These points require further investigation, and it is now necessary to undertake experiments on a large scale, to determine whether a continuance of all available methods of dust-laying will result in a significant reduction of the incidence of cross-infections in hospital wards.

Summary

Attention is drawn to the very large numbers of streptococci which may accumulate in the dust and in the bedclothes of hospital wards.

It is shown that many of these organisms are projected into the air every time a bed is made or in any way disturbed, and it is suggested that these represent a very real danger.

The treatment of bedclothes with liquid paraffin, while not visibly affecting them, causes a 95% reduction in the number of organisms distributed into the air during bed-making.

It is suggested that this method of dust-laying, combined with the use of spindle oil on floors, may assist in reducing the incidence of cross-infections in hospital wards.

We are indebted to Major-Gen. H. Marrian Perry, C.B., O.B.E., F.R.C.P., Director of Pathology, Army Medical Services, for allowing one of us to carry out his part of this work in a military laboratory; to Colonel E. B. Marsh, M.C., R.A.M.C., for placing so many facilities at our disposal; to Dr. C. H. Andrewes, F.R.S., and Dr. R. B. Bourdillon for much helpful advice; to Dr. Otho Fitzgerald, medical superintendent of the hospital, for the use of the hospital laundry; to the medical officers and nursing staff who have co-operated so readily with us; and to our assistants, Sergt. H. G. Stevens, R.A.M.C., and Cpl. T. Bury, R.A.M.C., for their continued help in the laboratory.

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It was recently announced by the Board of Trade that arrangements had been completed for the manufacture of an adequate supply of high-tension batteries to meet the needs of deaf persons who use hearing aids. A standard range of batteries to be manufactured in wartime has been drawn up and embodied in a specification to be issued by the British Standards Institution (B.S. 966). High-tension batteries for hearing aids must be as small in size and as light in weight as possible, and in peacetime these requirements were met by making up the batteries from very small unit cells. At the present time there are heavy demands for these midjet cells for batteries for other purposes, and it has become necessary to standardize a range of batteries for hearing aids made up from cells which, so far as can be seen at present, will be available in sufficient quantity to enable hearing aids to continue to be serviced with the minimum of inconvenience to all concerned. There are eleven batteries in the standard range, and these should prove adequate to cover the requirements of all existing makes of hearing aids which employ H.T. batteries, though it may be found that some instruments will need minor modification in order to accommodate them. Such modification applies to the battery casing only, and no modification to the mechanism of any instrument is called for. Copies of this new specification will be available shortly from the British Standards Institution, 28, Victoria Street, S.W.1, price 2s. 3d. post free.

RECENT EXPERIENCES IN THE TREATMENT OF GONORRHOEA IN THE MALE*

BY

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In military practice the incidence of venereal disease is surprisingly low, and in this I have no doubt that we are reaping the benefit not only of the far-sighted policy of the Ministry of Health, but also of the standard of work which medical officers in charge of clinics have maintained during the past twenty years. The Medical Services of the Army also deserve much credit. For many years the officers of the Royal Army Medical Corps have insisted on educating the troops for whose health they are responsible on the dangers of promiscuous intercourse; as is widely known, their preventive work in the venereal field has reached a very high standard. In the active treatment of venereal diseases their standards have been equally high, and the population at large owes a debt to the Army Medical Services which, while unrecognized by the majority—venereal disease not being a subject for public discussion—is nevertheless very real. Despite the disturbances of war the Medical Services have taken steps to ensure that the prevention of venereal diseases and the treatment of these diseases are in keeping with modern standards.

Experiences in the Use of Sulphapyridine

We have found that the local application of sulphapyridine to chancroidal ulcers is a satisfactory form of treatment.

Some of our experiences in the treatment of gonorrhoea with sulphapyridine may be of interest to the profession. At the outset I wish to emphasize that I here refer to practical work. A war is in progress, and it is our duty to get the men fit and back to their units as soon as possible. For this reason the necessarily slow methods of pure clinical research have not been possible; but our work is controlled by a system of surveillance after the patients leave hospital, and we are able to assess from this, with a great degree of accuracy, whether our belief in the methods of treatment we use is based on mere optimism or on therapeutic achievement. The fact that this surveillance is usually carried out by medical officers in districts remote from ours makes this form of control of our work more satisfactory and perhaps less liable to criticism than otherwise it might be. I will refer to this subject later in the paper.

