The patient was a woman, aged 32, who was to have an empyema drained. Anaesthesia was induced uneventfully with nitrous-oxide-oxygen and trichlorethylene. After a rib resection a large exploring needle was passed in several directions to locate the pus, but without result. At this point temporary apnoea occurred, but natural breathing was soon re-established, and the remainder of the operation was completed under pure nitrous-oxide-oxygen. Just as the wound was being closed the respiration and circulation ceased, apparently simultaneously, and all efforts at resuscitation failed.

The relevant findings at the necropsy were: (1) a localized empyema higher than the exploring needle had reached; (2) free blood in the pleural and peritoneal cavities; and (3) degeneration of the heart muscle. Some air was present in the cerebral arteries, but the diagnosis of air embolism could not be definitely established as the vessels were unfortunately not ligated before the brain was lifted out of the skull.

It is my opinion that trichlorethylene was not responsible for this patient's death, and I have knowledge of an almost exactly parallel case in which local analgesia only was employed. It might be noticed that, since no trichlorethylene had been used for five minutes before circulatory failure occurred, the concentration of the drug in the air passages (with a partial rebreathing circuit) must have been negligible.

Effects on Sugar Metabolism

Dr. A. Jordan kindly made some blood-sugar estimations before, during, and after anaesthesia with trichlorethylene. In no case was there much disturbance, and on taking an average it could be said that there was no significant change. This contrasts with the rise which constantly occurs with chloroform and ether (Hewer, 1939).

Chart showing range of change in blood-sugar level during trichlorethylene anaesthesia.

One diabetic patient was included in the series. An abdominal operation lasting 1 hour 15 minutes was performed under nitrous-oxide-oxygen-trichlorethylene. The sugar tolerance was tested one week after operation, and was found to be unchanged.

Effects on Blood Urea

Blood-urea estimations were made by Dr. Jordan upon 5 patients before, during, and after anaesthesia. The changes were so slight as to be within the range of experimental error. Here again the contrast with ether and chloroform is marked.

After-effects

Of the series of patients 61% had no nausea or vomiting, 26% had nausea or slight vomiting, and 13% had severe vomiting; 5% complained of headache. Those who had had experience of diethyl ether commented favourably on the absence of an unpleasant taste or smell.

In most cases the urine was tested as a routine on the day after operation. In one instance only was the presence of albumin found but acetone was always absent. This is in marked contrast with other anaesthetics. For example, albuminuria has been found almost constantly after the prolonged administration of ether and in about 20% of patients anaesthetized with chloroform (Stephen, 1929). Acetonuria has been demonstrated in 67% of patients operated upon under all forms of general anaesthesia and in 85% under local analgesia (Schulze, 1924).

No pulmonary complications were observed, and, as already mentioned, existing lesions did not appear to be affected.

Summary and Conclusions

This article must be regarded as an interim report, and it is not suggested that our present knowledge of trichlorethylene warrants its recommendation as an inhalation anaesthetic. At the same time the drug appears to have enough good qualities to render a more exhaustive investigation profitable.

It appears that trichlorethylene generally resembles chloroform but is less potent and less toxic.

It is desired to express thanks for much help from Mr. B. Rait-Smith, who made nineteen administrations; also to Dr. Keele for his electrocardiographic work and to Dr. Jordan for his biochemical investigations. C. L. H.

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USE OF SULPHAPYRIDINE IN SUBACUTE BACTERIAL ENDOCARDITIS

WITH REPORT OF A CASE

BY

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In the treatment of subacute bacterial endocarditis attention has recently been focused on the use of sulphapyridine combined with heparin. The rationale of this treatment is that the latter drug is thought to prevent the deposition of further thrombus on the affected valves. As a result the bacteria are exposed to the sterilizing action of the sulphapyridine, and the check in the growth of the vegetation gives the processes of repair an opportunity to gain the ascendancy. The results of published cases treated along these lines are noted in Table I.

TABLE I.—Cases treated with Sulphapyridine and Heparin

No.	Author	Result
1	Kelson and White (1939)	Death from pulmonary infarct 2 weeks after treatment stopped
2	"	Bedridden with congestive heart failure, but "no evidence of bacterial endocarditis" 19 weeks after treatment stopped
3	"	Symptom-free and negative blood cultures 18 weeks after treatment stopped. Returned to work
4	"	Death during treatment from subdural haemorrhages following emboli
5	"	Death during treatment following a reaction due to faulty heparin
6	"	Little change
7	"	Free from evidence of disease 4 weeks after treatment stopped
8	Friedman, Hamburger, and Katz (1939)	Death during treatment from cerebral haemorrhage. No sulphapyridine used in this case
9	Dockeray and Kawerau (1940)	Death 3 months after treatment stopped
10	Witts (1940)	Death during treatment from subarachnoid haemorrhage
11	Fletcher (1940)	Remained well for 6 months "
12	Petch (1940)	Death from intracranial haemorrhage
13	"	"
14	"	"
15	"	Death from toxic "aundice "

These results are not encouraging. Death from haemorrhage, particularly cerebral haemorrhage, is a very real danger.

