# MEDICAL GRAND ROUNDS Parkland Memorial Hospital April 12, 1973

## **VENEREAL DISEASES:** NO LONGER JUST AN OCCUPATIONAL HAZARD

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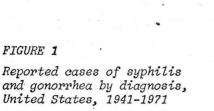
## MAGNITUDE OF THE PROBLEM

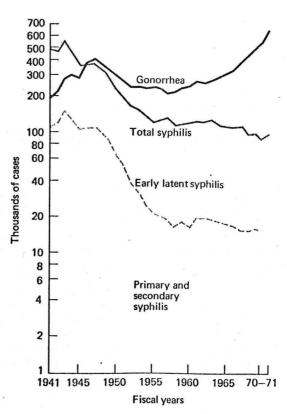
FIGURE 1

United States, 1941-1971

Gonorrhea is the commonest reportable infectious disease in the United States with syphilis holding a strong fourth place behind streptococcal disease and mumps. In 1971 some 625,000 cases of gonorrhea (~ 300 cases/100,000 persons), 24,000 cases of infectious syphilis and 71,000 cases of noninfectious syphilis were reported (1-4).

While there has been a steady increase in the number of cases of gonococcal infection since 1960, the prevalence of syphilis has remained relatively stable during the same period (Figure 1).





Because of inadequacies of reporting procedures, a more appropriate estimate would suggest that some 2 million cases of gonorrhea and 80,000 cases of infectious syphilis actually occurred during 1971 (5). Best estimates indicate that during 1972 there were 100,000 new cases of infectious syphilis and a record 2.5 million new cases of gonorrhea.

TABLE 1

REPORTING OF VENEREAL DISEASES, 1968

	Infectious Syphilis	''Other'' Syphilis	Gonorrhea
Number of cases treated and reported by public sources:	12,953	32,714	307,624
Number of cases treated and reported by private physicians:	7,229	45,299	123,756
Number of cases treated but not reported by private physicians (total estimated treated less total reported by them):	55,025	93,931	1,018,201
Estimated total number of cases treated during fiscal 1968 by all	25,425	32,33.	,,010,201
sources:	75,207	171,944	1,449,581

On a per capita basis in 1971, Texas ranked seventh in the nation in total reported venereal diseases, and of major cities, Dallas ranked fifth in cases of infectious syphilis and eleventh in gonorrhea (3).

Explanations for the recent increase in the major venereal diseases are speculative at best. The fact that there are more susceptibles probably contributes little; between 1956 and 1968, the population of the United States increased some 20%. During the same period, the number of reported cases of gonorrhea increased by 107%. Increased mobility of the population, changes in social mores, and the availability of the pill are intangible considerations. Treponema pallidum has retained its susceptibility to penicillin; contribution by the modest relative increase in resistance of N. gonorrhea to antibiotics is a consideration impossible to quantify. Epidemiological studies suggest that history of contact with a prostitute is obtained in 8 to 13% of persons with infectious syphilis and homosexual contact in 11 to 15% of cases; these figures have remained relatively stable for the past several years and would seem not to contribute significantly to the current "epidemic". Inadequate reporting and poor epidemiological followup of contacts probably are the most important factors in sustaining the diseases.

Age, sex, race and urbanization are important determinants in the distribution of the venereal diseases. Ninety-five per cent of persons with syphilis and 98% of those with gonorrhea acquire the diseases between the ages of 15 and 50.

TABLE 2

CIVILIAN CASES AND RATES OF PRIMARY AND SECONDARY SYPHILIS AND GONORRHEA PER 100,000 POPULATION BY AGE, COLOR, SEX, AND URBANIZATION, UNITED STATES, CALENDAR YEAR 1970

Population Group		Primary and Secondary Syphilis		Gonorrhea	
	Cases	Rate	Cases	Rate	
Age .					
0-14	254	0.4	7,515	12.5	
15-19	3,651	20.0	147,952	808.6	
20-24	6,213	41.9	239,466	1615.5	
25-29	4,424	34.0	110,001	845.6	
30-39 40-49	4,808	21.7	69,517	313.6	
50+	1,866 766	7.7 1.6	19,267 6,354	79.1 12.9	
2	-			-	
Total	21.982	10.9	600,072	297.5	
Color					
White	5,703	3.2	206,892	117.0	
Other	16,279	65.5	393,180	1581.6	
Total	21,982	10.5	600,072	297.5	
Sex	*				
Male	14,531	14.9	436,812	449.1	
Female	7,451	7.1	163,620	156.3	
Total	21,982	10.9	600,072	297.5	
Urbanization		¥.,			
Cities over 200,000 population	13,891	24.5	375,586	662.6	
50,000-200,000 population	3,445	10.3	113,099	336.9	
Smaller towns and rural	4,646	4.1	111,387	98.7	
Total	21,982	10.8	600,072	295.5	

### **GONORRHEA**

# Clinical Features and Treatment

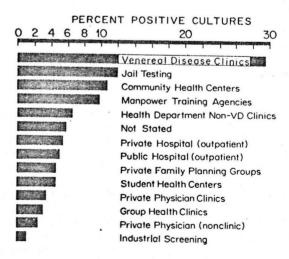
The commonest form of gonorrhea infection is probably an asymptomatic infestation, particularly in women (6-13).

