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Communicable Diseases Intelligence

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Contents:

VIRUS REPORTING SCHEME: A total of 1,125 reports were processed for this period.

Five cases of Q fever were reported, 2 from New South Wales and 3 from Queensland. Occupational exposure data were only available for 1 Queensland case, a male butcher of unknown age from Rockhampton. None of the five patients was involved in the Q fever vaccine field trial conducted in South Australia.

Cytomegalovirus was isolated from:

- the oesophageal biopsy of a 22 year old male with persistent upper respiratory tract infection.
- the leucocytes of a 44 year old HIV antibody positive male with CMV retinitis, being treated concomitantly with DHPG and AZT.
- the post-mortem tissues derived from the kidney of a 25 year old HIV antibody positive male who died of CMV retinitis.
- the breast milk of a 31 year old female during the early post-partum period. No other clinical details were available for the mother or her neonate.
- tissue of an aborted 11 week old foetus of a 32 year old female who had a primary CMV infection at 7 weeks gestation.

Rotavirus was isolated from the faeces of three males, two aged 3 years and one aged 5 with gastroenteritis.

Dengue was detected serologically in a 30 year old female with prolonged fever. The patient recently visited India.

Herpes simplex virus untyped was detected serologically in a 47 year old male with a severe upper respiratory tract infection.

Milker's nodule virus was isolated from a large haemorrhagic lesion on the face of a 2 year old male with a history of contact with a calf.

GONOCOCCAL SURVEILLANCE - AUSTRALIA

(Contributed by the Australian Gonococcal Surveillance Programme (AGSP) Co-ordinator Dr J.W. Tapsall, Prince of Wales Hospital, Randwick, New South Wales 2031)

The present report provides details of penicillin sensitivities for the periods:

- January-March 1987 with 1031 isolates (Table 1)
- April-June 1987 with 729 isolates (Table 2)

of Neisseria gonorrhoeae, examined by participating State and Territories laboratories using Standard Techniques and Procedures[1].

January - March 1987

In this quarter penicillinase-producing gonococci (PPNG) were isolated in all major centres and in Canberra and Darwin (Table 1). High rates of PPNG infection, observed in Sydney and in particular Melbourne, indicated that endemic cycles of PPNG transmission are well established, with approximately 60% of infections with PPNG being acquired by local Transmission. Local spread of PPNG was also recorded in most other centres but to a lesser extent.

TABLE 1: Penicillin sensitivity of isolates of N-gonorrhoeae[2] January-March 1987.

Centre	Percentage of isolates		
	Sensitive	Less sensitive	PPNG
Brisbane	20.2 (27.0)	62.3 (60.0)	10.9 (9.2)
Sydney	11.7 (7.5)	54.4 (54.5)	17.7 (27.6)
Melbourne	9.8 (15.5)	45.6 (53.0)	26.0 (12.6)
Adelaide	21.9 (47.9)	56.8 (37.3)	7.1 (3.5)
Perth	36.7 (32.9)	36.7 (34.1)	12.9 (8.5)

(Figures in parenthesis represent data for the corresponding period in 1986).

April - June 1987

In this quarter, the rates of PPNG infection declined in most major centres with the exception Melbourne where local spread of endemic PPNG appears to have accelerated (Table 2).

TABLE 2 Penicillin sensitivity of isolates of N. gonorrhoeae [2] April-June 1987.

Centre	Percentage of isolates		
	Sensitive	Less sensitive	PPNG
Brisbane	26.8 (21.6)	56.9 (58.6)	6.0 (13.8)
Sydney	8.7 (9.7)	46.7 (51.8)	21.2 (27.6)
Melbourne	8.6 (15.1)	41.4 (51.9)	34.8 (15.7)
Adelaide	21.6 (36.9)	49.1 (50.8)	3.4 (4.9)
Perth	15.2 (28.6)	56.5 (34.9)	3.5 (17.0)

(Figures in parenthesis represent data for the corresponding period in 1986).

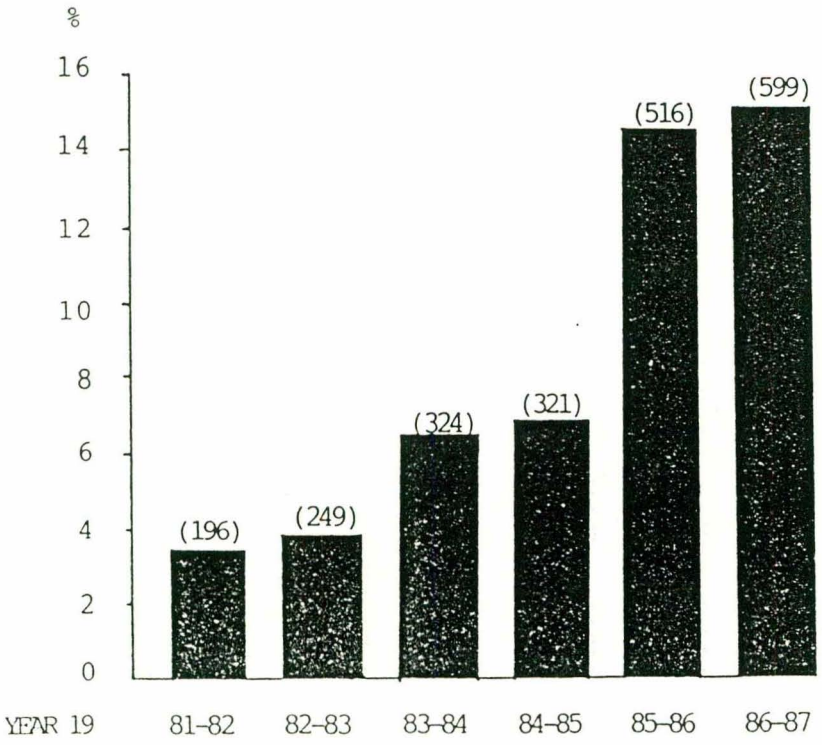
In the present report, penicillin resistance in Neisseria gonorrhoeae mediated by chromosomally controlled changes in the organism manifested as incremental changes in the minimal inhibitory concentration (MIC) of penicillin, was also examined.

Patterns of intrinsic resistance to the penicillins have remained essentially unaltered over the past 12 months.

CDI Editorial Comment:

Since the implementation of the Australian Gonococcal Surveillance Programme in July 1981, both the absolute number of PPNG isolates and the rates of PPNG isolation have shown dramatic increases for the past 6 years of surveillance (Figure 1).

FIGURE 1. Rate of PPNG isolations in Australia for the period July 1981 - June 1987.



() Figure in brackets represents absolute number of PPNG isolates.

In interpreting the above figure however, the following comments should be taken into account:

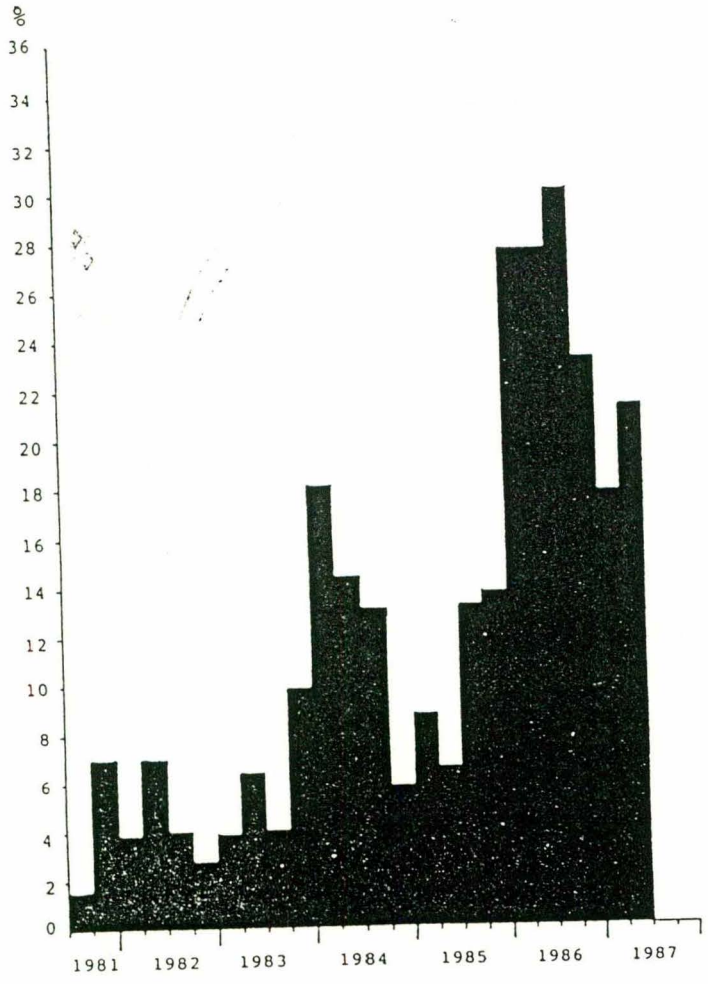
- Since the 1983-84 reporting period there has been an increase in the number of laboratories participating in the surveillance scheme for the first time, and
- the overall rate of PPNG reported for the whole of Australia would be of little value in monitoring the spread of gonococcal resistance since the rates fluctuate very widely between State centres with Sydney and Melbourne contributing the majority of data.

Despite the rise in PPNG incidences in the past 6 years of surveillance, the absolute number of gonoccal isolates has decreased steadily.

A review of PPNG isolations in each of the five major Australian centres is undertaken as follows:

Sydney (Figure 2)

FIGURE 2. Rate of PPNG isolation in Sydney for the period July 1981 - June 1987.



The increase in rates of PPNG infection observed during the period October 1983 - September 1984 has been primarily attributed to a continuing outbreak among prostitutes.

Although the high rates of PPNG would indicate endemicity of PPNG among infected women based on a conservative transmission rate of 22%[3], this proportion of cases linked to domestic tramsmission in Sydney was significantly contributed by foreign importation from hyperendemic centres in South East Asia and the Pacific.

