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## MONTHLY MORBIDITY REPORT

Provisional Statistics

DEPARTMENT OF HEALTH AND HUMAN RESOURCES  
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from  
EPIDEMIOLOGY UNIT AND PUBLIC HEALTH STATISTICS

### Disseminated Gonococcal Infection

Complications that may arise from untreated gonorrhea include either the local destructive action of the primary infection (i.e., urethral stricture, blindness); or local spread of the gonococcus with resultant paraurethritis, seminal vesiculitis, epididymitis, prostatitis in the male or Bartholinitis, salpingitis, pelvic inflammatory disease, tubo-ovarian abscesses, Fitz-Hugh Curtis syndrome in the female; or hematogenous spread of the organism (i.e., disseminated gonococcal infection [DGI]) to the joints, skin, liver, heart and meninges. If it were not for these complications, uncomplicated anogenital gonorrhea would not present a serious threat to the health of the patient.

It has been estimated that approximately two percent of patients with gonorrhea develop disseminated infection.<sup>1</sup> Next to acute salpingitis, infectious arthritis is the major cause of serious morbidity due to gonorrhea. Complications due to DGI range from a self-limited gonococcemia to life-threatening (gonococcal) endocarditis. A review of DGI focusing on the present body of information on the pathogenesis of dissemination, clinical manifestations, diagnosis, and treatment is presented in this issue of the STD Newsletter.

#### **PATHOGENESIS**

Dissemination may result if gonococci possess different virulence determinants which would allow them to overcome the body's defenses or if there is a breakdown or a deficiency of defense mechanisms there by allowing the organisms to migrate from the primary site of infection.

Factors which are said to facilitate the hematogenous spread of gonococci include asymptomatic gonococcal infection, pregnancy, menstruation, hepatitis, differences among strains of gonococci and host immunologic differences. Primary gonococcal infection of any site, particularly if the infection is asymptomatic, may lead to dissemination. The importance of asymptomatic gonorrhea in DGI may explain the changing sex distribution of DGI. In the preantibiotic era, DGI predominantly affected men but is currently seen more frequently in women.<sup>2</sup> The present sex distribution is related to the fact that most men with acute gonococcal urethritis are symptomatic and, therefore, receive prompt treatment, whereas most females are asymptomatic and untreated. However, in New York City, the male/female ratio of DGI is approximating equality. Comparison of the percentages between males and females with DGI to the total numbers of gonorrhea cases revealed that the proportion was roughly triple that for men in 1977, 2/3 that for men in 1978, and 1.2 times that for men in 1979. (Table 1). The overall decline in DGI in women is probably due to the introduction of the gonorrhea screening program where more cases of asymptomatic

female gonorrhea are now detected in earlier stages, thus preventing DGI.

The risk of dissemination, therefore, is greater in those sites where asymptomatic infection is common. Gonococcal pharyngeal infection, which is frequently asymptomatic, is a major source of gonococcemia.<sup>3</sup> The occurrence of gonococcal pharyngeal infection in heterosexual males with DGI is significantly greater than in heterosexual males with uncomplicated gonococcal urethritis.<sup>4</sup> Another potential source of gonococcemia is anorectal infection which is often asymptomatic. However, dissemination from this site does not occur as frequently as from the pharyngeal or endocervical site.

The risk of dissemination also increases during pregnancy, particularly in the second and third trimester, or during the first week of the menstrual cycle when endocervical shedding of gonococci is maximal.<sup>2,5</sup> Increased vascularity of the genital organs during pregnancy and hormonal or pH changes during menstruation may account for the increased risk.

The role of hepatitis as a risk factor is not clear. Holmes et al<sup>2</sup> cited one case of alcoholic hepatitis in their study group prior to development of DGI. However, both perihepatitis (Fitz-Hugh Curtis syndrome) and hepatitis may occur as a consequence of gonococcemia. The rare occurrence in the male of gonococcal perihepatitis is the result of hematogenous or lymphatic spread, whereas in the female it may involve either direct extension from the pelvis (via the fallopian tubes) to the perihepatic area, or hematogenous spread.