TABLE 3
GROUPS EXAMINED FOR ASYMPTOMATIC GONORRHEA

Groups Examined	Total	No. of Patients Asymptomatic	Percentage of Patients Asymptomatic With Gonorrhea
Female sex partners of known gonorrhea patients	211	211	36
Male sex partners of known gonorrhea patients ·	115	98	26
Female prisoners, new admissions	213	213	21
Male volunteers to venereal disease clinic	86	22	14
Female attending obstetric clinic	1,309	1,309	6
Male prisoners, new admissions	1,061	1,061	1
Males in military population	505	505	0.2

### FIGURE 2

Diagnostic screening of females for infection, reported by type of facility performing tests. Results are based on 511,316 cervical cultures from July 1968 through September 1970.



Of women found to have a positive culture on any occasion, 94% will have a positive culture one week later unless treatment is given (9); thus, the asymptomatic carrier serves as an important reservoir for transmission of the disease.

Holmes et al. in a study of 2100 servicemen after a 6-day leave in the Philippines where the prevalence of infection in women was 19.7% observed 88 cases of gonorrhea after the men returned to their ship. By epidemiological means, he estimated the risk factor of a single exposure to an infected woman to be approximately 22% (14). Thus, efforts at control of gonorrhea would reasonably include seeking out the sustaining reservoir by screening on each opportunity. Unfortunately, the definitive diagnosis of gonococcal infection in any form is still dependent upon demonstrating the organism by culture (15). Productivity of various culture sites is shown in the following two tables (9):

TABLE 4

DISTRIBUTION OF PATIENTS WITH POSITIVE CULTURES
AS ANALYZED BY CULTURE SITE

Site Cultured	Visit 1 (%)	Visit 2 (%)
Cervix	105 (93.8)	83 (88.8)
Rectum	55 (49.1)	54 (57.4)
Urethra	87 (77.7)	67 (71.3)
Vagina	87 (77.7)	77 (81.9)

TABLE 5 .

DISTRIBUTION OF PATIENTS WITH POSITIVE CULTURES
WHEN RESULTS OF TWO CULTURE SITES ARE TOTALED

Visit 1 (%)	Visit 2 (%)
112 (100)	90 (95.7)
104 (93.8)	86 (91.5)
105 (93.8)	89 (94.7)
96 (85.7)	78 (82.3)
99 (88.4)	87 (92.6)
95 (84.8)	81 (86.2)
	112 (100) 104 (93.8) 105 (93.8) 96 (85.7) 99 (88.4)

Unfortunately, in their current state of development, neither immuno-fluorescent studies looking for the organism in secretions nor serologic studies designed to detect antibody within serum dependably add to one's ability to detect gonococcal infection. Enthusiasm for the improvement of value of these techniques relates to the relatively recent observation that there are at least four colony types of N. gonorrheae with types 1 and 2 being pathogenic and 3 and 4 being nonpathogenic. The pathogenic potential apparently relates to the presence of pili which can be extracted from the cell wall proper. Pili have been shown capable of evoking an immune response when injected into volunteers and there is provocative evidence that their antigen specificity might enable the detection of antigonococcal antibody in the infected patient (15-23).

## Extragenital Manifestations of Gonococcal Infection

The commonest extragenital expression of gonococcal infection is arthritis or tenosynovitis, presumably resulting from bloodstream invasion from an anogenital or pharyngeal source. Whereas in the pre-antibiotic era these manifestations were most commonly seen in men, for the past several years some 70 to 80% of recognized cases occur in women. This change in sex distribution is logically presumed to be due to the fact that women are more likely to harbor predisposing asymptomatic urogenital infections than are men. Additionally, there is the empirical observation that pregnancy and puerperium predispose to the dissemination of the asymptomatic carrier state.

TABLE 6

RELATIONSHIP OF PREGNANCY AND OF WEEK OF MENSTRUAL CYCLE
TO DISSEMINATION OF GONOCOCCAL INFECTION IN 33 WOMEN

Status at Onset of Symptoms	Number of Women
Pregnant or puerperium	9
Nonpregnant, time in cycle: Day 1-7	14
Day 8-14 Day 15-21	3
Day 22-28 More than 28 days	- <b>3</b>
Total	33

The clinical manifestations in one large series of disseminated gonococcal infection are shown in the following table:

TABLE 7

MAJOR MANIFESTATION OF DISSEMINATED GONOCOCCAL INFECTION IN 42 PATIENTS; UNIVERSITY OF WASHINGTON HOSPITALS, 1960-1970

Manifestation	Number of Patients
Gonococcal arthritis	35
Gonococcal meningitis	2
Gonococcal endocarditis	2
Gonococcal bacteremia without arthritis	2
Gonococcal pericarditis	1
Total	42

TABLE 8

CLINICAL AND BACTERIOLOGICAL FEATURES OF SEQUENTIAL STAGES
OF GONOCOCCAL ARTHRITIS IN 37 PATIENTS

		Median	Number	Isola	tion of N.	gonorrheae
	Number of Patients	Number of Days With Symptoms	With Typical Dermatitis	Blood	Synovial Fluid	Anogenital
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Bacteremic stage	23	3	21	11	2	21
Septic joint stage	8	8	0	0	5	4
Indeterminate	6	4	0	0	0	6

Only approximately one-third of patients presenting with a clinical picture enabling a presumptive diagnosis of gonococcal arthritis and who subsequently respond to therapy will demonstrate viable neisseriae in joint or synovial fluid. Holmes (28) accounts for this observation on the basis of the probability that cell wall defective organisms or protoplasts exist within the fluid and that culturing the specimen on osmotically supported medium would increase the yield of positive cultures (23-29).