The subsequent decrease observed in 1984-85 was due to the containment of the disease spread, most probably by the effective use of appropriate antimicrobials and greater effort devoted to contact tracing.

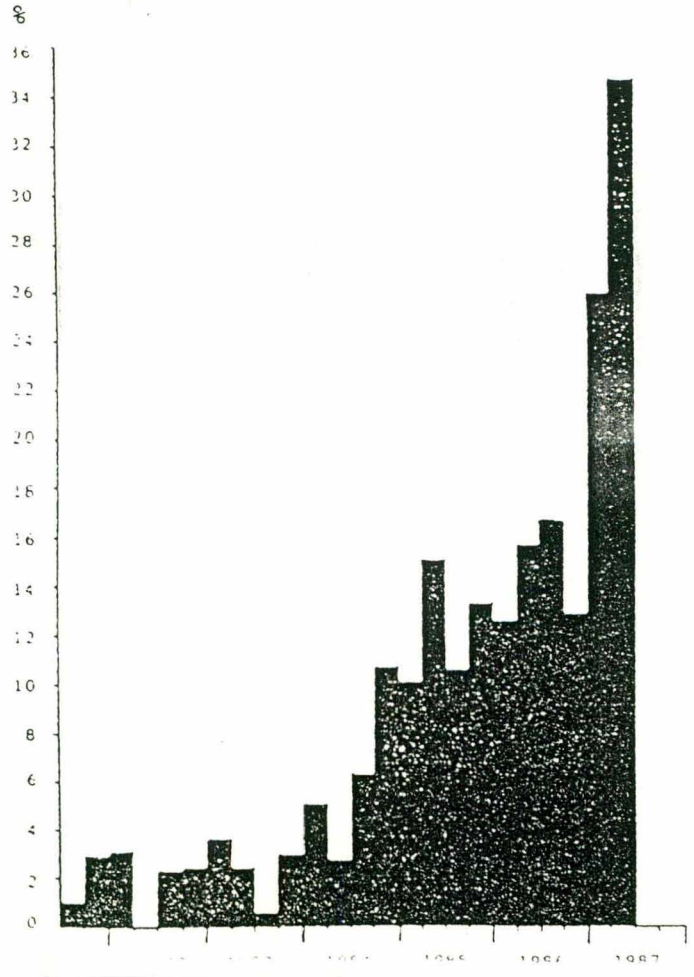
The rate of PPNG recorded for the 1st quarter of 1987 appeared to signal a downward trend following an outbreak of PPNG recorded during the latter half of 1985 and the whole of 1986. In this latter outbreak, PPNG accounted for up to 30% of all gonorrhoea isolates with the majority of PPNG infections being acquired locally.

This downward trend observed in the first quarter of this year needs to be monitored with caution since it may be expected to reflect:

- a change in transmission rate engendered by increasing AIDS awareness,
- a change in the rate of PPNG acquisition as the result of media campaigns advocating the use of condoms and safe sex practices,
- a successful PPNG control with the use of effective antimicrobials.

Melbourne (Figure 3)

FIGURE 3. Rate of PPNG isolations in Melbourne for the period July 1981 - June 1987.



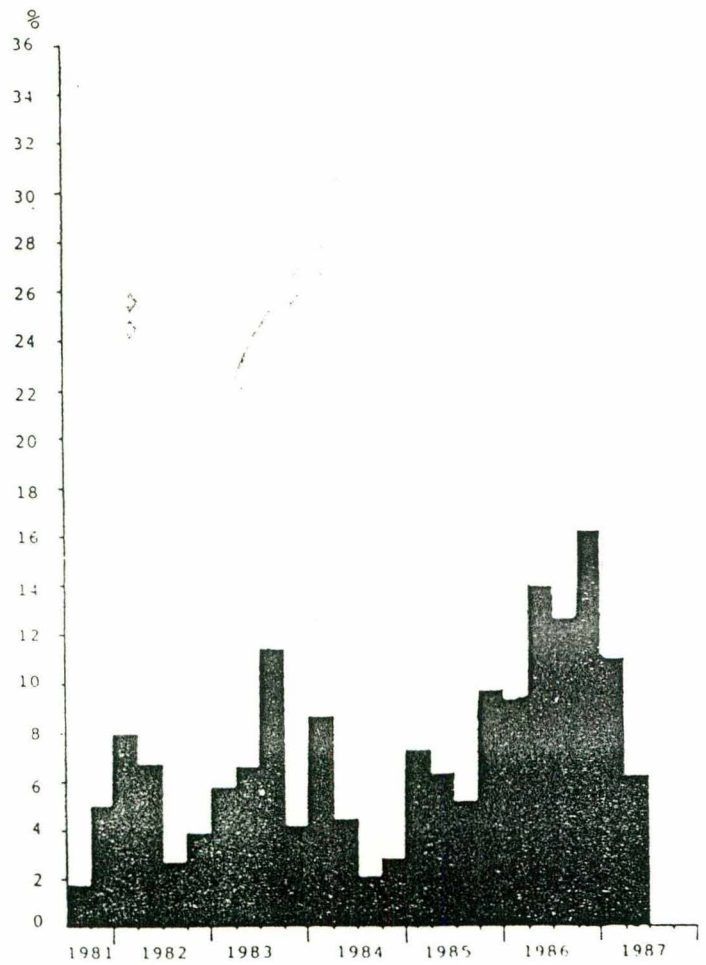
The rates of PPNG infection recorded for this city indicated a stepwise increase since the 3rd quarter of 1984. Although foreign importation would undoubtedly be responsible for the establishment of PPNG strains in the first instance, the subsequent gradual increase would indicate an increasing rate of endemicity of PPNG in the local transmission. The rate of PPNG infections accounted for up to 35% of gonorrhoea isolates recorded for the 2nd quarter of 1987.

Although this gradual increase might only reflect an increasing proportion of gonorrhoea isolates that have acquired penicillin resistance over time, other explanations have been put forward:

- an increase in the rate of PPNG transmission, and
- an increase in the rate of PPNG acquisition despite the recent implementation of preventive campaigns such as condoms and safe sex practices.

Brisbane (Figure 4)

FIGURE 4. Rate of PPNG isolations in Brisbane for the period July 1981 - June 1987.

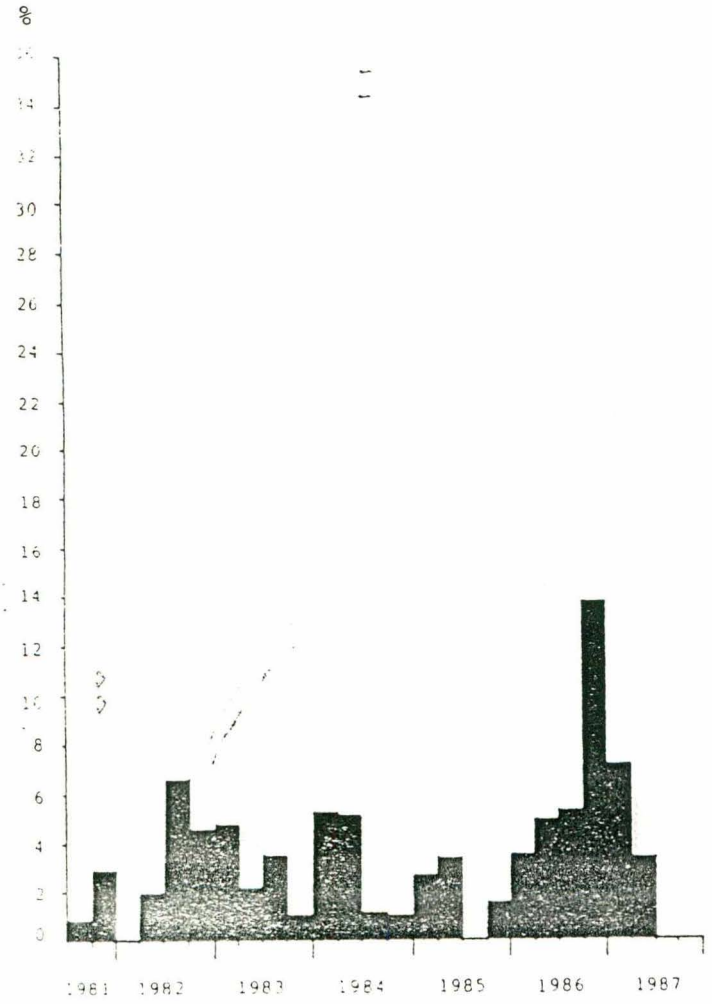


The rates of PPNG infections recorded for Brisbane exhibit cyclic increases every two years starting from the reporting year of 1981. However, if the increases observed in the 1981-82 and 1984-85 periods can be disregarded as artifacts of reporting since they are comparable and of the same small order of magnitude, the remaining profile resembles that of Sydney (Figure 1).

Such comparability between the two centres may support the rationale that in addition to an established local/intrastate acquisition, an interstate transmission of PPNG between Brisbane and other centres ie Melbourne and Sydney is also apparent, possibly due to an internal tourist movement.

Adelaide (Figure 5)

FIGURE 5. Rates of PPNG isolations in Adelaide for the period July 1981 - June 1987.