As for differences among gonococcal strains, it has been shown that sexual partners can both have disseminated infections, thus lending support to the

#### **SOURCE:**

New York City Health Department, *Sexually Transmitted Disease Newsletter*, November, 1980.



idea that certain strains of *N. gonorrhoeae* can have increased virulence that facilitates their dissemination.<sup>6</sup> The virulence of *N. gonorrhoeae*, as shown by its ability to disseminate, is surprisingly associated with low antibiotic resistance whereby the patient readily responds to treatment. In essence, the loss of virulence in any given strain of *N. gonorrhoeae* is accompanied by a gain in antibiotic resistance. Thus, in the antibiotic era, there has been an increase in relatively penicillin resistant organisms which tend to disseminate less than sensitive organisms.<sup>6</sup> Most isolates recovered from patients with DGI are highly susceptible to penicillin G, having penicillin minimum inhibitory concentrations (MIC) at levels less than 0.15 ug/ml. These highly penicillin susceptible strains of *N. gonorrhoeae* generally require arginine, hypoxanthine, and uracil (AHU) for growth.<sup>7</sup> In the population studied by Knapp and Holmes,<sup>7</sup> AHU auxotypes accounted for 89 percent of cases with DGI. These DGI auxotypes were found in 38 percent of uncomplicated gonococcal infections in this same population group. The AHU auxotype was not recovered from a study group of patients with gonorrhea in the Philippines, where DGI is uncommon.<sup>8</sup>

Specific complement component deficiencies may also play a role in DGI. It has been reported that both gonococcal and meningococcal bacteremia are associated with C6, C7, or C8 deficiency in patients and that patients with these complement deficiencies tend to have recurrent Neisserial bacteremias.<sup>9</sup> However, most patients with DGI have normal bactericidal complement.<sup>10</sup> It may be that defects in complement may predispose some individuals to DGI.

It has also been demonstrated that gonococci isolated from patients with DGI are more resistant to the bactericidal action of normal human serum.<sup>10,11</sup> McCutchan and co-workers<sup>12</sup> identified a natural blocking antibody of the IgG class which binds serum-resistant but not serum-sensitive gonococci. These investigators speculated that resistant strains have a second antigen to which blocking antibody attaches and that normal serum contains an IgG blocking antibody which competes with natural bactericidal antibody.

## CLINICAL MANIFESTATIONS

### Gonococcal Arthritis

Gonococcal arthritis is the most common form of infectious arthritis and the most common manifestation of gonococcal dissemination. Morbidity due to gonococcal arthritis ranges from minimal arthralgia to chronic disability (as a result of severe destructive arthritis). Two clinical forms of this disease have been described:<sup>2,13</sup>

- 1) a bacteremic stage characterized by fever, chills, malaise, polyarthritis with relatively little joint effusion, tenosynovitis and dermatitis, and
- 2) a septic joint stage with monoarticular involvement and signs of an effusive arthritis where gonococci are recovered from the synovial fluid cultures. Fever, chills skin lesions and bacteremia are absent in the septic joint stage.

These two clinical forms are sequential stages of the same disease with the bacteremic or hematogenous phase being the early manifestation.

The presence of skin lesions in the majority of patients (50% — 70%) with gonococcal arthritis has prompted investigators to designate this manifestation of gonococcemia as the arthritis-dermatitis syndrome. The skin lesions associated with gonococcal arthritis start as tiny red macules and progress to papular, petechial, vesicular and pustular stages with or without a necrotic center and usually on a hemorrhagic base. Rarely, large bullae which are often hemorrhagic may also occur. The skin lesions usually appear during the first few days of symptoms, are scanty, unevenly distributed, vary from 1 mm. to 20 mm. in diameter, and are often seen in various stages of development. The most common site of involvement is the distal portion of the extremities near the periarticular regions. Occasionally, lesions may be seen on the trunk. The scalp and oral mucosa are usually spared. The number of lesions vary from 1 to 40 or more. Individual lesions resolve spontaneously at any stage of development. Usually resolution occurs within four to five days, whereas the necrotic lesions may persist over a longer period and resolve as eschars.