A more recently recognized extragenital site of infection with the gonococcus is the oral-pharyngeal area, particularly in homosexual people (30-34).

TABLE 9

PREVALENCE OF PHARYNGEAL GONOCOCCAL INFECTION
IN 2224 VENEREAL DISEASES CLINIC PATIENTS

Category	No. Examined	No. Infected (All Sites)	No. With Pharyngeal Infection
Men:			
Heterosexual men	217	95	3 (1.4%)*( 3.2%)*
Homosexual men	143	67	14 (9.8%) (20.9%)
Women:			
11/70-3/71	538	310	32 (6.0%) (10.3%)
3/71-9/71	1,326	400	76 (5.7%) (19.0%)
Totals	2,224	872	125 (5.6%) (14.3%)

<sup>\* %</sup> of number examined

<sup>\* %</sup> of number infected

TABLE 10

ABSENCE OF CORRELATION OF GONOCOCCAL PHARYNGEAL INFECTION
WITH COMPLAINT OF SORE THROAT AMONG INFECTED WOMEN AND
HOMOSEXUAL MEN WHO PRACTICED FELLATIO

Category	No. Examined	No. Infected (All Sites)	No. With Pharyngeal Infection	No. With Pharyngeal Infection Only
Females: with sore throat without sore throat	293 904	101 260	23 (23%) 51 (20%)	5 (5.0%)* 5 (1.9%)
Homosexuals: with sore throat without sore throat	<b>32</b> 88	14 49	4 (29%) 10 (20%)	1 (7.1%) 4 (8.2%)

<sup>\*</sup> % of number infected

In addition to asymptomatic colonization of the rectum in both males and females, there has been at least one well documented case of ulcerative proctitis due to infection with the gonococcus (35).

#### Treatment of Gonorrheal Disease

The problem of increased resistance (36-43): Although the gonococcus remains susceptible to doses of penicillin which can be easily accomplished, the trend toward relative resistance has been associated with an increasing failure rate of low-dose one-shot therapy. There is excellent correlation between the minimum inhibitory concentration of penicillin against the organism and the failure rate.

TABLE 11

FAILURE RATES AFTER THERAPY WITH 5 MILLION UNITS AQUEOUS PENICILLIN PLUS PROBENECID RELATED TO MIC (PENICILLIN) OF INFECTING STRAINS

MIC	(u/ml)	No. Treated	No. Followed	Cured	Failed	Reinfection	Per Cent Fail
>2.	7	 13	12	8	4	0	33
0.1	17-2.7	69	67	59	5	3	8
<0.		244	230	221	2	7	1
		326	309	288	1.1	10	3.7

The trend toward relative resistance is most marked in Southeast Asia and the Philippines, but has been noted to a modest degree in the United States.

TABLE 12

PENICILLIN SENSITIVITY OF GONOCOCCI FROM DIFFERENT REGIONS OF THE WORLD

Area	Year	No. of Strains	Per Cei	nt Strains W (units/ml)	ith MIC		
		00141113	<0.10 0.10-0.50 >0.				
USA ·	1950-55	771	99	1	0		
USA	1965	1124	58	37	5		
USA	1968-69	649	35	51	14		
Sweden	1968	335	86	8	6		
England	1968-69	95	38	62	0		
Canada	1967	1916	35	47	19		
India	1968-69	216	33	46	21		
Philippines	1968-69	179	11	45	47		
Japan	1968-69	33	0	42	58		
Uganda	1968	173	19	24	57		

Prior to 1955, only 0.6% of isolates from the United States required more than 0.05 units/ml of penicillin to inhibit the organism; by 1969, this group had increased to 65% of the isolates.

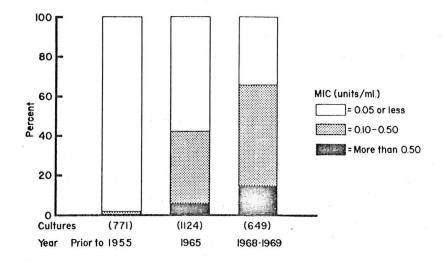


FIGURE 3

Penicillin susceptibility of cultures of N. gonorrheae obtained from routine clinic patients

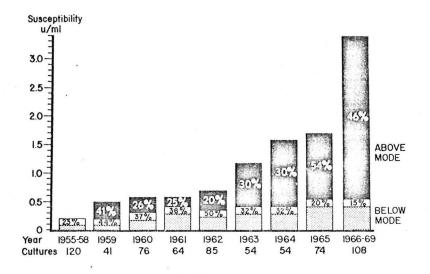


FIGURE 4

Penicillin susceptibility of cultures of N. gonorrheae obtained from treatment failure patients

<u>Selection of program</u>: A large number of therapeutic regimens have been evaluated in uncomplicated genital gonorrhea (44-62). A partial list of observations is shown in the following table:

TABLE 13

EFFICACY OF TREATMENT OF GONORRHEA (MALE)