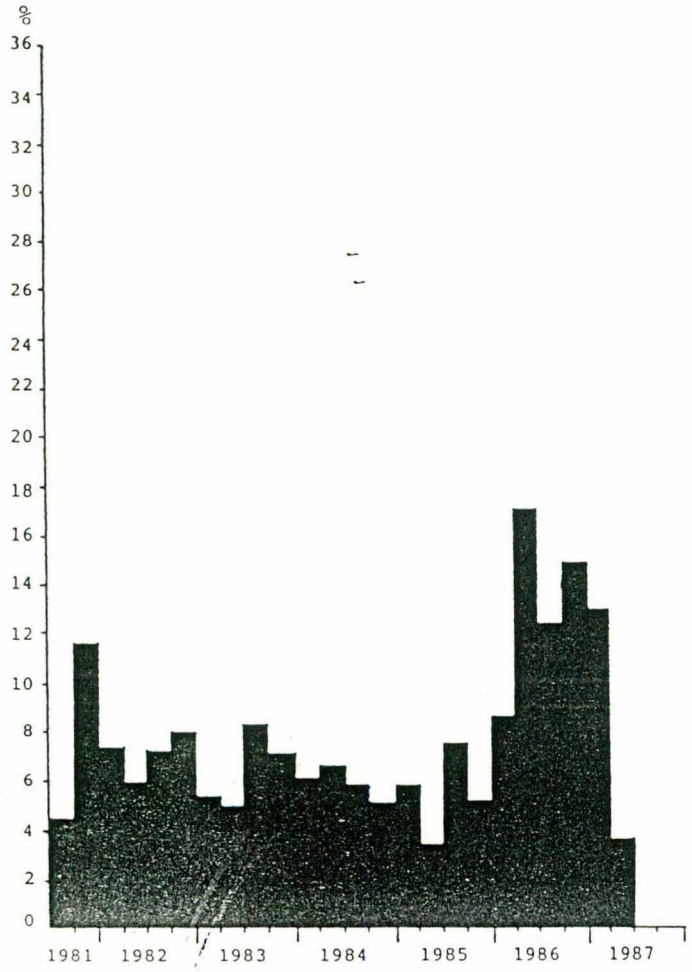


Despite the presence of two apparently small outbreaks recorded in the 3rd quarter of 1982 and the first half of 1984, the rates of PPNG infections reported for Adelaide fluctuate periodically and remained low until the major outbreak reported in the last quarter of 1986. Evidence of interstate spread of PPNG was also reported.

Although the reasons for this major outbreak are not known, Adelaide still reported fairly low rates of PPNG infections throughout the surveillance period, compared with other Australian centres.

Perth (Figure 6)

FIGURE 6. Rates of PPNG isolations in Perth for the period July 1981 - June 1987.



Apart from the high rate reported for the 2nd quarter of 1981 which could have been an artifact of the commencement of reporting, the rates of PPNG infections reported prior to 1986 remained fairly constant in the range of 5-8% of total gonorrhoea isolates.

The factors contributing to the 1986 major outbreak cannot be fully ascertained. Although the endemicity of PPNG strains is comparable to that of Adelaide, anecdotal explanations have been put forward to account for the increased rate of PPNG in Perth:

- the rate of Perth PPNG infections acquired from overseas is high because the tourist traffic between Perth and centres in South East Asia is preferred to that between Perth and Eastern Centres of Australia, and
- periodical visits of US naval forces to Perth may have contributed to cyclic changes in rates of PPNG infections.

NB: A fuller analysis of changes in the incidences of gonorrhoea including PPNG will be published by the Australian Gonococcal Surveillance Program in 1988.

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NEISSERIA GONORRHOEAE - SENTINEL SURVEILLANCE SYSTEM FOR ANTIMICROBIAL RESISTANCE IN CLINICAL ISOLATES

(Based on MMWR Vol. 36/No. 35, 11 September 1987)

Infections caused by strains of Neisseria gonorrhoeae that are resistant to recommended antimicrobials continue to be a growing public health problem. Over the past three years, the incidence of plasmid-mediated, penicillinase-producing N. gonorrhoeae (PPNG) has increased, and it now accounts for 2% of all reported gonococcal infections in the United States[1]. However, the proportions of infections caused by organisms with chromosomally mediated resistance to penicillin, tetracycline and spectinomycin and by gonococci with plasmid-mediated tetracycline resistance (TRNG) have been determined for only a limited number of localities[2,3].

The procedures for laboratory diagnosis and reporting of PPNG have been standardised, and over 90% of public health laboratories in the United States test every gonococcal isolate for production of β-lactamase. However, ascertainment and reporting of other types of antimicrobial resistance have been inconsistent. Whereas PPNG can be detected by a rapid diagnostic test, laboratory diagnosis of chromosomally mediated resistance and TRNG requires relatively expensive antimicrobial susceptibility determination procedures on subcultures of primary isolates. Until recently, surveillance of these strains had been based on a passive reporting system; consequently, geographical areas performing more susceptibility tests than other areas may appear to have higher incidences of these strains.

Because recommendations for therapy should be based on accurate and timely surveillance of antimicrobial resistance in N. gonorrhoeae, the Division of Sexually Transmitted Diseases, Center for Prevention Services (Centers for Disease Control - CDC), in co-operation with the Sexually Transmitted Diseases Laboratory Program, Center for Infectious Diseases (CDC), and State and local health departments, has organised the Gonococcal Isolate Surveillance Project (GISP).

In this project, each of four regionally based laboratories chosen for their expertise in performing antimicrobial susceptibility determinations processes a prospective consecutive sample of isolates from five sexually transmitted disease clinics. Each month, the first 25 urethral isolates from male patients in each clinic are submitted to the regional laboratories where a test for β-lactamase is performed and minimum inhibitory concentrations (MICs)to penicillin, tetracycline, spectinomycin, cefoxitin, and ceftriaxone are determined. Classification of the isolates is based on the CDC surveillance definitions of plasmid-mediated resistance (PPNG, TRNG) and chromosomally mediated resistance[4]. This report summarises the results from the first 15 participating clinics.

Between August 1986 and July 1987, 1420 gonococcal isolates were evaluated:

- 19 isolates (1%) were PPNG, and
- 64 isolates (5%) were TRNG.
  - 45 of the TRNG isolates were reported from Baltimore, where TRNG accounted for 15% (45/300) of gonococcal isolates (Table 1).

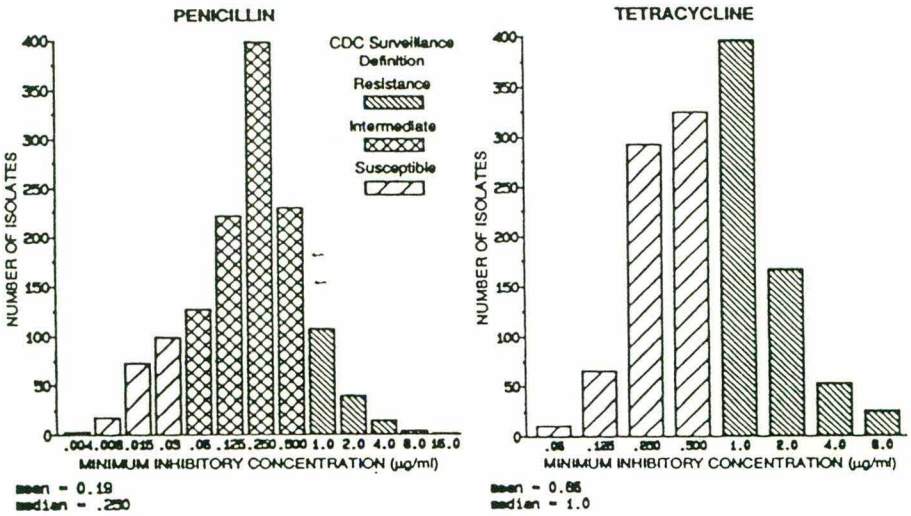
Table 1 Results of the initial phase of the Gonococcal Isolate Surveillance Project, by city - United States, August 1986- July 1987

City	Number of isolates			
	PPNG	TRNG	Without Plasmid-Mediated Resistance	Total
Albuquerque	3	1	69	73
Atlanta	0	2	63	65
Baltimore	0	45	255	300
Birmingham	0	5	58	63
Boston	1	4	120	125
Cincinnati	0	0	74	74
Denver	5	0	172	177
Honolulu	3	0	64	67
Long Beach, CA	0	0	95	95
New Orleans	0	5	99	104
Phoenix	0	0	23	23
San Diego	7	2	138	147
San Francisco	0	0	45	45
St. Louis	0	0	20	20
San Antonio	0	0	42	42
Total	19	64	1 337	1 420

For the 1 337 non-PPNG, non-TRNG isolates, the geometric mean MIC to penicillin was 0.19 µg/ml;
to tetracycline was 0.66 µg/ml;
to cefoxitin was 0.33 µg/ml;
to spectinomycin was 16/5 µg/ml; and
to ceftriaxone was 0.003 µg/ml.

Thirteen percent of the isolates without plasmid-mediated resistance were chromosomally resistant to penicillin, and 48% of them were chromosomally resistant to tetracycline (Figure 1). No isolates were resistant to spectinomycin or ceftriaxone.

FIGURE 1 Distribution of minimum inhibitory concentrations of chromosomally-mediated resistance - Gonorrhoea Isolate Surveillance Project, August 1986 - July 1987.



Editorial Note:

This is the first nationally based prospective survey of antimicrobial resistance in N. gonorrhoeae in the United States since the National Gonorrhoea Therapy Monitoring Study (NGTMS) was conducted from 1972 to 1977 [5, 6]. Previous nationally based reports of chromosomally mediated resistance and TRNG have been limited to summaries of outbreaks [7, 8] and the passive reporting of sporadically occurring cases [7, 8].

The preliminary Gonococcal Isolate Surveillance Project (GISP) survey data underestimate the proportion of infections caused by PPNG strains because New York and Florida, which accounted for 58% of PPNG reported in 1986 [11], are not represented in the initial GISP survey results. The distribution of TRNG reflects a high prevalence of disease in Baltimore, as previously reported [5]. Excluding the Baltimore cases, TRNG represents 2% (19/1,120) of the national sample.