The joints most frequently affected include the knees, ankles, wrists, elbows, and the small joints of the hands and feet. Other joints (shoulders, sternoclavicular, temporomandibular, hip) are infrequently involved.<sup>14</sup> During the bacteremic stage, *N. gonorrhoeae* can be isolated from the blood in approximately 50 percent of patients. Occasionally, identification of the organism can also be made from a lesion specimen by the fluorescent antibody technique, culture and Gram stain. Synovial effusions are usually minimal or absent and synovial fluid is sterile on culture.

In the untreated patient, the polyarthritic manifestations usually evolve into a purulent monoarticular arthritis shortly after onset of illness. Skin lesions either disappear or are in a healing stage, systemic symptoms abate and blood cultures invariably are sterile. Synovial fluid cultures are often positive for *N. gonorrhoeae*.

Arthropathy may range in severity from arthralgias without any evidence of inflammation, to signs of an inflammatory reaction involving the synovial membranes and periarticular tissues, to overt arthritis with intense pain, redness, swelling over the joint, and limitation of movement.

Rarely, conjunctivitis due to hematogenous spread may occur. In such cases, differentiation has to be made from conjunctivitis due to Reiter's syndrome.

### Gonococcal Endocarditis

Gonococcal endocarditis is a life-threatening complication that may occur when DGI is not recognized and promptly treated. The presence of pathological murmurs and valvular heart disease in a patient with gonococcemia, particularly if the gonococcemia persists longer than one or two weeks, further supports the diagnosis. Polyarthritides usually occurs in the majority of endocarditis. Maculopapular skin lesions appearing in crops are often observed. Splenomegaly, major arterial emboli, focal myo-



carditis and immune complex glomerulonephritis are additional manifestations of endocarditis. Myocarditis and pericarditis are very common in DGI and EKG abnormalities have been reported frequently

#### Gonococcal Meningitis

Gonococcal meningitis is a sequel of gonococcal septicemia, a serious illness in which endocarditis may be present and from which myopericarditis may follow

The clinical manifestations of gonococcal meningitis are similar to those of other causes of bacterial meningitis and most closely mimic those of meningococcal meningitis. The differentiation from the latter is based on different bacterial sugar fermentations or the direct fluorescent antibody test. Most of the reported cases fall roughly into two groups: meningitis in adults accompanying or following gonococcal infection of the genital tract, or meningitis in the newborn infant following infection at birth

#### DIAGNOSIS

Apart from the clinical presentation of acute arthritis or tenosynovitis and/or the presence of typical skin lesions, a confirmatory diagnosis for gonococcal arthritis depends on identifying *N. gonorrhoeae* either by culture or by direct fluorescent antibody stain. Since 25% - 50% of patients have evidence of gonococcal infection at the primary site, culture testing using modified Thayer Martin (MTM) or New York City (NYC) medium should be done on all primary sites of infection — i.e. cervical, pharyngeal, and anal for females and urethral, pharyngeal and anal in males — regardless of whether there are any local signs and symptoms of infection.

Additionally, blood, synovial fluid, skin lesion, and cerebrospinal fluid (for suspected gonococcal meningitis) specimens should be inoculated on chocolate agar medium (without antibiotics) and in TSY broth. Chocolate agar medium will not diminish the yield of gonococcal organisms nor inhibit the growth of nongonococcal pathogens which might occur with MTM or NYC medium. Since bacteremia may be intermittent or transient, several blood cultures (including aerobic and anaerobic) should be obtained.

Gram-staining of exudate from skin lesions may presumptively identify *N. gonorrhoeae*. Confirmation may be obtained by using the direct fluorescent antibody test on skin lesion specimens. The yield from such procedures, however, is low.

Thus, the diagnosis of DGI is established when *N. gonorrhoeae* is identified by culture or by specific FA testing from blood, synovial fluid, skin lesion, or cerebrospinal fluid specimens. Isolation of *N. gonorrhoeae* from primary sites of infection and not from systemic sites with clinical presentation of arthritis and/or dermatitis also establishes a diagnosis of DGI.