Maegraith and Vollum (1938) claim that sulphapyridine is the drug with the most definite inhibitory action on the

growth of *Streptococcus viridans*. On the other hand, Swain (1940) suggests that some strains of *Strep. viridans* may be resistant to sulphapyridine. Sulphapyridine, however, is probably the drug of choice if a chemotherapeutic agent is to be used. It would also be the drug of choice in those rarer cases due to *B. coli*, pneumococci, or haemolytic streptococci. A number of cases have been treated with this drug alone in various doses. The results of published cases are given in Table II.

TABLE II.—Cases treated with Sulphapyridine

No.	Author	Result
1	Whitby (1938)	Life undoubtedly prolonged. Clinical improvement in general health and comfort. Anaemia and fever lessened
2	Ellis (1938)	
3		
4	..	Symptomatic improvement, but death 3 weeks after stopping treatment
5	Andrews (1940)	Symptomatic improvement. Patient discharged
6	..	Improvement, but death 2 weeks after starting treatment
7	Richards (1940)	Apparent cure
8	Ravina (1939)	Recovery claimed
		Decided improvement

These results, admittedly in a very small series of cases, are encouraging. Two cases of cure are claimed. In others the authors are emphatic that a decided improvement in the general condition of the patient occurred and that life was undoubtedly prolonged. This is a striking advance. It is possible, also, that those cases treated with sulphapyridine and heparin, and showing an improvement, would have benefited equally with sulphapyridine alone. It would appear, as was pointed out by Donovan (1940), that in the treatment of subacute bacterial endocarditis there seems to be more hope in further chemotherapeutic development than in heparin as an adjunct.

The difficulty to be overcome is the mechanical one of attacking the bacteria embedded in the vegetations. If, however, an adequate concentration of sulphapyridine were maintained in the blood stream over a long period, then, in the event of bacteria becoming exposed—e.g., by the separation of a portion of thrombus—they would be liable immediately to be attacked by the chemotherapeutic agent already present. In the majority of the cases quoted above (Table II) treated with encouraging results with sulphapyridine alone, embolic phenomena were frequent.

That sulphapyridine may be given continuously over long periods is suggested by the work of Coburn and Moore (1940). These authors administered 3 grammes of sulph-anilamide daily continuously for periods of several months as a prophylactic measure in rheumatic children. No major toxic effects were noted. It is suggested, therefore, that in cases of subacute bacterial endocarditis treated with sulphapyridine an initial full course be given to sterilize the blood stream, followed by a smaller dose given continuously over a long period to maintain this sterilization and to attack the bacteria in the vegetation as the opportunity arises. A case treated along these lines is described.

Report of Case

The patient, a man aged 20, had had rheumatic fever when 9 years old and again when 13. On each occasion he had spent three months in bed, followed by two months' convalescence. His heart was said to be affected at the second attack. In September, 1940, he complained of tiredness, breathlessness on exertion, and, later, of poor appetite, nausea, constipation, and pains in the fingers. He was admitted to hospital on October 25.

On examination a pale, tired-looking young man was seen lying listlessly in bed. He was undersized, poorly developed, and poorly covered; height 5 ft. 5 in., weight 7 st. 8 lb. He had typical café-au-lait complexion and hot moist skin. There was slight clubbing of fingers; and two or three Osler's nodes appeared daily, at the outset, in the pulp of fingers and toes. Neither jaundice nor pitting oedema was present. The temperature was 100°, the pulse 100, and the respirations 20.

There was visible precordial pulsation in the fifth intercostal space lateral to the nipple line, and a systolic thrill could be felt in this area. The apex beat was forceful, 9 cm. from the midline; the mid-clavicular line was 8.5 cm. from the midline. Apical systolic and basal systolic and diastolic murmurs were present. These murmurs and the quality of the heart sounds varied considerably in character from day to day. A radiograph on March 10, 1941, revealed mitral heart—measurements: transverse diameter 14 cm., longitudinal diameter 17 cm. The spleen was not palpable, but dullness over the splenic area extended to the costal margin. The urine contained albumin and red blood cells.

The patient was kept strictly at rest in bed and was nursed as much as possible near an open window. He was given iron, yeast, and cod-liver oil and malt. On October 31 a blood culture yielded a profuse growth of haemolytic strepto-

The daily temperature noted above represents the highest reading recorded on a four-hourly chart. x = Negative blood culture.

cocci. His general condition remained extremely poor until sulphapyridine was started on November 5, 1 gramme being given four-hourly. A very decided improvement was evident in the course of a few days. The sulphapyridine was reduced on the 14th to 0.5 gramme thrice daily, but was increased on the 21st to 0.5 gramme four-hourly because of a return of fever. It was stopped on December 6, as persistent anorexia developed, but was restarted in doses of 0.5 gramme thrice daily on December 9 and was maintained continuously at this level until February 25, 1941.

