Serovar specific immunity to *Neisseria gonorrhoeae*: does it exist?

J D C Ross, A Moyes, H Young

Abstract

Objective—To determine whether the host immune response to gonorrhoea provides limited serovar specific protection from reinfection.

Subjects—508 episodes of gonorrhoea diagnosed at a city centre genitourinary medicine clinic including 22 patients with multiple infections over a 4 year period.

Methods—Patients with recurrent gonococcal infection were analysed with respect to the initial and subsequent serovars isolated.

Results—No significant difference was seen in the prevalence of serovars isolated following a repeat infection compared with those without repeat infections. The site of the initial infection did not appear to influence the subsequent serovar isolated.

Conclusion—We found no evidence of serovar specific immunity in our population. It remains possible that populations with a higher prevalence of gonorrhoea and more frequent infections may have a quantitatively greater immune response.

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Keywords: gonorrhoea, immunity, serotyping, sexual orientation

Introduction

The host immune response to gonococcal infection is primarily humoral in nature and, although a variety of antibodies can be detected both in serum¹⁻³ and in genital secretions,⁴⁻⁷ individuals with gonorrhoea do not appear to be protected from reinfection with *N gonorrhoeae* as occurs with many other bacterial infections. This lack of protective immunity gives rise to the "core group" theory of infection, where a small core group of individuals with multiple partners produce the majority of infections within a community.⁸ However, it has been suggested that limited serovar specific immunity may occur and reinfection of an individual with the same serovar of *N gonorrhoeae* may be less likely than with a different strain.⁹ In this context it is of interest that immunoglobulin in vaginal fluid reacts comparatively more with Protein I, the serotyping antigen, than does immunoglobulin in serum⁷.

This study was designed to examine recurrent gonococcal infections in patients attending a Department of Genitourinary Medicine

with respect to their initial and subsequent serovar as a surrogate marker of serovar specific immunity.

Methods

All patients presenting to the Department of Genitourinary Medicine at Edinburgh Royal Infirmary between January 1990 and December 1993 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 from all women.

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.¹⁰

Information was obtained from the casenotes of patients with a diagnosis of gonorrhoea on age, sex, sexual orientation and date of diagnosis. The data on serovar prevalence was then analysed with respect to the clinical information.

The data were entered into the dBase (Borland Software) database program and statistical analysis was performed using chi square on the Epiinfo statistical package (WHO public domain software).

Results

Five hundred and eight patient episodes of gonococcal infection occurred over the 4 year study period. Twenty one patients were infected with gonorrhoea on two separate occasions over the four year study period and one patient on three occasions (total of 45 infectious episodes). The sex, age, sexual orientation, time between infections, serovars isolated and serovars of sexual contacts are shown in the table. Eighteen of the patients were homosexual and four heterosexual (one male and three female). Six homosexual patients were initially infected with serovar 1B-2 and three of these were subsequently reinfected with the same serovar (50%). The

Department of
Genitourinary
Medicine, Edinburgh
Royal Infirmary,
Edinburgh
J D C Ross

Department of
Medical Microbiology,
University of
Edinburgh, Teviot
Place, Edinburgh
A Moyes
H Young

Address for correspondence:
Dr J Ross MRCP,
Department of GU
Medicine, Lauriston
Building, Edinburgh Royal
Infirmary, Edinburgh
EH3 9YW, UK

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Table Re-infection with gonorrhoea in Edinburgh

Sex	Age (years)	Sexual orientation	Time interval between infections (months)	Serovar (first/second/third)	Serovar of initial partner
F	17	heterosexual	28	1A-6/1A-2	1A-6
F	20	heterosexual	8	1B-2/1B-2	1B-2
F	18	heterosexual	5	1B-2/1B-2	1B-2
M	24	heterosexual	14	1B-6/1B-2	
M	39	homosexual	17	1B-6/1B-1	
M	32	homosexual	6	1B-6/1B-6	1B-6
M	23	homosexual	31	1B-6/1B-2	
M	32	homosexual	10	1B-2/1B-5	
M	34	homosexual	29	1B-3/1B-2	
M	38	homosexual	14	1B-3/1B-2	
M	29	homosexual	9	1B-2/1B-15	
M	23	homosexual	13/16	1B-2/1B-7/1B-2	
M	41	homosexual	19	1B-6/1B-2	
M	22	homosexual	15	1B-6/1B-2	
M	24	homosexual	17	1B-2/1B-2	1B-2
M	19	homosexual	35	1B-6/1A-6	1B-6
M	24	homosexual	28	1B-2/1B-6	
M	24	homosexual	4	1B-3/1B-2	
M	22	homosexual	4	1B-3/1B-6	
M	28	homosexual	1	1B-2/1B-2	1B-2
M	24	homosexual	9	1B-6/1B-2	
M	26	homosexual	7	1B-7/1A-6	