Program	No. Cases	Failure Rate (%)	Author
Procaine penicillin 2-4 mu	63*	28	Holmes
Procaine penicillin 2.4 mu + probenecid	391	.2.4	Holmes
Ampicillin 2 gm + probenecid	106*	0.9	Keys
Ampicillin 2 gm + probenecid	500	1.2	Gunderson
Kanamycin 2 gm	63	4.6	Farrell
Cephaloridine 2 gm	97	16.5	Keys
Cephaloridine 2 gm	84	2.4	Lucas
Spectinomycin 2 gm	121	9.8	Duncan
4 gm	122	7.1	
Tetracycline 9.5 gm	530	1.9	Holmes
Methacycline 600 mg	97	14.7	McLone
900 mg	95	12.9	
1.2 gm	97	3.6	

<sup>\*</sup> Pacific cases

The program currently recommended by the Center for Disease Control is as follows: Uncomplicated gonorrhea in man or woman: Aqueous procaine penicillin G, 4.8 million units intramuscularly, preceded by 1 gm of oral Probenecid. If oral therapy is elected, ampicillin 3 gm with Probenecid 1 gm administered simultaneously. If penicillin is contraindicated, spectinomycin is the recommended alternate drug, to be given in men in a dose of 2 gm in one intramuscular injection and in women 4 gm in one intramuscular injection. If oral therapy is elected, in men or women, tetracycline 1.5 gm initially followed by 0.5 gm 4 times a day for four days. For complications such as salpingitis, bacteremia or arthritis, large doses of penicillin are recommended. Our current and effective program involves 4.6 million units per day for a period of 10 days. However, preliminary studies being done at Parkland at present indicate that cures of gonococcal arthritis can be accomplished by the administration of 10 million units of penicillin per day, for a 3-day period.

It should be noted that while spectinomycin is effective against all gonococci relatively resistant to penicillin, the drug will not treat syphilis which might be in the incubating stage and therefore occult. This desirable feature is accomplished by penicillin (62).

## SYPHILIS

## Morbidity of Untreated Syphilis (63-66)

The controversial Tuskegee study serves as the best available source of information about the natural history of untreated lues. At the outset, 412 persons with syphilis and 192 controls were involved and the survivors were followed some 30 years. In first published report in 1936, the luetic persons under 40 had approximately 4 times the morbidity found in age-matched controls. Luetic involvement of cardiovascular system, CNS, and skeletal systems accounted for the difference  $(\theta 3)$ .

In the most recent evaluation the differences between groups (based on mortality) had lessened, presumably because of infirmities accruent to advancing age.

TABLE 14

CURRENT STATUS OF TUSKEGEE STUDY GROUP OF ORIGINAL 412 SYPHILITICS AND 192 CONTROLS

	Dead		Alive		Unknown	
	No.	%	No.	%	No.	%
Syphilitics	242	58.7	85	20.6	85	20.6
Controls	87	45.3	66	34.4	39	20.3

Based on the observations from the Tuskegee studies and those of Brunsgaard (64) and Rosah (65), an interesting epidemiological evaluation was made by Moore (66).

He estimated the consequences of untreated lues as follows:

Mortality 3000/year Blindness 1/200 Heart disease 1/13 Some associated incapacity 1/25

If one accepts a prevalence of 1.2 million untreated luetics, one can project a prevalence of 25,000 potential paretics, 6000 blind, 23,000 with taboparesis and 90 thousand with heart disease. Economic maintenance of the blind was estimated at \$6 million per year and the mentally defective at \$50 million per year. If one accepts a life expectancy of 10 years in the latter group, a debt of \$0.5 billion is accrued.

Fortunately, the incidence of latent lues is slowly diminishing, perhaps as a consequence of inadvertent treatment of early disease through antibiotic therapy directed at burgeoning gonorrhea or other infections.

## Serological Diagnosis of Syphilis (67-88)

The diagnosis of primary syphilis is best established by darkfield examination of suspicious lesions. Secondary syphilis is frequently clinically characteristic enough to make a strong presumptive diagnosis, but serological support is expected. In evaluation of latent lues one is entirely dependent upon serological evaluation since history of past contacts and/or lesions are of little benefit and physical findings are characteristically absent.

The tests used currently are of two antigenic types: flocculation tests using nonspecific cardiolipin antigens and treponemal tests using  $\underline{\mathsf{T}}$ .  $\underline{\mathsf{pallidum}}$  as the antigen. The VDRL and Kolmer are prototypes of the former and the  $\overline{\mathsf{TPl}}$  ( $\underline{\mathsf{Treponema}}$   $\underline{\mathsf{pallidum}}$   $\underline{\mathsf{immobilization}}$ ) and  $\underline{\mathsf{FTA-Abs}}$   $\underline{\mathsf{prototypes}}$  of the latter.

