

# Gonococcal infection in Edinburgh and Newcastle: serovar prevalence in relation to clinical features and sexual orientation

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## Abstract

**Aims**—The variable distribution of gonococcal serovars in different areas is well recognised but the factors that are important determinants of serovar prevalence are less clear. The aim of this study was to identify relevant clinical variables by comparing serovar prevalence in two cities over the same time period.

**Methods**—A prospective analysis of serovar prevalence was made between January and December 1992 in Edinburgh and Newcastle with respect to age, sex, sexual orientation, antibiotic sensitivity and presence of symptoms.

**Results**—224 infective episodes of gonorrhoea were studied. The serovar distribution varied between the two cities with serovar 1B-1 being more common in Edinburgh (20/91 cf. 4/133,  $p < 0.01$ ) and serovar 1B-6 more common in Newcastle (26/133 cf. 2/91,  $p < 0.01$ ). Serovar 1A-2 was associated with heterosexual infection (35/114 in heterosexuals cf. 0/85 in homosexuals,  $p < 0.01$ ) and was more sensitive to penicillin than average (39/39 1A-2 strains highly penicillin sensitive cf. 98/184 for all other strains,  $p < 0.01$ ) whilst 1B-6 was mostly acquired through homosexual contact (22/26 cf. 63/142 for all other strains,  $p < 0.01$ ) and tended to show reduced penicillin susceptibility (13/28 1B-6 strains less penicillin sensitive cf. 45/195 for all other strains,  $p < 0.01$ ). Infection with serovar 1A-2 was significantly less often symptomatic in heterosexuals than average (15/33 asymptomatic 1A-2 infections cf. 17/59 for all other serovars,  $p = 0.015$ ). Subgroup analysis of male heterosexual infections confirms an association between asymptomatic infection and serovar 1A-2 (2/14 asymptomatic 1A-2 infections cf. 1/72 for all other serovars,  $p = 0.02$ ). The distribution of infections over the year differed between the cities. **Conclusions**—A variety of factors including penicillin sensitivity and virulence may be important in determining the prevalence of gonococcal serovars within a given area.

detailed epidemiological studies of gonococcal infection over the past seven years.<sup>1-4</sup> A varying distribution of serovars has been demonstrated both geographically<sup>5,6</sup> and temporally.<sup>7,8</sup> Factors involved in producing geographical, temporal and sexual orientation associated differences in serovar prevalence are as yet unknown. Serovars isolated from groups within a population also differ with respect to serovar pattern. We have previously shown that serovars isolated from gay men in Edinburgh not only are different when compared with heterosexually acquired infections, but also that within the homosexual group dynamic change occurs in the prevalent serovar pattern.<sup>9</sup> The association between clinical presentation and gonococcal serotype may help to provide the answer to this question. This prospective study was designed to observe and compare the patterns of gonococcal serotypes isolated in two cities in the United Kingdom with respect to their clinical features.

## Methods

All patients presenting to the Departments of Genitourinary Medicine at Edinburgh Royal Infirmary or Newcastle General Hospital between January and December 1992 were analysed. The diagnosis of gonorrhoea was made on the basis of culture of *N gonorrhoeae* on modified New York culture medium from the urethra, rectum, endocervix and/or throat. All male patients had a single urethral swab taken whilst female patients had urethral and endocervical swabs cultured on two separate occasions to diagnose or exclude gonorrhoea. Throat cultures were performed in all partners of patients with gonorrhoea and when the history indicated that this site had been placed at risk. Rectal cultures were taken routinely from men who gave a history of homosexual contact and in all women in Edinburgh. In Newcastle rectal cultures were taken when the history indicated that the site had been placed at risk, in those admitting to casual contacts and in contacts of patients known to be infected with gonorrhoea.

