if the subject has an intercurrent infection or has taken alcohol or other drugs. Prolonged unconsciousness also results from taking mixtures of tranquillizers and hypnotic drugs when alcohol or dexamphetamine or barbiturates are ingredients.

I agree with Dr. H. J. S. Matthew (10 February, p. 380) that the evidence is extremely confusing. It would be interesting to know if people who have given L.S.D.-25 therapeutically have ever encountered prolonged coma. The first case of chronic psychosis following therapeutic L.S.D.-25 which I ever saw was a man who later died of leukaemia. This has given me much food for thought in the light of the present research on chromosomal aberrations after L.S.D.-25, and might be worth pursuing.—I am, etc.,

London W.2.

ELIZABETH TYLDEN.

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SIR,—At the present time all too little is known of the interaction between therapeutic agents, and the assimilation of such data is thus of great value. Nevertheless, it is important that information obtained of necessity outside the environment of the controlled clinical trial be subject to careful scrutiny.

In Dr. R. Clayton's report (20 January, p. 163), as in that by Milman,¹ the presumption is that the lysergic acid diethylamide (L.S.D.-25) ingested was of illicit origin. It is likely that material produced in such circumstances, while exhibiting hallucinogenic activity, will contain a low percentage of L.S.D.-25, proportions of other hallucinogenic lysergic acid derivatives, and non-hallucinogenic starting materials and intermediates. These proportions are likely to vary from batch to batch and from source to source. Distinctions should therefore be drawn between interactions resulting from legitimate and illicit sources of drugs. Indeed, in the past other therapeutic agents have been passed off as L.S.D.-25.² Furthermore, coma does not appear to have been encountered when L.S.D.-25 has been given alone.

In view of the very small dosage of L.S.D.-25 required to provide hallucinogenic effects in man its autonomic properties are unlikely to have been evident if pure material was administered.—I am, etc.,

D. S. FREESTONE,

Manager,
Clinical Research Department,
Sandoz Limited.

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Not Allowed to Die

SIR,—Palliative treatment, whether it involves a calculated surgical risk, the use of expensive equipment, complicated techniques, or simple drug therapy, should be carefully planned to give maximum ease through the probable life expectancy of the particular patient. When, however, the latter is un-

usually difficult to assess the semantics of life quality have to be considered and resolved. This is an ethical field which the profession should explore before another permissive Bill is thrust upon us.—I am, etc.,

Oxford.

EDWARD COPE.

Scientific, Technical, and Ethical Considerations in Cardiac Transplantation

SIR,—I think that it is very sad that nobody has attempted to answer the important points raised by Mr. W. J. Dempster and others (20 January, p. 177). Perhaps strong criticisms of the present practice of visceral transplantations are unanswerable, stemming as they do from people who have long experience in the field. This "heart-grafting business" has also been well and truly discussed from the scientific, ethical, and practical point of view by Dr. A. V. Mitchison, Sir George Pickering, and Professor Peter Beaconsfield,¹ and their evaluation as medical scientists not personally involved in transplantation has passed unnoticed by the profession.

Is this because the figures for survival rates for renal transplants done in Britain are not given in a true unequivocal form? I have spent many hours reading many articles without having been able to arrive at this necessary information. Figures should separate twin donors, other live donors, and cadavers, and give the survival rates for one, two, three, four, and five years.

On television, radio, and in the lay press a figure of 75% success for renal transplantation has been mentioned repeatedly. Who supplied this figure to the editors and journalists? Excluding twins, how many five-year survivals have there been in Britain? Moreover, the non-specialist reader must be informed of the common practice of transferring patients in whom a transplant has been unsuccessful to renal dialysis, and thereby prolonging life a further few months or maybe over a year. But this would not constitute an honest report of renal transplant success.

Are living donors still being used in British units? I know of a young woman in the later stages of pregnancy who was persuaded to be a donor and accepted. What about the man who was exhorted, "You cannot let your colleague down and let him die," who after he had donated a kidney was surprised that an insurance company would not accept him as a first-class life and felt that he should have been warned? Have the British units done a critical follow-up of all kidney donors? Again, I know of one definite case who later himself developed severe renal infection with serious consequences.

Has the problem of tissue rejection really been solved, even "adequately," as Professor Barnard has maintained? Does not all available critical evidence point to the fact that tissue rejection always occurs sooner or later after all visceral transplants? Is it not true that the length of the period prior to complete rejection cannot be predetermined, and may indeed be much shorter than the recipient's life expectancy without transplantation? Furthermore, it is claimed that the risks of transplantation surgery, however

great, are justifiable because the prognosis otherwise is hopeless. But hopeless in terms of weeks, months, or years? Are the prognostic abilities of these transplant surgeons so accurate that they can precisely contrast this expected period of survival against the period in which organ rejection will be complete, a period which is itself unpredictable?