#### DIFFERENTIAL DIAGNOSIS

Gonococcal arthritis has to be differentiated from the arthritic condition (bone pain) associated with the secondary stage of syphilis. The dermatitis seen in secondary syphilis is usually generalized and symmetrically distributed, with or without mucocu-

taneous lesions which are rarely, if ever, seen in gonococcal arthritis. Additionally, there is often generalized lymphadenopathy and high titer reactive serologic test results in patients with secondary syphilis.

Another venereal arthritic disorder that gonococcal arthritis has to be differentiated from is Reiter's syndrome. Reiter's syndrome usually presents with characteristic mucocutaneous lesions (keratoderma blennorrhagicum, circinate balanitis, aphthous ulceration) as well as skin lesions. In addition, migratory polyarthritis and fever are more common in gonococcal arthritis while spondylitis and sacroileitis are more common in Reiter's syndrome. Nongonococcal conjunctivitis will readily differentiate Reiter's syndrome.

Other skin conditions that may mimic those of DGI include septicemias caused by other microorganisms (meningococci, staphylococci, *Pseudomonas*) and fungi. However, they can be differentiated from DGI by laboratory analysis.

#### TREATMENT

##### Antibiotic Therapy

Most strains isolated from patients with DGI are extremely penicillin sensitive. Treatment may be entirely oral or a combination of parenteral and oral. Management of a patient with gonococcal arthritis may be done on an outpatient basis. However, hospitalization is required for unreliable patients, those with purulent joint effusion or other joint complications, endocarditis, meningitis, and those with uncertain diagnoses.

The drug of choice for DGI is aqueous crystalline penicillin G, 10 million units intravenously per day until clinical improvement occurs followed by 0.5 g ampicillin orally Q.I.D. to complete 7 days of antibiotic therapy. A rapid clinical resolution usually in 1 to 3 days should be evident in the majority of patients. However, joint swelling may persist for up to 10 days.

Orally administered ampicillin or amoxicillin may also be given in an initial dose of 3.5 g ampicillin or 3.0 g amoxicillin each with 1.0 g of probenecid followed by 0.5 g of either drug Q.I.D. for 7 days.

For those patients who are allergic to penicillin, tetracycline hydrochloride may be given in a dosage regimen of 0.5 g orally Q.I.D. for 7 days. Because of its bacteriostatic action tetracycline should not be used in patients with endocarditis or meningitis. Additionally, tetracycline should not be given to pregnant women. Erythromycin, 0.5 g orally Q.I.D. for 7 days may be used in pregnant women who are allergic to penicillin.

Overt endocarditis and meningitis requires a longer course of therapy. Ten million units of aqueous crystalline penicillin G intravenously daily for at least 10 days for meningitis and for 3 to 4 weeks for endocarditis is recommended. In penicillin allergic patients with endocarditis, desensitization and administration of penicillin are indicated. In penicillin allergic patients with meningitis, chloramphenicol may be used.

For treatment of DGI infections caused by PPNG (penicillinase-producing *N. gonorrhoeae*) strains, 2.0 g spectinomycin HCl given intramuscularly twice daily for 3 days is recommended.

All patients, regardless whether the infection was localized or disseminated, should also have test-of-cure follow-up cultures of specimens from previously infected sites.

#### Local Measures for Gonococcal Arthritis

Since penicillin is readily transported into the synovial cavity, intra-articular injection of penicillin is not recommended. Other than the hip, open drainage of joints is not necessary. Aspiration and irrigation of the joint with sterile saline may be indicated in severe cases to relieve pain and pressure and to remove inflammatory fluid that might result in destruction of joint tissue. In an involved weight-bearing joint, ambulation should not be permitted until evidence of effusion has disappeared.

