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CURRENT STATUS OF THE IN VITRO SENSITIVITY OF GONOCOCCI TO PENICILLIN IN FINLAND

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Abstract. During the period April 1, 1967 to June 30, 1969 specimens from 3095 consecutive gonococcal patients were examined for the sensitivity of gonococci to penicillin. In 765 cases (24.7%) a diminished sensitivity to penicillin was seen (MIC $\geq$ 0.2 IU/ml). The incidence of such cases was highest in 1969, (29.0%) and lowest in 1968, (21.2%). Seventy-seven (36.1%) of the 213 patients infected abroad had gonococci with decreased penicillin sensitivity.

Since its introduction 20 years ago, penicillin has been the drug of choice in the treatment of gonorrhoea. But since 1958 a number of papers have been published demonstrating strains of gonococci with a decreased sensitivity to penicillin (2, 3, 5, 7, 9). The increasing rate of failure of penicillin treatment has led to larger standard doses. Thus, where 300,000 units of a moderately long-acting penicillin sufficed 20 years ago, 1.2 to 2.4 mega-units is the usual dose today, with some using multiple doses (1, 6).

The purpose of this study was to determine the frequency of the in vitro penicillin-insensitive gonococci strains in Finland from April 1967 until June 1969. Special attention was paid to those cases in which infection occurred abroad.

MATERIAL AND METHODS

The Out-patient Department for Venereal Diseases at the University Central Hospital, Helsinki, routinely performs a gonococcal culture in all cases of suspected gonorrhoea, and since April 1967 a penicillin sensitivity test has also been performed in positive cases. The series comprised 3095 consecutive patients showing positive gonococcal culture during the period April 1, 1967 until June 30, 1969. The series represents about one-sixth of the total number of reported cases of gonorrhoea in Finland during that period. Of the series, 778 were females and 2317 male patients. All attended the out-patient clinic of their own free will, which suggests that the series included few prostitutes. In 213 cases the infection had been contracted abroad and 257 patients were sailors. Samples were taken from all the patients for both direct microscopy and culture. Only the patients with a positive culture are included in the present series. The specimens for culture and sensitivity tests were taken from the urethra (males) and urethra, cervix and rectum (females). The samples were brought to the laboratory in Stuart's medium, arriving within 24 hours of being taken. Gonococci were classified under the usual morphological, cultural and bio-chemical groups. The penicillin sensitivity test was performed using the plate dilution method, described by Reyn et al. (8) and inoculation was according to Juhlin (4). The penicillin concentrations used were 0.01, 0.03, 0.05, 0.07, 0.1, 0.2, 0.3, 0.4, 0.5, 0.7, 1.0, 2.0 IU/ml, and each test was duplicated. A minimum inhibitory concentration (MIC) value of 0.2 IU/ml to penicillin was regarded as indicative of decreased sensitivity.

RESULTS

Table I shows that 765 (24.7%) of the total 3095 cases had an MIC value $\geq$ 0.2 IU/ml; this was 202 (26.0%) of the 778 female patients and 563 (24.3%) of the 2377 male patients. Seventy-seven of the patients infected abroad showed gonococci with decreased sensitivity to penicillin. When the patients infected abroad were excluded the total number of cases infected by strains with a decreased sensitivity to penicillin was 688 (23.9%) of 2882. In 653 (85.4%) of the 765 patients infected with gonococci with a decreased sensitivity to penicillin, the decrease was only moderate (MIC value 0.2–0.4 IU/ml) while in the remaining 112 cases the MIC values ranged from 0.5 and 2.0 IU/ml. The latter group was 5.8% of all patients in 1967, 2.1% in 1968 and 4.5% in 1969.