Reinfection with same virus marked in bold.

prevalence of 1B-2 infections in all gay men over the same period was not significantly different at 48% (87/182 [$p = 0.76$]). Seven gay men had 1B-7 infections initially with one subsequently becoming reinfected with the same serovar (15%). The overall prevalence of 1B-7 infections in gay men was similar at 12% (22/182 [$p = 0.68$]).

Six homosexual patients initially presented with infection at multiple sites, two of whom had rectal infections. In total six of the gay men with repeat infections initially presented with rectal infections, two of whom were subsequently reinfected with the same serovar. Of eight gay men initially with pharyngeal infections three re-presented with an infection of the same serovar and of 10 urethral infections the same serovar was subsequently isolated in one.

Discussion

Protein I forms the basis for serotyping and the immune response to Protein I depends on a variety of factors including previous immune status,^{11 12} site of infection⁷ and duration of infection.¹³ Following gonococcal infection antibodies to Protein I can sometimes be detected in serum particularly following local or systemic spread of infection.^{2 3 14} Although Protein I is less immunogenic than pili or Protein II⁷ when serum antibody is measured there is a better antibody response to Protein I in vaginal secretions. In serum, Protein I interacts with antibody and complement to produce a bacteriocidal reaction that can kill *N gonorrhoeae*¹⁵ but the importance of this interaction in the mucosa is unclear. *N gonorrhoeae* expressing Protein IB are more readily killed by this interaction than Protein IA gonococci.¹⁶ Both Protein IA and Protein IB antibodies can activate complement via the classical pathway^{17 18} and act as opsonins.^{12 17}

A study of prostitutes in Africa found that women infected with one Protein I gonococcal strain are less likely to become reinfected with

the same strain subsequently.⁹ Our data do not support the presence of such immunity with no difference observed in the reinfection rates for patients previously infected. Unlike the African study the reinfections that we observed occurred primarily in homosexual men who may differ from women in the magnitude of their immune response to infection. The serum antibody response is greater in women than men, possibly reflecting a greater infective burden in the female genital tract or a more chronic infectious process.^{19 20} Infection at multiple sites might also be expected to invoke a greater immune response. The site of initial infection did not appear to influence the serovar subsequently isolated although the numbers involved are small and a significant difference cannot be ruled out.

There are other important differences between the two studies. The time period for the African study was 16 months during which period the women had an average of four gonococcal infections. Our study took place over four years during which period patients had on average only 1.04 infections although this was higher in gay men (1.11 infections). Nevertheless the time interval between infections in our study averaged 14.7 months (range 1–35) allowing more time for an antibody response, particularly a local mucosal response, to wane. Therefore the conclusion from the African study⁹ that infection with a specific gonococcal serovar results in specific but incomplete protection against subsequent infection with the homologous serovar only holds for a highly active population with frequent exposure after a short time interval.

It is also possible that some of those re-presenting with isolates of the same serotype had been inadequately treated or non compliant with therapy rather than reinfected. This may account for some episodes which re-presented after a short time interval but is unlikely to be a major factor for those with a longer interval between infections. Although one case of presumed re-infection in the study occurred after one month the remainder had a time interval of at least four months making it unlikely that this would compromise the study's conclusions.

The results of our study do not support the concept of serovar specific immunity to gonococcal infections occurring in homosexual men. Because of the low level of gonorrhoea in this population and the limited number of infections immunity does not appear to be a major variable in determining the prevalence of infection.

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