During this time the improvement in the patient's condition continued, although it was interrupted temporarily on several occasions by minor upsets (see Chart). Four successive blood cultures were negative. The fifth unfortunately was contaminated, but the sixth was again negative. There was a striking decrease in the frequency of Osler's nodes while sulphapyridine was being given. A blood count on December 3 showed red cells, 4,400,000 per c.mm.; haemoglobin, 70%; colour index, 0.8; white cells, 8,600 per c.mm.—polymorphs, 74%; eosinophils, 1%; lymphocytes, 24%; monocytes, 1%. On March 1 the readings were: red cells, 4,530,000 per c.mm.; haemoglobin, 85%; colour index, 0.9; white cells, 21,800. Leucocyte counts, made at frequent intervals throughout, varied between 7,000 and 22,000 per c.mm. (see Chart). The blood concentration of sulphapyridine while 0.5 gramme was being given thrice daily was: free 1.2 mg., acetylated 1.3 mg. per 100 c.cm. The sulphapyridine was discontinued on February 25 in view of the very decided improvement. As fever returned it was restarted on March 10 and was continued until discharge.

By the date of discharge the patient was up for the greater part of the day, and was out for several hours in the afternoon. He insisted on being discharged because he felt so well.

Comments

The outstanding result of the treatment was the change in the patient's condition. From a miserable tired young man bathed in sweat he became cheerful and active and had long periods free from fever. An advanced case of subacute bacterial endocarditis was arrested and very decidedly improved. As occurred in Whitby's (1938) cases the anaemia also improved. Another interesting result was the striking diminution in the number of Osler's nodes while sulphapyridine was being given.

A total of 241.5 grammes of sulphapyridine was administered. Apart from transient nausea and anorexia, no toxic effects were noted. Whitby (1938) states that resistance to the drug may develop. That this did not occur in the case reported here is suggested by the fact that when the drug was discontinued after 226.5 grammes had been given the fever that followed was readily controlled by further small doses.

The case is unusual in that the streptococcus isolated was of the haemolytic type, and the encouraging results obtained may have been due in part to the fact that this organism is more readily destroyed by sulphapyridine than is the *Strep. viridans*. The outstanding problem, however, in the treatment of subacute bacterial endocarditis is the inaccessibility of the organisms in the heart valves rather than the sterilization of the blood stream, and it is probable, therefore, that, as has been argued above, cases in which the infecting organism is a *Strep. viridans* will also show a good response to similar treatment.

Summary

Published cases of subacute bacterial endocarditis treated with sulphapyridine and heparin and with sulphapyridine alone are reviewed briefly.

The encouraging results in those cases treated with sulphapyridine alone are noted.

A scheme of treatment is suggested, and a case so treated with considerable benefit is described and briefly discussed.

I am indebted to the Department of Health for Scotland for permission to publish this case. My thanks are also due to Dr. A. A. F. Peel for helpful criticism throughout.

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HYPERVENTILATION TETANY IN TROPICAL CLIMATES

BY

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It seems clear that tetany is only one of the many clinical manifestations which can result from hyperventilation. The early experimental and clinical observations of Haldane and Poulton (1908), Vernon (1909), Henderson (1909-10), Hill and Flack (1910), Henderson and Haggard (1918), Collip and Backus (1920), Grant and Goldman (1920), Davies, Haldane, and Kennaway (1920), Barker and Sprunt (1922), and Goldman (1922) established the importance of hyperventilation as a cause of tetany, and the subject has been widely discussed in recent years. Its literature has now become tremendous, but an excellent review of the then known facts was published by Thomson and Collip in 1932.

It is now recognized that there are many aetiological factors, of which psychic changes and pain would seem to be the most important. McCance (1932) showed that in certain persons tetany could be induced by attacks of overbreathing which were scarcely perceptible to casual observation; he considered that these persons must be peculiarly susceptible to an alkalosis. It is widely agreed that there are great variations in individual susceptibility to hyperventilation, and in this connexion the work of Schultzer and Lebel (1939) is of interest. Serum calcium is generally accepted to be normal in these cases, while Fowweather, Davidson, and Ellis (1940) have shown that immediately after the attack the serum inorganic phosphorus may be considerably below the normal level. All the evidence at present goes to show that overbreathing produces an alkalosis by washing out carbon dioxide from the blood. The mode of production of tetany by alkalosis is still in doubt. The conclusion of Fowweather and his colleagues (1940) that it is due to tissue alkalosis seems to be fairly well founded.

Effect of Temperature upon Ventilation

Bazett and Haldane (1921) described the effects of the immersion of four men in hot baths for a long period. They noted that sweating occurred early, and that a rapid rise of temperature produced hyperpnoea, which was accompanied by faintness, mental confusion, and tingling. They also observed that these symptoms could be relieved by breathing mixtures containing high percentages of carbon dioxide. The secretion of a large amount of highly alkaline urine was also recorded. This work was confirmed by Landis and others (1926), who noted the occurrence of tetany and found that the degree of change in the blood pH did not appear to be in direct relation to the onset of tetany. One of the cases recorded by McCance (1932) was that of a nursing sister whose first and only spon-