Table I. *The incidence of gonococcal strains with decreased sensitivity to penicillin (MIC ⩾ 0.2 IU/ml) excluding patients infected abroad*

Period of study		Total	Decreased sensitivity	Per cent	Total	Decreased sensitivity	Per cent
April–June	1967	272	67	24.6	243	57	23.5
July–Sept.	1967	570	94	25.4	346	86	24.9
Oct.–Dec.	1967	318	97	30.5	289	84	28.7
Total	1967	960		Mean 26.9			
Jan.–March	1968	305	65	21.3	288	61	21.2
April–June	1968	356	65	18.3	333	55	16.5
July–Sept.	1968	442	97	22.0	412	87	21.1
Oct.–Dec.	1968	352	83	23.6	331	78	23.6
Total	1968	1455		Mean 21.2			
Jan.–March	1969	322	93	28.9	306	88	28.8
April–June	1969	358	104	29.1	334	92	27.5
Total	1969	680		Mean 29.0			
TOTAL		3095	765	24.7	2882	688	23.9

Table I also illustrates the frequency of gonococcal strains with decreased sensitivity to penicillin for isolated 3 month periods within the period of the overall study. In 1967 the mean proportion of cases with decreased sensitivity was 26.9%, but in 1968 it was 21.2% and in 1969 a rising trend was observed, 29.0%. This trend was marked even when cases infected abroad were excluded.

In the first period of 1967 (April 1 to June 30) 272 patients were examined, 37 (13.6%) of whom showed gonocci with MIC values of 0.5–2.0 IU/ml, while of the remaining 688 patients examined that year only 19 (2.8%) had gonococci with sensitivity to penicillin equally low. Twenty-two (10.3%) of the patients infected abroad and 90 (3.1%) of the patients infected in Finland harborued gonococci with a MIC value of 0.5–2.0 IU/ml.

Table II. *Incidence of gonococcal strains with decreased sensitivity to penicillin (MIC ⩾ 0.2% IU/ml) among patients infected abroad*

Place of infection	Total	No. of those with decreased sensitivity	Per cent
Scandinavia	70	14	20
Eastern Europe	48	16	33
Central and Western Europe	53	21	40
Southern Europe	24	13	54
Outside Europe	18	13	72
Total	213	77	36

In Table II the patients infected abroad are broken down according to the area of the world in which the infection was contracted. Patients infected in Scandinavia showed no higher frequency of gonococci with decreased penicillin sensitivity than those infected in Finland. But those infected in other parts of Europe showed a higher incidence of gonococcal strains with decreased penicillin sensitivity.

CONCLUSIONS

The study reveals that in Finland more than 20% of the gonococcal strains have a decreased penicillin sensitivity. Despite a fall in 1968 the percentage appeared to be growing and by 1969 it had almost reached 30%. The frequency of occurrence should be followed continuously, because routine doses of penicillin must be sufficiently high to cure even those patients harbouring a gonococcal strain with reduced sensitivity to penicillin.

The increasing frequency of occurrence may be the result of a too-low standard dose of penicillin in the past, which allows the relatively insensitive mutants to multiply and disseminate. Because of large variations in individual blood concentrations after identical dosages of penicillin, low blood

concentration of penicillin may permit the growth of relatively insensitive gonococci. The present series shows that in Finland, infections contracted abroad are more often caused by relatively insensitive gonococci, than those contracted in Finland. This may also be a reason for the increasing frequency of strains with diminished sensitivity. For example, from April until June 1967 most of the cases with strains showing MIC values of 0.5–1.0 IU/ml could be traced back to a single source coming from England.

REFERENCES

1. Amies, C. R.: Development of resistance of gonococci to penicillin: an eight-year study. Canad Med Ass J *96*: 33, 1967.
2. Cradock-Watson, J. E., Shooter, R. A. & Nicol, C. S.: Sensitivity of strains of gonococci to penicillin, sulphathiazole, and streptomycin. Brit Med J *1*: 1091, 1958.
3. Curtis, F. R. & Wilkinson, A. E.: A Comparison of the in vitro sensitivity of gonococci to penicillin with the results of treatment. Brit J Vener Dis *34*: 70, 1958.
4. Juhlin, I.: Problems in diagnosis, treatment and control of gonorrhoeal infections. II. Routine sensitivity tests with the plate dilution and disc methods. Acta Dermatovener (Stockholm) *45*: 223, 1965.
5. King, A. J.: "These dying diseases" Venereology in decline? Lancet *1*: 651, 1958.
6. Medical News. Venereal disease escalation. No. 244: June 9, 1967.
7. Rantasalo, I., Salo, O. P. & Wallenius, J. O.: High doses of penicillin in the treatment of gonorrhoea. Results of the causative gonococcal strains. Brit J Vener Dis *40*: 273, 1964.
8. Reyn, A., Korner, B. & Bentzon, M. W.: Effects of penicillin, streptomycin and tetracycline on N. gonorrhoeae isolated in 1944 and in 1957. Brit J Vener Dis *34*: 227, 1958.
9. Reyn, A.: Current problems in the diagnosis and therapy of gonorrhoea from the laboratory point of view. Acta Dermatovener (Stockholm) *43*: 380, 1961.

