USE OF SULPHUR-CONTAINING COMPOUNDS, PARTICULARLY PENTOTHAL SODIUM, IN CONJUNCTION WITH SULPHAPYRIDINE

BY

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It has been said that sulphapyridine should not be given to a patient if he has recently received pentothal sodium for the induction of anaesthesia, and, conversely, that a patient under treatment with sulphapyridine must not be given pentothal sodium. This prohibition may be inconvenient in both directions because subsequent to an operation during which pentothal has been employed it may become advisable to start sulphapyridine therapy for some unexpected infective complication. On the other hand, a patient with a large infected wound who is receiving sulphapyridine might well be given some pentothal for the first dressings or for opening of abscesses, etc.

In April, 1940, a soldier (Case 1) was admitted to this hospital with a history suggestive of acute perforation of a peptic ulcer some fourteen hours before. The peritoneal cavity was found to be full of thick pus, and his condition appeared to be so desperate, as so long a time had elapsed since the perforation, that it was obviously necessary to employ every means at our disposal to combat the infection. Having decided to give him sulphapyridine intravenously during the operation I then discovered that he had just received 1.75 grammes of pentothal (containing some 3 grains of sulphur) intravenously for the induction and maintenance of anaesthesia. Despite this I felt that we must proceed, and he was given 1 gramme of sulphapyridine intravenously while still on the operating table. He made an amazingly rapid recovery in every way, and in particular there were no complications that could be attributed to the administration of sulphapyridine together with pentothal.

Shortly afterwards casualties from France and Belgium began to arrive in large numbers. In one convoy there were many cases of gas gangrene as well as other infections. Sulphapyridine was given to very large numbers of men, and indeed some had received it before admission, both for gas gangrene and for other infective conditions. Pentothal was widely used by certain anaesthetists here for the induction of anaesthesia, and sometimes throughout the operation as well. It seemed worth while taking the risk of administering sulphapyridine to every case needing it, exactly in the same way as if no pentothal had been given. Table I shows seven cases in which anaesthesia

TABLE I.—Cases Receiving Sulphapyridine Intravenously at End of Operation

Case No.	Date of Operation	Amount of Sulphapyridine I.V.	Amount of Pentothal I.V.
1	8/4/40	1 gramme	1.75 grammes
2	25/5/40	1 "	0.3 gramme
3	28/5/40	1 "	0.5 "
4	27/5/40	1 "	0.5 "
5	24/6/40	1 "	0.5 "
6	4/7/40	1 "	0.5 "
7	4/7/40	1 "	0.5 "

had been produced by pentothal either alone or with other anaesthetic substances and in which sulphapyridine was given intravenously during the operation. Table II shows two further cases which received sulphapyridine intravenously within twenty-four hours of operation. In all cases medication was continued by mouth.

Other cases were taking sulphapyridine by mouth when an anaesthetic became necessary, and these were given pentothal, therefore, at a time when their blood had a

high concentration of sulphapyridine. Patients falling into this group were those given sulphapyridine on admission

TABLE II.—Cases Receiving Sulphapyridine Intravenously within 24 Hours of Operation

Case No.	Date of Operation	Amount of Sulphapyridine I.V.	Amount of Pentothal I.V.
8	3/6/40	1 gramme	0.5 gramme
9	4/6/40	1 "	0.5 "

while awaiting operation; and those taking sulphapyridine after a first operation who developed complications requiring further operation under anaesthesia. At the time of the evacuation from Dunkirk this hospital received several hundred cases in the space of a few days, so that many large dressings, removals of tubes, etc., had to be done in a short time. Not enough portable gas apparatuses were available, and the difficulty was met by organizing teams consisting of one R.M.O. and students who went round the wards giving pentothal for these dressings. In these cases all were treated alike whether they had had sulphapyridine or not. Table III shows cases taking sulphapyridine by mouth when they received pentothal. Table IV shows cases which were not receiving sulphapyridine at the time of operation but had it within the next twenty-four hours; and Table V those cases which began their sulphapyridine within three days of the receipt of pentothal.

TABLE III.—Cases Receiving Sulphapyridine Orally at Time of Operation

Case No.	Date of Operation	Amount of Sulphapyridine by Mouth	Amount of Pentothal I.V.
10	24/5/40	Wound pack	0.5 gramme
11	25/5/40	8 grammes	0.5 "
12	25/5/40	8 "	0.5 "
13	26/5/40	15 "	0.5 "
14	27/5/40	6 "	0.5 "
15	28/5/40	6 "	0.75 "
16	2/6/40	8 "	0.75 "
17	4/7/40	8 "	0.5 "

TABLE IV.—Cases Receiving Sulphapyridine Orally within 24 Hours of Operation

Case No.	Date of Operation	Amount of Sulphapyridine by Mouth	Amount of Pentothal I.V.
18	25/5/40	6 grammes	0.5 gramme
19	25/5/40	12 "	0.5 "
20	25/5/40	8 "	0.5 "
21	27/5/40	14 "	0.5 "
22	28/5/40	14 "	0.5 "
23	28/5/40	6 "	0.5 "
24	30/5/40	6 "	0.5 "
25	2/6/40	6 "	0.5 "
26	19/6/40	6 "	0.5 "

TABLE V.—Cases Receiving Sulphapyridine Orally within Three Days of Operation

Case No.	Date of Operation	Amount of Sulphapyridine by Mouth	Amount of Pentothal I.V.
27	14/5/40	6 grammes	0.5 gramme
28	27/5/40	6 "	0.5 "
29	31/5/40	6 "	0.33 "
30	25/6/40	6 "	0.5 "

Pentothal sodium contains 12% of sulphur. Case 1 therefore received over 3 grains of sulphur direct into his veins and within half an hour was given 1 gramme of sulphapyridine intravenously. Such a concentration of sulphur in the blood would surely never be reached by a diet containing many eggs and onions. I have been unable to discover how long the sulphur of pentothal remains in the body. Even Abbotts, the manufacturers of pentothal, had no information available in this country concerning that point. As it may be that the sulphur is excreted rapidly, no case has been recorded which was not receiving sulphapyridine within seventy-two hours of operation. The combination of drugs has been given to

very many more patients than the thirty here reported, but for certain reasons it is only possible at the moment to have access to the complete notes, with medicine cards, of these thirty. Both in the recorded cases and in the more numerous unrecorded ones there have been no complications other than the usual nausea and vomiting, and the incidence of the latter would appear to be lower rather than higher than that always experienced in any series of cases treated with sulphapyridine. There has been no cyanosis whatever.