The high incidence of gonococci with chromosomally-mediated resistance to penicillin and tetracycline confirms published reports of geographically limited studies in Seattle and Vancouver [2, 3]. Although no organisms in our sample were resistant to Ceftriaxone, 27 (2%) of the isolates had MICs of 0.06 - 0.25µg/ml and met the criteria for intermediate susceptibility. Trends in ceftriaxone susceptibility will require continued monitoring as this and other third-generation cephalosporins are used more frequently in the treatment of gonorrhoeae. These results, when compared with those from the NGTMS, show a marked decrease in susceptibility to penicillin and tetracycline. Limited GISP trend data suggest that the incidence of chromosomally mediated resistant organisms will continue to increase.

In localities where the proportion of gonococcal strains meeting CDC surveillance definitions of antimicrobial resistance is 1% for 2 consecutive months, treatment and disease-intervention protocols may require modification. Management and treatment guidelines for infections caused by antimicrobial-resistant N.gonorrhoeae are reviewed in the following article.

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ANTIBIOTIC - RESISTANT STRAINS OF NEISSERIA GONORRHOEAE POLICY GUIDELINES FOR DETECTION, MANAGEMENT, AND CONTROL.
(based on MMWR Vol. 36/No. 55, 11 September 1987)

NB. The following guidelines should not be construed as rules, but rather as a source of guidance within the United States.

INTRODUCTION

Background

Although most strains of Neisseria gonorrhoeae in the United States are susceptible to a broad range of antimicrobial agents, relative or absolute resistance to some agents, especially penicillin, is a rapidly growing problem:

- with the introduction and regular use of sulfonamide and penicillin in the 1940s and 1950s, progressive resistance to these drugs evolved; the recommended therapeutic dose of aqueous procaine penicillin G for uncomplicated gonorrhoea rose from 2×10^5 units in 1945 to 4.8×10^6 units in 1972 - a 24-fold increase.
- since the emergence of plasmid-mediated resistance to penicillin (penicillinase-producing Neisseria gonorrhoeae, PPNG) in 1976, clinically significant resistance has been described for the three most widely used classes of drugs

  - the penicillins,
  - the tetracyclines, and
  - the aminoglycosides.

Antimicrobial resistance in the gonococcus can be:

- plasmid-mediated,
- chromosomally-mediated, or
- both.

In the United States, many variations have been identified. The three most important, from a public health standpoint, are:

- PPNG;
- Chromosomally mediated resistance to penicillin (CMRNG); and
- plasmid-mediated, high-level tetracycline resistance (TRNG).

PPNG: are gonococcal strains that have acquired an extra chromosomal element or plasmid that encodes for β-lactamase, and enzyme that destroys the β-lactam ring of penicillin. Of the resistant strains, PPNG has had the greatest impact on public health programs and resources in the mid 1980s:

- the first case of PPNG in the United States was reported in March 1976;
- incidence rose slowly through 1979, and most infections were acquired outside the United States or could be traced to imported cases.
- from 1980 through 1982, reported incidence rose rapidly, and most cases were no longer linked to foreign travel.
- over 4,500 cases of PPNG were reported in 1982.
- the incidence dropped in 1983 to below 3,800 cases, but rose again in 1984, nearly reaching the 1982 level.
- in 1985, reported cases more than doubled, reaching over 8,800; the only states in 1985 that did not report at least one case of gonorrhoea caused by a resistant strain were Nevada and South Dakota.
- in 1986, only Nevada reported no cases; in that year, the total number of cases for the United States was 16,648.

CMRNG: unlike strains with plasmid-mediated resistance, strains with chromosomal resistance to penicillin do not produce β-lactamase. Chromosomally mediated resistance is not limited to penicillin, but is a more general phenomenon that can include resistance to tetracycline, the cephalosporins, spectinomycin, and other aminoglycosides. In most instances to date, these strains have not been associated with treatment failure, either because the levels of resistance have not been high, or because the antibiotic in question was not used for therapy.

- The first outbreak of gonorrhoea in the United States caused by strains with high-level chromosomal resistance to penicillin occurred in North Carolina in 1983; since then, similar organisms have been reported from several areas.
- Between January 1983 and October 1984, reports of 185 CMRNG cases were received from 22 states other than North Carolina.
- Testing for high-level chromosomal resistance to penicillin is still not widespread therefore, the true scope of the problem remains unclear.

TRNG: gonococcal isolates with plasmid-mediated, high-level resistance to tetracycline (minimum inhibitory concentration [MIC] $\geq$ 16µg/ml) were first identified in 1985. Although many individual cases and clusters of TRNG have since been reported, investigation has shown that in most instances, CDC treatment guidelines were followed regarding dual therapy with penicillin and tetracycline, thus avoiding therapy failure. For nearly all patients with TRNG who have been treated with tetracycline alone, the therapy has not been effective.

Rationale for action

No clinical distinctions occur between the infections caused by resistant strains of N. gonorrhoeae and the infections caused by sensitive strains. In a community with a high prevalence of resistant strains, however, the sequelae of acute gonococcal infection, such as:

- pelvic inflammatory disease (PID),
- gonococcal ophthalmia, and
- disseminated gonococcal infection (DGI),

are likely to increase as the numbers of preventable conditions of the "inadequately treated" are added to those of the "never treated". Inadequate therapy can also result in an extended period of infectiousness and an increase in the number of sex partners who become infected.

Resistant strains of N.gonorrhoeae in a community also have an adverse impact on the costs of patient management:

- additional laboratory tests,
- added drug costs,
- extra clinic visits, and
- more extensive disease intervention activities.

Although some of these costs (eg, alternative drugs) are more directly attributable to antimicrobial resistance than others (eg the costs of supervising disease intervention specialists), the aggregate fiscal impact on the public health budget of an infected area is substantial.

The aim of these guidelines is to reduce the adverse health and financial consequences of gonorrhoea through limiting the transmission of those strains that are resistant to one or more antimicrobial drugs. Success will depend on the accomplishment of a wide variety of complementary activities at the program management, laboratory clinic, and community levels.

Scope and approach

These policy guidelines are divided into four sections:

- surveillance,
- control,
- laboratory methods, and
- treatment.

Within each section, several alternatives may be suggested for each recommended course of action. A preferred alternative is often identified as such; however, varied legal, fiscal, demographic, and other factors will determine which options are preferable for specific localities.

A graduated approach is recommended for many of the program elements discussed in these guidelines. This strategy emphasises different degrees and types of activities to be implemented as specific prevalence levels of PPNG are reached in a community. Three levels of response are proposed on the basis of the percentage of all gonorrhoea caused by β-lactamase-producing strains (PPNG) reported in a 2-month period:

. < 1%,
. 1%-3%, and
. > 3%

For such a strategy to be effective, a sensitive management information system needs to be established and maintained in addition to disease surveillance systems based on clinical diagnoses and laboratory tests. The utility of this approach for controlling CMRNG and TRNG has not been established.

Surveillance

Surveillance for antibiotic-resistant gonorrhoea must fulfill two requirements:

1. surveillance data must be processed with little or no delay, and
2. a system must be in place for the prompt review and analysis of data so that appropriate adjustments can be made in disease intervention activities and therapy recommendations.

Testing

At the local level, the primary aim of surveillance is to detect PPNG. Although the detection of all types of resistance is ideal, the technical, difficulties and costs of performing disc-diffusion and agar-dilution susceptibility tests often preclude comprehensive surveillance for CMRNG and TRNG. The following stratified approach is recommended:

. All isolates of N. gonorrhoeae should be tested for β-lactamase production
. If a sexually transmitted disease (STD) project area cannot arrange for TRNG and CMRNG testing of all isolates, selected priority isolates should be tested. Priority isolates are of two kinds:

1. - Positive post-treatment isolates,
   - Isolates from patients with DGI, and
   - Isolates from patients with gonococcal ophthalmia (A determination of susceptibility in these instances may have direct impact on the clinical course of the case); and

2. Isolates from members of specific risk groups that are known to have a high incidence of infection with resistant strains (These groups should be determined locally on the basis of the epidemiologic data compiled in a management information system).

Adequate surveillance depends upon laboratory support. STD programs need to ensure that appropriate funds are maintained for performing these procedures. In areas with a low incidence of gonorrhoea, the establishment of multistate regional laboratories for testing should be considered.

Reporting of Gonorrhoea

A useful surveillance system must be both representative and timely. A surveillance system that is representative must accurately observe over time:

1. The occurence of a health event; and
2. the distribution of that event within the population "Timeliness" is a qualitative measure of the period between the occurrence of a health event and the report of that event to the public health agency responsible for instituting control and prevention measures. Gonorrhoea caused by antibiotic-resistant strains unually occurs within the same population groups as gonorrhoea caused by penicillin-sensitive strains. To attempt to disrupt the transmission of resistant strains without having knowledge of the total community burden of gonococcal infections would be unrealistic. A gonorrhoea morbidity reporting system that is incomplete, or slow, or that excludes the private sector would be of little or no value in designing, implementing, and appropriately modifying an effective control program. To be of value in controlling antibiontic-resistant strains, a local gonorrhoea morbidity reporting system must:

   a. include cases reported by emergency rooms, community clinics (both government and non-government), private physicians, and the military;
   b. provide basic demographic information on patients; and
   c. limit to 14 calendar days the period from provider's diagnosis to the first aggregation of data by the responsible public health agency.

Laboratories should report infections caused by antibiotic-resistant strains by telephone the same day they are identified.

Building a Local Surveillance Network

Data on the rates of gonococcal resistance in the United States are derived primarily from cases seen in public health clinics. The coordination of individual STD project areas with other components of the health-care system will greatly increase surveillance effectiveness. Some of the more

important of these components are:

. United States military preventive medicine commands.
. Health maintenance organisations, community health centres, and correction/detention facilities.
. Large commercial laboratories serving the private sector.
. Professional medical groups and organisations, such as the College of American Pathologists, local and state medical societies, and specific groups of hospital staff members.

