SULPHATHIAZOLE AND SULPHAPYRIDINE IN ACUTE GONORRHŒA

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SULPHONAMIDE preparations, in particular sulphapyridine, are now firmly established in the therapy of gonorrhœa. It has, however, been repeatedly observed that while in most cases early cure results from intensive administration of these drugs, some cases prove refractory (Cokkinis and McElligott 1939, Prebble 1940, Batchelor, Lees and Thomson 1940). The sulphonamide preparations vary considerably in their potency for different organisms and it is therefore important to determine if the recently introduced compound, sulphathiazole, has a greater action on the gonococcus than the earlier preparations. The value of sulphathiazole (M. & B. 760) in the treatment of acute gonorrhœa in men was compared with that of sulphapyridine, the compound used in the routine treatment of these cases. Acute cases were selected in which gonococci were found in urethral smears, and alternate patients, as far as possible, were given sulphapyridine and sulphathiazole and were kept under close daily observation until the tests for cure were satisfactory.

METHOD

The diagnosis was established in all cases by the demonstration of gonococci in urethral smears stained by Gram's and Sandiford's (1937) methods.

Group 1 : sulphapyridine.—Over five days all patients received sulphapyridine, 22 g., the tablets being crushed in water (table I); 1 g. (two tablets) was given at 7 A.M., 10 A.M., 2 P.M. and 6 P.M., except on the first two days when 2 g. was given at 6 P.M. During the five days the patients were kept in bed and urethral smears were taken daily.

If the patients were free from symptoms on the sixth day and remained so until the eighth day tests for cure were carried out; and if these were satisfactory the patient was discharged after two further days observation. If the urethral discharge continued, anterior urethral irrigation with 1/10,000 potassium permanganate was given for the next three days, and afterwards, if necessary, posterior urethral irrigations were carried out until the discharge ceased; tests for cure were then performed. In persistent cases prostatic massage was used with posterior irrigations.

Group 2 : sulphathiazole.—Over seven days all patients were given sulphathiazole, 22·5 g. in water (table I), the tablets again being crushed; on the first day, 1·5 g. (three tablets) was given at 8 A.M., 2 P.M. and 6 P.M. and 4·5 g. at 10 P.M. On the second, third and fourth days 1 g. was given at 10 A.M., 2 P.M. and 6. P.M.; on the fifth, sixth and seventh days 0·5 g, was given at each of these times. During this first week the patients were kept in bed and urethral smears were collected daily.

TABLE I—DOSAGE IN GRAMMES

Day	Sulphapyridine g.	Sulphathiazole g.
1	5	9
2	5	3
3	4	3
4	4	3
5	4	1·5
6	—	1·5
7	—	1·5
Total	22	22·5

Tests for cure.—After the patient had been dry for three days the following tests were carried out:

1. A Kollman dilator was passed and the degree of dilatation and presence of tenderness noted; if discharge was present, a smear was prepared from it.

2. Prostatic massage and preparation of a smear. Smears were stained by Gram's and Sandiford's methods and examined for gonococci and pus cells. The presence of pus cells, even if they were only few in number, was considered at all stages to indicate persistence of infection, and treatment was continued. This practice is carried out as a routine measure and has undoubtedly reduced the incidence of relapses, which have been low in this clinic.

If tests 1 and 2 were satisfactory the patient was kept under observation for two days, after which the final tests were carried out.

3. On the third day urine was not passed in the morning until the tests were completed. Anterior urethroscopy was done, the obturator being used for massage purposes, and any abnormality noted. The four-glass test was then carried out:

(*a*) The anterior urethra was washed out with a pint of mercuric oxycyanide (1/10,000) into a conical glass, which was examined with the naked eye for the presence of threads.

(*b*) Into a second glass about an inch of urine was passed—this represented the washings from the posterior urethra and the residue from the anterior urethra.

(*c*) Procedure (*b*) was repeated into a third glass.

(*d*) Thorough prostatic and vesicular massage was carried out and a smear collected.

(*e*) The remainder of the urine was passed into a fourth glass; this represented the prostatic and vesicular washings.

Only those cases in which the urines were clear and the smears did not show pus cells or gonococci were considered cured; if satisfactory after two more days observation they were discharged from hospital. Patients returned after three months for another complete examination. The gonococcal complement-fixation test was not employed because in many cases the test never becomes positive, so that it has only a limited value.

