RESULTS OF TREATMENT OF GONORRHOEA WITH PENICILLIN ALONE AND WITH PENICILLIN AND SULPHONAMIDE*

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The "single injection" treatment of uncomplicated gonorrhoea has been in general use for several years since the introduction of long-acting preparations of penicillin. Penicillin-oil-beeswax, penicillin-aluminium monostearate, and procaine penicillin in oily or aqueous suspension have been used in turn as they have become available. Various authoritative statements have been made on the dose required to ensure a high cure-rate, but there has been a singular scarcity of published reports of clinical experience (especially with the more recent preparations) to support such statements.

The dose of long-acting preparations of penicillin commonly recommended is 300,000 units (with or without 100,000 units crystalline penicillin G), and this is the dose that is probably most often used. This recommendation is partly influenced by the fact that the dose has to be the smallest compatible with efficiency in order to reduce the risk of "masking" the possible development of syphilis which may have been acquired at the same time as the gonorrhoea. It is probably also influenced by the fact that the dose is contained in 1 ml. of many of the standard proprietary preparations.

Smaller doses are recommended by some authorities, for example 150,000 to 200,000 units by Osmond (1952), although there is little published evidence of the effect of such doses in gonorrhoea. It has been shown that 150,000 units of procaine penicillin in oil maintains a bacteriostatic blood level (0.03 units penicillin per ml. serum, or more) for about 9 hours, which is just over the minimum period apparently necessary for the cure of uncomplicated gonorrhoea (Horne, 1950). It is unlikely, however, that 150,000 units of the soluble sodium salt, also recommended by Osmond, would be very effective in view of its more rapid absorption and excretion.

Procaine penicillin in aqueous suspension (with or without crystalline penicillin G) is probably the

most popular preparation in current use. It is easy to administer, comfortable for the patient, and has practically no side-effects. Nevertheless, the opinion is held by some that it is less effective in the treatment of gonorrhoea than the earlier preparations, although this is difficult to explain in view of the high blood levels it produces. There has also been debate about the value of combining a course of sulphonamide with penicillin in the treatment of gonorrhoea, especially in the female, in order to enhance the cure-rate. It is also believed that sulphonamide may help to reduce the incidence of the urethritis that sometimes persists in the male after the gonorrhoea has been cured by penicillin.

In view of these controversial opinions and the lack of authoritative evidence, an analysis has been made of the effects of different schedules of treatment, and as a result of this analysis it is possible to conclude that a single injection of 300,000 units procaine penicillin in aqueous suspension (with or without 100,000 units crystalline penicillin G) is a very satisfactory method of treating uncomplicated gonorrhoea.

Clinical Material

An analysis has been made of all cases of uncomplicated gonorrhoea in white patients treated in this Department, with the schedules under review, from January 1, 1950, to December 31, 1951. Some of the patients were treated on more than one occasion during this period. In the analysis, observation after treatment is considered to have ceased at the end of March, 1952.

Male Patients (321 individuals with 349 infections).—This number includes every adult diagnosed as having uncomplicated gonococcal urethritis. Cases are included in which the urine in the second glass of the "two-glass" test was hazy, but in none of these was there clinical evidence of prostatitis or of other complications of urethritis.

Female Patients (135 individuals with 143 infections).—This number includes every adult diagnosed as having uncomplicated gonococcal cervicitis and/or urethritis.

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Diagnostic Criteria

Male.—The presence of Gram-negative diplococci, morphologically resembling gonococci, in stained smears of the urethral discharge was the principal diagnostic criterion. Cultural investigations were made in a small number of cases in 1950, and in nearly every case in 1951.

Female.—Stained smears and cultures from the cervix and urethra were examined in every case. A diagnosis of gonorrhoea was made, and treatment started, in every case in which one or more of these four investigations were positive.

The reliability of the cultural methods is illustrated in Table I, where it will be seen that in many female cases gonococci were cultured from secretions which yielded "negative" results in stained films. In some of the cases with "negative" cultures in spite of "positive" smears, the organisms may have been *Neisseria* other than the gonococcus (Wilkinson, 1952), but no data are available on this point.