The relative sensitivity of the various tests is shown in the following table (67):

TABLE 15

REACTIVITY OF VDRL, FTA-ABS AND TPI TESTS
DURING VARIOUS STAGES OF SYPHILIS

	No. Tested	% Reactive			
Category		FTA-Abs Test	TPI Test	VDRL Test	
Primary syphilis	191	85	56	78.	
Secondary syphilis	270	99	94	97	
Late syphilis	117	95	92	77	
Latent syphilis	954	95	94	74	
Presumably normal	384		0	0	

Thus, the FTA-Abs test seems the most sensitive test currently available. Its durability in chronic infection is supported in the following table:

TABLE 16

Reference	Patients	Duration of Disease	% Positive		
		or Time After Therapy	VDRL	TPI	FTA-Abs
67	Lues without therapy	30 years	66	91	97
72	Latent lues + penicillin CNS lues + penicillin	10 years 10 years	60 60	81 91	92 96
71	Late lues + penicillin	13 years	78	90	98

Since the FTA-Abs is the most sensitive test for syphilis, there is no mechanism by which the rate of occurrence of false negative can be precisely quantitated. In a serological study of 250 lifelong celibates, all had negative VDRL tests, 3 had positive FTA-Abs and one had a weakly reactive TPI. These observations led to the conclusion that fewer than 1% of normal persons had BFP FTA-Abs (79). If one accepts that a BFP FTA-Abs can be defined as a patient without clinical evidence of lues, a positive FTA-Abs, negative TPI and VDRL, there is increasing evidence of this spurious finding in persons having underlying disease predisposing to abnormal globulins, i.e., cirrhosis, rheumatoid arthritis, lupus, etc. (80-83).

## FTA-Abs in Evaluation of CNS Syphilis (84-88)

It is well recognized that patients with a neurological syndrome can have a positive VDRL in the CSF and a negative serum VDRL (5% PMH series). A pertinent question involves the patient with a neurological syndrome consistent with meningovascular lues with a positive serum serology (FTA-Abs and/or VDRL) and a negative CSF VDRL. In view of the possibility that the VDRL is as insensitive in the CSF as it is in serum, there are continuing efforts to evaluate the efficacy of a form of the FTA-Abs in determining whether luetic CNS infection is present. Studies to date, using the TPI test and clinical status of the patient as markers, have shown the FTA to swing heavily in the direction of falsely negative and falsely positive. Until the test can be sophisticated, the CSF VDRL should be considered the best serological test and one should give consideration to empirical therapy to a patient with clinical evidence of inflammatory CNS disease, a positive serum serology, a negative CSF serology and no definitive diagnosis.

#### Treatment of Syphilis (89-114)

Penicillin is clearly the drug of choice in all forms of syphilis and its efficacy approaches 100% in primary and secondary stages of the disease. All other drugs which have been studied sufficiently to evaluate their efficacy have varying failure rates; thus, clinical and serological followup is essential in patients treated with alternate drugs because of penicillin sensitivity.

The efficacy of any form of therapy against latent lues is difficult to evaluate since seroconversion occurs with similar frequency in treated and untreated groups.

Relapse of central nervous system lues is seen with disappointing frequency in the programs thus far evaluated.

TABLE 17

FAILURE OF THERAPY OF NEUROSYPHILIS

lumber of Therapy		Failure Rate	
26	BPG 4.8 mu	8%	
298	2.4-4.0 mu aqueous penicillin	10%	
	Repository penicillin 9 mu	10%	
112	Repository penicillin 4.8 mu	9%	
756	Penicillin 2.4-9 mu	9.5%	
47	BPG 2.4 mu	24%	
53	Repository penicillin 4-5 mu	16%	

Adapted from Short (92)

There are several reports (107-114) of spirochete-like organisms isolated from the CSF and/or from aqueous humor obtained from patients having undergone prolonged penicillin therapy. Whether these are indeed  $\underline{\text{T. pallidum}}$ , non-pathogenic "contaminants" or artifacts is actively being argued by two offsetting groups.

#### RECOMMENDED PROGRAMS OF THERAPY FOR SYPHILIS - USPHS

## Primary, Secondary Syphilis

Rx: Benzathine penicillin G - 2.4 million units total (1.2 million units in each buttock) by intramuscular injection

or: PAM - 4.8 million units total usually given 2.4 million units at first session, as above, and 1.2 million units at each of two subsequent injections 3 days apart

or: Aqueous procaine penicillin G - 600,000 units daily for 8 days to total 4.8 million units

#### Latent Syphilis

Rx: Benzathine penicillin G - If no spinal fluid examination is done, treatment must encompass the possibility of asymptomatic neurosyphilis. In this case, 6.0-9.0 million units total, given 3.0 million units (1.5 in each buttock each session) at 7-day interval. With nonreactive spinal fluid examination, 2.4 million units (as primary).

or: PAM - Aqueous penicillin G - Same as primary syphilis

## Late Syphilis

Asymptomatic neurosyphilis Symptomatic neurosyphilis Cardiovascular syphilis

Late benign (cutaneous, osseous, and visceral gumma) syphilis

Rx: Benzathine penicillin G - 6.0 to 9.0 million units total, given 3.0 million units at 7-day intervals

or: PAM - 6.0-9.0 million units total, given 1.2 million units at 3-day intervals

or: Aqueous procaine penicillin G - 6.0-9.0 million units total, given 600,000 units daily

Any benefit from more than 10 million units has not been demonstrated.

## Syphilis in Pregnancy

Syphilis in pregnancy should be managed in the same manner as with any non-pregnant patient. Urgency of treatment is the keynote to therapy.

## Alternate Antibiotics

When sensitivity precludes use of penicillin, erythromycin and tetracycline are the best alternate drugs. Recommended dosage orally is  $30-40~\rm gm$  of erythromycin and  $30-40~\rm gm$  of tetracycline given over a period of  $10-15~\rm days$ .