Magnesium sulphate and saline purgatives in general have been forbidden to cases receiving sulphapyridine or prontosil, as such a combination is said to cause cyanosis. If this is really so it is again unfortunate, because there are certain types of case requiring both drugs. I refer particularly to those frequent cases of head injury in which there is both an actual or a potential infection of the brain or scalp and the existence of a state of high intracranial pressure due to oedema and congestion of the brain. Perhaps less important in war are those cases of high pressure due to cerebral tumour, etc., which develop an infection—for example, a pneumonia after operation. These cases require sulphapyridine for their infection and also magnesium sulphate by various routes for cerebral dehydration. Both at the National Hospital for Nervous Diseases, London, and at Horton I have dehydrated such patients by oral and rectal magnesium sulphate during sulphapyridine medication without anything untoward arising.

This short paper has been written because it is felt that patients receiving sulphapyridine can safely be given pentothal and magnesium sulphate at the same time. Although this is not directly concerned with the matter of diet one is caused to wonder whether various sulphur-containing foods, such as eggs, need be withheld from the now very numerous patients receiving sulphapyridine.

USE OF PROFLAVINE AND ACRIFLAVINE IN A THROAT AND NOSE DEPARTMENT

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Various preparations of proflavine and acriflavine have been widely used as antiseptics for a number of years now. Although much has been written about them we consider that our experience of the application of some of these to certain phases of the work of a throat and nose department is encouraging enough to warrant a brief communication. We shall confine ourselves to two of the most striking examples of the efficacy of these antiseptics. One refers to a special method of treatment of a malignant condition from which septic complications have now been eliminated, and the other to the prevention of post-operative scarlet fever such as is encountered from time to time in these special wards.

Malignant Tumours of Accessory Nasal Sinuses

In a previous communication one of us described the definite place which proflavine oleate had come to occupy in certain spheres of radium therapy (Charteris, 1937). Among those only briefly mentioned then was the treatment of malignant tumours of the accessory nasal sinuses,

for which experience has led us to favour as a rule exploration of the affected part combined with cavitary application of radium. The antrum is opened by the Caldwell-Luc method and the tumour tissue scooped out. Any invasion of the bony walls is noted, and the antro-nasal wall removed if necessary. In almost every case the operation is carried on so as to throw the antrum, ethmoid cells, and even the sphenoid sinus into one more or less regular cavity: this procedure, though extensive, is not dangerous, and enables one to see clearly how far the gross disease has progressed. Into the convenient cavity so formed a series of radium applicators of known output is placed, and held in position with packing. We do not intend here to say anything of the method except that a uniform dosage can be obtained, giving excellent results. The applicators are left undisturbed for seventy-two hours, and the parts therefore tend to become very septic and foul, causing the patient much distress. Moreover, various septic complications may ensue: the most important of these is localized osteomyelitis. We have not observed meningeal infection. Before the employment of proflavine oleate in 1936 sepsis constantly ensued, and, although rarely so serious as to threaten life, gave rise to unnecessary suffering and retarded convalescence, probably also interfering with the response of the tumour to the radium treatment. Soaking of the packing in proflavine oleate (1% in liquid paraffin) at once ended all gross sepsis where other procedures had failed. The patients now have very little discomfort, the temperature never shows more than the usual transient reactionary rise of about 1° F. on the day after operation, and not only does the packing come away without sticking but it is reasonably clean and almost free from objectionable odour. No local or other complications have followed treatment since then, even where the field has been very extensive, nor have the usual troublesome crusts formed afterwards in the affected zone. So remarkable a result, maintained over four years now, may well suggest other uses of this material in cases in which a temporarily closed cavity must be kept clean. It is not necessary to stress the importance of combating infection in a region subjected to radiation in dosage adequate to deal with malignancy.

Prevention of Post-operative Scarlet Fever

The second way in which such a preparation has been helpful is concerned with the prevention of infectious disease in throat and nose wards. Many of the cases are inevitably complicated by local sepsis, and the occasional occurrence of infectious disease after operation is a general experience: the chief difficulty is with post-operative scarlet fever. Such infections are not only unfortunate from the patient's point of view, but cause disorganization, since the ward affected has to be closed for a suitable period. Some six years ago the routine was established of giving all patients a mouth-wash and gargle of watery acriflavine 1 in 5,000 twice daily: this was started immediately on admission and was continued throughout the stay in hospital. Before the introduction of this simple measure one of the throat, nose, and ear wards had been closed no fewer than thirteen times during the preceding winter, and this was by no means an exceptional frequency, but since then the two wards have not had more than a total of five cases of post-operative scarlet fever up to date. This practical proof of the efficacy of acriflavine is not less striking than the first example when one realizes that the change is due entirely to a single procedure of extreme simplicity, and that the good result has also been maintained over a period of years.

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REFERENCE

Charteris, A. A. (1937). *Lancet*, 2, 627.