The Ministry of Health has been bludgeoned into setting up renal transplant units at enormous cost in money, manpower, and space. But should not these empire builders who have campaigned for these units have used what influence they have for the more needed and more urgent requirements, such as hospital rebuilding? Where is their sense of priorities?

Further, the Medical Research Council, the Royal College of Physicians, and the Minister of Health, in answer to previous criticisms of mine on human experimentation,² have pointed out the various ethical codes on human experimentation, all of which insist on prior animal experiments, and thus have many of my criticisms been summarily dismissed. Yet when some surgeons carry out transplants without adequate prior animal experimentation, especially from the immunosuppressive viewpoint, they are not condemned but lauded as heroes. Why this two-faced attitude?—I am, etc.,

London W.1.

M. H. PAPPWORTH.

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Royal Malady

SIR,—Dr. G. Dean's letter (17 February, p. 443) is patterned so closely upon that of Professor C. E. Dent (3 February, p. 311) that our reply to the latter (24 February, p. 509) affords an answer to both except for the following points.

Dr. Dean does not accept the description of James I's illness as indicative of porphyria for a number of reasons. Firstly, because "porphyria causes constipation, not diarrhoea." This is factually incorrect. Waldenström¹ has observed the occurrence of diarrhoea in porphyria, and in Professor A. Goldberg's^{2,3} series diarrhoea was present in 12% of his cases—a figure which tallies well with our 2 out of 17 in the royal personages. Since paralysis of the gut may be segmental, as demonstrated by x-rays, it is not surprising that constipation or diarrhoea may occur, or an alternation of both. Although constipation is experienced by the majority of porphyrics—Frederick the Great, to quote but one of our cases, complained of "being constipated like a Turk"—hypermotility of the gut can and does occur,⁴⁻⁷ and an acute attack may be ushered in by this symptom.

Secondly, Dr. Dean prefers Mayerne's 350-year-old "diagnosis of kidney disease and haematuria and some form of arthritis, perhaps gout" as "much more probable than recurrent attacks of acute porphyria." He says "our ancestors were notoriously liable to gravel in the seventeenth century." It would perhaps be more exact to say that they were more liable to the *diagnosis* of gravel, as indeed they were to the diagnosis of witchcraft and possession. Every urine which left any sediment was considered to con-

tain "gravel," as sixteenth- and seventeenth-century medical texts show. We⁸ felt compelled to exclude haematuria because after passing red urine (which incidentally Mayerne called *urina cruenta*—just as Thudichum⁹ (1867) called haematoporphyrin "Cruentine") James passed, "a few hours later," a specimen which was "white as water" and "clear as if filtered" (see plate⁹). Had the red colour been due to bleeding from the urinary tract it is unlikely that it would have disappeared so abruptly without leaving a trace of discoloration or smokiness—the very circumstance which mystified Mayerne. But that such rapid changes in colour do occur in porphyria and in what circumstances we have already touched on in our previous letter (24 February, p. 509).

Dr. Dean does not accept James's skin lesions as "characteristic"—they ought to be "water-blisters." A glance at our paper⁸ would have shown him that this is exactly what they were—namely, "vesicular"—and what is more they broke out "in the blazing sun," and, more typical still, were severest on the forehead and only healed at the end of September. Lastly, Dr. Dean doubts our statement that James had one congenitally malformed, non-functioning kidney, which like the other healthy one could not have been the seat of repeated calculus formation. Our evidence for it is contained in a contemporary necropsy report by a physician¹⁰ which runs: "The right kidney was found with difficulty, buried in much fat, very small and hardly exceeding an inch in length. It was not contracted from any disease but in shape it was formed naturally."

The existence of the X porphyrins, porphyrin-peptide conjugates, has only recently been discovered by one of us (C. R.) and their chemistry elucidated (Rimington, Lockwood and Belcher, *Clinical Science*, in press) by work over the past three years. The method for their determination, which demands considerable skill, has been passed on request to a few colleagues, and in our opinion the figure we quote for patient B is above normal.

However, Dr. Dean's overall objection to all our findings is that "this inherited disorder of metabolism, as far as we know from family studies [our italics], caused no significant symptoms, except light-sensitive skin, until the introduction of modern drugs." It has repeatedly been stated in your columns that severe symptoms do occur independent of drug intake, as by Professor A. Goldberg,³ Professor A. L. Cochrane,¹¹ and by those workers whom we quote in our previous letter (24 February, p. 509). This is therefore no valid ground on which to reject their appearance in the past. His dictum that porphyria caused no symptoms but skin sensitivity in the past is based on his own study where he traced the genealogy of living porphyrics in South Africa to an immigrant in 1688. His information was derived almost exclusively from verbal tradition or entries in family Bibles or church registers where in some, but not all, cases skin sensitivity was noted as a family peculiarity, called the "van Rooyen's skin." One would naturally not expect clinical observations or description of disease to be forthcoming from such sources. Dr. Dean cannot seriously argue that because he found no mention of clinical symptoms in his cases none occurred and therefore cannot have occurred in any porphyric. Would he maintain that because he saw no record of, say, smallpox his patients' families were exempt from it or that smallpox did not then exist? It was the advantage of finding detailed medical records—such as only exist for

historic figures—which gave us the opportunity of detecting evidence of symptoms of porphyria centuries before it was recognized as a clinical entity.—We are, etc.,

IDA MACALPINE.