Treatment with such alternate antibiotics must be accompanied by close followup of the syphilitic patient since none of these drugs has had adequate evaluation in all stages of syphilis. Spinal fluid examinations must be done as part of followup after this type of therapy.

### Preventive Treatment

If the patient is known to have been exposed to lesion syphilis, it is a fallacy to wait for the disease to develop to the clinical or reactive serologic stage, meanwhile allowing reinfection of treated patients and the infection of additional persons. However, every effort should be made to arrive at a diagnosis, including a complete physical examination, before administering preventive treatment.

Adequate preventive treatment may consist of 2.4 million units of benzathine penicillin G.

#### CASE REPORT

The patient is a 77-year-old woman with longstanding mild diabetes mellitus who was admitted with a 3- to 4-month history of decreasing mental acuity and increased difficulty in getting about and caring for herself. For several weeks there had been progressive mental deterioration to the point of total confusion. Urinary and fecal incontinence developed shortly prior to admission. It is of note that the patient was found to have a positive peripheral serology some four months prior to admission and for that was treated with 7.2 million units of Bicillin. No CSF evaluation was done prior to therapy.

On admission, she had normal vital signs. She was confused in all spheres. Whether her inability to walk was secondary to peripheral muscular weakness or failure of cortical function could not be ascertained. A lumbar puncture revealed 420 leucocytes which were 96% mononuclear, a protein of 115 mg.%, and a glucose of 456 mg.% with a concomitant blood glucose of 122 mg.%. The peripheral serology (VDRL) was non-reactive, but the CSF Wasserman was reactive to 64 dilutions. She was treated with procaine penicillin 1.2 million units daily for 12 days and in the face of that program became alert, oriented and appropriately responsive. Neurological exam done after she regained her mental faculties revealed no evidence of posterior column disease. She did manifest difficulty in abstract thinking. At the time of discharge, she was regaining her ability to walk alone. When last seen in clinic some five months after her hospitalization, she was alert and able to care for herself.

#### REFERENCES

- Sexually transmitted diseases. Extract from the Annual Report of the Chief Medical Officer to the Department of Health and Social Security for the year 1970. Brit. J. Ven. Dis. 48:313, 1972.
- Internal Medicine at large: VD climb continues. Arch. Int. Med. 130:14, 1972.
- Lucas, J. B.: The national venereal disease problem. Med. Clin. No. Amer. 56:1073, 1972.
- 4. Today's VD Control Problem. A Joint Statement by the American Public Health Association.
- 5. Fleming, W. L., et al.: National survey of venereal disease treated by physicians in 1968. JAMA 211:1827, 1970.
- 6. Hart, M.: Gonorrhea in women. JAMA 216:1609, 1971.
- 7. Thatcher, R. W., et al.: Asymptomatic gonorrhea. JAMA 210:315, 1969.
- Pariser, H., and Farmer, A. D.: Diagnosis of gonorrhea in the asymptomatic female: Comparison of slide and culture technics. South. Med. J. 61:505, 1968.
- 9. Schmale, J. D., et al.: Observations on the culture diagnosis of gonorrhea in women. JAMA 210:312, 1969.
- 10. Cave, V. G., et al.: Gonorrhea in the obstetric and gynecologic clinic. Incidence in a voluntary hospital in an urban community. JAMA 210:309, 1969.
- 11. Ackerman, A. B., and Calabria, R.: Asymptomatic gonorrhea, the gonococcal carrier state, and gonococcemia in man. JAMA 196:221, 1966.
- 12. Sarrel, P. M., and Pruett, K. A.: Symptomatic gonorrhea during pregnancy. Obst. & Gyn. 32:670, 1968.
- 13. Schroeter, A. L., and Pazin, G. J.: Gonorrhea. Ann. Int. Med. 72:553, 1970.
- 14. Holmes, K. K., et at.: An estimate of the risk of men acquiring gonorrhea by sexual contact with infected females. Am. J. Epidem. 91:170, 1970.
- 15. Schroeter, A. L., and Lucas, J. B.: Gonorrhea. Diagnosis and treatment. Obst. & Gyn. 39:274, 1972.
- 15A Serologic detection of gonorrhea [Editorial]. Ann. Int. Med. 72:594, 1970.
- 16. Welch, B. G., and O'Reilly, R. J.: An indirect fluorescent-antibody technique for study of uncomplicated gonorrhea. I. Methodology. J. Inf. Dis. 127:69, 1973.
- 17. Kellogg, D. S., et al.: Neisseria gonorrhoeae. 1. Virulence genetically linked to clonal variation. J. Bacteriol. 85:1274, 1963.

