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.

REFERENCES

- Waldenström, J., *Acta. med. scand.*, Suppl. No. 82, 1937, pp. 70, 72, 73.
- Goldberg, A., *Quart. J. Med.*, 1959, 28, 183.
- Goldberg, A., *Brit. med. J.*, 1968, 1, 509.
- Garrod, A. E., and Hopkins, F. G., *J. Path. Bact.*, 1895, 3, 434.
- Günther, H., *Ergebn. allg. Path. path. Anat.*, 1922, 20, 1, Abt. 608.
- Hymans, van den Bergh, A. A., Dellaert, R., Grotepass, W., Nyssen, R., and Van Bogaert, L., *Ann. Méd.*, 1937, 42, 510.
- Goldberg, A., and Rimington, C., *Diseases of Porphyrin Metabolism*, 1962, Springfield, Ill.
- Macalpine, I., Hunter, R., and Rimington, C., *Brit. med. J.*, 1968, 1, 7.
- Thudichum, J. L. W., *Tenth Report Med. Off. Privy Council*, 1867, p. 152, London.
- Munk, W., 1885, *Marvodia*, Exeter.
- Cochrane, A. L., *Brit. med. J.*, 1968, 1, 443.

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.

Leeds

H. FLASHER.

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

Wales 44% of the men and 56% of the women who committed suicide used coal gas. McCulloch, Philip, and Carstairs (1967)² reported that of the 216 suicides in Edinburgh in the years 1963-5 40% were due to coal gas, the proportion being the same for both sexes. Your opening sentence should thus have referred to common methods in completed suicides.

The last paragraph of your leading article indicates that the neurological prognosis of patients who have inhaled carbon monoxide is generally good, and with this we would agree; but you close with the sentence: "It is a paradox that many patients might not wish it so." You have failed to appreciate that the vast majority of poisoned patients do not wish to kill themselves, and the motive is unknown for many who die. Kessel¹ pro-

posed the term "self-poisoning" as being more appropriate than "attempted suicide," as he considers the latter not only misleading but positively wrong. If these acts have a purpose it is nearly always to alter the social situation, rather than self-destruction.—We are, etc.,

R. C. B. AITKEN.
R. J. DALY.
N. KREITMAN.
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REFERENCES

- ¹ Kessel, N., *Brit. med. J.*, 1965, 2, pp. 1265 and 1336.
- ² McCulloch, J. W., Philip, A. E., and Carstairs, G. M., *Brit. J. Psychiat.*, 1967, 113, 313.

Fluphenazine Enanthate in the Maintenance Treatment of Schizophrenia

SIR,—We read with interest the letter by Dr. N. S. Capstick (20 January, p. 181) and review briefly our own experience with fluphenazine enanthate in a 107-bedded unit based on a general hospital. Our experience with this drug is similar to that of Dr. Capstick, but, because of the reluctance on the part of some psychiatrists to use this preparation we feel the need to enlarge on one or two aspects of treatment.

To date we have treated a total of 79 patients, of whom 70 are still receiving maintenance therapy. The failures showed: 7, inadequate response; 1, absconded (therefore excluded); 1, discontinued (abnormal fear of hypodermic needles).

Of the 70 patients 66 are now discharged from inpatient care and are attending the hospital for injection. Four are being stabilized as inpatients.

The following Table may be of interest:

Period of Treatment (Months)	No. of Patients
0-6	26
6-12	18
12-18+	26

These figures should help to dispel doubts regarding the efficiency of the drug in maintaining patients in gainful occupation in society, thus relieving pressure on the bed state. The readmission rate and the need for further E.C.T. have also greatly diminished. A detailed report of our findings will be published at the end of the year.

It is our practice to start medication as an inpatient, giving fluphenazine orally, followed some two weeks later by 0.25 ml. intramuscularly as a test dose, then by 0.5 ml. about two weeks later. The doses are then adjusted to the individual response, depending upon what the patient can tolerate with minimal side-effects. If there are any side-effects we have a chance to observe them in the initial stages and have been able to control them with orphenadine or procyclidine. In this group of chronic schizophrenic patients we have found fluphenazine enanthate highly effective, and we feel that psychiatrists need have few qualms concerning toxicity, side-effects, or patient control with a long-acting preparation

such as fluphenazine enanthate.—We are, etc.,

MAURICE SILVERMAN.
WILFRED P. LOPES.

Queen's Park Hospital,
Blackburn.