TABLE I
BACTERIOLOGICAL INVESTIGATIONS MADE IN CASES
OF GONORRHOEA IN 1951
(To illustrate reliability of technique)

Sex of Patient	Male	Female
Cultures from cases with "positive" smears ..	129	38
"Positive" cultures obtained	121	33
"Negative" smears with "positive" cultures ..	0	17

Treatment Schedules

MALE

- (a) 93 Cases.—Single intramuscular injection (into the buttock) of 300,000 units procaine penicillin in aqueous suspension, plus 20 g. "sulphatriad". Patients were instructed to take two tablets—1 g.—four times daily, spread over as long a period of the 24 hours as possible, for 5 days.
- (b) 104 Cases.—300,000 units procaine penicillin only.
- (c) 70 Cases.—300,000 units procaine penicillin only. (Two different proprietary preparations of penicillin were used in (b) and (c).)
- (d) 43 Cases.—Single injection of 300,000 units procaine penicillin together with 100,000 units crystalline penicillin G. in aqueous suspension.
- (e) 39 Cases.—As in (d), plus 20 g. "sulphatriad".

FEMALE

- (a) 114 Cases.—Single injection of 300,000 units procaine penicillin in aqueous suspension, plus 20 g. "sulphatriad".
- (b) 29 Cases.—Single injection of 300,000 units procaine penicillin together with 100,000 units crystalline penicillin G. in aqueous suspension.

Surveillance After Treatment

All the patients were treated and observed as out-patients, and it was not considered justifiable to insist on their attendance for examination at very short intervals. When the period of observation after treatment was short it was not necessarily due to default. Other reasons included the transfer elsewhere of patients, treatment of concomitant syphilis with penicillin, and re-infection.

Male Patients.—Only a small proportion were seen within 1 or 2 days of receiving penicillin, but nearly all were seen within 3 to 7 days. At the second and subsequent visits, the patient was questioned with regard to symptoms, the urethra was examined for the presence of any discharge, and the urine examined for any abnormality. If the progress at the end of a week was considered satisfactory further observation was usually arranged at approximately weekly intervals until the "test of cure" was carried out, and thereafter at approximately monthly intervals, for varying periods of time. The total period of observation is recorded in Table II. A blood Wassermann reaction was always done at the first visit and about 7 to 10 days later; then at the time of the test of cure, and at approximately monthly intervals thereafter.

Female Patients.—Nearly all the cases were seen approximately a week after receiving penicillin, when cultures from the urethra and cervix were repeated. If the progress was considered satisfactory subsequent attendances were arranged so that the patients were seen as soon as possible after a menstrual period, for varying periods of time. The total time of observation is recorded in Table III. A blood Wassermann reaction was always done at the first visit, and then usually at approximately monthly intervals thereafter.

Test of Cure

Male Patients.—The test was nearly always carried out during the third or fourth week after the injection of penicillin. The urethra was examined for the presence of any discharge. The urine was examined macroscopically for any abnormalities, and the centrifuged deposit was examined for pus cells. If an excess of pus cells was seen (more than one or two per high-power field, and especially if there were any clumps) a stained preparation of the deposit was examined. The prostate gland was massaged, and the secretion inoculated directly on to a culture plate, and a stained smear also examined microscopically. The

TABLE II
RESULTS OF TREATMENT OF GONORRHOEA (MALE CASES) WITH DIFFERENT SCHEDULES OF TREATMENT

Treatment Schedule								(a)	(b)	(c)	(d)	(e)
Period								January— June 1950	July— December 1950	January— June 1951	July—December 1951	
Drug	Crystalline penicillin (units)							—	—	—	100,000	100,000
	Procaine penicillin (units)							300,000	300,000	300,000	300,000	300,000
	Sulphonamide (g.)							20	—	—	—	20
Cases originally treated								93	104	70	43	39
Cases receiving adjuvant treatment on account of		Coincidental disease						2	1	1	1	2
		Persistent non-gonococcal urethritis						1	7	7	2	3
Treatment Failures								3	0	3	0	1
Successful Cases	Period of Observation (weeks)		Less than 1					13	13	11	16	5
			1— 4					10	18	14	12	8
			5— 8					12	17	9	5	3
			9—12					10	13	10	1	8
			13—20					33	30	12	6	9
			More than 20					9	5	3	0	0
	Test of Cure	A (including centrifugation of urine)						24	61	36	19	23
		B (excluding centrifugation of urine)						35	5	2	0	0
Re-infections (weeks since original treatment)								8 10 10 12 17 60 86 88 93 100	1½ 7 9 42 50 50 53 —	1* 1* 1½ 2 7 9 15 17 28 39	5 2 6 9 —	6 4 —

* The same patient.