- 18. Kellogg, D. S., et al.: Neisseria gonorrhoeae. II. Colonial variation and pathogenicity during 35 months in vitro. J. Bacteriol. 48:596, 1968.
- 19. Ward, M. E., and Watt, P. J.: Adherence of N. gonorrhea to urethral mucosal cells: an electron-microscopic study of human gonorrhea. J. Inf. Dis. 126: 601, 1972.
- 20. Jephcott, A. E., and Reyn, A.: Neisseria gonorrhoeae. Colony variation 1. Acta Path. Microbiol. Scand. 79:609, 1971.
- 21. Swanson, J., et al.: Studies on gonococcus infection. I. Pili and zones of adhesion: Their relation to gonococcal growth patterns. J. Exp. Med. 134: 886, 1971.
- 22. Buchanan, T. M., et al.: Antibody response to gonococcal pili in patients with gonorrhea. [Abstract]
- 23. VD Meeting: How close is an anti-gonococcal vaccine? [Editorial]. Hosp. Practice, p 35, August 1972.
- 23A Graber, W. J., Sanford, J. P., and Ziff, M.: Sex incidence of gonococcal arthritis. Arth. & Rheum. 3:309, 1960.
- 24. Holmes, K. K., et al.: Disseminated gonococcal infection. Ann. Int. Med. 74:979, 1971.
- 25. Partain, J. O., et al.: Arthritis associated with gonorrhea. Ann. Rheum. Dis. 27:156, 1968.
- Cooke, C. L., et al.: Gonococcal arthritis. A survey of 54 cases. JAMA 217: 204, 1971.
- 27. Fink, C. W.: Gonococcal arthritis in children. JAMA 194:387, 1965.
- 28. Hormes, K. K., et al.: Recovery of Neisseria gonorrhoeae from "sterile" synovial fluid in gonococcal arthritis. New Eng. J. Med. 11:318, 1971.
- 29. Metzger, A. L.: Gonococcal arthritis complicating gonococcal pharyngitis. Ann. Int. Med. 73:267, 1970.
- 30. Weisner, P. J., et al.: Clinical spectrum of oropharyngeal gonococcal infections. New Eng. J. Med. 288:131, 1973.
- 31. Owen, R. L., and Hill, J. L.: Rectal and pharyngeal gonorrhea in homosexual men. JAMA 220:1375, 1972.
- 32. Weisner, P. J., et al.: Clinical spectrum of pharyngeal gonococcal infections. New Eng. J. Med. 288:181, 1973.
- 33. Fiumara, N. J., et al.: Gonorrheal pharyngitis. New Eng. J. Med. 276:1248, 1967.
- 34. Cowan, L.: Gonococcal ulceration of the tongue in the gonococcal dermatitis syndrome. Brit. J. Ven. Dis. 45:228, 1969.

- 35. Kilpatrick, Z. M.: Gonococcal proctitis. New Eng. J. Med. 287:967, 1972.
- Sparling, P. F.: Antibiotic resistance in N. gonorrheae. Med. Clin. No. Amer., p 1133, September 1972.
- 37. Martin, J. E., Jr., et al.: Comparative study of gonococcal susceptibility to penicillin in the U. S. 1955-1969. J. Inf. Dis. 122:459, 1970.
- 38. Maurer, L. H., and Schneider, T. J.: Gonococcal urethritis in males in Vietnam. JAMA 207:946, 1969.
- 39. Willcox, R. R.: A survey of problems in the antibiotic treatment of gonorrhea, with special reference to South-East Asia. Brit. J. Ven. Dis. 46:217, 1970.
- 40. van der Wielan, A. W.: Sensitivity to antibiotics of gonococcal strains isolated from sailors at Rotterdam. Brit. J. Ven. Dis. 47:190, 1971.
- 41. Lynn, R., et al.: Further studies of penicillin resistant gonococci. Brit. J. Ven. Dis. 46:404, 1970.
- 42. Moses, M., et al.: Present pattern of antibiotic sensitivity of gonococcal strains isolated in Bombay. Brit. J. Ven. Dis. 47:273, 1971.
- 43. Silver, P. S., and Darling, W. M.: Penicillin-insensitive gonococci in the Bolton area. Preponderance in young women and immigrants. Brit. J. Ven. Dis. 47:367, 1971.
- 44. Holmes, K. K., et al.: Studies of venereal disease. I. Probenicid-procaine penicillin G combination and tetracycline hydrochloride in the treatment of "penicillin-resistant" gonorrhea in men. JAMA 202:461, 1967.
- 45. Cornelius, C. E., et al.: Variations in serum concentrations of penicillin after injections of aqueous procaine penicillin G with and without oral probenecid. Brit. J. Ven. Dis. 47:359, 1971.
- 46. Pedersen, A.H.B., et al.: Spectinomycin and penicillin G in the treatment of gonorrhea. JAMA 220:205, 1972.
- 47. Velasco, J. E., et al.: Minocycline in the treatment of venereal disease. JAMA 220:1323, 1972.
- 48. Jones, S. R., and Gilleland, H. E.: Using one dose of doxycycline or penicillin to treat men with gonococcal urethritis. HSMHA Health Reports 86: 849, 1971.
- 49. Pedersen, A.H.B., et al.: Spectinomycin and penicillin G in the treatment of gonorrhea. JAMA 220:205, 1972
- 50. Smith, E. B.: Cephalothin in GC urethritis. Curr. Therap. Res. 9:79, 1967.
- 51. McLane, D. G., et al.: Gonorrheal urethritis in males treated with one oral dose of ampicillin. South. Med. J. 61:278, 1968.