SIR,—The contributions from Dr. N. S. Capstick (20 January, p. 181), Dr. R. Hicks and Dr. I. M. K. Ovenstone,¹ and Dr. C. M. Parks *et al.*,² bring forward for consideration whether or not the time is opportune to recognize that the phenothiazines exert at least two significantly different effects on the central nervous system. These two separable effects comprise a general sedative effect at subcortical level, and a more specifically directed antipsychotic effect which, if exerted over a sufficient length of time, conceivably may be associated with a destructive lesion, possibly in the strio-nigral system.

In a manner of speaking it is coincidental that we have come to think of these drugs as divisible into a "broad spectrum" group (of which chlorpromazine is a good exemplar) and a "narrow spectrum" group. I say "coincidental" because probably those phenothiazines which are utilized by us primarily for their general sedative effect do not produce a specific antipsychotic effect unless we use them in sufficiently high dosage to procure an antipsychotic effect; and *vice versa* with the narrow-spectrum antipsychotic group. If these hypotheses correspond to fact then it may be that in many patients a rational therapy would be to combine the use of small doses of a broad-spectrum (sedative) drug such as chlorpromazine with a narrow-spectrum antipsychotic drug.

What is now emerging from your columns is that there are an increasing number of patients, especially in the older age groups (who are predisposed to degenerative lesions by virtue of their impaired cerebral circulation) who develop these choreiform movements, and less frequently ballismus and athetosis. I think it possible that with some of these patients (especially the older group) these effects are not reversible and are not easily covered up by such drugs as orphenadrine, because, I believe, there has in fact accrued a destructive lesion.

These notions tie up with the nowadays well-documented observation that if one subjects a number of chronic schizophrenics to long-standing phenothiazine therapy (for example, over a period of 10 to 15 years) the time arises when these drugs can be reduced very considerably and indeed in many instances withdrawn completely. In such cases it seems possible that what we have done is not only to sedate a brain but in addition to destroy nerve cells (or interfere with enzyme system activity) and thereby eradicate delusions and hallucinations. The comparison with leucotomy is invalid if it be a fact that we are not interfering with tracts but attacking relatively specific centres of activity in the mid-brain. Further, if these hypotheses correspond to fact then it might seem that a logical therapeutic regimen would be to subject our patients to an intensive barrage of narrow-spectrum antipsychotic phenothiazines for a limited period (which might prove to be about three months at most), then switch over to a broad-spectrum sedative phenothiazine for a period of two or three years, during which latter period one would aim at rehabilitation by means of psychotherapy and social therapy. The place of E.C.T. and insulin sopor within such a regimen would be justified on empirical grounds, though doubtless these latter methods ultimately also will be reducible to scientific consideration. One need hardly stress the importance of having regard to the medico-legal responsibilities involved in such notions if it be true that with the use of certain of these narrow-spectrum antipsychotic phenothiazines one is indeed destroying neural tissue and endangering in certain instances (especially the older age group) the risk of permanent damage and the emergence of these choreiform movements to which your correspondents are drawing attention.

In fact, from the records available to me, I possess one patient who I believe may have become incurably choreiform (age 61) and three other patients who I suspect possess permanent relic of minor "movements." As against these four patients, there are hundreds of beneficiaries, and the occasional "miraculous" recovery.

May I suggest in conclusion (if these hypotheses be correct) that we should cease thinking about "the sedative" phenothiazines as opposed to the "stimulating" phenothiazines (though still retaining the notion of "sedation" for the broad-spectrum group) but now speak simply of the "more potent" phenothiazines, recognizing that these latter possess a more potent "antipsychotic" effect. It seems possible that certain of the butyrophenones (for example, haloperidol) possess a target "antipsychotic" effect very similar to that possessed by the "more potent phenothiazines." One may of course think of a narrow-spectrum "sedative" phenothiazine such as promazine.—I am, etc.,

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HAROLD PALMER.

REFERENCES

- ¹ Hicks, R., and Ovenstone, I. M. K., *Brit. med. J.*, 1966, 2, 1071.
- ² Parks, C. M., Brown, G. W., and Monck, E. M., *Brit. med. J.*, 1962, 2, 1262.

Identification of Tablets

SIR,—I understand that there is, at present, a working party appointed by the B.M.A., the Pharmaceutical Society, and the Ministry discussing this matter. It would appear to me that the case for identification of tablets is overwhelming and this system should indeed have been introduced many years ago. In fact such a system was introduced by an individual firm (under the trade name of "Co-tabs"), but instead of receiving support this firm's individual effort was censured.