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ROLITETRACYCLINE BY INJECTION AND TETRACYCLINE PHOSPHATE COMPLEX BY MOUTH GIVEN IN A SINGLE SESSION IN THE TREATMENT OF GONORRHOEA IN MALES

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Abstract. Forty-eight male patients with uncomplicated acute gonorrhoea have been treated with single intramuscular injections of 350 mg of rolitetracycline plus 500 mg of tetracycline phosphate complex by mouth at one session. Of 45 patients followed there were 7 failures, as judged by a history of no further sexual exposure, within three post-treatment months (15.6% of those followed). Three patients (6.6% of those followed) developed Reiter's syndrome within two weeks of treatment. While this may not be significant in view of the size of the series its occurrence or non-occurrence is worthy of noting by other workers who use these drugs. The results obtained in this series are contrasted with those of 18 other personally conducted series using single-session methods. Although somewhat less good than those obtained with penicillin by injection they are in line with those obtained with single oral doses of other tetracyclines or of ampicillin.

With signs of increasing resistance of the gonococcus to penicillin in a number of world areas, and a consequent significant narrowing between the minimum effective dose and the maximum injectable dose of procaine penicillin possible at a single session, and with additional problems posed by the not inconsiderable numbers of patients with a history of penicillin allergy for whom other antibiotics are necessary, there is a continuing need for the investigation of alternative drugs capable of use by single session methods.

The present paper concerns the use of injectable and oral tetracyclines in combination. The injectable tetracycline employed was pyrrolidino methyl tetracycline nitrate (Tetrex PMT)—or rolitetracycline—and the oral preparation, the tetracycline phosphate compleh ("Tetrex").

CASE MATERIAL

The average age of the 48 patients was 25.4 years (extremes 19–41): 16 were married and 32 were single. Six of the patients were West Indian Negroes and of the remainder 31 were born in the United Kingdom, 6 in Pakistan and one each in Cyprus, France, Germany, Italy and Spain.

No previous venereal incident had been experienced by 24 patients but the remainder had had 27 previous attacks of gonorrhoea, 8 of non-gonococcal urethritis and one each of balanitis, herpes genitalis and pediculosis pubis—a total of 38 previous incidents. The six West Indian patients accounted for 5 of these, all of gonorrhoea.

The disease had been present before treatment for 1–3 days in 23 cases, for 4–7 days in 19 and for 8–14 days in 6: all but five patients complained of some dysuria. The apparent incubation period was 1–3 days in 15, 4–7 days in 13, 8–14 days in 11, 15–21 days in 2 and longer than this time in 2: in 5 cases it was unknown. The disease was acquired from a stranger in 25 cases, from a friend in 17, from the wife in 4 and from a male in one, while one patient denied having had sexual intercourse during the previous three months.

The routine Wassermann and VDRL reactions were negative in all cases and the gonococcal complement-fixation test was positive in three and negative in 45.

