

Imported penicillinase producing *Neisseria gonorrhoeae* becomes endemic in London

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SUMMARY We review all cases of gonorrhoea caused by penicillinase producing *Neisseria gonorrhoeae* (PPNG) seen between 1976 and 1983 at the sexually transmitted disease (STD) clinic of this hospital, which accounted for 11% of all such cases reported in that period in the United Kingdom. While the overall incidence of gonorrhoea remained relatively stable in this clinic, that of PPNG rose to 4.4% of all such cases by 1982. Until last year, 75% of these cases were imported, mainly from Nigeria and Ghana, but a marked change was seen in the second half of 1982, when 71% of cases were indigenous in origin. Casual partners and prostitutes in London were mentioned as the source of infection by 34% of patients, a much higher percentage than that seen previously. Such sources are notoriously difficult to trace and these figures show a very disturbing trend.

Although rectal infection tends to be asymptomatic, PPNG was isolated in rectal cultures from two of five homosexuals and 19 of 26 women. There is therefore a risk that PPNG could spread rapidly through the homosexual population. We suggest that spectinomycin should no longer be the first drug of choice in the treatment of gonorrhoea caused by PPNG but should be replaced by the newer cephalosporins.

Introduction

In 1976 Phillips reported isolating the first β -lactamase producing strain of *Neisseria gonorrhoeae* at this hospital;¹ these strains are now often referred to as penicillinase producing *N gonorrhoeae* (PPNG). At the same time a similar isolate was reported in the United States of America,² while in the same year these strains caused an outbreak of gonorrhoea in Liverpool.³ Fifteen isolates of PPNG were reported in the United Kingdom in 1977, but since then there has been a dramatic increase in their incidence⁴ with 1033 cases reported in 1982.⁵ PPNG strains appear to have originated in South East Asia and West Africa and have spread widely around the world. Initially most strains isolated in the United Kingdom were either directly imported or could be linked epidemiologically with imported strains, but recently it has been suggested that an increasing proportion of the PPNG strains reported in the United Kingdom are indigenous.⁴

The incidence of PPNG at this hospital has risen in parallel with the increase in the United Kingdom, and many of our patients with PPNG strains were born in Ghana and Nigeria. As this is the largest clinic serving the population of South London, it appeared worthwhile to examine the problem in some detail, and we report our findings here.

Patients and methods

We reviewed all patients found to have gonorrhoea caused by PPNG between September 1976 and the end of 1982. For comparison we also reviewed 220 consecutive patients with gonorrhoea caused by non-PPNG strains and 154 men with non-specific urethritis (NSU) attending for the first time in the first quarter of 1982. For this study NSU was defined by the presence of at least 10 polymorphonuclear leucocytes in at least 10 microscope fields of a Gram stained smear examined with a $\times 100$ objective. All men with NSU gave negative results for *Trichomonas vaginalis* in wet films and for gonococci from urethral cultures. Cultures for chlamydia were performed in only a few cases.

To diagnose gonorrhoea, material was collected from the urethra and, when indicated, from the

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rectum and pharynx in men, from the urethra and cervix in all women, and from the rectum and pharynx in known contacts. The material was plated on selective culture medium⁶; *N gonorrhoeae* was identified and β -lactamase production detected as already described.¹

Demographic details of age, country of birth, place of residence, marital status, and occupation were provided by the patients. The source of infection with *N gonorrhoeae* was determined by interviews with health advisers (contact tracers). Casual sexual partners were untraceable as the patients knew little or nothing of their personal details.

We followed the principles outlined by Evans in assessing cure and failure after treatment.⁷

Results

A total of 214 patients (148 men and 66 women) were identified as having gonorrhoea caused by PPNG during the seven year period. Three men and one woman who were seen in other hospital departments were excluded from this study as full details were not available, leaving 210 patients (145 men and 65 women).

