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LETTERS

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Detection of *Neisseria gonorrhoeae* by PCR using *orf1* gene as target

Nucleic acid amplification tests have the ability to specifically amplify small quantities of DNA and hence have been used successfully in the diagnosis of STDs.^{1,2} An in-house polymerase chain reaction (PCR) method was developed and evaluated for the detection of *Neisseria gonorrhoeae* DNA in the urogenital specimens collected (with consent) from patients visiting an STD clinic in India.

The primers (forward primer 5'-CAACTATCCCGATTGCGA-3' and reverse primer 5'-GTTATACAGCTTCGCTGAA-3') amplify the 221-480 bp region of *orf1* gene. Clinical isolates (n = 40) of *N gonorrhoeae* were recovered from urethral or cervical swabs by inoculation onto modified Thayer-Martin medium and identified by Gram stain, colony

morphology, positive oxidase, and rapid carbohydrate utilisation test. For PCR the clinical samples (n = 489) were centrifuged (30 minutes, 14 000 g) and the cell pellet was lysed with 50 mM TRIS-HCl (pH 7.5) 1% Triton X-100, 1 mM EDTA, 250 µg of proteinase K per ml at 37° for 1 hour, boiled for 10 minutes, and centrifuged. Eight µl of lysate was used for amplification (40 cycles) under standard conditions. Each cycle consisted of 30 seconds at 94°C, 30 seconds at 52°C, and 1 minute at 72°C. The amplified PCR product (10 µl) was analysed by electrophoresis in a 2% agarose gel and characterised by sequencing.

An amplified product of 260 base pairs (bp) of *orf1* gene was observed with all *N gonorrhoeae* isolates but not when DNA from the other non-gonococcal strains (17 closely related *Neisseria* species, *Corynebacterium*, *Chlamydia trachomatis*, *Candida*, syphilis, and members of Enterobacteriaceae) was used as template. For the 427 clinical swabs collected from men, 379 were positive and 46 were negative by both culture method and *orf1*-PCR assay. Urethral specimens from two men were culture negative but PCR positive for *orf1* gene. Since these two samples tested PCR positive for *cppB* gene of *N gonorrhoeae*³ they were considered true positives. Thus, a total of 381 men (89%) were classified as true positives based on the PCR assay (table 1). Of the 62 women tested, 52 were true positives, and five were true negative as they gave concordant results irrespective of the site of collection and the diagnostic method used (table 1). Four culture negative specimens tested positive by the PCR assays using primers specific to *orf1* as well as *cppB* gene and were, therefore, considered positive. One culture negative specimen was positive by the *orf1*-PCR assay for its endocervical specimen but negative for urethral specimens. For the *cppB* gene amplification, the specimen yielded a negative result for both the sites. This was therefore classified as true negative. The sensitivity, specificity, positive predictive value, negative predictive value for the PCR method described here would be 100%, 98%, 99.7%, and 100% respectively. The gold standard has been reported as having a sensitivity of 85-95%.^{4,5}

The high specificity and sensitivity (25 fg DNA per assay, equivalent to 10 cells) coupled

with low cost and rapidity of the in-house PCR assay described here can serve as a promising diagnostic method for the detection of gonococcus directly from clinical swab samples.

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References

- Farrell DJ. Evaluation of Amplicor *Neisseria gonorrhoeae* PCR using *cppB* nested PCR and 16S rRNA PCR. *J Clin Microbiol* 1999;37:386-90.
- Kehl SC, Georgakas K, Swain GR, et al. Evaluation of the Abbott LCx assay for detection of *Neisseria gonorrhoeae* in endocervical swab specimens from females. *J Clin Microbiol* 1998;36:3549-51.
- Ho BS, Feng WG, Wong BK, et al. Polymerase chain reaction for the detection of *Neisseria gonorrhoeae* in clinical samples. *J Clin Pathol* 1992;45:439-42.
- Hook EW III, Handsfield HH. Gonococcal infections in the adult. In: Holmes K, Straling F, Wiesner P, Cates W, Lemon S, Stamm W, ed. *Sexually transmitted diseases*. New York: McGraw Hill, 1990:149-65.
- Ching S, Lee H, Hook E, et al. Ligase chain reaction for detection of *Neisseria gonorrhoeae* in urogenital swabs. *J Clin Microbiol* 1995;33:3111-14.