CASE MANAGEMENT

Diagnosis was established by means of Gram-stained urethral smear in all cases prior to treatment when blood for routine serum tests for syphilis was also taken. The patients were given an intramuscular injection of 350 mg of pyrrolidinomethyl tetracycline nitrate (rolitetracycline —"Tetres PMT") in 2 ml of distilled water plus 500 mg of "Tetrex" tetracycline phosphate complex in one or two capsules in one session by mouth. The patients were subsequently seen 2–5 days later when a further post-treatment smear was made after which they were instructed to attend a week later. It was planned that they should be seen subsequently at two, four, eight and

Table I. *Follow-up and results*

Follow-up	Followed	Satis.	Non-gonococcal urethritis	Reiter's syndrome	Reinfection	Failure
0	48	—	—	—	—	—
1–3 days	45	2	—	1	—	1
4–7 days	41	3	2	1	2	3
8–14 days	32	5	—	1	—	2
15–21 days	22	1	1	—	—	—
22–28 days	20	—	1	—	—	—
1–2 months	19	4	2	—	2	—
2–3 months	13	3	—	—	—	1
More than 3 months	7	5	1	—	1	—
Total	45	23	7	3	5	7

twelve weeks from treatment when the urethra was examined for discharge, a smear being taken if present, and the urine inspected for haze and threads. It was intended also that at least one examination of the prostatic secretion be made during surveillance and a final serum test for syphilis be performed at three months.

Sufficient time has elapsed before writing this report to allow all patients to have been watched for three months but by no means all patients, however, attended at the times instructed.

SIDE EFFECTS

Some patients complained of slight pain for some hours after injection; in one case it was very severe during the first hour and subsequently lasted for two days, but by and large the injection was well tolerated and few patients complained of pain unless specifically asked. No other side effects were noted.

FOLLOW-UP AND RESULTS

The follow-up and results obtained are shown in Table I.

Of 48 patients treated 45 were followed. Of these, six were given additional treatment for non-gonococcal urethritis, within three post-treatment months as were three others who developed Reiter's syndrome. There were also four reinfections within this time and seven treatment failures as judged by a history of no further sexual exposure (15.6 % of those followed).

No adequate criteria exist to distinguish relapse from reinfection apart from a history or absence of same of further sexual exposure. However, if all recurrences regardless of history occurring within one week are regarded as failures, as has been recommended by some authors [e.g. Curtis & Wilkinson (2)], the failure rate would be 13.3 % and if two weeks was chosen the figure of 17.8 % would be obtained.

Of possible interest is that three cases of Reiter's syndrome developed within 2–14 days of treatment, all of whom had a non-gonococcal urethral discharge at the time. One patient subsequently admitted having previously received treatment for iritis and spondylitis on the occasion of an earlier infection but the other two had had no earlier rheumatic disorder. Tetracyclines in higher dosages and other drugs were then given to these patients. In two cases the disease ran a protracted course, admission to hospital being required in one, but ultimately a good recovery was obtained in all. That three patients of the 45 followed (6.6 %) should develop Reiter's syndrome may not be significant in regard to the size of the series but, as its anticipated occurrence in patients treated for gonorrhoea would be 1 % or less, its occurrence or otherwise in other series treated in this way should be noted.

COMPARISON WITH OTHER SINGLE-SESSION METHODS

A comparison is made in Table II of the personal results obtained with other antibiotics using single-session methods.

While the findings of the present series are apparently somewhat less good than those ob-

Table II. *Results compared with other single session procedures*

Antibiotic	Dose	How given	Treated	Followed	Fail	% fail
Penicillins						
Procaine penicillin[a]	2.4 mega units	Injected	280	240	14	5.8
Procaine penicillin[a] (1966–1967)	1.2 mega units	Injected	238	200	17	8.5
Procaine penicillin[b] (1964)	1.2 mega units	Injected	279	207	23	11.1
Ampicillin[b]	0.5–1.0 g	By mouth	200	174	26	14.9
Tetracyclines						
Oxytetracycline[c]	500 mg	Injected	15	14	1	7.1
Tetracycline phosphate[c]	500 mg	Injected	31	23	4	17.4
Tetracycline phosphate[c]	250 mg	Injected	8	7	2	28.0
Oxytetracycline[c]	250 mg	Injected	19	17	5	29.4
Pyrrolidine methyl tetracycline[c]	250 mg	Injected	14	11	4	36.4
Demethylchlor-tetracycline[d]	1.2 g	By mouth	52	46	6	13.0
Limecycline[e]	1.22 g	By mouth	50	43	8	18.6
Demethylchlor-tetracycline[d]	0.9 g	By mouth	33	30	6	20.0
Limecycline[e]	0.816 g	By mouth	25	23	5	21.7
Other antibiotics						
Spiramycin[f]	3–4 g	By mouth	30	25	—	—
Spectinomycin[g]	1.6 g	Injected	151	134	23	9.7
Rifampicin[h]	0.9 g	By mouth	103	84	10	11.9
Spiramycin[f]	2.0 g	By mouth	24	22	6	27.2
Streptomycin[i]	1.0 g	Injected	130	104	33	31.7
This series	See text	By mouth and injection	48	45	7	15.6