Table I shows the racial group and country of origin of these patients. West Africans were the most common, with 53 patients born in Nigeria and 26 in Ghana. Three of them were born in Sierra Leone, but other West African countries were not represented. Among those born elsewhere were four patients from the other main endemic area, south east Asia (two from Hong Kong, one from Singapore, and one from Indonesia). The country of birth for patients with non-PPNG strains is also shown in table I, and the preponderance of patients from West Africa with PPNG and from the UK with non-PPNG strains is striking

TABLE I Comparison of racial groups and countries of birth of patients with gonorrhoea caused by PPNG and non-PPNG strains

Racial group	Country of birth	Gonococcal strain	
		PPNG	non-PPNG
White	Britain	39	68
Black	Britain	22	52
Black	West Indies	26	50
Black	Ghana	26	5
Black	Nigeria	53	5
Other	Elsewhere	44	3
Total		210	183

Table II shows the rise in gonorrhoea caused by PPNG in the United Kingdom and in this hospital in particular. While the proportion of PPNG strains is still relatively low, the rate of increase is alarming.

TABLE II Incidence of all reported cases of gonorrhoea and those caused by PPNG strains in the United Kingdom and St Thomas' Hospital between 1976 and 1982

Year	In the United Kingdom		St Thomas' Hospital	
	All cases	PPNG	All cases	PPNG
1976	65 281	77	1513	1
1977	65 963	15	1793	1
1978	63 596	31	2054	5
1979	61 616	104	2029	17
1980	60 850	211	2025	24
1981	58 301	443	2095	61
1982	NA	1033	2319	101
Total		1914	13 818	210

NA = not yet available.

Table III shows the age distribution of patients with gonorrhoea caused by PPNG and non-PPNG strains and of men with NSU. Men with PPNG strains were older than those in the other two groups, while women with PPNG strains were slightly older than those with non-PPNG strains.

TABLE III Comparison by ages of men with NSU and patients with gonorrhoea caused by PPNG and non-PPNG strains

Age (years)	Men with NSU	Gonorrhoea caused by			
		PPNG strains		Non-PPNG strains	
		Men	Women	Men	Women
15-19	10	2	11	45	15
20-24	71	38	25	61	29
25-29	38	37	14	21	7
30-34	21	30	8	12	6
35-39	8	16	5	4	1
40-44	2	7	1	6	2
45-49	1	10	0	5	0
50 and over	3	5	1	5	1
Total	154	145	65	159	61

Men with PPNG and non-PPNG under 25 years v 25 and over: $\chi^2 = 46.4, p < 0.001$;
 Women with PPNG and non-PPNG under 25 years v 25 and over: $\chi^2 = 3.8, p = 0.05$;
 Men with PPNG and NSU under 25 years v 25 and over: $\chi^2 = 19.4, p < 0.001$;
 Men with non-PPNG and NSU under 25 years v 25 and over: $\chi^2 = 6.4, p < 0.02$.

Table IV shows the marital status of the three groups of patients. In the group with gonorrhoea caused by PPNG similar proportions of men and women were married and single, though in six patients the marital status was not recorded. More men with PPNG were married compared with those with non-PPNG strains and NSU. In contrast, the marital status of women with PPNG strains was similar to that of women with non-PPNG strains.

TABLE IV Comparison by marital status of men with NSU and patients with gonorrhoea caused by PPNG and non-PPNG strains

Marital status	Men with NSU	Gonorrhoea caused by			
		PPNG		Non-PPNG	
		Men	Women	Men	Women
Single	132	92	49	149	41
Married	17	44	13	8	16
Divorced or separated	5	2	1	1	1
Widowed	0	1	1	1	1
Not recorded	0	6	1	0	2
Total	154	145	65	159	61

Men (single v other marital status):

in all disease groups $\chi^2 = 49.2$, $p < 0.001$;

in PPNG v non-PPNG $\chi^2 = 42.3$, $p < 0.001$;

in non-PPNG v NSU $\chi^2 = 5.45$, $p < 0.05$;

Women (single v other marital status):

in PPNG v non-PPNG $\chi^2 = 1.02$, not significant.