Gonococcal isolates were identified on the basis of biochemical and immunological tests and serotyping was performed using the American panel of monoclonal antibodies as has been described previously.<sup>10</sup> Minimum inhibitory concentrations (MICs) of penicillin were determined by an agar plate dilution method<sup>5</sup> using a series of plates incorporating 0.015, 0.06, 0.12, 0.5 and 1.0 mg/l of peni-

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Accepted for publication  
13 October 1993

(*Genitourin Med* 1994;70:35-39)

## Introduction

The ability to serotype *Neisseria gonorrhoeae* using monoclonal antibodies has permitted

collin: MICs less than or equal to 0.12mg/l were classed as sensitive and isolates with MICs greater than or equal to 0.5 as reduced susceptibility.

Information was obtained from the casenotes of patients with a diagnosis of gon-

Table 1 Distribution of serovars in Edinburgh and Newcastle

Serovar	Edinburgh	Newcastle	Total
1A-2	16	24	40
1B-1	20†	4	24
1B-2	24	48	72
1B-6	2	26†	28
1A-6	4	1	5
1A-16	5	3	8
1A-25	2	0	2
1B-00*	0	2	2
1B-3	4	15	19
1B-4	0	1	1
1B-5	4	2	6
1B-7	6	2	8
1B-16	1	1	2
1B-19	0	2	2
1B-26	1	2	3
1B-29	1	0	1
Not Typed	1	0	1
Total	91	133	224

\*untypable strains. †p < 0.01.

Table 2 Comparison of Edinburgh and Newcastle cohorts

Characteristic	Edinburgh	Newcastle
Age Group (years)	15-19	9
	20-24	23
	25-29	31
	30-34	11
	over 34	15
Sex	Male	64
	Female	26
Sexual Orientation	Heterosexual	51
	Homosexual	31
	Bisexual	4
Serogroup	1A	27
	1B	63

orrhoea on sex, sexual orientation, antibiotic sensitivity, date of diagnosis and presence of symptoms. The data on serovar prevalence in Edinburgh and Newcastle were then analysed with respect to the clinical information. The data were entered into the DBase (Borland Software) database programme and statistical analysis was performed using chi-square on the Epiinfo statistical package (WHO public domain software).

## Results

In Edinburgh, 91 episodes of gonorrhoea in 91 patients were analysed. Gonococcal serovar data was available in 90 (99%) cases, sexual orientation in 86 (95%), antibiotic sensitivity in 91 (100%), date of diagnosis in 91 (100%) and details of symptoms in 85 (93%). Newcastle had 133 episodes of gonorrhoea in 126 patients. Serovar data was available in 133 cases (100%), sexual orientation in 125 (94%), antibiotic sensitivity in 132 (99%), date of diagnosis in 133 (100%) and details of symptoms in 120 (90%).

For analysis the four commonest serovars, which accounted for 73% of infections (1A-2, 1B-1, 1B-2 and 1B-6), were looked at separately whilst the other "minor" serovars were grouped together. Serovar incidence is shown in table 1.

No significant differences were seen in the age ( $p = 0.24$ ), sex ratio ( $p = 0.24$ ), sexual orientation ( $p = 0.43$ ) or ratio of 1A to 1B infections ( $p = 0.17$ ) in infections in Edinburgh compared with Newcastle (table 2). The relative frequency of gonococcal serovars in the two cities is shown in fig 1. Serotype 1B-1 infection was significantly more common in Edinburgh while 1B-6 infection was seen more frequently in Newcastle over the 12 month study period (table 1). The distribution of infections through the year differed between Edinburgh and Newcastle with the peak number of infections occurring in the 2nd quarter in Newcastle ( $p = 0.05$ ) (fig 2).

Serovar 1A-2 was associated exclusively with heterosexual infection (fig 3). 1B-2 infections were significantly associated with