[a] Morrison et al. (3). [b] Willcox (7). [c] Willcox (10). [d] Willcox (9). [e] Willcox (8). [f] Willcox (5). [g] Willcox (6). [h] Cobbold et al. (1). [i] Spitzer & Willcox (4).

tained with penicillin by injection, and with those of some other antibiotics, they are in line with previous experience of oral tetracyclines given in a single dose and also of ampicillin administered in this way.

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REFERENCES

1. Cobbold, R. J. C., Morrison, G. D. & Willcox, R. R.: Brit Med J *14* (Dec.), 685, 1968.
2. Curtis, F. R. & Wilkinson, A. E.: Brit J Vener Dis *34:* 70, 1958.
3. Morrison, G. D., Cobbold, R. J. C., Bor, S., Spitzer, R. J., Foster, D. N. & Willcox, R. R.: Brit J Vener Dis *44:* 319, 1968.
4. Spitzer, R. J. & Willcox, R. R.: Acta Dermatovener (Stockholm) *48:* 537, 1968.
5. Willcox, R. R.: Brit J Vener Dis *32:* 117, 1956.
6. — Acta Dermatovener (Stockholm) *43:* 399, 1963.
7. — Postgrad Med J, Suppl. *202*, 1964.
8. — Unpublished data. 1965.
9. — Brit J Vener Dis *43:* 157, 1967.
10. — Current Problems in Dermatology, Antibiotic Treatment of Venereal Diseases (ed. A. Luger), p. 101. Karger, Basel and New York.

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GONORRHOEA IN 1968

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Abstract. An analysis is presented of 756 outpatient cases of gonorrhoea (456 males and 300 females) treated at the Department of Dermatology, Karolinska Sjukhuset, Stockholm, in 1968. The standard treatment was 1.0 megaunit aqueous benzyl penicillin and 1.5 megaunit aqueous procaine penicillin given intramuscularly in a single injection to both males and females. This therapy was given in 670 cases. True recurrence of gonorrhoea after this treatment occurred probably in thirteen cases. Primary curses were obtained in 97.6%. No difference was noted between males and females. The "standard" treatment of penicillin used in this study is still regarded as being satisfactory. The importance is stressed of following possible further changes in the penicillin sensitivity pattern of gonococci and the efficacy of the treatment.

During the last decade several studies have been undertaken of the outpatients attending Karolinska Sjukhuset for gonorrhoea, relating the results of penicillin therapy to the sensitivity of the gonococci to this antibiotic (2, 3, 4, 5). The treatment during this period was increased in dosage from 300,000 units of aqueous procaine penicillin in 1957 to 1.0 megaunits of aqueous benzyl penicillin plus 1.2 megaunits of aqueous procaine penicillin in a single session in 1966, i.e. a sevenfold increase. In 1966 primary cures were obtained with this therapy in 99.1% of the patients. Since then the procaine penicillin therapy component has been increased to 1.5 megaunits. The present report deals with those cases treated during 1968.

CLINICAL MATERIAL

The study comprises all outpatient attending the Dermatology Clinic of Karolinska Sjukhuset during 1968 in whom cultures showed the presence of gonococci. The age distribution of the 456 males and 300 females concerned is presented in Table I. The youngest patients were a boy of fourteen and five girls fifteen years of age. Cases were excluded in which direct microscopy of smears indicated the presence of gonococci, but in which cultures did not confirm the diagnosis—a total of 192 males and 36 females.

The relatively high number of males in the age group 20–24 years relates partly, as in previous reports, to the function of the outpatient clinic as a treatment center for military conscripts in addition to civilians.

