exact nature remains uncertain. The suggestion of Mr. Slapak *et al.* that it may have an immunological basis does not seem to us to be either premature or unreasonable.—We are, etc.,

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Antiserum in Gas Gangrene

SIR,—Gas gangrene occurs sporadically in civilian surgical practice, commonly after amputation for peripheral vascular disease,^{1,2} or after operations breaching the gastrointestinal tract, or in association with contaminated traumatic wounds.

The present therapeutic approach is empirical, and may be summarized as follows. Gas gangrene is a highly lethal disease. Therefore if its presence is merely suspected it is justifiable to discharge a battery of therapeutic measures, whose efficacy, singly or in combination, will never be put to the acid test of controlled clinical trial, given due regard for medical ethics.

Therefore the use of any of the four mainstays of treatment—namely, amputation, penicillin, gas gangrene antiserum, and hyperbaric oxygen—is based on hope rather than expectation of success. My only purpose in writing is to examine the place of antiserum in the treatment of gas gangrene. Recourse to the literature for guidance is disappointing. The use of antiserum seems to be based on extensive animal experimental work of questionable relevance to the human condition. However, in war wounds it has been found³ that the mortality in 20 patients who received no antiserum was 90%, but this was reduced to 57% in 100 patients who received antiserum. The authors confess that this series probably comprises only 50–60% of the actual incidence of the condition in their theatre of war. This was a retrospective survey, with all the inherent pitfalls of this method of measurement.

There is therefore very little evidence in favour of the therapeutic efficacy of antiserum. But there is indirect evidence that it is ineffective—namely, in a separate series of 9 of the 12 fatal cases treated with antiserum had therapeutically adequate blood levels of antiserum at the time of death.⁴ Furthermore, antiserum was widely used in the first world war, inconsistently in the second world war, and rarely in the Korean war. The incidence of gas gangrene in three representative series is as follows:

	First World War (France) Pettit (1919) ⁵	Second World War (India) North (1947) ⁶	Korean War Howard and Inui (1954) ⁷
No. of wounds ..	4,377	4,600	4,900
Gas gangrene ..	221	32	4
% incidence ..	5%	0.7%	0.08%
Case fatality rate	27%	31.3%	0

In addition, North⁶ reported that he treated Chinese and American soldiers, but that antiserum was available only for the latter. On

analysis there was no significant difference in the mortality from gas gangrene between the two groups, so its use was discontinued.

One might conclude from these figures that antiserum caused positive harm. In fact the decreased incidence has been attributed to more rapid clearance of casualties with speedy debridement of wounds, and may have been influenced by other factors such as increased use of penicillin; but I submit that it is unlikely to have been due to antiserum and that the use of this substance should be discontinued.—I am, etc.,

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Rehabilitation after Head Injury

SIR,—Mr. Walpole Lewin (24 February, p. 465) is to be congratulated on emphasizing the need for proper facilities for rehabilitation after head injury. The problem has of course increased markedly—for example, in Edinburgh our admissions from head injury have doubled in the last five years. There, as in Cambridge, these patients are under the care of the surgical neurologist, but in Edinburgh they are admitted to a head and spinal traumatic unit, part of the accident/emergency service and quite separate from elective surgical neurology. Our admissions now total between 1,200 and 1,300 a year, but the number of severely injured (post-traumatic amnesia of more than 24 hours) is higher—13%, as opposed to Mr. Lewin's figure of 7%.

As he so rightly emphasizes, our concept of recovery from brain injury is outmoded. Long-term improvement appears to be increasingly possible even after severe head injury, but more often in the young, who have an inherent capacity to learn. Thus planned rehabilitation of a progressive and imaginative kind designed for each patient's particular needs is throwing a new light on the understanding of recovery by the use of alternative cerebral pathways.

In the south-eastern region of Scotland, the injured from the last war were cared for in the brain injuries unit of Bangor Hospital under the care of Professor Norman Dott. As in Oxford with the late Sir Hugh Cairns, rehabilitation was already advanced in 1941, and it has continued since in a more elaborate form. Even the mildly concussed are seen in a follow-up clinic after one week so that their return to work can be planned successfully, and this step would seem to have reduced the incidence of the post-concussional syndrome. The more severely injured are rehabilitated at the Astley Ainslie Hospital (rehabilitation hospital of 230 beds in a large park 1½ miles from the centre of the city), on an inpatient basis in the first instance, by a skilled team of physiotherapists, occupational therapists, speech therapists, social workers, and nursing and medical staff. They are allowed home as soon as this important step

would seem wise, and sometimes it is an important one in furthering the progress of the patient. However, if the adult members of the family are out at work then these patients are treated at the "day unit" of the hospital by the same staff. Thus there is complete continuity of management, with the general practitioner being brought in increasingly at this stage.

Those patients who remain unconscious to all intents and purposes for many months or even years may well be required to be cared for in a special part of the rehabilitation unit. Such a special unit is now being planned.

I warmly support Mr. Lewin's recommendation that an organization for co-ordinating services for head injuries be set up and that some special rehabilitation centres should be developed to deal with brain-injured patients.—I am, etc.,

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Problems Associated with L.S.D.

SIR,—Many cannabis smokers are aware that prolonged coma occurs with an excessive intake of this drug. I saw the patient reported by Dr. R. Clayton (20 January, p. 163) shortly before his admission to hospital, as he was under my care for psychotherapy at University College Hospital. He had begged me to prescribe him tincture of cannabis, as his anxiety was intolerable and he wanted to be "stoned out of his mind all the time for the rest of his life." He refused to consider admission as an inpatient, and agreed to try diazepam. I have seen him since his episode with Dr. Clayton and had his account of what happened.

It was not clear to anybody exactly how much of anything this patient had taken, but it was clear to me that after a period in which the police had closed up the supply of cannabis temporarily the patient was only too anxious to get as good a "high" as possible as soon as he laid hands on the drug again. During the 24 hours before admission he had smoked cannabis in large quantities, as well as taking lysergic acid diethylamide (L.S.D.), diazepam, and probably paracetamol.

I have seen two previous episodes where a patient became semicomatose for a long period when taking cannabis. On one occasion the patient, aged 14, combined his first reefer with two or three "purple hearts" and two or three double whiskies. On the other a cannabis habitué smoked several cannabis cigarettes to ward off the symptoms of impending influenza—he may have taken paracetamol as well, but, like the patient shared with Dr. Clayton, he "couldn't rightly remember."

The literature on cannabis reports potentiation of barbiturates by cannabis,^{1,2} and Miras' reports prolongation of the barbiturate sleeping time in rats which had been given sublethal doses of cannabis, which lasted for 30 days after the last dose. The same sensitivity to barbiturates after cannabis had been put in the food for six months was present for the same length of time but to a lesser degree. It is more likely to occur

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.

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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.,

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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.,

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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.,

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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-