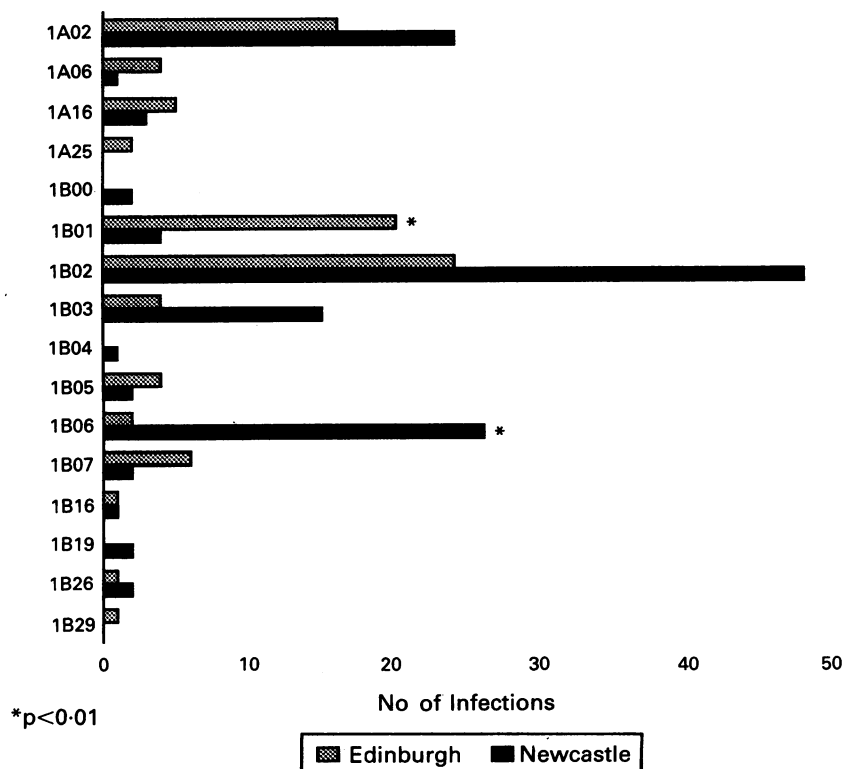


Figure 1 Frequency of gonococcal serovars in Edinburgh and Newcastle.

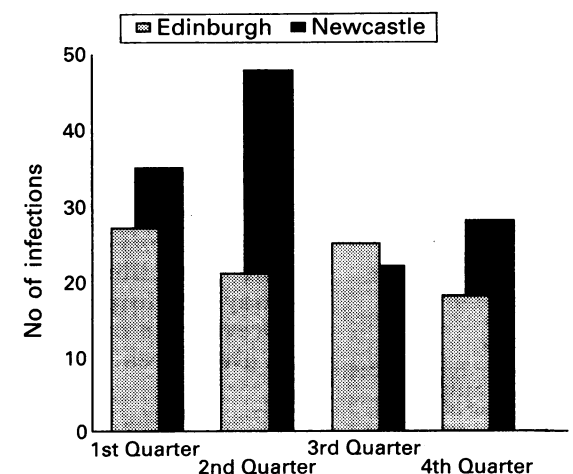


Figure 2 Quarterly frequencies of gonococcal infection in Edinburgh and Newcastle.

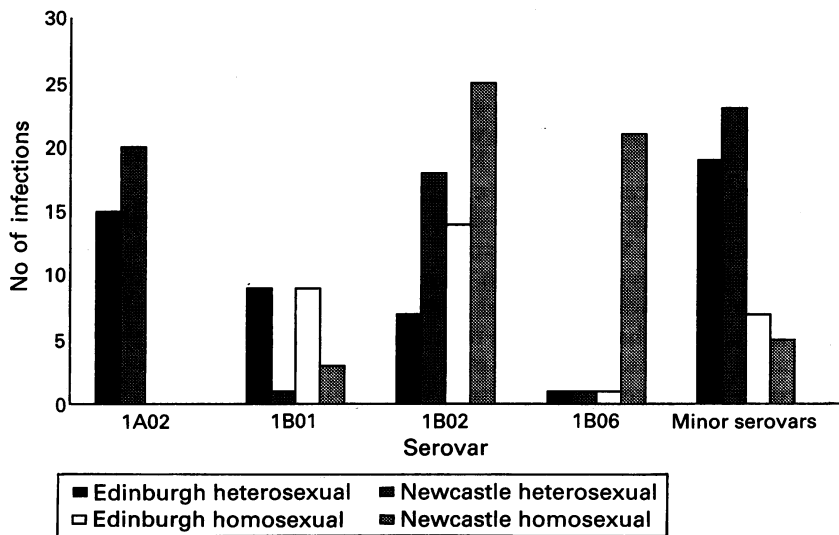


Figure 3 Frequency of gonococcal serovars in Edinburgh and Newcastle subdivided by sexual orientation.