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Nevirapine + efavirenz based salvage therapy in heavily pretreated HIV infected patients

The emergence of protease inhibitors (PIs) and multiple drug therapy for HIV infection has greatly decreased mortality in countries where these medications are available. Unfortunately, many patients eventually develop viral resistance to treatment because of HIV virus mutations. As clinicians await development of new drugs to combat resistant virus, innovative strategies with existing drugs may be particularly valuable. Patients having failed regimens containing nucleoside reverse transcriptase inhibitors (NRTIs) and PIs face limited options for future therapy. A regimen containing the two potent non-nucleoside reverse transcriptase inhibitors (NNRTIs), nevirapine (NVP) and efavirenz (EFV), could provide an effective alternative, since both can be conveniently dosed once daily^{1,2} and have demonstrated efficacy in patients with high viral loads.²⁻⁴

A retrospective chart review at an urban HIV hospital clinic identified 13 patients who had initiated an NVP + EFV based salvage

Table 1 Comparison of culture and PCR method for detection of *Neisseria gonorrhoeae* in urogenital specimens from men and women

No of specimens from men	Urethra			Patient status	
	Culture	Gram stain	PCR (<i>orf1</i> / <i>cppB</i> gene)		
46	−ve	−ve	−ve	Not infected	
367	+ve	+ve	+ve	Infected	
12	+ve	−ve	+ve	Infected	
2	−ve	−ve	+ve/+ve	Infected	
No of specimens from women	Urethra		Endocervix		Patient status
	Culture	PCR	Culture	PCR	
5	−ve	−ve	−ve	−ve	Not infected
52	+ve	+ve	+ve	+ve	Infected
1	−ve	−ve	−ve	+ve	Not infected*
4	−ve	+ve	−ve	+ve	Infected

*The individual was categorised as not infected after confirming with the *cppB* gene PCR.

Table 1 Baseline characteristics and outcome for NNRTI naive and experienced patients

Patient No	Regimen	Previous drugs	Baseline viral load (copies/ml)	Baseline CD4+ cell count (cells $\times 10^6/l$)	Months of follow up	Last viral load (copies/ml)
1	NVP+EFV+d4T	d4T, ddl, RTV, IDV, ABC	37100	290	15	164000
2	NVP+EFV+d4T	NFV, CBV, IDV	436000	183	7	<50
3	NVP+EFV+ABC	IDV, d4T, NFV, ddC	27000	–	13	<50
4	NVP+EFV+d4T	CBV, NFV, SQV	151000	161	9	<50
5	NVP+EFV+d4T	NFV, CBV	31900	392	18	<50
6	NVP+EFV+d4T+ddl	d4T, ddl, NFV	5000	440	6	<50
7	NVP+EFV+RTV+IDV	IDV, NFV, d4T, CBV	750000	20	10	<50
8	NVP+EFV+d4T	NFV, CBV	750000	2	11	<50
9	NVP+EFV+ddl	IDV, ddl	–	–	12	<50
10	NVP+EFV+ddl	RTV, other PI	35900	180	3	<50
11*	NVP+EFV+RTV+IDV	DLV, RTV, d4T	3100	190	14	<50
12*	NVP+EFV+RTV+IDV	SQV, NFV, NVP, ddl, DLV	8900	276	13	<50
13*	NVP+EFV+RTV+IDV	SQV, d4T, ddl, EFV, IDV	3900	235	11	33000

*NNRTI experienced patients.