TABLE III
RESULTS OF TREATMENT OF GONORRHOEA (FEMALE CASES) WITH DIFFERENT SCHEDULES OF TREATMENT

Treatment Schedule					(a)	(b)
Period					Jan. 1950- June 1951	July-Dec. 1951
Drug ..	Crystalline penicillin (units) Procaine penicillin (units) Sulphonamide (g.)				— 300,000 20	100,000 300,000 —
Cases originally treated					114	29
Cases receiving adjuvant treatment on account of coincidental disease					6	0
Treatment Failures					3	1
Successful Cases	Period of Observation (weeks)	Less than 1	5	1		
		1- 4	8	3		
		5- 8	16	10		
		9-12	28	11		
		13-20	19	3		
		More than 20	29	0		
	Post- treatment Cultures	1	2	2		
		2	11	5		
		3	4	4		
		4 or more	83	16		
Re-infections (weeks since original treatment)			3	4	14	
			6	8	24	
			30	30		
			32	50		

urine passed after prostatic massage was examined macroscopically for abnormalities, and the centrifuged deposit examined for pus cells. As with the first specimen of urine, a stained preparation was examined if necessary.

Centrifugation of the urine was not carried out in every case, and in the analysis tests of cure including this investigation are referred to as (A), those excluding it as (B). In treatment schedule (a) the test of cure included the passage of a metal urethral sound, and in some cases, anterior urethroscopy, but these procedures were abandoned after June, 1950.

Female Patients.—As soon as possible after the end of a menstrual period, the patients were clinically examined, and cultures taken from the cervix and urethra. At least three post-menstrual examinations of this type were made whenever possible, the actual numbers being shown in Table III.

Progress after Treatment

No reaction of any kind to penicillin was observed.

Male Patients.—Nearly all stated that within 24 to 48 hours of the injection of penicillin (and sometimes earlier) all their symptoms were completely relieved and the discharge had disappeared. This was confirmed in those patients who were seen

within the first day or two. At the end of a week there was very rarely any residual urethral discharge or even any stickiness of the urinary meatus, and pus threads were seldom seen in the urine. If at the end of a week the urinary meatus was no more than moist no action was taken. If there was still a definite discharge, however, or if a discharge had reappeared after a period of freedom, the material was always examined and further treatment given if indicated (see below).

Tests of cure were carried out in 206 cases, and in only one of these were gonococci found in the prostatic secretion (Case 6, below). In a very small proportion of cases (and principally in those in which the test of cure was done early) a slight excess of pus cells, with occasional clumps, was seen in the centrifuged first urine, or in prostatic smears, or in the centrifuged urine after prostatic massage, but in all these cases subsequent examination a week or two later revealed no abnormalities in spite of the fact that no further treatment had been given.

Female Patients.—The symptomatic response to treatment was similar to that in the male. The procedure for post-treatment observation and investigations has been described.

Results of Treatment

The difficulty of assessing the results of treatment of gonorrhoea, and in particular the calculation of the "cure-rate", is notorious, since it is so often necessary to decide whether the recurrence of a urethral discharge containing gonococci in the male, or the reappearance of positive smears or cultures or both in the female, is due to a relapse of the original infection (treatment failure) or to a new infection following intercourse. Discrimination between these two alternatives involves a careful analysis of all the information available, and, while in some cases there may be no doubt about the explanation, in others a decision may be very difficult, and different observers might even interpret the facts differently.

However, the setting of an arbitrary time-limit after treatment before a true re-infection will be admitted (for example, 3 months, as suggested by King, Curtis, and Nicol, 1950) would seem to be unscientific and unrealistic, in view of the frequency with which re-exposure to possible infection occurs within even a few days of treatment, although such an arbitrary time-limit may be useful from the point of view of analysis (see below). Recurrence of the gonococcal discharge after a satisfactory bacteriological test of cure, however, can be accepted

fairly confidently as evidence of re-infection rather than relapse.

The analysis of this series of cases has been recorded in such a way as to show every infection of every individual during the period under review. If treatment failure was discounted, the subsequent infection is recorded in Tables II and III as a number which indicates the number of weeks since the treatment of the previous infection. By this means the failure rate may be calculated on the basis of any arbitrarily selected time-limit if desired, should the criteria of cure adopted here not be acceptable.