homosexually acquired infection (fig 3) but also occurred in heterosexual patients. Whilst in Newcastle 21 of 24 infections with 1B-6 were homosexually acquired, in Edinburgh 1B-6 occurred only twice (one heterosexual infection and one homosexual). Serovars 1A-2 and 1B-2 were more sensitive to penicillin than average ( $p < 0.01$ ) and serovar 1B-6 and the "minor" serovars tended to be less susceptible ( $p < 0.01$ ) (table 3). Penicillinase producing *Neisseria gonorrhoeae* (PPNG) were isolated uncommonly in our population: three isolates from Newcastle and four isolates from Edinburgh. Serovar 1B-5 was isolated on a total of six occasions (four Edinburgh, two Newcastle) but was associated with PPNG in four cases (two Edinburgh, two Newcastle). Genital (urethral or endocervical) infection with serovar 1A-2 in heterosexual patients was associated with no symptoms (table 4) and a subanalysis of genital infection in male heterosexuals also

Table 3 Serovar sensitivity to penicillin

Serogroup	Sensitive (MIC $\leq$ 0.12mg/l)	Reduced susceptibility (MIC $>$ 0.5mg/l)
1A-2	39†	0
1B-1	19	5
1B-2	60*	12
1B-6	15	13†
Other	32	28†
Total	165	58

\* $p < 0.05$ . † $p < 0.01$ .

Table 4 Serovar associations with symptoms in heterosexual genital infections

Serovar	Asymptomatic	Symptomatic
1A-2	15*	18
1B-1	2	8
1B-2	6	18
1B-6	0	2
Other	9	31
Total	32	77

\* $p = 0.015$ .

showed an association between asymptomatic infection and serovar 1A-2 (2/14 asymptomatic male genital infection for serovar 1A-2 cf. 1/72 for all other serovars,  $p = 0.02$ ). The age distribution of infected patients did not differ for individual serovars.

## Discussion

The observed pattern of gonococcal serovars varies between Edinburgh and Newcastle although geographically the cities are not far apart. Certain serovars, such as 1A-2 and 1B-2, are observed in both cities whilst others predominate in one area only: 1B-6 in Newcastle and 1B-1 in Edinburgh, despite the patients being similar with respect to age, sex and sexual orientation. As has been previously reported some serovars are associated with certain sexual behaviour patterns<sup>17</sup> and we found 1A-2 to be exclusively heterosexually acquired while 1B-6 was usually acquired through homosexual contact, although 1B-2 was found in substantial numbers of both homosexual and heterosexual patients. Although serovar 1B-6 was isolated only very infrequently in Edinburgh in 1992, compared with Newcastle, previous reports have showed that this serovar was prevalent in gay men in Edinburgh in 1991 and was also increasing in prevalence in Glasgow during the same time period.<sup>5</sup> It has been postulated that serovars may "cross over" from homosexual to heterosexual populations or vice versa via bisexual men. It is also possible that certain gonococcal strains have a selective advantage in gay men by, for example, being able to thrive more successfully in the rectal environment.<sup>11</sup>

Plummer *et al*<sup>6,12</sup> and Buchanan *et al*<sup>13</sup> have suggested that there may be a serovar specific immune response which gives partial protection against reinfection with the same gonococcal strain. This implies that the success of a "new" strain within any particular community would depend on that community's previous exposure and may explain the differences observed in this and other studies which have compared serovar patterns in different geographical areas of even relatively close proximity.<sup>5</sup>