R. HUNTER.

C. RIMINGTON.

London W.C.1.

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Steroids and Nephrotic Syndrome

SIR,—In your leading article on steroid treatment for nephrotic children (2 March, p. 530) you mention that there is no means of identifying those likely to relapse.

For over a decade I have used a regimen that has successfully achieved this. On discharge from hospital after the initial admission the mother is taught how to test her child's urine with Esbach's reagent each day and she is instructed to match the daily dose of prednisolone with the reading obtained. Thus if albumin is present amounting to four parts per thousand she gives four tablets of prednisolone in the following 24 hours, if 10 parts she would give 10 tablets, etc. It is surprising how great are the fluctuations recorded in her daily notebook. With colds and other infections a rapid rise to 12 parts is common, but the prompt administration of an adequate dose of steroid prevents the formation of significant oedema. As the child improves less frequent Esbach readings are taken. Experience has shown that the mothers successfully prevent relapses with this regimen, and, since steroids are only given when required, growth inhibition is kept to an absolute minimum.—I am, etc.,

Stock, Essex.

IAN G. WICKES.

Dental Anaesthesia

SIR,—A recent press report¹ concerning an inquest on a patient who died following anaesthesia for conservative dental treatment has prompted us to write this letter.

We wish to make it clear that we strongly deprecate the present practice employing the use of intravenous anaesthetic agents (for example, methohexitone) by single-handed practitioners for the purpose of carrying on any form of dental treatment. In our respective dental practices we do make use of general anaesthesia for conservative dental treatment. However, our incidence of general anaesthesia for these procedures is small and we each average about one to two patients per month (this is a lot less than the 5% figure quoted in the *Sunday Times*). Also the patient's airway is safeguarded by an endotracheal tube and packing.

During the preparation of a cavity in a tooth with the air turbine drill considerable water is used as coolant. Much of this water can be aspirated by the highly efficient aspirator used in most dental practices. This aspirator is many times more efficient than the best suction apparatus found in operating-theatres. However, it is still not possible to recover all this coolant, and the top of the pack is invariably wet if a large number of cavities have been prepared. Also, during the packing, condensation, and subsequent carving of the amalgam restoration, it is possible to dislodge small pieces of material into the mouth, which presents a further hazard. How can the operator-anaesthetist working on posterior teeth safeguard his patient's airway at all times? The answer is he cannot, and recent events prove the point.

Local analgesia with efficient premedication is the logical alternative. For the completely unmanageable patient, the subnormal or very nervous patient, an endotracheal anaesthetic. In conclusion let us remember that treatment shall not be more dangerous than the disease.—We are, etc.,

JOHN E. DE B. NORMAN.

R. C. TURNER.

H. FLASHER.

Leeds

REFERENCE

- Sunday Times*, 25 February, 1968.

Coal Gas and the Brain

SIR,—In the opening sentence of your leading article (17 February, p. 398) you state: "The common methods of attempting suicide in Britain are inhalation of carbon monoxide and the ingestion of barbiturates and aspirin." This may have been true in the distant past but it has not been the recent experience in Edinburgh, and there is no reason to think that the methods used here differ from elsewhere in the country. Kessel¹ reported that in 1962–3 9% of 522 patients who poisoned themselves used coal gas, while 55% ingested barbiturates. To equate the frequency of carbon monoxide with barbiturates as a means of attempting suicide is clearly misleading. This is further supported by a provisional analysis of the poison used by 974 patients admitted to this unit in 1967:

Method of Poisoning	No.	%
Barbiturates	286	29
Salicylate	141	14
"Mandrax"	107	11
Benzodiazepines	86	9
Carbon monoxide	46	5
Tricyclic compounds	46	5
Phenothiazines	35	4
Others	227	23

The admission rate to the Regional Poisoning Treatment Centre has doubled in the past five years, but the annual numbers of those who have ingested barbiturates or inhaled carbon monoxide have remained remarkably constant. The increased admission rate can be attributed to poisoning with Mandrax, benzodiazepines, tricyclic antidepressant drugs, and phenothiazines. The Registrar General reports that in 1959 in England and