National Surveillance of Antimicrobial Resistance

- National surveillance of antimicrobial-resistant strains of N. gonorrhoeae will be conducted through a Gonococcal Isolate Surveillance Project, which is being implemented by the Division of Sexually Transmitted Diseases and The Sexually Transmitted Diseases Laboratory Program, CDC.
- This system will test approximately 400 cultures per month from clinical gonorrhoea cases in 20 participating cities. A broad range of antimicrobial susceptibilities will be determined by using a reference method.
- Quarterly reports summarising the trends in national N. gonorrhoeae resistance will be prepared and published.

CONTROL

With the increasing proportion of gonorrhoea in the United States caused by PPNG, every health jurisdiction must have surveillance, patient-care, and outbreak-management procedures in place to identify new cases rapidly and thereby limit transmission. Different strategies and mixes of control efforts will be needed in different areas. In addition to incidence and prevalence levels, other factors that might be considered in the design of control efforts include:

1. available resources,
2. total and "at-risk" population sizes and characteristics,
3. travel patterns of infected persons, and
4. proximity of the locality to known endemic areas.

The success of disease intervention efforts is directly related to the availability of adequate resources. The greatest impact an disease incidence achieved when intervention personnel are effectively mobilised before resistant strains become thoroughly "seeded" in traditional gonorrhoea core areas. STD control programs should concentrate staff and other resources in the specific neighbourhoods reporting cases of PPNG. In the absence of reported cases of PPNG, staff members need to be concentrated in the neighbourhoods traditionally reporting a high incidence of gonorrhoea and other STDs.

To enhance monitoring and to focus control efforts, each STD project area should evaluate PPNG:

1. using an area no larger than a local health jurisdiction (county, health district, or area served by a clinic) for the analysis; and
2. on the basis of prevalence, or the percentage of all reported cases of gonorrhoea in the area that are caused by β-lactamase-producing strains.

Levels of Control Activity

Multiple STD program elements are involved in controlling antibiotic-resistant strains of N. gonorrhoeae. Three levels of activity are proposed for each element, corresponding to the proportion of all gonorrhoea in the target area that is caused by PPNG during a 2-month period (Table 1).

The 2-month period and the PPNG proportion cutoff levels (<1%, 1-3%, >3%) were empirical from a review of county-specific PPNG morbidity data reported to the Division of Sexually Transmitted Diseases, CDC, from January 1985 through September 1986.

Non-Endemic Areas

A basic control program should be in place in all areas, REGARDLESS OF WHETHER RESISTANT STRAINS HAVE BEEN DETECTED. The basic control program is appropriate for non-endemic areas, which are defined as localities in which <1% of gonorrhoea reported in a 2-month period is caused by PPNG. In Table 1, this level of activity is described in the left-hand column.

Endemic areas

Activities in addition to those of a basic program should be undertaken in endemic areas, defined as localities in which 1%-3% of gonorrhoea reported in a 2-month period is caused by PPNG. The purpose of the additional activities is to focus existing STD control resources on PPNG and intercept the spiraling trend before a hyperendemicity level is reached. In Table 1, this level is described by the combination of the left and centre columns. The efficacy of these activities in controlling CMRNG and TRNG has not been demonstrated.

Hyperendemic areas

Some different activities are appropriate for hyperendemic areas - those in which more than 3% of the gonorrhoea cases reported in a 2 month period are caused by PPNG. In a hyperendemic area, an antibiotic effective against resistant strains should be provided to ALL patients with gonorrhoea. Because of this treatment policy, intervention priorities should be based not on the laboratory identification of PPNG, but rather on epidemiologic profiles of high-risk gonorrhoea patients. In Table 1, this level is described in the right-hand column. The efficacy of these activities in controlling CMRNG and TRNG has not been demonstrated.

Management Information System

The success of any STD program in controlling PPNG (as well as other STDs) depends on accurate information, adequate resources, and the energetic application of proven control methods. Accurate information is the keystone. Each STD control program needs a data collection system that permits the quick retrieval of complete information on patients. Hence, every STD program should maintain a continually updated database for all reported cases of PPNG. At a minimum, this database should reflect the demographic characteristics, disease-intervention data, and risk-factor information that can be used to develop patient profiles for the high-risk population. When all relevant information is computerised, timely decisions on prevention and control can often be put into effect before an endemic situation develops.

TABLE 1. Elements of PPNG control for state and local STD programs

Element	Non-endemic areas (PPNG < 1%) Basic control program	Endemic areas (PPNG 1%–3%) Basic control program PLUS	Hyperendemic areas (PPNG > 3%) Intensified/targeted program
Management information system	Develop a high-risk patient profile. Identify geographic target areas. Identify key providers. Track impact (individual and collective) of Disease Intervention Specialists (DIS).		Maintain the management information system of a basic program.
GC* culturing	Include: known exposures to PPNG, GC treatment failures, all females 30 years of age seen in STD clinics and at GC screening sites, as well as those with clinical or epidemiologic justification seen by a) public and private care providers in high-GC-incidence areas; and b) detention centres, and all exposed and/or symptomatic individuals with history of recent travel to endemic or hyperendemic areas or with history or contact with a prostitute.	Include: all males seen in STD clinics, as well as those with clinical or epidemiologic justification seen by a) public and private primary care providers in high-GC-incidence areas; and b) detention centres, all male urethritis patients in high-GC-incidence areas, and all females 30-44 years of age seen in STD clinics.	Include: GC treatment failures, selected high-risk asymptomatic persons in appropriate health care settings, and periodic representative samples of GC patients from both high-and low- incidence areas for monitoring trends.
Testing for antimicrobial resistance	Test all GC isolates in public and military laboratories for β-lactamase production; further test all positive test-of-cure (TOC), ophthalmia, and DGI isolates for antimicrobial sensitivity.	Test all GC isolates in private laboratories for β-lactamase production. Test all isolates from children and PID patients for antimicrobial sensitivity.	Test all GC isolates for β-lactamase production. Also test isolates from periodic representative samples for resistance to public STD clinic's drug of choice for uncomplicated GC.

Element	Non-endemic areas (PPNG <1%) Basic control program	Endemic areas (PPNG 1%-3%) Basic control program PLUS	Hyperendemic areas (PPNG >3%) Intensified/targeted program
GC screening quality assurance	Determine monthly smear-culture correlations for all STD Clinics. Conduct a semiannual quality assurance (QA) review of all STD clinics and screening sites. Conduct a semiannual QA review of hospitals and GC screening sites with their own laboratories. Offer annual QA review service to other providers testing in volumes of >20/ month.	Replace annual QA reviews of other providers doing GC testing with a system of ongoing voluntary self-assessment with mail-in reports.	Conduct all standard activities of a basic program.
Reporting	Ensure that ALL laboratories report PPNG isolates by telephone the same day they are identified.	Initiate active surveillance of key private providers.	Ensure that ALL laboratories report PPNG isolates by telephone the same day they are identified.
Treatment	Observe CDC guidelines for prevention and treatment of GC in all STD clinics. Inform all other providers of CDC Treatment Guidelines, and periodically monitor their GC treatment practices. Review all PPNG cases to ensure proper treatment. Selectively treat for PPNG all patients at STD clinics who meet the PPNG patient profile developed through the management information system.	Urge selected providers in PPNG-affected neighbourhoods to treat all GC initially with recommended anti-PPNG regimen. Treat with recommended anti-PPNG regimen all GC patients in STD clinics who meet PPNG patient profile.	Provide anti-PPNG therapy as primary regimen for prevention or treatment of GC in STD clinics. Urge all providers in key PPNG-affected neighbourhoods to treat initially with recommended anti-PPNG therapy; periodically monitor actual treatment practices. Urge providers in other areas to offer all GC patients anti-PPNG therapy.
Test of cure	Refer for TOC all female GC patients from STD clinics. Recommend to all other providers that females be referred for TOC. Refer for TOC all PPNG patients, and following up to ensure return visit.	Refer high-risk male patients for TOC. Refer all PPNG patients for 1 to 2 month reculture.	Refer for TOC a representative sample of male GC patients seen in STD clinics (without field follow-up).

Element	Non-endemic areas (PPNG <1%) Basic control program	Endemic areas (PPNG 1%-3%) Basic control program PLUS	Hyperendemic areas (PPNG >3%) Intensified/targeted program
Disease Intervention Specialist activities	Apply related case analysis, clustering, and reinterviewing techniques to all PPNG cases. Set DIS process performance standards. Ensure that DIS are provided ongoing, interactive first-line supervision and training.	Reorder disease priorities for intervention efforts, and relieve DIS from all activities not related to patient management. Interview all clinic patients who fit the PPNG patient profile, and provide field follow-up of their sex partners. Assign DIS (if available) to major hospitals and other provider sites in high-incidence neighbourhoods.	Interview all clinic patients who fit the PPNG patient profile, and provide field follow-up of their sex partners. Apply reinterviewing and clustering techniques on a selective basis.
Education	Develop educational objectives that are specific, measurable, and applicable to PPNG control for GC patients, health providers, members of risk groups, and the community as a whole.	Issue medical alerts to all providers, emphasizing culture methods, presumptive PPNG treatment, and reporting. Visit key providers to reinforce their essential role, update recommendations, and provide feedback. Target high-incidence neighbourhoods for posters, pamphlets, and radio public service announcements. Issue press releases on the PPNG problem and the control actions being taken.	Maintain educational activities of a basic control program.

* Gonorrhoea

LABORATORY PROCEDURES

Ongoing surveillance for antimicrobial resistance in gonococcal strains should be an integral part of a standard STD laboratory program. The laboratory plays an important role in two areas:

- first, among those patients with clinical evidence that treatment has not been effective, the laboratory can often help differentiate true drug failure from reinfection.
- second, the laboratory can help define the characteristics of the strains present in the community, enabling health officials to make a rational choice of therapeutic regimens.