NVP = nevirapine, EFV = efavirenz, d4T = Stavudine, ABC = abacavir, ddl = didanosine, RTV = ritonavir, IDV = indinavir, CBV = carbociclovir, SQV = saquinavir, DLV = delavirdine.

regimen (table 1). Inclusion of these patient charts in this study was approved by a research ethics committee at Bellevue Hospital. All patients received NVP + EFV at standard doses. The lower limit of quantitation was determined at 50 HIV RNA copies/ml using Roche Amplicor HIV-1 Monitor (RNA) (Roche Diagnostics, Branchburg, NJ, USA). Median baseline values were: viral load 33 900 copies/ml (range 3100–750 000 copies/ml) and CD4+ count 190 cells $\times 10^6/l$ (range 2–440 cells). After a median follow up of 11 months (range 3–18 months), 85% (11/13) had viral loads <50 copies/ml. Considering previous treatment experience, 90% (9/10) of NNRTI naive patients had viral loads <50 copies/ml and 67% (2/3) of NNRTI experienced patients had viral loads <50 copies/ml. Effectiveness of the dual NNRTI combination in heavily pretreated patients is in contrast with a study using a single NNRTI plus two NRTIs in NRTI experienced patients in whom rapid virological failure was observed.⁵ These results suggest that the combination of two potent NNRTIs may be able to overcome development of NNRTI associated resistance, even when there are only one or two NRTIs in the combination. These data accord with those of Jordan and colleagues who demonstrated a sustained response to NVP + EFV in combination with only didanosine (ddl) in 19/21 patients after 12 months.⁶

The most common adverse event was elevated liver function test results (more than three times upper limit of normal) in three patients. One case of liver toxicity was attributed to Bactrim, and a second case resolved following interruption of EFV (EFV rechallenged in this patient was successful). No specific cause of liver toxicity could be identified in the third case, suggesting a possible association with antiretroviral treatment. Other adverse events included anaemia. The patient with EFV induced hepatotoxicity also had anaemia and EFV related central nervous system disturbances. None of the patients discontinued therapy because of adverse events. The relatively low incidence of adverse events and the absence of NNRTI associated metabolic disorders make this dual NNRTI based regimen additionally appealing.

This retrospective analysis demonstrated the effectiveness of the combination of two NNRTIs (NVP and EFV) in heavily pretreated PI experienced patients, with no apparent increase in NNRTI related side effects. Since few new antiretrovirals with novel resistance

profiles are forthcoming in the near future, this regimen may provide a much needed alternative in heavily pretreated patients.

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References

- 1 Van Heeswijk RPG, Veldkamp AI, Mulder JW, *et al.* The steady-state pharmacokinetics of nevirapine during once daily and twice daily dosing in HIV-1-infected individuals. *AIDS* 2000;**14**:F77–82.
- 2 Staszewski S, Morales-Ramirez J, Tashima KT, *et al.* Efavirenz plus zidovudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infection in adults. *N Engl J Med* 1999;**341**:1865–73.
- 3 Pollard R. Factors predictive of durable HIV suppression in randomized double-blind trial with nevirapine (NVP), zidovudine (ZDV), and lamivudine (3TC) in treatment-naïve (ARV-n) patients with advanced AIDS. 7th Conference on Retroviruses and Opportunistic Infections, San Francisco, USA, 30 Jan–2 Feb 2000 [abstract 517].
- 4 Podzamczar D, Ferrer E, Consiglio E, *et al.* A randomized, open, multicenter trial comparing Combivir plus nelfinavir or nevirapine in HIV-infected naive patients (the Combine study). 8th Conference on Retroviruses and Opportunistic Infections, Chicago, USA, 4–8 Feb 2001 [abstract 327].
- 5 D'Aquila RT, Hughes MD, Johnson VA, *et al.* Nevirapine, zidovudine, and didanosine compared with zidovudine and didanosine in patients with HIV-1 infection. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1996;**124**:1019–30.
- 6 Jordan WC, Jefferson R, Yemofio F, *et al.* Nevirapine (NVP) + efavirenz (EFV) + didanosine (ddl): a very simple, safe, and effective once-daily regimen. 13th International AIDS Conference, Durban, South Africa, 9–14 July 2000; abstract TuPeB3207.