It was not ascertained whether the patients had received penicillin or other anti-gonococcal drugs elsewhere while under observation—a factor which must nowadays be taken into account in the assessment of the results of treatment of both gonorrhoea and syphilis.

Male Patients.—In no case did gonococci persist in the urethral discharge after treatment. In only one case did any complication of urethritis develop after treatment had been started (one man developed unilateral epididymitis—see Case 7 below).

In a number of cases there was a recurrence of a urethral discharge containing gonococci at intervals varying from a few days to more than a year after treatment of the original infection. In only five of these did careful analysis of all the data available (including in some instances, information from the consorts) lead to the belief that treatment failure had occurred, and in another case gonococci were found in the prostatic secretion at test of cure. All six appeared to be cured after re-treatment with varying doses of penicillin; four then had a satisfactory test of cure, but two defaulted before this could be carried out. In all the other cases in which the possibility of treatment failure had to be considered the evidence was interpreted to mean that the patient had been re-infected.

Female Patients.—In no case did gonococci persist after treatment, nor did any complication develop. In a number of cases positive smears or cultures were obtained at intervals varying from a few weeks to a year after treatment of the original infection.

In only four cases did careful analysis of all the available data lead to the belief that treatment failure had occurred. In three of these cases, repetition of the same or of a similar schedule of treatment resulted in cure, and the fourth one was given a larger course of penicillin. In all the other cases in which the possibility of treatment failure had to be considered the evidence was interpreted to mean that the patient had been re-infected.

Re-infections and Treatment Failures

For the purpose of illustrating the criteria used here in assessing the results of treatment, an arbitrary period has been selected of 12 weeks after the initial treatment—a detailed account is given only of those patients who had a “recurrence” of the gonorrhoea within this period.

Male Patients.—None of the fifteen patients who returned to the department with gonococcal urethritis 12 weeks or longer after their initial treatment were considered to be treatment failures. All of them admitted intercourse within the accepted incubation period for gonorrhoea. Of the fifteen, ten had had a satisfactory test of cure after their previous infection; of the five who had not, one had been observed for only four days after treatment, and the others from 4 to 12 weeks, but all appeared to be clinically cured at their last visit.

Twenty patients returned to the department with gonococcal urethritis less than 12 weeks after the initial treatment, and of these, three had three attacks each during the period of 2 years under review.

Eight of these twenty were believed to have re-infected themselves from the wife or regular consort before she had been treated, and two of these eight re-infected themselves twice from the same source in this way. This conclusion was confidently drawn in every case by assessing the history and clinical findings of each partner.

Seven of the twenty patients were believed to have re-infected themselves from a new source, and one of these had three infections during the period under review. In every case a new exposure was admitted, and in the only two cases in which the consorts were found, both had gonorrhoea. Two of the seven patients had had a satisfactory test of cure following the original infection; four developed their new infection 4, 7, 9, and 10 weeks after their initial treatment; and the seventh had two re-infections at 6-week intervals.

These fifteen (eight re-infected from the same source and seven from a different source) were not considered to have been treatment failures. The other five, and, in addition, one patient who was found to have gonococci in the prostatic secretion at test of cure, and one patient who developed epididymitis a few days after treatment were, however, considered to be treatment failures. The case histories of these seven treatment failures are briefly summarized below.

Case 1 (Ukrainian).—Seen on fourth day after treatment with 300,000 units procaine penicillin (Schedule c). Stated that the discharge had cleared up the day after

treatment, but had recurred. Found to have acute gonococcal urethritis. Denied further intercourse, but admitted drinking. Since he also had latent syphilis he was given a large course of penicillin.

Case 2.—Seen on 2nd and 9th day after treatment with 300,000 units procaine penicillin and 20 g. sulphatriad (Schedule a). On each occasion there was no urethral discharge, and the urine was clear but contained a few pus threads. On the 9th day the Gonococcal Complement-Fixation Test was positive (he admitted having had gonorrhoea in 1945). Reported on 24th day with acute gonococcal urethritis. His previous records indicated that he was highly promiscuous and untruthful, but since on this occasion he stoutly denied further intercourse, he has been classified as a treatment failure. He was given 600,000 units procaine penicillin, but defaulted after one more visit.

