients on dialysis, 254 (11·2%) received kidney transplants. There are three transplant centres in the Northern California/Northern Nevada area. The number of patients on the transplant waiting list was 463 at Dec. 31, 1980, of whom 120 (26%) were above 50 years of age.

Data from the U.K. are not strictly comparable with these. Patients of all ages and all conditions are accepted in the dialysis programme here—no-one is allowed to die because he is old (904 patients, 40% of the total on dialysis, are above 60 years of age) or because he has diabetes or an irreversible cardiovascular condition. The motivation for nephrologists referring patients for transplantation differs on the two sides of the Atlantic. Additionally, no patients here need to be transplanted to have his or her machine available for someone else. The factors in common are apathy and unwillingness of other physicians to take part in the organ donation procedure, which is less complex here than in the U.K. due to the integrated working of the transplant coordinators in the United States. We also have our fair share of refusal to consent from the next of kin. The enactment of the law of "opting in to donate organ" by signing consent on the back of a driver's licence has not appreciably increased the availability of cadaver donors.

The source of these data is the report of the Northern California/Northern Nevada ESRD Network Coordinating Council.

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