When, a little over a year ago, I took over my duties as officer in charge of a dermatological division, the cases of gonorrhoea were being treated on routine lines. Sulphapyridine was administered thrice daily, the average dosage being 3 grammes a day. Treatment was given for a week or ten days, during which time the men were kept in bed and on a light diet. The results were satisfactory, but not outstandingly so.

As you probably know, in the Army cases of gonorrhoea are treated in hospital and the men are not allowed to carry on with their duties. This confinement to hospital may be irksome to the individual, but from the medical standpoint it is of the greatest benefit both to the patient and to the physician. I soon came to the conclusion that with the

* Being part of an address delivered to the North of England Branch of the British Medical Association at Newcastle-upon-Tyne, October 31, 1940.

patients under observation and their diet under control very much larger doses of sulphapyridine could safely be given. I therefore instituted an "eight-day course," during which the men were strictly confined to bed, received only milk diet, and were encouraged to drink as much barley-water as they could stomach. The course of treatment was as follows: On the first day they received 6 grammes of sulphapyridine. This dose was repeated on the second day; on the third and fourth days they were given 4 grammes daily, and on the remaining days 3 grammes. The tablets were given thrice daily, and the course consisted of 32 grammes of sulphapyridine in eight days. Somewhat to my surprise there was no difficulty in keeping the men on milk diet for that length of time. As one philosopher sadly remarked: "Those d—n tablets makes you feel so lousy you doesn't want to eat."

On this course, which was given to several hundred cases, there were no severe complications, but there was too high a proportion of generalized scarlatiniform eruptions associated with a brisk rise of temperature. This complication usually developed between the seventh and the tenth days (usually the ninth) after the course began. It caused the patient some discomfort, but, as the rash and the fever seldom lasted longer than forty-eight hours, it did not give us much anxiety. For the majority of the patients the chief disadvantage of the treatment was that when on the ninth day they had to get up they were weak from the combined effects of the action of the drug and the low diet. Nevertheless the method was successful and relapses were few.

After this routine had been employed for some months I asked Major R. T. Wordingham to concentrate on the treatment of gonorrhoea in my department, and to alter and amend the method as he thought fit. We had the benefit of a consultation with Dr. R. Forgan, who told us that in his opinion it was the initial heavy dose of sulphapyridine which was the essential factor in curing the disease. We kept this opinion in mind, and Wordingham began his investigations.

Requirements in Sulphapyridine Treatment

We agreed that in sulphapyridine treatment there are certain desiderata. These may be tabulated as follows:

1. That the first dose should be the maximum which the average patient would tolerate.
2. That it was a mistake to administer the drug only during the day. The administration should be maintained throughout the whole of the twenty-four hours so as to keep the concentration in the blood as high as possible.
3. That the patients should be kept on milk diet during the course of treatment. We were, and still are, convinced that this is beneficial.
4. That barley-water should always be available in the wards, and that the patients should be encouraged to drink as much of it as possible.
5. That particular care should be taken to avoid constipation. We had noticed that the scarlatiniform eruption due to sulphapyridine was invariably preceded by constipation for forty-eight hours or longer. There is no doubt that failure to defaecate is an important predisposing factor in the development of the complications of sulphapyridine therapy.

Wordingham's first task was to discover the optimum initial dose of the drug and to curtail the length of the course. This necessitated a long series of clinical observations and some biochemical investigations. During these he discovered two things: first, that if the patients are not allowed to smoke, nausea and vomiting—those two bug-bears of this form of treatment—are reduced; secondly, that the administration of potassium citrate in large doses (30 grains in a simple mixture, two-hourly) is beneficial. By a process of trial and error Wordingham devised a routine which we have used in many hundreds of cases,

and during this time we have had only one death. This case, examined at necropsy by an independent pathologist, was found definitely not to be due to sulphapyridine poisoning. The findings of the pathologist, with notes on the case, were submitted to Lieut.-Colonel T. E. Osmond, R.A.M.C., who agreed that death could not be attributed to the drug.

The course consists in the administration of 22 grammes of sulphapyridine in forty-eight hours. The tablets are crushed and are given in milk every four hours during the day and night. Two important points should be noted—namely, that the tablets are *crushed*, and that there is no interruption of the treatment during the night. The first dose is 5 grammes; the second, 4 grammes; the third, 3 grammes; the fourth, 2 grammes; the remaining eight doses are each of 1 gramme. If a patient begins treatment at noon he will be given 10 crushed tablets (each tablet of sulphapyridine containing 0.5 gramme); at 4 p.m. he receives 8 tablets, and at 8 p.m. 6 tablets. At midnight he is awakened and given 4 tablets, and at 4 a.m. he has 2 tablets. And so the course continues until he has received the total dose of 22 grammes.