TABLE II—DAY OF DISCHARGE FROM HOSPITAL AFTER TREATMENT

Drug	No. of cases	Discharged after		
		14 days	14–21 days	21 days
Sulphapyridine ..	51	9 (18%)	27 (54%)	14 (28%)
Sulphathiazole ..	30	6 (20%)	17 (57%)	7 (23%)

RESULTS

In this series, 30 cases received sulphathiazole and 51 sulphapyridine. In both groups good results were obtained; dysuria disappeared within 24–48 hours and the patients were as a rule free from discharge in two or three days. There was little difference in the end-results of the two drugs; in both groups most patients (72% with sulphapyridine and 77% with sulphathiazole) had passed the tests for cure and were discharged from hospital within three weeks (table II).

There was, however, an appreciable difference in the toxicity of the two drugs; sulphathiazole was more readily tolerated than sulphapyridine. The patients were under close observation, particularly during the stages of chemotherapy when they were kept in bed and temperatures were taken twice daily. Manifestations of intolerance were shown with both drugs (table III).

TABLE III—INCIDENCE OF SYMPTOMS OF INTOLERANCE

Symptoms	Sulphathiazole (30 cases)	Sulphapyridine (51 cases)
Nausea	3 (10%)	25 (50%)
Headache ..	2 (7%)	39 (78%)
Vomiting	0	2 (4%)
Pyrexia	3 (10%)	17 (34%)

These symptoms mostly persisted for two or three days; pyrexia when present was only slight, the temperature being raised to about 99° F. The more serious signs of toxicity, such as hæmaturia, cyanosis and anæmia, were not noted. Most patients returned for examination three months after treatment and no relapse has been observed.

DISCUSSION

The number of cases investigated has been small, but the trial was carried out under strictly controlled conditions such as are impracticable in civilian practice. Thus while it is not possible to draw final conclusions from the results, they are worth recording. They show that while sulphathiazole is a useful therapeutic agent in gonorrhœa (as indicated by Lloyd and Erskine 1940), it differs little in efficiency from sulphapyridine. Sulphathiazole is, however, much more readily tolerated than

sulphapyridine; even though the large dose of 9 g. was given on the first day of treatment toxic symptoms were seldom encountered.

These findings suggest that, since the amount of sulphathiazole available is limited, in the treatment of gonorrhœa it should be reserved for the cases which show serious intolerance to other sulphonamide preparations.

SUMMARY

In two strictly comparable groups of men with acute gonorrhœa sulphathiazole and sulphapyridine both proved efficient therapeutic agents and there was little to choose between the results. Sulphathiazole produced fewer toxic symptoms than sulphapyridine.

We wish to thank Messrs. May and Baker for supplying M. & B. 760.

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IMPROVED APPARATUS FOR CONTINUOUS INTRAVENOUS ANÆSTHESIA

BY

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IN a recent communication (*Lancet*, 1940, **2**, 650) we described an apparatus for the continuous administration of intravenous anæsthetics. Further experience confirms the advantages of this route in certain operations, and we now present modifications of our original apparatus which make it simpler and safer in use. The new features to which we wish to draw attention are:

The use of a standard British Drug Houses or Crookes bottle of saline and/or glucose (1 in fig. 1) as a reservoir for the anæsthetic solution greatly increases the applicability of this method. The chosen anæsthetic is added directly to the 560 c.cm. (1 pint) of solution already in the bottle and the mixture is ready for use immediately after it has been well shaken.

The " safety " dropper (2), which differs from the ordinary dropper in that it has a side tube, and contains a glass float