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Comparing cost effectiveness of screening women for *Chlamydia trachomatis* in systematic and opportunistic approaches

Screening women for asymptomatic *Chlamydia trachomatis* (CT) infections is indicated to prevent the spread of CT and the development

of complications such as pelvic inflammatory disease (PID), chronic pelvic pain, ectopic pregnancy, tubal infertility, and neonatal pneumonia (major outcomes averted; MOA). Cost effectiveness presents an important aspect in the decision making regarding actual implementation. Recently, in this journal Van Valkengoed *et al.* published a paper on the cost effectiveness of systematic screening among women in Amsterdam (Netherlands), using pharmacoeconomic modelling.¹ Using the same model, results on the cost effectiveness of an opportunistic screening in the same city have also been published.² Specific model assumptions differed in both publications. The aim of this letter is to compare cost effectiveness of systematic and opportunistic screening using similar model assumptions and correcting for potential biases.

Opportunistic screening was done during May 1996 to May 1997 in a pilot study.³ Women visiting the participating GPs were eligible for screening if they considered themselves heterosexually active, were aged 15–40 years, and did not visit their GP for sexually transmitted disease complaints (participation among women: 96% compared with 50% in the systematic screening). In this letter we report on the age group 15–30. Obviously, the effectiveness of this type of screening depends on the frequency of visiting the GP; 87% of Dutch women aged 15–30 visit the GP at least once per year.² As in the systematic universal screening, testing was done with ligase chain reaction (LCR) on urine. Participating GPs in the opportunistic screening had an overrepresentation compared to the general Amsterdam situation of participants from Caribbean and Surinam ethnicity with relatively high CT prevalence.³ To enhance valid comparison with the systematic screening, asymptomatic CT prevalence rates in the opportunistic screening were recalculated standardising for the distribution of the Amsterdam population over the ethnic groups of Caribbean, Surinam, and other (source: Statistics Amsterdam).

Parameters in the pharmacoeconomic model were kept similar to the previous paper in this journal, except for the probability of PID after asymptomatic infection.¹ For this probability we applied 20% compared to 10% in the paper by Van Valkengoed *et al.*¹ We even consider 20% as a very conservative estimate for the risk of PID in our model.⁴ Cost effectiveness was estimated as net costs per MOA in baseline analysis using assumptions

Table 1 Cost effectiveness in net costs per major outcome averted (in US\$) for Amsterdam (Netherlands) of screening 15–25 year aged women (15–30 in parentheses) for asymptomatic *Chlamydia trachomatis* in systematic and opportunistic approaches for the baseline and in sensitivity analysis (PID risk at 10% instead of 20% in the baseline; assuming high performance testing* and pooling†)

	Systematic	Opportunistic
Baseline	5300 (6300)	1700 (3100)
PID risk at 10%	11100 (12900)	4100 (6900)
High performance testing	4100 (4900)	1300 (2600)
Pooling	2000 (2400)	500 (1200)

*PCR testing with sensitivity of 98.8% and specificity of 99.9%; †pooling of urine specimens by five with relative sensitivity and specificity of 100%.

above and sensitivity analysis (PID risk at 10%, high performance testing and pooling).^{1,5}

In the baseline analysis cost effectiveness is US\$5300 per MOA for systematic screening of women aged 15–25 and \$1400 for opportunistic screening of that same age group. Including sensitivity analysis, cost effectiveness of systematic screening ranges from \$2000–\$11 100 per MOA (see table 1). For opportunistic screening this range is \$500–\$4100 per MOA. For the age group of 15–30, cost effectiveness is estimated to be generally slightly less favourable.

We conclude that opportunistic instead of systematic screening reduces net costs per MOA up to 75% (age groups 15–25) and by approximately 50% (age groups 15–30) over a range of plausible assumptions. Opportunistic CT screening in Amsterdam is therefore more attractive than systematic screening from a pharmacoeconomic point of view. Obviously, pharmacoeconomics only present one aspect in decision making concerning CT screening, others being, for example, implementation issues and budgetary constraints.