The course differs considerably from the routine treatment, devised by Lieut.-Colonel T. E. Osmond, R.A.M.C., which is generally used in the Army. That treatment is as follows: On the first day the patient receives 2 grammes of sulphapyridine as soon as the disease is diagnosed, and thereafter 0.5 gramme every four hours during the day and 2 grammes at bedtime. On the second day he receives a total of 4 grammes of sulphapyridine, and from the third to the seventh day, inclusive, 3 grammes of the drug every day. Irrigation of the urethra with potassium permanganate or oxycyanide of mercury may be used in conjunction with the sulphonamide therapy, at the discretion of the medical officer. This treatment is followed by the usual investigations of the prostate gland, etc.

Lieut.-Colonel Osmond, to whom we are much indebted, gave us the benefit of his opinion both by writing and verbally. Wordingham's intensive course was adopted only after consultation with him and with his concurrence.

During the intensive course of sulphapyridine most of the patients have some degree of frontal headache; about 10% suffer from sickness; and many show a slight degree of cyanosis, but this disappears within twenty-four hours of the termination of the course. The cyanosis is little more than a slight blueness of the lips, and, in some men, a very slight degree of slate-blue discoloration of the face and ears. In this respect Buttle (1939) may be quoted: "Cyanosis seems to be partly due to the elaboration of pigments from condensation of the drug itself, and it is usually thought that it can be neglected from consideration as a symptom of overdose."

Vomiting is a variable factor. If it occurs it usually develops about eighteen hours after starting treatment—that is, about two hours after the taking of the fifth dose. Thereafter the patient may not vomit again, or if he vomits he will do so an hour or two after each administration of the tablets. The wastage by vomiting is therefore not great. At the present time we are having a series of biochemical investigations carried out to determine the average loss of the drug in those patients who vomit. So far as our investigation has gone the actual loss appears to be very small; this confirms the clinical findings, for we have not experienced any marked delay in response to treatment in those cases in which vomiting has occurred. Vomiting is, of course, influenced by psychological factors. If two or three men in a ward vomit, the majority of their companions will follow their example. If before the course begins they are warned that they may be sick, they usually are sick.

Complications of Sulphapyridine Therapy

Headache, lassitude, nausea, and vomiting are the only complications which we anticipate. We have not seen a case of agranulocytosis or of haemolytic anaemia.

There are, however, two complications which are seen and which must be remembered. In a few cases during the course of treatment, and usually early in the second day, the patient may complain of pain in the lumbo-costal area, extending thence to the epigastric region. Usually it is felt on only one side of the body, but it may be bilateral. The pain is severe and the patient may be restless. There is marked tenderness on deep palpation of the upper lumbar area, and there may be tenderness on pressure over the ureter. Occasionally before the pain develops, but as a rule shortly after, the patient's urine becomes blood-stained, and a brisk haematuria may occur. In severe cases there is usually a visible precipitate of crystals if the urine is allowed to stand in a conical urine glass. When these symptoms develop there is a diminution in the amount of urine passed, with nitrogen retention. Vomiting usually occurs, and may be severe. We regard the condition as a pyelonephritis caused by the formation of a compound known as acetyl-sulphapyridine. The crystals of this compound take the form of sharp needles, and we presume that the haematuria is produced in a manner analogous to the bleeding in oxaluria.

In most cases there are no further signs or symptoms, out in a few instances anuria occurs, and may persist for as long as thirty-six to forty hours. During this time no grave symptoms have developed in the cases we have had, but, needless to say, the condition is one which we have viewed with some anxiety.

The treatment given has been simple but successful. The administration of sulphapyridine is stopped; the pain is relieved by 1/3 grain of morphine; barley-water is given in large amounts; and the administration of potassium citrate is continued. If vomiting is troublesome rectal salines are given so that the maximum fluid intake is obtained. Constipation is treated by cascara and, if necessary, by enemata. Here I should like again to emphasize the importance of avoiding constipation during sulphapyridine therapy: in almost all these cases the bowels have not been open for two or three days before the appearance of the symptoms. The pain and haematuria usually disappear within forty-eight to sixty hours of their onset, and as a rule the gonorrhoea is cured. I have not had an opportunity to work out the exact incidence of this complication, but it does not occur in more than 1 in 600 cases.