Case 3 (Homosexual).—Observed on four occasions over a period of 5 weeks after treatment with 300,000 units procaine penicillin (Schedule c). On each occasion there was no urethral discharge and the urine was clear and free from pus. On the 16th day he had a satisfactory test of cure, except that there was an excess of pus cells in the urine following prostatic massage, but no organisms were seen in the prostatic fluid and no growth was obtained on culture. However, 6 weeks after the initial treatment he was found to have a mild urethritis, and gonococci were seen in a smear of the discharge (no culture was made). Since he stoutly denied further intercourse, he has been classified as a treatment failure. He was given 600,000 units procaine penicillin, had a satisfactory test of cure, and then defaulted.

Case 4 (Polish).—Observed on five occasions during 39 days following treatment with 300,000 units procaine penicillin and 20 g. sulphatriad (Schedule a). On each occasion there was no urethral discharge and the urine was clear but showed a few pus threads at the last two visits. On 25th day test of cure was satisfactory. However, on the 41st day he was found to have acute gonococcal urethritis, and since he stoutly denied further intercourse he has been classified as a treatment failure. He was retreated with the same schedule, had a satisfactory test of cure, and was discharged 10 weeks after treatment.

Case 5.—Seen on 3rd and 8th day after treatment with 300,000 units procaine penicillin (Schedule c). Discharge did not completely clear up and urine remained slightly hazy. On 15th day had acute gonococcal urethritis. Denied further intercourse. His wife (Case 11), whom he had infected after extramarital intercourse, and who was treated on the same day, also relapsed, but denied intercourse. He was retreated with 300,000 units procaine penicillin, had a satisfactory test of cure, and was discharged 3 months later.

Case 6.—Seen on 17th and 33rd day after treatment with 300,000 units procaine penicillin and 20 g. sulphatriad (Schedule a). On each occasion there was no

urethral discharge and the urine was clear and free from pus threads. On the 75th day there was no discharge but the urine contained pus threads. Further intercourse was denied but he admitted heavy drinking. A prostatic smear showed an excess of pus cells, and gonococci were reported on culture of the prostatic secretion. He was given further penicillin but defaulted immediately.

Case 7.—Pain in right testicle began 2 days after treatment with 400,000 units penicillin and sulphonamide (Schedule *e*). When seen on 4th day after treatment he had a moderately severe acute epididymitis; a smear and culture from urethral bead were negative for gonorrhoea, and the urine was clear. This has nevertheless been considered a treatment failure. He was given a further injection of 800,000 units penicillin, and subsequently had a satisfactory test of cure.

Female Patients.—None of the six who were found to have gonorrhoea 12 weeks or longer after their initial treatment were considered to be treatment failures. All of them admitted intercourse within the accepted incubation period for gonorrhoea. All six had had between two and four negative post-treatment cultures, and they had been observed for from 8 to 12 weeks.

Eight patients were found to have gonorrhoea less than 12 weeks after their initial treatment. Three of these infected themselves again from the same man before he had been treated. One was believed to have re-infected herself from a new source 4 weeks after her initial treatment (she had had two negative post-treatment cultures in the interval). These four cases were not considered to have been treatment failures. However, four others were considered to have been treatment failures, and their case histories are briefly summarized below.

Case 8.—Had negative cultures 1 and 2 weeks after treatment with 300,000 units procaine penicillin and 20 g. sulphatriad (Schedule *a*), but a week later smears and cultures were positive. Although she was known to be a prostitute and had had gonorrhoea several times previously, she admitted recent intercourse with only one man, who showed no evidence of gonorrhoea. Retreated with the same schedule and had five negative post-treatment smears over a period of 3 months.

Case 9.—Had negative cultures 2 weeks after treatment with 400,000 units penicillin (Schedule *b*), but positive cultures a week later. Stoutly denied further intercourse, but known to be promiscuous, and had had gonorrhoea before. Retreated with same schedule and had four negative post-treatment cultures over a period of 3 months.

Case 10.—Had negative cultures 2 weeks after treatment with 300,000 units procaine penicillin and 20 g. sulphatriad (Schedule *a*), but positive cultures 2 weeks later. She had been infected by her husband but denied

intercourse with him since treatment. Retreated with same schedule and had four negative post-treatment cultures over a period of 3 months.

Case 11.—Had negative cultures one week after treatment with 300,000 units procaine penicillin and 20 g. sulphatriad (Schedule *a*), but positive smear and culture two weeks later. She had been infected by her husband (Case 5) but denied intercourse with him since treatment. She was retreated with a large course of penicillin and had three negative post-treatment cultures over a period of 4 months.