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References

- 1 Van Valkengoed IGM, Postma MJ, Morré SA, et al. Cost effectiveness analysis of a population based screening programme for

asymptomatic *Chlamydia trachomatis* infections in women by means of home obtained urine specimens. *Sex Transm Inf* 2001;77:276–82.

- 2 Postma MJ, Welte R, Van den Hoek JAR, et al. Opportunistic screening for genital infections with *Chlamydia trachomatis* among the sexually active population in Amsterdam. II. Cost-effectiveness of screening women. (in Dutch) *Ned Tijdschr Geneesk* 1999;143:677–81.
- 3 Van den Hoek JAR, Mulder-Folkerts DKF, Coutinho RA, et al. Opportunistic screening for genital infections with *Chlamydia trachomatis* among the sexually active population in Amsterdam. I. Over 90% participation, almost 5% prevalence. (in Dutch) *Ned Tijdschr Geneesk* 1999;143:668–72.
- 4 Postma MJ, Welte R, Van den Hoek JAR, et al. Cost-effectiveness of screening asymptomatic women for *Chlamydia trachomatis*: the importance of reinfection and partner referral. *Health Economics in Prevention and Care* 2000;1:103–10.
- 5 Morré SA, Welte R, Postma MJ. Major improvements in cost effectiveness of screening women for *Chlamydia trachomatis* using pooled urine specimens and high performance testing. *Sex Transm Inf* 2002;78:72–8.

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Major improvements in cost effectiveness of screening women for *Chlamydia trachomatis* using pooled urine specimens and high performance testing

Screening of asymptomatic *Chlamydia trachomatis* (CT) infections is indicated to prevent the spread of CT and the development of secondary complications like pelvic inflamma-

tory disease, ectopic pregnancy, and tubal infertility. Cost effectiveness presents an important aspect in the decision making regarding actual implementation. A recent paper in this journal by Van Valkengoed *et al*¹ addressed cost effectiveness, using an established pharmacoeconomic model,² of a systematic screening programme for asymptomatic CT infections in women registered in general practices in Amsterdam, based on mailed home obtained urine specimens.³ The aim of this letter is to extend the application of the pharmacoeconomic model with regard to pooling and improved test performances (sensitivity and specificity).

We recently determined the sensitivity and specificity for two commercially available CT detection assays for urine specimens from asymptotically CT infected women and men.⁴ In total, 2906 mailed home obtained urine specimens were tested for CT using both ligase chain reaction (LCR) and polymerase chain reaction (PCR) testing. We showed that for individual testing, the test sensitivity/specificity for LCR and PCR could be estimated at 78.6%/99.7% and 98.8%/99.9%, respectively. Furthermore, we recently showed by using individual urine samples (n = 650) and samples pooled by five (n = 130) that pooling has a relative sensitivity and specificity of 100%. Since only CT positive pools have to be analysed for the individual CT positive cases approximately 60% of the number of tests could be saved in our population with an estimated CT prevalence of 2–3%.⁵

In the pharmacoeconomic model test performances of 85.0% sensitivity and 99.0% specificity were previously assumed.¹ Furthermore, the model included population based estimates of CT prevalence, the costs of the programme, the health gain effects and the related monetary benefits. Health gain effects considered were averted pelvic inflammatory disease, chronic pelvic pain, ectopic pregnancy, infertility, and neonatal pneumonia (major outcomes averted; MOA). Both direct and indirect costs and benefits were considered. We investigated the effects on baseline cost effectiveness of pooling and improvements in test performance.