Ideally, all isolates should be screened for clinically important antimicrobial resistance. If resources are limited, clinically or epidemiologically important isolates should be tested, using the priority schedule outlined above (SURVEILLANCE - Testing). Clusters of treatment failures may suggest an outbreak of a resistant strain. When an outbreak is suspected, a consecutive sample of at least 50 isolates should be evaluated in consultation with a reference laboratory.

β-Lactamase Assay

All gonococcal isolates should be tested for β-lactamase. β-lactamase tests may be done on primary cultures or on pure subcultures. A chromogenic cephalosporin test is preferred, although the iodometric or acidometric procedures can be used. β-lactamase-positive and -negative control strains of N. gonorrhoeae should be tested with each batch of clinical isolates. No direct method for detecting β-lactamase in patients specimens (eg urethral exudate) is currently recommended.

Determination of Antimicrobial Susceptibility

Test results for antimicrobial susceptibility are only a measure of the in vitro susceptibility of an isolate to an antibiotic. Treatment failure may result from a variety of causes, and patients may experience failure of therapy even when infected with isolates that manifest in vitro susceptibility. Test results must be used as an adjunct to-not in place of - clinical evaluation.

A. Agar-dilution method

Agar-dilution susceptibility testing is the most reproducible and accurate method currently available. The Centers for Disease Control (Atlanta) recommends testing of isolates for susceptibility to penicillin, tetracycline, spectinomycin, cefoxitin, and ceftriaxone:

- the recommended medium is a GC base with a defined supplement, such as Isovitalex;
- Mueller-Hinton medium should not be used;
- inoculum size is 10^4 organisms/ml.

This method should be standardised in accordance with the protocols of the National Committee for Clinical Laboratory Standards (NCCLS). Further details of the protocol, dilution ranges of the antibiotics, and reference strains are available from the The Sexually Transmitted Diseases Laboratory Program, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Georgia 30333.

B. Disc-diffusion method

Disc-diffusion testing is the most common method for determining antibiotic susceptibility in N. gonorrhoeae. Test results should correlate with data from reference strains tested with the agar-dilution technique. The protocol and reference strains for the disc-diffusion method may be obtained from The Sexually Transmitted Diseases Laboratory Program. If disc-diffusion susceptibility tests are performed by using non-standardised reagents, the results must be considered presumptive and should be confirmed by using the reference or standardised alternative procedures.

- the recommended medium for disc-diffusion testing is supplemented GC agar base.
- recommended discs are - penicillin (10 IU),
  - tetracycline (30 µg),
  - spectinomycin (100 µg), and
  - ceftriaxone (30 µg)
- culture-plate inoculation and test-reading procedures should conform to the M7-A dilution standards of the NCCLS.

Unfortunately, current data that correlate disc-diffusion test results with clinical outcome are not available for each antibiotic. Three categories of results for susceptibility tests are proposed (Tables 2, 3):

1. A susceptible result implies a <5% likelihood of treatment failure.
2. An intermediate result indicates predictable failure rates of 5% - 15% if the patient is treated with the tested antibiotic in the standard dosage (in most cases of intermediate susceptibility, a higher dose or prolonged therapy results in >95% cure rates).
3. A resistant result is associated with clinical treatment failure rates of >15%.

TABLE 2. Interpretive categories for penicillin and spectinomycin zone size results

	Size (mm)	Agar-dilution Correlates (µg/ml)
Penicillin (10 IU):		
Resistant*	≤ 25	≥ 1
Intermediate	26-29	0.06-0.5
Susceptible	≥ 30	≤ 0.03
Spectinomycin (100 µg):		
Resistant	≤ 15	≥ 64
Intermediate	16-18	***
Susceptible **	≥ 19	≤ 32

* zone sizes with isolates that produce plasmid-mediated β-lactamase are usually < 20mm.
** if a zone of inhibition is observed, it may contain resistant colonies.
*** dilutions between 32 and 64 are not usually performed.

TABLE 3. Interpretive categories for tetracycline and ceftriaxone zone size results

	Size (mm)	Agar-dilution Correlates (µg/ml)
Tetracycline (30 µg):		
Resistant*	<20	≥ 16
Resistant**	≤ 30	≥ 1
Susceptible	≥ 35	≤ 0.5
Ceftriaxone (30 µg):		
Resistant	≤ 30	>1
Intermediate	31-34	0.06-0.5
Susceptible	≥ 35	≤ 0.03

* plasmid-mediated, high-level resistance (TRNG)
** chromosomal resistance

Tetracycline and ceftriaxone disc-diffusion testing

Disc-diffusion tests for susceptibility to tetracycline are particularly prone to problems with reproducibility, even when standardised methods are used. Additionally, the wide range of susceptibility to tetracycline and the presence of determinants for both plasmid-mediated and chromosomally mediated resistance have made if difficult to interpret sensitivities determined by tetracycline disc:

- tetracycline is recommended as the sole therapy only in unusual situations;
- routine screening for tetracycline resistance remains important, however, because of the propensity of strains of TRNG to acquire other resistance determinants; and
- in most cases, tetracycline screening should be targeted at identifying TRNG strains.

Preliminary interpretive criteria for testing susceptibility to ceftriaxone (Table 3) are based on regression data from a similar spectrum-class drug (cefotaxime). These recommendations must be considered tentative, since the incidence of organisms with minimum inhibitory concentrations of >0.03 ug/ml is $<5\%$.

Antibiotic - Containing Media

Penicillin-containing selective media have not been sufficiently evaluated to be recommended as a screening method for identifying resistance of directly plated specimens.

For subculture screening:

- supplemented GC-agar base containing 1µg/ml penicillin can be used to screen for penicillin resistance, and
- media containing 10µg/ml tetracycline can be used to screen for plasmid-mediated high-level tetracycline resistance.

Further details of these procedures can be obtained from the Sexually Transmitted Diseases Laboratory, CDC.

Vancomycin - sensitive N. gonorrhoeae

Vancomycin-sensitive strains may not be grown on selective media, which commonly contain 4ug/ml vancomycin. If N. gonorrhoeae isolation rates are abnormally low, strains may be vancomycin-sensitive. Vancomycin-sensitive strains can be detected either by using a biplate culture system that contains chocolate agar plus a selective medium or by using a selective medium that contains only 2µg/ml vancomycin.

THERAPY

These guidelines are not intended to cover all treatment regimens. Rather, they provide guidance for selected regimens that meet general criteria of;

- efficacy,
- ease of administration, and
- acceptability by the patient.

In addition, they reflect a consensus of public health opinion about a regimen of treatment for gonorrhoea that will effectively treat the commonly associated - but often undetected - chlamydial infection.

Therapy may fail for patients infected with PPNG or TRNG strains of N. gonorrhoeae when they are treated solely with either penicillin or tetracycline. Similarly, gonococci with chromosomally mediated resistance to penicillin or tetracycline, as well as gonococci that are only moderately susceptible to these drugs, are associated with unacceptably high treatment-failure rates when currently recommended penicillin and tetracycline regimens are followed.

Choice of Regimen

These guidelines suggest an approach to the treatment of patients with gonorrhoea based on the known prevalence of PPNG in a community. In cases of chromosomally mediated penicillin resistance, alternative drug therapy is unnecessary unless the community prevalence of strains associated with treatment failure exceeds 5% in a 2-month period. In that instance, the same therapy approach as indicated for endemic community levels of PPNG would be appropriate. The designation of three levels of prevalence of PPNG follows the scheme outlined above (CONTROL - levels of Control activity).

- In Non-Endemic Areas

  In areas where PPNG accounts for < 1% of all gonorrhoea, patients should be routinely treated with a regimen of proven efficacy at all anatomical sites against penicillin-sensitive strains. If regimens such as **ceftriaxone** with **probenecid** (or others known to be less effective against antibiotic-resistant strains) are employed, routine susceptibility testing and comprehensive test-of-cure evaluations will be required to assure continued therapeutic efficacy. If budgetary and logistic conditions are amenable, **ceftriaxone** intramuscularly (IM) would be a highly desirable alternative.

. In Endemic Areas

In areas in which PPNG accounts for 1%-3% of all gonorrhoea strains, a regimen of proven efficacy against all strains of N. gonorrhoeae should be used by selected public and private providers in neighbourhoods with increased levels of gonorrhoea caused by resistant strains. It should also be used by STD clinics for all patients meeting high-risk profile criteria. The drug of choice in this case would be **ceftriaxone** IM;

- all isolates associated with apparent treatment failure,
- all isolates from children, and
- all isolates from patients with complicated gonococcal infections (eg, disseminated gonococcal infection, pelvic inflammatory disease, and ophthalmia)

should be tested for antimicrobial sensitivity. Monitoring of therapeutic responses is as important as monitoring antimicrobial susceptibilities.

. In Hyperendemic Areas

In areas in which PPNG accounts of > 3% of all gonorrhoea, all public and private providers in infected neighbourhoods should use therapy effective against resistant strains. The drug of choice in this case would be **ceftriaxone** IM. Another indicator of the need for this therapy is the occurrence of true treatment failures (eg positive cultures for N. gonorrhoeae from patients who return for test-of-cure evaluations 3 to 5 days after completion of therapy and who report having had no sexual exposure during this time) at levels of 3% - 5% for patients treated with the amoxicillin-probenecid regimen.

- Other **third-generation cephalosporins** may prove to be as efficacious as **ceftriaxone**.
- In all indications for **ceftriaxone** treatment, **spectinomycin** is an alternative.
- Some site specificity is lost, however, especially for infections of the pharynx.

Dosage of Ceftriaxone

At present, 250mg of ceftriaxone IM in a single dose is the regimen favored for patients with uncomplicated gonorrhoea caused by antimicrobial-resistant strains:

- Although some investigators report therapeutic success with a lower dose (eg 125mg), insufficient data preclude a general recommendation at this time, especially for areas having a high prevalence of resistant strains.
- A major concern is that use of the 125 mg dose may accelerate the development of strains resistant to ceftriaxone. As data accumulate from providers who routinely use the 125mg dose to treat patients with uncomplicated gonorrhoea, that choice may be recommended.