METHODS AND PRINCIPLES OF TREATMENT

Direct smears and specimens for culture and gonococcal sensitivity tests were made at each examination from most of the patients. In males specimens were taken from the urethra, in a few cases also from the rectum; in females from the urethra, cervix and rectum.

The smears were stained with methylene blue, in doubtful cases also by the Gram technique, and immediately studied by the examining doctor. The technique of bacterial culture and of sensitivity testing and the criteria used in the bacteriologic diagnosis were the same as in earlier reports (1).

The standard treatment during 1968 was 1.0 megaunits of aqueous benzyl penicillin plus 1.5 megaunits of aqueous procaine penicillin given intramuscularly in a single injection to both males and females. The change from the 1966 therapy was made both to increase the penicillin dosage and for a practical reason, i.e. ease of injection of the whole dosage. The efficacy of the therapy was checked by the weekly examinations. Routine procedure comprised three follow-up examinations in male patients and four in females.

RESULTS

History of previous episodes of gonorrhoea was recorded in 33% of the male and 16% of the female patients (Table II). The time between the occurrence of the first symptoms and the first medical consultation is shown in Table III. The stated interval between presumed exposure to infection and onset of symptoms is summarized in Table IV. It is noted that the interval was estimated as more than three weeks in as many as twenty cases.

Table I. *Age and sex distribution of cases*

	< 20	20–24	25–29	30–40	> 40	Total
Males	44	246	111	46	9	456
Females	105	115	43	23	14	300
Total	149	361	154	69	23	756

The results of cultures compared with microscopy of stained smears are presented in Table V. The sensitivity to penicillin of the gonococci isolated is shown in Table VI. The number of primary cures following the standard treatment is given in the various sensitivity groups. Table VII further identifies the initial treatment and reasons for failure. Complications of gonorrhoea, such as shown in Table VIII, were treated with higher dosage and/or prolonged administration of "standard" penicillin—or other varieties of penicillin combined with other antibiotics. Tetracyclines were given to patients with a history of hypersensitivity to penicillin. Sulphonamide was used in one case in whom coexistent syphilis was suspected. Cases with salpingitis were managed in collaboration with the Gynecology and Obstetric Clinic of the hospital.

The cure rate after a single injection of the indicated therapy among patients with information on strain sensitivity to penicillin was 97.6%. No difference between the sexes was noted.

Only two side-reactions to penicillin therapy were noted (shock and urticaria).

DISCUSSION AND COMMENTS

The aim of the present study was to analyze the results of the gonorrhoea therapy, comparing the composition of the material and the efficacy of treatment.

The primary cure rate in 1968 was 97.6%.

Table II. *Number of previous gonorrhoeal infections*

	0	1	2	3	4	> 4	Not known	Total
Males	250	93	31	8	15	4	55	456
Females	208	42	4	2	0	0	44	300
Total	458	135	35	10	15	4	99	756

Table III. *Number of days between first symptom and first medical consultation*

	No symptoms	1–3	4–7	8–14	15–21	22–28	> 28	Not known	Total
Males	35	181	167	36	2	2	11	17	456
Females	129	15	25	8	4	4	11	96	300
Total	164	196	192	44	6	6	22	113	756

Table IV. *Number of days between presumed exposure to infection and onset of symptoms*

	No symptoms	1–3	4–7	8–14	15–21	22–28	> 28	Not known	Total
Males	35	150	142	57	10	3	5	54	456
Females	129	8	20	14	7	1	11	110	300
Total	164	158	162	71	17	4	16	164	756

Table V. *Results of direct microscopy and culture*

	Pos. culture and pos. smear	Pos. culture and neg. smear	Pos. culture without smear	Total
Urethra				
Males	388	64	4	456
Females	54	121	55	230
Cervix	63	124	66	253
Rectum				
Males	0	7	0	7
Females	8	116	25	149

Table VI. *Sensitivity of gonococci to penicillin: first positive culture*

	Minimum inhibitory concentration u. penicillin/ml serum			Culture positive but no sensitivity test	Total
	< 0.1	0.1–1.0	> 1.0		
Males					
Total	389	53	3	11	456
Primary cure with standard treatment	286	32	1	5	324
Females					
Total	243	33	0	24	300
Primary cure with standard treatment	178	18	0	15	211
Probable true recurrence					
Males	4	4	1	0	9
Females	1	3	0	0	4
Total	5	7	1	0	13

This is not significantly lower than that obtained in 1966, i.e. 99.1 %.