- 52. Neumann, H. H., and Baecker, J. M.: Treatment of gonorrhea. Penicillin or tetracyclines. JAMA 219:471, 1972.
- 53. Groth, O., and Hallquist, L.: Oral ampicillin in gonorrhea. Brit. J. Ven. Dis. 46:21, 1970.
- 54. Gunderson, T., et al.: Treatment of gonorrhea by one oral dose of ampicillin and Probenecid combined. Brit. J. Ven. Dis. 45:235, 1969.
- 55. Farrell, L.: Kanamycin sulphate in the management of gonorrhea failing to respond to penicillin. Brit. J. Ven. Dis. 45:232, 1969.
- 56. Domescik, G., et al.: Use of a single oral dose of doxycycline monohydrate for treating gonorrheal urethritis in men. Public Health Reports 84:182, 1969.
- 57. McLane, D. G., et al.: Gonorrheal urethritis in men treated with one oral dose of methacycline. Public Health Reports 93:87, 1968.
- Enfors, U., and Malin, L.: Demethylchlortetracycline compared with penicillin in the treatment of gonorrhea in women. Brit. J. Ven. Dis. 46:209, 1970.
- 59. Duncan, W. C., and Knox, J. M.: Cephalosporin antibiotics in V.D. Postgrad. Med. J. (London) Suppl.:119-122, Feb. 1971.
- 60. Ayra, 0. P., et al.: Rifadin (rifampicin) in the treatment of gonorrhea in Uganda. Brit. J. Ven. Dis. 47:184, 1971.
- 61. Caldwell, J. G., et al.: Current therapy of gonorrhea. JAMA 218:714, 1971.
- 62. Schroeter, A. L., et al.: Therapy for incubating syphilis. Effectiveness of gonorrhea treatment. JAMA 218:711, 1971.
- 63. Rockwell, D. H., et al.: The Tuskegee study of untreated syphilis. The 30th year of observation. Arch. Int. Med. 114:792, 1964.
- 64. von Bruusgaard, E.: Uber das Schicksal der nicht spezifisch behandelten Luetiker. (Aus der Dermatologischen Universitätsklinik in Oslo)
- 65. Rosahn, P. D.: Studies in syphilis. VII. The end results of untreated syphilis. J. V.D. Information, pp 293-301, December 1946.
- 66. Moore, M. B.: The epidemiology of syphilis. JAMA 186:831, 1963.
- 67. Sparling, P. F.: Diagnosis and treatment of syphilis [Medical Progress]. New Eng. J. Med. 284:642, 1971.
- 68. Atwood, W. G., and Miller, J. L.: Fluorescent treponemal antibodies in fractionated syphilitic sera. The immunoglobulin class. Arch. Derm. 100:763,
- 69. Sartoris, S., et al.: FTA test on early syphilis [Abstract]. Minerva Derm. 43:23, 1968.

- 70. Harner, R. E., et al.: FTA-ABS test in late syphilis: A serological study in 1,985 cases. JAMA 203:545, 1968.
- 71. Atwood, W. G., et al.: The TPI and FTA-ABS tests in treated late syphilis. JAMA 203:107, 1968.
- 72. Forstrom, L., and Lassus, A.: The fluorescent treponemal antibody absorption test (FTA-Abs) in treated and late syphilis. Acta Dermatovener. 49:326, 1969.
- 73. Nicholas, L.: A simplified schema for the evaluation of reactive serologic tests for syphilis. J. Chron. Dis. 24:281, 1971.
- 74. Deacon, W. E., et al.: Fluorescent treponemal antibody-absorption (FTA-ABS) test for syphilis. JAMA 198:624, 1966.
- 75. Sepetjian, N., et al.: Investigation of a specific IgM antibody test in neonatal congenital syphilis. Brit. J. Ven. Dis. 46:18, 1970.
- 76. Alford, C. A., et al.: Gamma-M fluorescent treponemal antibody in the diagnosis of congenital syphilis. New Eng. J. Med. 280:1086, 1969.
- 77. LeClair, R. A.: Evaluation of a qualitative hemagglutination test for antibodies to <u>Treponema pallidum</u>. J. Inf. Dis. 123:668, 1971.
- 78. Wilkinson, R. E.: Recent progress in venereal disease: Serology of syphilis. Brit. Med. J. 2:573, 1972.
- 79. Goldman, J. N., and Lantz, M. A.: FTA-ABS and VDRL slide test reactivity in a population of nuns. JAMA 217:53, 1971.
- 80. Mackey, D. M., et al.: Specificity of the FTA-ABS test for syphilis: an evaluation. JAMA 207:1683, 1969.
- 81. Jokinen, Z. J., et al.: Fluorescent treponemal antibody (FTA) reaction in sera with antinuclear factors. Ann. Clin. Res. 1:77, 1969.
- 81A Bradford, L. L., et al.: Fluorescent treponemal absorption in syphilitic patients and biologic false positive reactors. Am. J. Clin. Path. 47:525, 1967.
- 82. Kraus, S. J., et al.: Fluorescent treponemal antibody-absorption test reactions in lupus erythematosus. Atypical beading pattern and probable false-positive reactions. New Eng. J. Med. 282:1287, 1970.
- 83. Salo. O. P., et al.: False-positive serological tests for syphilis in pregnancy. Acta Derm.-Venereol. 49:332, 1969.
- 84. Duncan, W. P., et al.: Fluorescent treponemal antibody-cerebrospinal fluid (FTA-CSF) test. A provisional technique. Brit. J. Ven. Dis. 48:97, 1972.
- 85. Mahoney, J.D.H., et al.: Evaluation of the CSF FTA-abs test in latent and tertiary treated syphilis. Acta Dermatovener. 52:71, 1972.