Thus, it is particularly important that those areas with a high proportion of resistant strains maintain a sensitive monitoring system for ceftriaxone resistance.

The national Gonococcal Isolate Surveillance Project co-ordinated by the Centers for Disease Control (SURVEILLANCE - National Surveillance of Antimicrobial Resistance) will be examining ceftriaxone resistance in selected areas of the United States and reporting results regularly in the Morbidity and Mortality Weekly Report (MMWR). Some minimal ceftriaxone resistance has been sporadically, but none approaches clinical significance to date.

Recommendations for Therapy

For adults with uncomplicated

. urethral,
. endocervical,
. pharyngeal, or
. rectal infections

IN PPNG-ENDEMIC AND HYPERENDEMIC AREAS

Ceftriaxone: 250mg IM

PLUS

Doxycycline*: 100mg, orally twice a day for 7 days

OR **Tetracycline HCl** 500mg, orally 4 times a day for 7 days

OR for patients for whom tetracyclines are contra-indicated (pregnant women and prepubertal children) or not tolerated, the single-dose regimen may be followed by:

erythromycin base or stearate: 500mg, orally 4 times a day for 7 days
OR **erythromycin ethylsuccinate:** 800mg, orally 4 times a day for 7 days
OR equivalent doses of other approved **erythromycin** preparations

* in the United States, the daily cost of generic doxycycline is now equivalent to the daily cost of tetracycline. The twice-a-day regimen results in better compliance on the part of most patients.

The treatment recommendations for other conditions diagnosed in PPNG-endemic and -hyperendemic areas:

. follow the format of the Centers for Disease Control *1985 STD treatment Guidelines*[1], and
. are detailed below:

I. Disseminated Gonococcal Infection

Antibiotic-resistant gonococcal strains may cause disseminated gonorrhoea. Hospitalisation is recommended in these instances, especially for persons who:

- cannot reliably comply with treatment,
- have uncertain diagnoses, or
- have purulent synovial effusions or other complications.

Attempts should be made to exclude endocarditis or meningitis.

When, - antibiotic-resistant gonococcal strains are suspected in disseminated gonorrhoea,
OR - in all disseminated gonorrhoea cases occurring in PPNG -endemic or -hyperendemic areas,

the following treatment schedule is recommended:

Ceftriaxone: 1g, intravenous (IV), once a day for 7 days.

An equivalent **third-generation cephalosporin** may be used in appropriate doses. Most authorities recommend at least a week of antibiotic therapy for patients with purulent arthritis or gonococcal septicaemia. If early hospital discharge is required, an expert should be consulted to determine appropriate outpatient follow-up therapy.

II Meningitis and Endocarditis

Patients with gonococcal meningitis or endocarditis occurring in PPNG -endemic and -hyperendemic areas should be treated with high-dose intravenous **third-generation cephalosporins** in consultation with an expert.

Optional therapy may be guided by results from in-vitro susceptibility tests. Most authorities recommend treating patients with meningitis for 10-14 days and those with endocarditis for at least 1 month.

III Ophthalmia

A. Gonococcal Ophthalmia in Adults

In PPNG-endemic and -hyperendemic areas, adult patients with gonococcal ophthalmia should be hospitalised and treated with either

Ceftriaxone, 1g, once a day, IM or IV, for 5 days
OR equivalent doses of another effective **third-generation cephalosporin**.

An ophthalmologist should evaluate the patient for ocular complications. Adjuvant topical antibiotics are not thought to offer any significant advantage. Irrigation of the eyes with saline or buffered ophthalmic solutions may be a useful adjunctive therapy to eliminate discharge.

B. Gonococcal Ophthalmia in Neonates

Untreated gonococcal ophthalmia in neonates is highly contagious and may rapidly lead to blindness:

. all neonates with gonococcal ophthalmia in PPNG - endemic and -hyperendemic areas should be treated with

ceftriaxone, 25mg-50mg/kg body weight/day, IV or Im, for 7 days;

. an equivalent **third-generation cephalosporin** may be used in appropriate doses;
. topical antimicrobial preparations alone are not sufficient and are not required when appropriate systemic therapy is given;
. irrigation of the eyes with saline or buffered ophthalmic solutions may be useful adjunctive therapy to eliminate discharge;
. both parents of newborns with gonococcal ophthalmia must be treated; and
. simultaneous ophthalmic infection with Chlamydia trachomatis has been reported and should be considered if a patient does not respond satisfactorily to recommended treatment.

C. Neonatal Prophylaxis and Prophylactic Treatment

. All newborns should receive ocular prophylaxis with either

1% **silver nitrate** solution,
1% **tetracycline** solution (or ointment)
OR

1% **silver nitrate** solution
0.5% **erythromycin** ointment.

. Prophylaxis should be given within 1 hour after birth.
. No one regimen is completely effective.
. **Tetracycline** and **erythromycin** are also active against C. trachomatis.

. The prophylaxis failure rate of the antibiotic preparations for infections with resistant gonococcal strains is unknown. However, the intraocular antibiotic concentrations achieved with routine prophylaxis are high. Studies are currently under way to evaluate this problem.
. Neonates born to mothers with documented gonococcal infection peripartum should be treated with **ceftriaxone**, 125mg, IM, in one dose.
. Low-birth-weight infants should receive 25mg-50mg/kg body weight.

IV Acute Pelvic Inflammatory Disease (PID) (Endometritis, Slapingitis, Parametritis, and/or Peritonitis)

Acute PID refers to the acute clinical syndrome (unrelated to pregnancy or surgery) attributed to the ascent of microorganisms from the vagina and endocervix to the endometrium, fallopian tubes, and/or contiguous structures. Many cases of PID are caused by more than one organism.

Causative agents include:

- N. gonorrhoeae (antibiotic-sensitive and antibiotic-resistant strains),
- C. trachomatis,
- Anaerobic bacteria,
- facultative gram-negative bacilli,
- Mycoplasma hominis, and rarely,
- Actinomyces israelii.

In the individual patient it is often impossible to identify and differentiate among the various causative agents. Because of this difficulty, all persons who have PID in areas endemic or hyperendemic for resistant gonorrhoea should be treated with agents effective against a broad range of pathogens, including antibiotic-resistant N. gonorrhoeae. Although the treatment of choice is not established, combination therapy is usually indicated. Patients with antibiotic-resistant gonococcal infection who are inappropriately treated are at high risk of developing PID.

A. Hospitalisation and Inpatient Treatment

Hospitalisation of patients with acute PID is indicated when:

1. the diagnosis is uncertain,
2. surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded,
3. a pelvic abscess is suspected,
4. the patient is pregnant,
5. the patient is a pre-pubertal child,
6. severe illness precludes outpatient management,
7. the patient is unwilling or unable to follow an outpatient regimen,
8. outpatient therapy has not been effective for the patient, or
9. clinical follow-up within 72 hours of starting antibiotic treatment cannot be arranged.

Many experts recommend that all patients with PID be hospitalised for treatment. Special consideration should be given to adolescents because their compliance with therapy is unpredictable, and the long-term sequelae of PID are particularly severe in this group.

B. Combination Regimens with Broad Activity Against Major Pathogens.

Inpatient Regimens

. Regimen A (preferred when N. gonorrhoea or C. trachomatis is suspected as the primary pathogen):

Doxycycline: 100mg, IV, twice a day
PLUS Cefoxitin*:2g, IV, four times a day

- Continue drugs IV for at least 4 days, and at least 48 hours after the patient improves (defervescence, decreased symptoms an signs).
- Then continue **doxycycline**, 100 mg, orally, twice a day to complete 10-14 days of total therapy.

. Regimen B (preferred when facultative gram-negative baccilli or anaerobes are suspected as the primary pathogens):

Clindamycin: 900mg, IV, 3 times a day

MIXED in the same infusion with

Gentamicin: 2mg/kg, IV,

. followed by 1.5mg/kg, 3 times a day for patients with normal renal function;

- serum gentamicin levels should be monitored, and dose or dose interval adjusted to maintain a gentamicin serum level of 5-10µg/ml 30 minutes post-administration;
- continue drugs IV for at least 4 days and at least 48 hours after the patient improves; and
- then continue clindamycin, 450mg, orally, 4 times a day to complete 10-14 days of therapy.

N.B. At present, most antibiotic-resistant strains of N. gonorrhoeae are susceptible in-vitro to the aminoglycosides.

* The regimen is unchanged from that found in the *1985 STD Treatment Guidelines*. PID is a polymicrobial infection which may include N. gonorrhoeae, C. trachomatis, anaerobes, and facultative gram-negative bacilli. Some published studies have shown cefoxitin to be a more effective agent than ceftriaxone against anaerobic infection.

