Analysis of an Outbreak of Penicillinase-Producing Neisseria gonorrhoeae in Rhode Island, 1987

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In June of 1987, an outbreak of penicillinase-producing Neisseria gonorrhoeae (PPNG) occurred in Rhode Island. PPNG persists as an endemic pathogen despite a concerted statewide effort to eradicate the organism. Detailed analysis of PPNG isolates demonstrated that multiple strains are circulating concurrently, complicating control efforts.

The incidence of infections caused by penicillinase-producing Neisseria gonorrhoeae (PPNG) has been steadily rising in the United States in recent years. In 1987, approximately 26,000 cases of PPNG infection, or 3.2% of all gonorrhea cases, were reported to the Centers for Disease Control, a threefold increase over the previous year. Before 1986, PPNG infections had been concentrated in New York, California, and Florida (13). However, since that time PPNG outbreaks have been reported in such diverse geographic areas as Denver, Colo. (3), and King County, Wash. (4).

Until 1987, PPNG infections had occurred episodically in Rhode Island and its control had posed few problems. Between 1976, when the first case of PPNG was identified, and 1986, a total of 62 cases were reported to the Rhode Island Department of Health. This pattern abruptly changed in 1987 when 211 cases were reported to the Department of Health, with the frequency of PPNG isolates increasing from 0.42 to 19.6% of all reported gonorrhea cases. This led to major changes in the approach to gonorrhea treatment throughout the state. By the end of 1987, Rhode Island’s PPNG case rate of 21.4/100,000 population was the fourth highest in the United States. In this report, we describe the PPNG epidemic in Rhode Island that began in June 1987 and link epidemiologic features of the outbreak with plasmid, auxotype, and serovar analysis of the PPNG isolates.

Surveillance and case finding for gonorrhea in Rhode Island occur primarily through two mechanisms: reporting from three state-funded sexually transmitted diseases clinics and a state regulation requiring all laboratories to submit each gonorrhea isolate to the Rhode Island Department of Health Laboratory. Epidemiologic data on all PPNG cases are collected and recorded by Department of Health personnel. Statistical analyses were performed using the 2-by-2 contingency table analysis and Fisher’s exact test. All N. gonorrhoeae isolates were screened for β-lactamase with a chromogenic cephalosporin (BBL Microbiology Systems, Cockeysville, Md.)(11). Susceptibility testing was performed using a standard agar dilution technique (7). Plasmid profiles were obtained by the technique of Kado and Liu (8). Auxotyping was performed by the method of Hendry and Stewart (6). Identification and characterization of β-lactamase were performed using isoelectric focusing in polyacrylamide gels developed with a chromogenic cephalosporin (10). Serovar determinations were made by using monoclonal antibodies to gonococcal outer membrane protein I by previously described methods (9, 12). Plasmid DNA from one strain of PPNG was transformed into Escherichia coli HB101 (14).

The outbreak began in June of 1987 when 24 isolates of PPNG were reported. During the next 6 months, an average of 30 cases were reported each month, bringing the total by the end of 1987 to 211 cases (Fig. 1). This represents 9.5% of all N. gonorrhoeae isolates reported to the state health department for 1987, compared with 0.8% of all gonorrhea isolates in 1986 (P < 0.0001). The total number of reported cases of gonorrhea (both PPNG and non-PPNG) increased from 1,842 in 1986 to 2,212 in 1987, a 20% increase (P < 0.05) (Fig. 2).

Most of the PPNG cases (73%) occurred in residents of Providence, R.I., compared with 55% of all the non-PPNG cases (P < 0.0001). Whereas patients attending publicly funded sexually transmitted diseases clinics in the state accounted for only 42% of non-PPNG cases in 1987, they accounted for 63% of all PPNG isolates (P < 0.05). PPNG infections in blacks and Hispanics accounted for 68% of all reported PPNG cases, compared with 48% of all non-PPNG cases (P < 0.05). Men accounted for 56% of all cases of PPNG, and 67% of the PPNG cases occurred in persons aged 15 to 29 years. Both sex and age distributions were similar among PPNG and non-PPNG cases.

**FIG. 1.** PPNG cases by month, 1987.
The epidemiologic investigation of PPNG cases, which occurred at the beginning of the epidemic in June 1987, revealed that two heterosexual males infected with PPNG had multiple sexual partners, some of whom were prostitutes. In addition, two patients diagnosed that same month had a history of recent travel to areas where PPNG was endemic. Because these individuals did not know the names of many of their contacts, partner identification and treatment was incomplete.