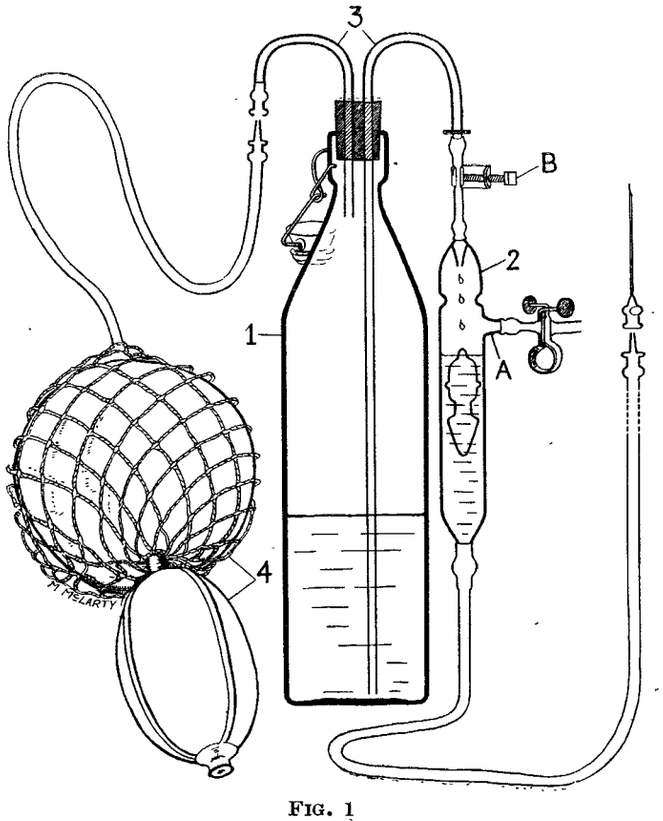

FIG. 1

the lower surface of which is ground to fit into a seating at the bottom of the dropper. When there is fluid in the dropper chamber the float is kept away from its seating by its natural buoyancy; but if the chamber should become empty of fluid, as it will if the supply in the bottle is exhausted, the float seats down and the air which is under pressure in the bottle cannot escape into the patient's veins. The whole dropper and float are made from thick Pyrex glass and can therefore be boiled.

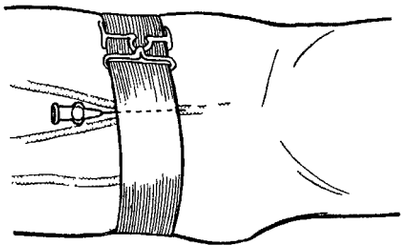

FIG. 2

The rigid tubes (3), which pass through a rubber bung of correct size to fit the standard bottles, are made of stainless steel to eliminate risk of breakage.

The hand bellows (4) provide sufficient pressure to maintain a rapid flow when needed, so that anæsthesia can be rapidly induced or deepened. Once anæsthesia has been induced the bellows act as a reservoir of air sufficient to keep up a slow flow of anæsthetic mixture for many minutes.

METHOD OF USE

A sealed standard bottle of sterile saline or glucose solution is opened and the selected anæsthetic added to it. A small sterilised package containing the necessary connexions is opened and the bung firmly fixed into the neck of the bottle. The hand bellows are now attached and a small pressure created within the bottle. With the side tube (A) of the dropper open, fluid is allowed to run into it until the chamber is about two-thirds full, when the flow is cut off and the side tube clamped. It may be necessary now to displace the float from its seating by squeezing the tube below it. The remainder of the tubing is filled in the usual manner and the needle introduced into a suitable vein.

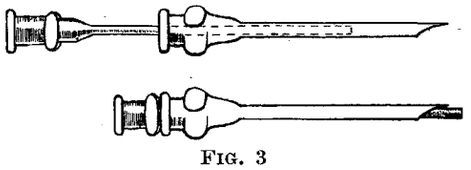

FIG. 3

It has been found convenient to retain the needle in the vein by means of a narrow adjustable garter which encircles the arm, and covers that part of the needle which lies beneath the skin, but leaves free the tip of the needle within the vein (fig. 2).

When a large vein is available we have used a 1·5 mm. needle through which passes a blunt-ended cannula to the proximal end of which is attached the tubing from the dropper (fig. 3). The cannula, at first partially withdrawn, is pushed home after the needle has been introduced into the vein. The blunt end of the cannula now projects into the vein beyond the point of the needle and is not readily displaced.

The screw clip (B) allows the flow to be maintained at a uniform rate, or to be varied at will between a slow drop and a continuous stream. The flexibility in the rate of administration which results from adjustment of the screw clip allows a weak anæsthetic solution to be used, and thus dispenses with the necessity for a supply of an " inert " solution such as glucose or saline for keeping the needle patent when anæsthesia is deep.

We have used this apparatus for various operations, including major abdominal surgery, and consider it particularly suitable for operations on the head and neck in which it is not desirable to pass an endotracheal tube. For example, for ophthalmic operations, or for toilet of wounds or burns of the face, the anæsthetist can sit well away from the surgeon's field, keep a free airway by supporting the chin with the finger, and maintain an even level of light anæsthesia by adjusting the rate of flow of anæsthetic solution. Anæsthetic solutions which we have administered by this method include Pentothal 0·5–1%, ether 5–7%, Avertin 1%, alcohol 33%, and various mixtures of these drugs. The apparatus has also been used to give glucose and insulin in a case of diabetic coma, and should be of value as a readily transportable apparatus for administering blood.