REFERENCE

1. MMWR (1985) 34 (Suppl 45): 835-865, 925-945.

AUSTRALIA - COMMUNICABLE DISEASES INTELLIGENCE

REPORTING PERIOD - 16-11-87 to 29-11-87 BULLETIN NUMBER CDI 87/24
VIRAL IDENTIFICATIONS FROM CONTRIBUTING LABORATORIES

VIRUS OR VIRAL ANTIGEN	ICPMR (NSW)/ WVH (ACT)	RAHC (NSW)	PHH/ POW (NSW)	FAIR-FIELD (VIC)	RCH (VIC)	IMVS (SA)	STATE LAB (QLD)	STATE LAB (WA) *	Total
0100 ADENOVIRUS NOT TYPED		1	3	5	11	1	10	2	33
0101 ADENOVIRUS TYPE 1					1			2	3
0102 ADENOVIRUS TYPE 2		1		1				1	3
0103 ADENOVIRUS TYPE 3				2				1	3
0104 ADENOVIRUS TYPE 4								1	1
0199 ADENOVIRUS TYPING PENDING			1		3				4
0201 INFLUENZA A VIRUS			2			2	1	1	6
0202 INFLUENZA A VIRUS SUBTYPE H3N2						2			2
0203 INFLUENZA B VIRUS			1	3	4	14		5	27
0206 INFLUENZA A VIRUS SUBTYPE H1N1						1			1
0301 PARAINFLUENZA VIRUS TYPE 1					3	3			6
0302 PARAINFLUENZA VIRUS TYPE 2					1				1
0303 PARAINFLUENZA VIRUS TYPE 3	3	1		3	6	3	10	4	30
0400 RESPIRATORY SYNCYTIAL VIRUS (RS)	4			6	7		2		19
0500 RHINOVIRUS (ALL TYPES)				1	6	2	7		16
0600 MYCOPLASMA PNEUMONIAE	8		6	3	5	6	10	12	50
0700 ORNITHOSIS-PSITTACOSIS	1			3				1	5
0800 COXSACKIEVIRUSES GROUP A - NOT TYPED								1	1
0809 COXSACKIEVIRUS A9				1	2			1	4
0816 COXSACKIEVIRUS A16				1	2				3
0901 COXSACKIEVIRUS B1				1					1
0902 COXSACKIEVIRUS B2		1		3	3				7
0903 COXSACKIEVIRUS B3					1		1		2
0904 COXSACKIEVIRUS B4						1		1	2
1000 ECHOVIRUS NOT TYPED						2			2
1022 ECHOVIRUS TYPE 22				2					2
1027 ECHOVIRUS TYPE 27								1	1
1100 POLIOVIRUS NOT TYPED			4		1		1		6
1101 POLIOVIRUS TYPE 1				1					1
1102 POLIOVIRUS TYPE 2		2		2	1				5
1103 POLIOVIRUS TYPE 3				1					1
1200 MUMPS VIRUS	2	1	2					2	7
1300 HERPES VIRUS GROUP-NOT TYPED	3		4	1					8
1301 HERPES SIMPLEX VIRUS NOT-TYPED		2		2				2	6
1302 EPSTEIN-BARR VIRUS (EB VIRUS)	13	4	1	2	1	2	3	10	36
1303 VARICELLA-ZOSTER VIRUS	3		4	2			5	3	17
1306 HERPES SIMPLEX TYPE 1			6	34		9	34	27	110
1307 HERPES SIMPLEX TYPE 2			9	55		27	49	67	207
1399 HERPES VIRUS TYPING PENDING					3	2			5
1401 COXIELLA BURNETI	2						3		5
1502 PICORNA VIRUS-NOT TYPED			10				5	2	17
1516 MILKERS NODULE VIRUS		1							1
1521 MEASLES VIRUS			2	1					3
1522 RUBELLA VIRUS	1					1			2
1532 HEPATITIS B ANTIGEN	20	2	3	13	2	16	19	17	92
1535 HEPATITIS A ANTIBODY	1		1	4		3		6	15
1541 CHLAMYDIA A - C TRACHOMATIS	36		2	29	1	30	22	43	163
1556 CMV - CYTOMEGALOVIRUS	4		6	27	5		50	9	101
1564 ROTAVIRUS	12	15	2	8	4	16	3	2	62
1599 ENTEROVIRUS TYPING PENDING			6		6		1		13
9990 AUSTRALIAN ENCEPHALITIS							1		1
9992 ROSS RIVER VIRUS							2	1	3
9995 DENGUE							2	1	3
Total	113	31	75	217	79	143	241	226	1,125

*
Includes 9 reports from the Princess Margaret Hospital for Children.

AUSTRALIA - COMMUNICABLE DISEASES INTELLIGENCE

PERIOD : 16-11-87 to 29-11-87 BULLETIN NO 87/24

Viral Identifications by Clinical Information Table 1.
Code 00,99 -No ill or data; 01,02,11,12 -Respiratory; E3 -Encephalitis; M3 -Meningitis; 04 -Paralysis; 05,13 -CNS other unspec.; 07,49 -GI; 17,47 -Hepatic; 19 -CVS; 89 -Urinary; 06 -Skin/mucous.

VIRUS OR VIRAL ANTIGEN	No-ill or data	Respir atory	Enceph alitis -	Mening -itis	Para- lysis	CNS other unspec	GI	Hepa -tic	CVS	Urin -ary	Skin/ mucs memb
0101 ADENOVIRUS TYPE 1.....		1									
0102 ADENOVIRUS TYPE 2.....		2									
0103 ADENOVIRUS TYPE 3.....		1									
0104 ADENOVIRUS TYPE 4.....			1								
0201 INFLUENZA A VIRUS.....		4								2	
0202 INFLUENZA A VIRUS SUBTYPE H3N2		2									
0203 INFLUENZA B VIRUS.....	1	21				1	1	1			
0206 INFLUENZA A VIRUS SUBTYPE H1N1		1									
0301 PARAINFLUENZA VIRUS TYPE 1....		6									
0302 PARAINFLUENZA VIRUS TYPE 2....		1									
0303 PARAINFLUENZA VIRUS TYPE 3....	1	27									
0400 RESPIRATORY SYNCYTIAL VIRUS (RS).....	1	16									
0600 MYCOPLASMA PNEUMONIAE.....	7	41								1	1
0700 ORNITHOSIS-PSITTACOSIS.....	1	2									
0800 COXSACKIEVIRUSES GROUP A - NOT TYPED.....		1									
0809 COXSACKIEVIRUS A9.....		1		2							
0816 COXSACKIEVIRUS A16.....											3
0901 COXSACKIEVIRUS B1.....		1									
0902 COXSACKIEVIRUS B2.....		4		2							
0903 COXSACKIEVIRUS B3.....		1		1							
0904 COXSACKIEVIRUS B4.....		2									
1000 ECHOVIRUS NOT TYPED.....		1									
1022 ECHOVIRUS TYPE 22.....							2				
1101 POLIOVIRUS TYPE 1.....		1									
1102 POLIOVIRUS TYPE 2.....		1					3				1
1103 POLIOVIRUS TYPE 3.....					1						
1200 MUMPS VIRUS.....	1		1	1							
1300 HERPES VIRUS GROUP-NOT TYPED..		1								1	
1301 HERPES SIMPLEX VIRUS NOT-TYPED		3					1				1
1302 EPSTEIN-BARR VIRUS (EB VIRUS).	7	5	1				1	3			
1303 VARICELLA-ZOSTER VIRUS.....	1	1	1	1		1					11
1306 HERPES SIMPLEX TYPE 1.....	3	10						1			64
1307 HERPES SIMPLEX TYPE 2.....		1									89
1401 COXIELLA BURNETI.....									2		1
1516 MILKERS NODULE VIRUS.....											1
1521 MEASLES VIRUS.....	2										
1522 RUBELLA VIRUS.....											1
1532 HEPATITIS B ANTIGEN.....	21							64			1
1535 HEPATITIS A ANTIBODY.....								14			
1541 CHLAMYDIA A - C.TRACHOMATIS...	19	2									2
1556 CMV - CYTOMEGALOVIRUS.....	11	21			1	1	2	4	1	1	2
1564 ROTAVIRUS.....	1						61				
9992 ROSS RIVER VIRUS.....											2
9995 DENGUE.....	1										
Total.....	78	182	4	7	2	3	71	87	3	5	180

AUSTRALIA - COMMUNICABLE DISEASES INTELLIGENCE

PERIOD : 16-11-87 to 29-11-87 BULLETIN NO 87/24
Viral Identifications by Clinical Information Table 2.
Code 10 -Eye; 59 -Genital; 39 -Endo/sal gland;
38 -RES; 29 -Muscle/joint; 69 -Congenital; P8 -PUO;
G8 -Fever/malaise; 09 -Other; A1 -SIDS ...

VIRUS OR VIRAL ANTIGEN	Eye	Genital	Endo/sal gland	RES	Muscle/joint	Congenital	PUO	Fever/malaise	Other	SIDS
0101 ADENOVIRUS TYPE 1.....				1						1
0102 ADENOVIRUS TYPE 2.....								1		
0103 ADENOVIRUS TYPE 3.....	1							1		
0201 INFLUENZA A VIRUS.....								1		
0203 INFLUENZA B VIRUS.....							3	6		
0303 PARAINFLUENZA VIRUS TYPE 3....								1	1	
0400 RESPIRATORY SYNCYTIAL VIRUS (RS).....								1	1	
0600 MYCOPLASMA PNEUMONIAE.....		1		1	2			5		
0700 ORNITHOSIS-PSITTACOSIS.....		2						1		
0809 COXSACKIEVIRUS A9.....								1		
0902 COXSACKIEVIRUS B2.....								1	1	
1000 ECHOVIRUS NOT TYPED.....									1	
1022 ECHOVIRUS TYPE 22.....								1		
1027 ECHOVIRUS TYPE 27.....									1	
1200 MUMPS VIRUS.....			1						1	
1300 HERPES VIRUS GROUP-NOT TYPED..			1						1	
1302 EPSTEIN-BARR VIRUS (EB VIRUS).			4	7			3	2	6	
1303 VARICELLA-ZOSTER VIRUS.....				1					1	
1306 HERPES SIMPLEX TYPE 1.....	4	27						1	3	
1307 HERPES SIMPLEX TYPE 2.....		118								
1401 COXIELLA BURNETI.....							1	1	1	
1521 MEASLES VIRUS.....									1	
1522 RUBELLA VIRUS.....									1	
1532 HEPATITIS B ANTIGEN.....									6	
1535 HEPATITIS A ANTIBODY.....		1								
1541 CHLAMYDIA A - C.TRACHOMATIS...	2	139								
1556 CMV - CYTOMEGALOVIRUS.....	6	5	4	2	1	7	1	18	33	
9990 AUSTRALIAN ENCEPHALITIS.....									1	
9992 ROSS RIVER VIRUS.....					1			2		
9995 DENGUE.....							1	1		
Total.....	13	293	10	12	4	7	9	45	60	1