Population based prevalence in the systematic screening was 2.2% for women aged 15–40 and 2.9% for women aged 15–25. Van Valkengoed *et al* estimated baseline cost effectiveness for systematic screening in Amsterdam using LCR at net costs of US\$11 100 for women aged 15–25 and \$15 800 per MOA for women aged 15–40 (table 1).¹ High performance testing of 98.8% sensitivity and 99.9% specificity was estimated to reduce net cost per MOA by approximately 20%. Pooling urine specimens by five was estimated to reduce net costs per MOA by 57%. A total decrease of 67%

Table 1 Cost effectiveness in net costs per major outcome averted (in US\$) for Amsterdam (Netherlands) of two screening strategies for asymptomatic *Chlamydia trachomatis* (women aged 15–25 and women aged 15–40), in the baseline, assuming high performance testing*, pooling†, and both

	Women aged (years)	
	15–25	15–40
Baseline	11100	15800
High performance testing	8900	12400
Pooling	4800	6800
High performance testing and pooling	3700	5200

*PCR testing with sensitivity of 98.8% and specificity of 99.9%; †pooling of urine specimens by five with relative sensitivity and specificity of 100%.

was estimated if both high performance testing and pooling are assumed (table 1).

We conclude that with pooling and application of high performance testing major improvements in cost effectiveness of screening women for asymptomatic CT can be obtained.

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References

- 1 **Van Valkengoed IGM**, Postma MJ, Morré SA, *et al.* Cost effectiveness analysis of a population based screening programme for asymptomatic *Chlamydia trachomatis* infections in women by means of home obtained urine specimens. *Sex Transm Inf* 2001;**77**:276–82.
- 2 **Postma MJ**, Welte R, Van den Hoek JAR, *et al.* Opportunistic screening for genital infections with *Chlamydia trachomatis* among the sexually active population of Amsterdam. II. Cost-effectiveness of screening women. [in Dutch] *Ned Tijdschr Geneesk* 1999;**143**: 677–81.
- 3 **Morré SA**, Van Valkengoed IGM, de Jong A, *et al.* Mailed, home-obtained urine specimens: a reliable screening approach for asymptomatic *Chlamydia trachomatis* infections. *J Clin Microbiol* 1999;**37**:976–80.
- 4 **Morré SA**, Van Valkengoed IGM, Moes RM, *et al.* Determination of the *Chlamydia trachomatis* prevalence in an asymptomatic screening population: performance of LCx and COBAS AmpliCor in urine specimens. *J Clin Microbiol* 1999;**37**:3092–6.
- 5 **Morré SA**, Meijer CJLM, Munk C, *et al.* Pooling of urine specimens for the detection of *Chlamydia trachomatis* by PCR in a low prevalence population: cost saving strategy for epidemiological studies and screening programs. *J Clin Microbiol* 2000;**38**: 1679–80.

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Anti-HIV serology in patients with sexual dysphoria in screening test before sex change surgery

The health and behavioural issues of homosexual men and women have recently become a focus of research and interest. A well conceived framework within which to consider the uniqueness of problems faced by homosexual youths and the role of healthcare providers is needed.¹ Significant physical morbidity occurs among homosexual men and women because healthcare providers are often unaware of their actual or potential

Table 1 Demographic data and anti-HIV serology

Demographic	Anti-HIV serology	
	Positive (n=2)	Negative (n=33)
Sex		
Male	2	31
Female	0	2
Occupation		
Beauty salon workers	1	17
"Gay show" workers	1	12
Private business	0	2
Secretary	0	1
Student	0	1
Injecting drug use		
Ever	0	0
Never	0	33
Previous plastic surgery		
Ever	1	5
Never	0	29
Hormone injection		
Ever	0	20
Never	0	15
Abnormal sexual intercourse		
Ever	2	14
Never	0	19

health concerns. Physical health concerns mainly include HIV disease, hepatitis, and other sexually transmitted diseases. Healthcare professionals, who are clinically competent in the care of homosexual men and women, should have the opportunity to reduce the risk of disease, while providing unbiased, quality care which recognises the unique problems of this population.² In this study, we report the prevalence of HIV infection among the homosexual men and women who visited the pre-admission clinic, King Chulalongkorn Memorial Hospital, Bangkok, for further sex change surgery.