These short case histories show that if there has been any bias in interpretation it has been against the treatment schedule, since in some cases the circumstances seemed to favour a re-infection and the patient's denial of re-exposure was accepted with some misgiving. Only Case 1 would appear to have been an unequivocal failure.

Other Observations of the Results of Treatment

(a) **Intramarial Infections.**—Supporting evidence for the efficiency of the treatment schedules is provided by a study of the group of intramarial infections. During the period under review, 54 men were found to have infected their wives following extramarial intercourse, and the wives were also treated in the department. As has been stated, a few of these men infected themselves a second time, but after both partners had been treated further evidence of infection was found in only one pair, both of whom appeared to be true treatment failures (Cases 5 and 11). Also, the wives of twelve other men were examined and found to be free from infection. None of these wives was known to develop gonorrhoea subsequently, and none of the men had a recurrence of infection. In most cases in both groups marital intercourse was restored before observation ended.

(b) **Persistent Non-Gonococcal Urethritis in the Male.**—Nearly every one of the few cases in which the urinary meatus remained moist or pus threads persisted in the urine for more than a few days after penicillin had been given, eventually cleared up without further treatment. However twenty patients still had a persistent slight though definite urethral discharge after 5 to 7 days. No gonococci were seen in stained smears from any of these cases, and in twelve in which the discharge was cultured no gonococci were isolated. Most of these were given a course of 20 g. "sulphatriad", a few streptomycin, and one aureomycin. In every case the residual urethritis cleared up completely. These (and seven other patients who received adjuvant treatment for a coincidental disease, usually latent syphilis) are

not included in the "successful" cases in Table II, but sixteen eventually had a satisfactory test of cure. One was transferred elsewhere, and three defaulted before tests of cure could be carried out.

Since sixteen of these twenty cases occurred in the series who were given penicillin only, the inclusion of a course of sulphonamide in the treatment schedule may have had an effect in reducing the incidence of non-gonococcal urethritis, although when this did persist after a course of penicillin only it cleared up readily with further treatment.

(c) **Coincidentally acquired Syphilis.**—Six male and four female patients were found to have positive serological tests for syphilis at their first visit when gonorrhoea was diagnosed. One of these had aortitis and the other nine had a latent infection. No patients developed clinical or serological evidence of syphilis while under observation after treatment. The exact period of observation is recorded in Tables II and III, where it will be seen that 112 patients had serological tests for syphilis for as long as between 12 and 20 weeks after treatment, and 46 for even longer. Up to the end of the period reviewed (end of March, 1952) only one of the patients treated for gonorrhoea was found to have developed syphilis at a later date :

Case 12.—Reported in September, 1951, with non-gonococcal urethritis, and found to have positive serological tests for syphilis, although there was no history of suspicious lesions, and no clinical evidence of the disease. He had been treated in October, 1950, for gonorrhoea with Schedule (b). At that time there had been no clinical evidence of syphilis, the blood Wassermann reaction was negative at his first visit and again 2 weeks later, but he defaulted immediately and was not seen again until a year later. He admitted having had opportunities of acquiring syphilis.

It is therefore not possible to determine whether the small dose of penicillin given for gonorrhoea in this particular case had any masking effect on incubating syphilis in view of the short observation period.

Comment

No calculation has been made of the treatment failure rate in individual schedules, but over the whole series it was 2.2 per cent. in the male cases and 2.9 per cent. in the female cases (omitting from the calculation of the "successful" cases all those receiving adjuvant treatment, and thus probably augmenting the failure rate). Most of the treatment failures occurred surprisingly in cases treated under schedules in which sulphonamide was combined with penicillin, but there is of course no guarantee that all or any of the patients took the sulphonamide as instructed.

Nevertheless, there would appear to be little or no indication to use sulphonamide in addition to penicillin to ensure cure of gonorrhoea, at least in the male. The female series is probably too small to allow definite conclusions to be drawn. Indeed, there are several contraindications to the use of sulphonamides :

(i) They are potentially dangerous, especially if taken without regular supervision, and side-effects are occasionally seen, even with the dosage used here.

(ii) The tablets may not all be swallowed, especially if symptoms are relieved immediately after the injection of penicillin, and the unused tablets may then be put to other purposes.*

(iii) Sulphonamides entail an additional, and probably unnecessary, expense.