It may be asked what permanent effects accrue as a result of these events. Needless to say we have watched with particular interest the men who have suffered in this way. In no case have any signs of permanent renal damage been found. Ten days after the haematuria has disappeared the urine has been clear: there has been no albuminuria, and casts and red blood cells have not been demonstrated in centrifugal specimens. Also the blood urea has been normal, and urea-concentration tests have given no evidence of impaired renal function. These tests, repeated after an interval of three or four months, have produced similar satisfactory results.

Recently doubt has been cast on the belief that saline purgatives should not be given during the administration of sulphonamide compounds. Forgan (1939) has said that "it might be proved that there was no advantage, possibly even a disadvantage, in eliminating foods with a high sulphur content from the diet of patients receiving moderate doses of sulphapyridine (M & B 693)." With regard to these two points we have known cases in which,

despite instructions to the contrary, some patients have taken magnesium sulphate in fairly large doses whilst receiving sulphapyridine, and others have had eggs and onions while taking sulphanilamide. In no case have we noted any ill effects from these departures from the customary regime.

I have described in some detail Wordingham's course of sulphapyridine therapy because I am convinced that, provided the patient has an average tolerance to the drug, the ideal line is to attack with a maximum dose and to give a short course of treatment. This method succeeds where other methods fail, as in the case (referred to at page 982 of this issue) of the young officer suffering from chronic meningococcal septicaemia, who was not cured by small doses of sulphapyridine, but who rapidly responded to the short intensive course. Quite rightly it may be said that in the Army we are dealing with young men chosen after a medical examination, and we cannot presume that this method of treatment would be so successful if applied to the community at large. We appreciate this, but we have noted that older men in the fourth decade have usually tolerated the course well. Social distinctions sometimes make a difference in therapeutics, and particularly in gonorrhoea, from which the average hospital patient seems often to make better recovery than the private patient; but we have had no complications or difficulties arising in those officers whom we have treated.

There is one obvious precaution on which we do insist: we consider it inadvisable to administer the treatment to patients who have a history suggesting that they may have suffered from gastric or duodenal ulcer, for in these cases there is a risk that severe vomiting may develop and haematemesis may ensue.

The Routine followed by Gonorrhoea Treatment

It must not be imagined that the treatment of gonorrhoea in my department is confined to the administration of sulphapyridine. The full routine is as follows:

As soon as possible after the diagnosis has been confirmed by microscopical examination of the urethral discharge the patient is put to bed. If he is considered to be a suitable subject for intensive therapy he is given a milk diet, and mist, potassii citratis and barley-water as already indicated. He receives 22 grammes of sulphapyridine in forty-eight hours. On the third day he gets up. He is usually a little weak and lethargic, but is quite fit to take his meals in the dining-room and to go to the irrigation room for treatment. Usually his urethral discharge has almost ceased, but there may be a slight muco-purulent urethritis. On microscopical examination of this discharge pus cells and epithelial cells may be found, but gonococci can seldom be demonstrated. He is then kept for two or three days on irrigations of potassium permanganate 1 in 8,000, or oxycyanide of mercury of the same strength. Treatment is given thrice daily and the "grand lavage" is used, the irrigating fluid being allowed to flow into the bladder. On the sixth day the patient, who has not urinated for at least eight hours, reports at 6.30 a.m. for a "morning urethral smear." Very often a smear is not obtainable. If there is any moisture in the meatus it is usually found on microscopical examination to consist of mucoid secretions, probably prostatic in origin, with a few epithelial cells and spermatozoa. Later in the day a two-glass urine test is made, and if this is satisfactory a prostatic smear is taken. Usually no evidence of prostatic infection is found.

If these tests are favourable the patient takes two bottles of stout with his evening meal, for alcohol is a good test of cure. The "morning smear" and the urine examination are repeated on the seventh day, and if these are satisfactory a provocative dose of gonococcal vaccine containing three hundred million gonococci is given. On the eighth day the patient reports for yet another "morning smear"; a prostatic smear is taken and the usual urine test is made. If these tests are all satisfactory the anterior urethra is examined through a urethroscope. At this stage we expect to find a diffuse reddening of the urethra, but no litritis—no inflamed follicles. A curved sound of suit-

able size is passed. If possible we keep the patient under observation for a further two days, as occasionally there is a delayed reaction to the vaccine.

You will note the frequency with which the "morning smear" is investigated, and the fact that every patient has at least two prostatic examinations. This is because we are well aware that one of the dangers of sulphapyridine therapy is that in some cases pus formation, the cardinal sign of gonorrhoea, is decreased, while gonococci may occasionally be present in the urethra or in the prostatic secretion.