All but four of the patients with gonorrhoea caused by PPNG were resident in the United Kingdom. In the hospital's main catchment area of the West Lambeth health district and its immediate environs in South London more patients had gonorrhoea caused by PPNG than gonorrhoea caused by non-PPNG or than NSU. Most of the patients with gonorrhoea caused by PPNG lived in the western part of the catchment area. Another difference between those with gonorrhoea caused by PPNG and non-PPNG strains was in occupations, with 46 students in the former group compared with seven in the latter. In 1982 three of 33 women with PPNG strains were prostitutes compared with two of the 32 women seen in the previous six years, and in 1982 twelve men cited prostitutes in London as the source of their infection, compared with only two in the previous six years. Casual partners in London appeared to be the source of 23 infections in 1982 compared with only six between 1976 and 1981.

Table V shows that gonorrhoea caused by PPNG originated abroad in 106 (75%) men but in only 32 (48.5%) women. Most of the imported infections came from Ghana and Nigeria. Of the 24 cases seen by the end of 1979 only six (25%) appeared to be indigenous, and importation was noticeable until 1982. In that year only five (20%) of the first 25 cases compared with 34 (44% of the 77 cases in the second half of the year, 71% of the total) appeared to be indigenous. In 1982 only three infections came from Ghana, though Nigeria was the source of 18 infections.

Two patients acquired a second infection with PPNG, one of whom was reinfected by an untreated partner. Five men had homosexually acquired infection, and PPNG strains were isolated from the

rectum of two of three homosexuals. Of the 65 women with PPNG strains in the series, cultures were taken from the rectum before treatment in 26, 19 of which yielded PPNG strains.

TABLE V Geographical origin of gonorrhoea caused by PPNG and non-PPNG strains

Origin within United Kingdom or abroad	PPNG strains		Non-PPNG strains	
	Men	Women	Men	Women
Probably in UK	39	33	149	58
Acquired in UK but probably imported	4	16	0	0
Definitely from overseas	102	16	10	3
Total	145	65	159	61

Table VI shows the main treatment regimens used and the results obtained. Ampicillin and probenecid gave unsatisfactory results, cotrimoxazole marginally better, while spectinomycin and cefotaxime gave the best results, with no failures in the 96 patients treated with the latter. In vitro tests showed sensitivity to spectinomycin in the two isolates from patients in whom this drug failed. Two further isolates of PPNG strains from contacts of patients who had been treated with cefotaxime were resistant in vitro to spectinomycin at a concentration of 512 mg/ml.

TABLE VI Results of treatment of gonorrhoea caused by PPNG strains

Treatment regimen	Cure	Failure
Ampicillin 1 g + probenecid 1 g orally	1	31
Ampicillin 2 g + probenecid 1 g orally	7	53
Cotrimoxazole 480 mg tabs 3.84 g (single dose)	3	5
2.4 g every 12 hours for 3 doses (total 7.2 g)	13	6
Spectinomycin 2 g intramuscularly	20	2
Cefotaxime 0.5 g intramuscularly	96	0

Discussion

A high proportion of our patients with gonorrhoea caused by PPNG were born in Ghana and Nigeria and frequently visited West Africa, while very few of our patients infected with non-PPNG strains were born there. West Africa is one of the original foci of PPNG strains and is second only to the Far East as the main source of their import into the United Kingdom.⁴ Prevalence of PPNG strains in Nigeria in 1980 was reported to be 20%.⁸

Although the overall incidence of gonorrhoea seen in this hospital has remained more or less stable for the past few years, the proportion caused by PPNG strains has increased from 0.07% in 1976 to 4.4% in 1982. If the proportion continues to rise at this rate our initial treatment of choice, ampicillin 2 g plus probenecid 1 g, may have to be reconsidered, with obvious financial implications. Initial treatment is prescribed on the basis of a positive Gram stained smear before results of sensitivity tests are available. Gonorrhoea imported from West Africa or the Far East should be treated initially with antimicrobials resistant to β -lactamase, but it is uneconomic to extend this first line treatment to all cases of gonorrhoea.