All cases considered as being probable true recurrences had positive cultures on control examination one to two weeks after the initial treatment. All denied repeated coitus. In another nine cases (eight males and one female) direct smear microscopy was found to be positive but the culture did not confirm the diagnosis. In twenty-two repeated cases, coitus had occurred and reinfection rather than recurrence was regarded as probable.

A rise in frequency of gonorrhoea in the region of Stockholm has taken place during the recent years. The number of patients treated for gonor-

Table VII. *Initial treatment of gonorrhoea and failure to respond*

	♂	♀	Total
1. Standard treatment	411	259	670
Primary cure	324	211	535
Reinfection during follow up	11	11	22
Probable true recurrence	9	4	13
Defaulter from follow up	59	32	91
2. Other reatment	45	41	86
Other doses or variety of penicillin	24	32	
Tetracycline	21	8	
Sulphonamide	0	1	

Table VIII. *Complications of gonorrhoea*

	♂	♀
Arthritis	4	2
Bartholonitis	—	1
Epididymitis	8	—
Proctitis (with clinical symptoms)	1	1
Prostatitis	3	—
Salpingitis	—	17
Urethral abscessus	1	—
Total	17	21

rhoea at the Karolinska Sjukhuset during 1968 is greater than in earlier studies. However, the twofold increase in patients from 1966 to 1968 is probably also a result of improved facilities for taking care of the venereal patients at the clinic.

As in earlier materials a number of patients were foreigners with language difficulties. This may to some degree explain the several "unknowns" in Tables II and III and IV.

The group of defaulters in the follow-up is large, namely 14% in males and 12% in the females. This high rate is probably due to the complex circumstances in large cities, but makes appraisal of therapy results more difficult.

A high frequency of positive cultures in female specimens taken from rectum, 50% is notable. The findings agree with other studies, i.e. by Scott & Stone (6) who found 42%. At the Karolinska Sjukhuset the 1966 figure was 29%. This increase is, at least in part, explained by improved facilities for culturing of gonococci at the bacteriological laboratory. All males with positive rectal cultures were homosexual.

The number of gonococcal strains with decreased penicillin sensitivity has increased in the reports from the clinic, i.e. 1962 (4), 1964 (5) and 1966 (3). In the present material (1968) there is no significant change in sensitivity as compared with 1966.

The penicillin dosage schedule recommended as "standard" treatment for acute gonorrhoea in Sweden has apparently given slightly less favourable results compared with those reported from 1966. Nor further increase of the dosage has been regarded as necessary. Nor does this study support the necessity for higher doses of penicillin given to females. However, it is of great importance to follow carefully the changes of penicillin sensitivity of gonococci and the efficacy of the treatment recommended.

REFERENCES

1. Ericsson, H.: Rational use of antibiotics in hospitals. Scand J Clin Lab Invest *12:* Suppl. *50,* 1960.
2. Gentele, H., Lodin, A. & Rosengren, S.: Gonorrhoea in man: a 3-year outpatient serie. Acta Dermatovener (Stockholm) *40:* 386, 1960.
3. Gip, L., Lodin, A., Molin, L. & Nyström, B.: Gonorrhoea in 1966. Acta Dermatovener (Stockholm) *48:* 272, 1968.
4. Lodin, A., Nyström, B. & Rosengren, S.: Gonorrhoea in 1962. Acta Dermatovener (Stockholm) *44:* 127, 1964.
5. Lodin, A., Nyström, B. & Stigell, P. O.: Gonorrhoea in 1964. Acta Dermatovener (Stockholm) *46:* 245, 1966.
6. Scott, J. & Stone, A. H.: Some observations on the diagnosis of rectal gonorrhoea in both sexes using a selective culture medium. Brit J Vener Dis *42:* 103, 1966.

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