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Table 1 MALE/FEMALE RATIO OF PERCENTAGES OF DGI IN NEW YORK CITY			
YEAR	RATIO	MALES DGI/TOTAL Gc*	FEMALES DGI/TOTAL Gc*
1977	1.0:2.9	36/28,936	37/10,339
1978	1.0:0.7	35/28,650	10/11,558
1979	1.0:1.2	36/28,927	18/12,007
*Gc = gonorrhea cases			



# **SELECTED REPORTABLE DISEASES** (By Place of Residence)

STATE AND PARISH TOTALS REPORTED MORBIDITY DECEMBER, 1980	VACCINE PREVENTABLE DISEASES					ASEPTIC MENINGITIS	HEPATITIS A AND UNSPECIFIED	HEPATITIS B	LEGIONNAIRES DISEASE	MALARIA**	MENINGOCOCCAL INFECTIONS	SHIGELLOSIS	TUBERCULOSIS, PULMONARY	TYPHOID FEVER	OTHER SALMONELLOSIS	UNDERNUTRITION SEVERE	GONORRHEA	SYPHILIS, PRIMARY AND SECONDARY	RABIES IN ANIMALS (PARISH TOTALS CUMULATIVE, 1980)
	MEASLES	RUBELLA*	MUMPS	PERTUSSIS	TETANUS														
TOTAL TO DATE 1979	268	32	32	18	4	106	873	303	7	6	151	123	509	5	196	10	23990	1130	43
TOTAL TO DATE 1980	15	13	69	35	5	82	903	308	5	51	93	228	479	2	212	7	22803	1426	19
TOTAL THIS MONTH	2	0	1	1	0	6	86	33	0	4	5	16	32	0	29	0	1886	166	3
ACADIA																	15		
ALLEN																	1		
ASCENSION																	8	2	
ASSUMPTION																			
AVOYELLES																	4	1	1
BEAUREGARD																	3	1	
BIENVILLE																	2		2
BOSSIER								1									21	1	
CADDO						2	3	2				1	2		4		165	3	4
CALCASIEU							4	3					3		3		75	4	
CALDWELL																	1		
CAMERON							2												
CATAHOULA								1											
CLAIBORNE																	11		
CONCORDIA																	7		1
DESOTO																	4	1	
EAST BATON ROUGE							3						1				6		
EAST CARROLL																	171	37	
EAST FELICIANA							1										6		
EVANGELINE							1				1		1				8		1
FRANKLIN																			
GRANT															1		8		
IBERIA							3	1									2		
IBERVILLE																	9	1	
JACKSON																	8	2	
JEFFERSON			1			1	18	5					9				8		
JEFFERSON DAVIS							5	3			1						120	13	
LAFAYETTE							4	2					1				9	1	
LAFOURCHE													1				29	1	
LASALLE																	14	1	
LINCOLN							2												2
LIVINGSTON							9										52		
MADISON																	8	1	
MOREHOUSE													1				7		
NATCHITOCHES								1				1			1		14		
ORLEANS	2						4	6		3		2	5		3		2		4
OUACHITA						1	9	3					2				730	60	
PLAQUEMINES						1	1										101	14	
POINTE COUPEE																	5	1	
RAPIDES							2	1					2		1		1	1	
RED RIVER																	73	3	2
RICHLAND																			
SABINE																	26	1	
ST. BERNARD							2										3		
ST. CHARLES																	6		
ST. HELENA																			
ST. JAMES																	5		
ST. JOHN																	4		
ST. LANDRY				1			2	1			3		3				5		
ST. MARTIN													1				6	1	
ST. MARY							1										5		
ST. TAMMANY							1										8		
TANGIPAHOA																	18	4	
TENSAS																	5		
TERREBONNE						1	7					12			13		11	1	
UNION																	6	3	
VERMILION							1	2							1		3	1	
VERNON								1									8	2	
WASHINGTON							1								2		9		
WEBSTER																	18		4
WEST BATON ROUGE																	7		
WEST CARROLL																	3		
WEST FELICIANA																	1	3	
WINN																	9		
OUT OF STATE										1							12		

\* Includes Rubella, Congenital Syndrome.

\*\* Acquired outside United States unless otherwise stated.

From January 1, 1980, through December 31, 1980, the following cases were also reported: 7-Leptospirosis; 4-Brucellosis; 1-Blastomycosis; 1-Cryptococcosis; 28-Trichinosis; 1-Poliomyelitis, non-paralytic; 4-Rocky Mountain Spotted Fever; 12-Encephalitis, Anthropod-Borne; 3-Reyes Syndrome.



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