The men with gonorrhoea caused by PPNG were older than those infected with non-PPNG strains or those with NSU (who had similar age distributions). Women infected with PPNG strains were also older than those with non-PPNG strains, though this difference was less pronounced. These findings agree with those of McCutchan *et al.*⁴ More of the men infected with gonorrhoea caused by PPNG were married than those with non-PPNG strains and NSU, but the marital status of women infected with PPNG and non-PPNG strains was similar.

Few of our patients were involved in business, in contrast to the findings of McCutchan *et al* who ascribe importation of these strains to businessmen visiting areas where they are endemic.⁴ We found that importation was more often by students, many of whom were older than their British counterparts, returning from visits to their homes.

These findings suggest that this hospital's catchment area includes a particular population which exhibits a greater local concentration of patients with gonorrhoea caused by PPNG than those with non-PPNG strains or NSU. Our finding in Ghanaians and Nigerians in this area accords with a similar observation of Ellis *et al*,⁹ who noted that whereas *Plasmodium vivax* malaria was the commonest species seen in Birmingham and in the United Kingdom as a whole, *Plasmodium falciparum* was the predominant species identified at this hospital, mostly in patients from Ghana and Nigeria. In 1982, in contrast to the reduction in PPNG strains in Ghanaians, there were equal numbers (10 of each) of Ghanaians and Nigerians with falciparum malaria.

Until early in 1982 75% of our PPNG strains came from abroad. Thereafter there was an abrupt change and, in 1982 nearly the same percentage of infections appeared to originate in the United Kingdom. Our experience until the second half of 1982 is at variance with the conclusions of McCutchan *et al*⁴ in that there was little evidence of PPNG strains being endemic among patients attending this hospital. The

West African patients living in south London tend to pick their sexual partners from those of similar geographical origin and it is very unusual, for example, for a Ghanaian or Nigerian to have a West Indian sexual partner. Our West African population has probably contributed little to the endemic levels of PPNG strains in our community. The reduction in the number of Ghanaian infections contrasts with the continued importation of PPNG infection from Nigeria. This change may be related to the increased fees charged to overseas students studying in the United Kingdom which Nigeria, with her oil based economy, may be in a better position to afford. It might also reflect the increased use of antimicrobials resistant to β -lactamase. The increase in infections from prostitutes and casual partners in London is causing concern as they are notoriously difficult to trace, and infections from these sources may therefore be expected to increase. Spread of PPNG strains to these sources of infection has probably occurred in other towns and cities in the United Kingdom and elsewhere. It is fortunate that only two patients were infected twice and only five men had homosexually acquired infection. Some homosexuals change partners frequently and once introduced into the homosexual population PPNG strains could spread rapidly. Furthermore, our data show that PPNG strains can infect the rectum asymptotically, so a reservoir of PPNG strains might develop among homosexuals.

It was recently suggested that spectinomycin was the drug of choice for the treatment of PPNG,¹⁰ but our findings are at variance with this. Not only has spectinomycin resistant β -lactamase producing *N gonorrhoeae* been reported,^{11 12} but treatment with this drug may result in clinical failure despite in vitro sensitivity, as in our two spectinomycin treatment failures. A preliminary report showed the value of cefotaxime.¹³ The findings here support this view, and cefotaxime 0.5 g intramuscularly is now our treatment of choice for PPNG strains and for patients likely to be infected with them. Cefoxitin has been recommended for treatment of PPNG strains¹⁴ and cefuroxime is also effective,¹⁵ but in the dose used in this study (0.5 g) cefotaxime is at present cheaper in the United Kingdom.

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