The incidence of persistent non-gonococcal urethritis in the male was very low in the whole series, although most patients in which it was prominent had received penicillin only. The condition cleared up quickly after further treatment had been given, and thus there would appear to be little or no indication to combine sulphonamide with penicillin for this purpose either.

It is not possible to assess the effect on the treatment failure rate of the additional 100,000 units crystalline penicillin G used in some schedules, but it seems unlikely to have had much influence.

The risk of a small dose of penicillin "masking" syphilis has probably been overstressed, and it is debatable whether the prolonged observation after treatment of gonorrhoea (as recommended, for example, by Reekie, 1951) is nowadays justifiable. In the present series, none of the patients developed clinical or serological evidence of early syphilis while under observation, and there is thus no evidence one way or the other to show whether the small dose of penicillin had any effect in prolonging the incubation period of syphilis or in suppressing its clinical manifestation. On the other hand, a large proportion of the patients were observed for periods even longer than the accepted outside limit of the incubation period for syphilis. In view of the incidence of infectious syphilis in the area at the time of investigation, it is surprising that apparently no patient with gonorrhoea contracted syphilis coincidentally. This may mean, of course, that the small dose of penicillin was adequate to abort syphilis.

The necessity for any observation at all, at least in men, after treatment from the point of view of gonorrhoea is also debatable, but will not be

* One patient recently admitted having tried the effect of some tablets "left over" after a previous attack before reporting for treatment.

discussed here. It may be noted that in all the male treatment failures (except one—Case 6) there was a recurrence of obvious symptoms and signs of the disease, but nevertheless, the symptomless male “carrier” does exist, and several have recently been encountered in the Department.

A progressive drop in the treatment failure rate as time goes on may not be attributable only to increasing efficiency of treatment. Most analyses tend to be conservative in that when a decision has to be made between treatment failure or re-infection in any particular case it is always recorded as the former. As the total incidence of gonorrhoea falls (as has been happening during the last few years) the risk of re-infection diminishes, and with it the total number of “failures”.

Although it seems therefore that a single injection of 300,000 units procaine penicillin in aqueous suspension (with or without 100,000 units soluble penicillin) will cure nearly every case of uncomplicated gonorrhoea in the male and probably also in the female, the importance of making a prior diagnosis (clinical and bacteriological) cannot be too greatly stressed. A single injection of this dose is unlikely to cure gonorrhoea when such complications as prostatitis or salpingitis are present; these conditions must be eliminated before reliance is placed on this method of treatment.

Summary

(1) During 1950 and 1951, 349 male and 143 female cases of uncomplicated gonorrhoea were treated with different schedules of penicillin and sulphonamide. The circumstances under which the cases were observed were favourable for analysis of the results of treatment. The criteria of cure were stringent, and many of the cases were observed at intervals for periods long enough to conduct bacteriological tests of cure.

(2) Reasons are given why in most of the cases of recurrence, re-infection rather than treatment failure was considered to have been the cause.

(3) In the male series, a single injection of 300,000 units procaine penicillin in aqueous suspension (in some cases together with 100,000 units

crystalline penicillin G) was used. Some cases were given 20 g. sulphonamide in addition.

(4) In the female series, either a single injection of 300,000 units procaine penicillin with 20 g. sulphonamide, or 300,000 units procaine penicillin with 100,000 units crystalline penicillin G alone, was used.

(5) The treatment failure rate, calculated according to the criteria used here, was 2.2 per cent. in the male series and 2.9 per cent. in the female series.

(6) In the male series, there was no evidence that the addition of sulphonamide reduced the treatment failure rate, although there was some evidence that it did reduce the incidence of non-gonococcal urethritis persisting after successful treatment of the gonorrhoea. There was insufficient evidence to show whether the additional 100,000 units crystalline penicillin G had any effect in reducing the treatment failure rate.

(7) In the female series, the number of cases receiving penicillin alone was insufficient to justify definite conclusions, but the treatment schedule using 300,000 units procaine penicillin with 100,000 crystalline penicillin G alone appeared to give very satisfactory results.

(8) No evidence was obtained of the penicillin having a “masking” effect on syphilis.

(9) It is stressed that, in spite of the apparent simplicity of treatment, it is still important to establish a clinical and bacteriological diagnosis before treatment is started.

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