Over the past decade the incidence of gonorrhoea has fallen dramatically in many parts of the Western world<sup>14</sup> although there has recently been an increase reported in England and Wales.<sup>15</sup> No such increase has thus far occurred in Edinburgh, with the exception of an unsustained rise in homosexually acquired gonorrhoea,<sup>16</sup> but the observed decline in the incidence of gonorrhoea has plateaued (unpublished data). Widespread media campaigns directed at preventing HIV infection over the same time period would therefore appear to have affected sexual behaviour as measured by the incidence of other sexually acquired infections although this effect is of short duration.<sup>17</sup> If serovar characteristics themselves were important in determining their prevalence within a population then selective pressure on gonococcal strains

may be expected to increase as the overall incidence of gonorrhoea declines with the emergence of a few successful serovars. We have however, observed a comparatively large number of different serovars with relative success occurring in only a few. This implies that either there is a continual influx of unsuccessful strains from other geographical areas or else population factors are also important. We have previously shown that certain serovars can persist at low levels within a population whilst others appear only transiently<sup>9</sup> which lends support to the importance of population behaviour in a serovar's success. Homosexual populations often have infections with serovars that are uncommon in the heterosexual population<sup>9</sup> and this is likely to be due, at least partially, to relatively infrequent sexual mixing via bisexual men.

The presence of different serotypes of *N gonorrhoeae* is presumably as a result of the antigenic heterogeneity which occurs secondary to genetic mutation and indeed a number of "evolutionary trees" have been proposed.<sup>18</sup> The relevance of this "antigenic drift" to changing serovar patterns over time is not known as the rate of mutation in vivo has never been assessed. One way of estimating this is by comparing serovar patterns in named sexual contacts although this has given conflicting results with some authors finding a high correlation between partners<sup>19</sup> and others less so.<sup>20</sup>

The quarterly frequencies of gonococcal isolation in Edinburgh, peaking in the 1st and 3rd quarters, were the reverse of that observed in Newcastle. The pattern seen in Edinburgh follows that reported in the whole of Scotland in the past<sup>21</sup> which was postulated to be secondary to the increased mobility of the young sexually active population during holiday periods.

The absence of symptoms would in theory be advantageous to a serovar in natural selection by increasing the chance of more contacts being infected prior to detection and treatment. Serovar 1A-2 produces less symptoms than average in heterosexually acquired genital infections in men and is also one of the most successful strains in both Edinburgh and Newcastle. Although Crawford *et al*<sup>22</sup> found that the AHU auxotype of gonorrhoea was less likely to produce symptoms a recent article by Horner *et al*<sup>23</sup> found no difference in the symptoms caused by 1A and 1B serogroups. The possible explanations for the disparity between our results and those of Horner may relate to either the different populations studied or methodological differences. Serotype 1A-2 was the predominant 1A serovar in our population and if lack of symptoms were related to this particular serovar rather than serogroup 1A in general this may bias the serogroup analysis in areas where 1A-2 is less prevalent. There are also a number of potential flaws in the analysis of Horner's results. The number of patients included for most of their analysis is small (55) and 15% of the patients who completed questionnaires were not serogrouped. The

analysis of presence or absence of symptoms was based on 91 patients in 68 of whom the information appeared to have been obtained from questionnaire while in 36 the notes were used which makes valid interpretation difficult. No comparison between data obtained from case notes and questionnaire was made. The association between symptoms and serotype is further complicated by the observation that symptoms associated with gonococcal infection may not necessarily remain static over time and an increase in the incubation period from 1932 to 1989 has been reported.<sup>24</sup>

In common with other studies we found serogroup 1A more sensitive to penicillin than serogroup 1B.<sup>25-30</sup> In particular serovar 1A-2 was universally sensitive although others have demonstrated that this strain can become chromosomally resistant with one study showing 6/278 (2.2%) of 1A-2 infections to be CMRNG.<sup>31</sup> Despite this sensitivity to antibiotics, infections with 1A-2 are very successful in the community indicating that there may be some selective advantage associated with this trait.

The results of this and other studies indicate a complex interaction between the characteristics of the individual, the population and the gonococcal strain itself in determining the prevalence of a particular serovar in the community. Further research at both the epidemiological and molecular levels will be required before these issues can be resolved.

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