Analysis of the 77 PPNG isolates obtained from July through September 1987 revealed identical antimicrobial susceptibility results (MICs for 90% of isolates tested), including the following: penicillin, > 16.0 µg/ml; ceftriaxone, 0.01 µg/ml; tetracycline, 1.0 µg/ml; spectinomycin, 16 µg/ml; and cefoxitin, 0.25 µg/ml. The β-lactamase produced by PPNG was of the TEM-1 class. Plasmid profiles were identical, with 24.5-, 3.2-, and 2.6-megadalton plasmids. Transformation of the 3.2-megadalton plasmid into E. coli HB101 confirmed the presence of the β-lactamase gene on this plasmid.

Despite similar antimicrobial susceptibility and plasmid patterns, auxotyping revealed a total of five auxotypes among the 77 isolates tested. These included two major auxotypes, prototrophs (NR) (70%) and proline auxotrophs (Pro-) (17%). Other auxotypes included ornithine (ORN+) (7%); proline, citrulline, uracil (PCU-) (2%); and phenylalanine sensitivity in 2% of NR isolates. Auxotyping of penicillin-susceptible N. gonorrhoeae isolates (n = 47) from the same period demonstrated a similar distribution of auxotypes, including NR, 44%; Pro-, 32%; Orn-, 15%; and PCU-, 5.4%. PPNG isolates were prototrophs more often than were penicillin-susceptible strains (70 versus 44%; P < 0.01).

Serotyping also demonstrated that multiple serovars were found simultaneously in this outbreak. Of the 25 isolates studied by serotypic analysis, five different serotypes were identified; 17 isolates belonged to serovar IB-3, the most common serovar. The other predominant serovar, IA-2, was found in all proline auxotrophs and in none of 20 prototrophs (P < 0.0001).

The demographic characteristics of patients with PPNG infection in Rhode Island are similar to those of patients in other geographic areas where PPNG has become endemic (1, 2, 5). Those characteristics include a higher percentage of black and Hispanic patients among those infected with PPNG than among those infected with antibiotic-susceptible strains, a high percentage of inner-city residents, and a higher number of PPNG infections reported by publicly funded clinics than by private offices or laboratories.

Although the rapidity with which this outbreak spread is consistent with dissemination of a single strain of PPNG, multiple strains were isolated concurrently. The diversity of auxotype and serovar classes suggests that the epidemic in Rhode Island has been a series of mini-outbreaks caused by different strains of PPNG. Similar observations were also reported regarding outbreaks in Denver, Colo., and Miami, Fla. (1, 3). It is not known whether multiple-strain outbreaks arise because plasmids that code for β-lactamase are transferred from PPNG strains to other penicillin-susceptible gonococci or because of the importation of different PPNG strains into the community.

Medical advisories were issued in the fall of 1987 requesting that laboratories routinely screen gonococcal isolates for β-lactamase and recommending treatment of patients with suspected cases of gonorrhea and their sexual partners with ceftriaxone (250 mg intramuscularly), followed by a 7-day course of tetracycline to treat coexistent Chlamydia trachomatis infections. Despite this advisory, PPNG infections persisted through 1988, with PPNG representing 27% of all N. gonorrhoeae isolates in Rhode Island (485 of 1,967) in 1988. That this epidemic was caused by multiple PPNG strains may account for its persistence in the Rhode Island community. It has been hypothesized that single-strain epidemics are easier to eradicate from the community than are multiple-strain outbreaks (4).

Single-strain outbreaks may be traced to a point source of introduction which can be tracked through an epidemiologically defined community. These factors could enhance control measures, including contact tracing, case identification, and rapid institution of effective treatment regimens (5).

The emergence of gonococcal strains that are resistant to multiple antibiotics also underscores the importance of continued monitoring of antibiotic susceptibility patterns of N. gonorrhoeae in the community. Because PPNG infections are becoming endemic in several geographic areas in the United States, standard sexually transmitted diseases recommendations for gonorrhea treatment may need to be altered. In all suspected cases of gonorrhea, there should be a thorough laboratory workup of gonococcal isolates, including β-lactamase and antibiotic susceptibility testing; an aggressive approach to contact tracing; and empiric treatment with a broad-spectrum cephalosporin (ceftriaxone) if PPNG is prevalent in the community.

**LITERATURE CITED**


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