When our tests of cure and the period of observation are finished the patient returns to duty, but observation on the case does not end. Three weeks later the man reports to a military hospital, where he is examined by a medical officer who has had a training in the treatment of venereal disease. He is examined for signs of urethral discharge; the two-glass urine test is made, a prostatic smear is taken, and usually a curved sound is passed. The same investigation is repeated during the following two weeks. Although all the tests may be negative (and if they are not he is immediately referred back to us for treatment) he is not yet passed as cured. Three months after his discharge from hospital he is sent either to us or to some other centre. Another provocative injection of gonococcal vaccine is given, and all the usual tests—macroscopic, microscopical, and urethrosopic—are carried out. Only if these are negative is he discharged as cured. During the period of surveillance Wassermann tests are carried out to ensure that a concomitant infection with syphilis has not been missed.

I think, therefore, that we can claim that our work, though purely clinical, is well controlled: this being so, it is satisfactory to find that the relapse rate is under 5%.

Summary

The incidence of venereal disease is discussed, together with the part played by the Medical Services of the Army in prevention.

An intensive method of treating gonorrhoea is described at some length.

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ACUTE GONORRHOEA

FURTHER OBSERVATIONS ON TREATMENT BY SULPHAPYRIDINE FOLLOWED BY LAVAGE

BY

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In my original article (Sommerville, 1939) I reviewed 152 consecutive cases of acute gonorrhoea treated with sulphapyridine alone, without adjuvant therapy, in 90% of which early cures without complications were obtained. By comparison Dr. J. G. McGregor-Robertson (1938), using the drug in connection with lavage, claimed 100% early cures, but with 3% complications.

Technique

In a final note to that article I stated that I had altered my technique. This alteration was made in an attempt to maintain the freedom from complications and at the same time to improve the percentage of early cures. The present article is a review of 300 consecutive cases treated according to the new technique, which is as follows.

Sulphapyridine is given, the dosage being 0.5 gramme (one tablet) four times a day for one week. Irrespective of the clinical results at the end of this period, irrigation with 1 in 8,000 potassium permanganate daily is instituted for a week, followed by similar lavage on alternate days for another week. In most cases this completes the treatment, but if the clinical and urinary examinations are not entirely satisfactory at the end of three weeks lavage is persisted with until the desired result is obtained. Thereafter observation for three weeks is maintained, and a prostatic smear is then taken; if this is satisfactory (less than four pus cells per field) urethrosopic examination, followed by the passing of a curved bougie, is carried out a week later. If there is no response to instrumentation a routine Kahn test is done the following week; and finally, all being well, the patient is discharged at the end of nine weeks.

It is now fairly well established that if sulphapyridine is going to act satisfactorily, as it does in 90% of cases, it will do so in approximately three days. If a urethral discharge of any type exists after a week I believe that the virulence of the gonococcus is so diminished that any danger of complication arising as a result of irrigation is at a minimum.

Survey of Results in 300 Cases

The results obtained from the present series serve to prove my contention that large doses of the drug are not necessary, and that practically 100% of early cures can be obtained with almost the same percentage of freedom from complications. This article is published not simply because I think the results are satisfactory but more especially as a plea for economy in the use of the drug and with all due deference to those who believe in and employ massive or intensive dosage.

In going over the case records I find that my original enthusiasm in investigating the time interval required for urethral smears to become gonococcus-negative has waned considerably, and such observations were noted in 103 cases only. The average time interval in these was 1.74 days, compared with 1.92 days in my original series.

For the purpose of "dry" observations 9 cases are excluded from the record of figure averages. Of these 9 patients 7 were irregular attenders and, later, defaulters with no dry observations of any value owing to the time intervals in their attendance, 1 (a chronic persistent alcoholic who defaulted after nineteen days) failed to clear up or even improve, and 1 (one of two cases which showed repeated relapse, and the subject hereafter of a special note) relapsed before a completely dry observation could be obtained. I have divided the remaining 291 into four groups, as shown in Table I.

TABLE I

Type	No. of Cases	Urethra Dry. Day Average
Average case	250	4.98
Avowed alcoholics	33	23.09
Admitted re-exposures	5	25.60
Complications before therapy	3	30.00
Total	291	7.66

This division has been made because there is such a marked discrepancy between the figures of the normal average case and the other three groups. Especially interesting is the alcoholic group. The intake of alcohol quite evidently makes a considerable difference in the prognosis of a case, as the figures prove. It is also scarcely fair to slump all the cases together and thus alter materially the statistics obtained. The results obtained in the present series conform very closely to those of my previous one. Thus from the figures already given it can be seen that out of 293 cases 2 (0.68%) may be recorded as failures.