A prospective study on the data concerning anti-HIV test for 35 cases (33 homosexual men and two lesbian women) with sexual dysphoria who attended the pre-admission clinic, King Chulalongkorn Memorial Hospital, Bangkok for further sex change surgery, during years 1999 and 2000 was performed. The demographic data about occupation, injecting drug use, previous plastic surgery, hormone injection, and abnormal sexual intercourse (as oral and anal sex) were also reviewed for each case.

For all 35 cases of sexual dysphoria, only two cases of anti-HIV seropositivity were detected. The prevalence was equal to 5.71%. These two cases were homosexual. The demographic data of HIV seronegative and HIV seropositive cases are shown in table 1.

Currently, the two major routes of transmission of HIV are blood borne and sexual propagation. Sexual propagation also includes the abnormal sexual behaviour such as oral and anal sex found in the "gay" population.³ Unique aspects of Thai culture have shaped the response of homosexual men and women to HIV infection in Thailand. Thailand is a relatively homogeneous society that has, by and large, felt invulnerable to AIDS, viewing it primarily as a Western phenomenon. This attitude has also been common in the gay community and has resulted in some homosexual men and women engaging in high risk behaviour.

In Thailand it has been argued that HIV infection is still a major health problem

among homosexual men and women. The current HIV epidemic among young homosexual men and women is a major public health concern. Nevertheless, hardly any specific HIV education interventions have been designed for this population. In this study, the rather high rate of HIV infection among the homosexual men and women attending the hospital for further sex change surgery was detected. Compared with the rate in the general population in Thailand,⁴ this rate is five times higher. Therefore, this population is still a target group for HIV infection, and thus, proper control for this population is necessary.

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References

- 1 **Perrin EC**, Sack S. Health and development of gay and lesbian youths: implications for HIV/AIDS. *AIDS Patient Care STDS* 1998;**12**:303–13.
- 2 **Ungvarski PJ**, Grossman AH. Health problems of gay and bisexual men. *Nurs Clin North Am* 1999;**34**:313–31.
- 3 **De Wit JB**. The epidemic of HIV among young homosexual men. *AIDS* 1996;**10**:S21–5.
- 4 **Brown T**, Sittitai W, Vanichseni S, *et al.* The recent epidemiology of HIV and AIDS in Thailand. *AIDS* 1994;**8**:S131–41.

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Neuropsychiatric reaction induced by clarithromycin

We read with interest the case report by Prime and French¹ describing a person with HIV infection who developed a severe neuropsychiatric reaction during clarithromycin, zidovudine, didanosine, and nevirapine treatment. The authors suggest that this reaction was caused by the clarithromycin and not the antiretrovirals. Indeed, central nervous system (CNS) symptoms are a known side effect of clarithromycin.² CNS adverse effects, however, have also been reported with zidovudine³ and efavirenz.⁴

So far with nevirapine neuropsychiatric side effects have not been described. For this reason we would like to report the case of a patient who developed CNS side effects shortly after starting nevirapine.

A 40 year old woman with HIV infection was initially treated with zidovudine, didanosine, and nevirapine. Because she developed lipodystrophy she was switched to nevirapine, lamivudine, and zidovudine. Shortly after starting this treatment, she started to feel depressed and to experience bad dreams. Her CD4+ lymphocyte count was 727 × 10⁹/l and her viral load was undetectable. She was living under stressful conditions (her husband was also living with HIV) but according to her there was no recent change in her life to explain this depression. The nevirapine was replaced by abacavir and from then on the CNS side effects rapidly disappeared.

This case report strongly suggests that the nevirapine was responsible for the CNS symptoms.

CNS side effects related to antiviral treatment may be caused by high drug levels. Clarithromycin is known to increase nevirapine levels by about 26%.⁵ The fact that in the patient described by Prime and French the neuropsychiatric symptoms disappeared within 72 hours after stopping the clarithromycin suggests this drug was responsible for

causing these symptoms. However, it is also possible that after stopping the clarithromycin the nevirapine levels decreased and that therefore potential nevirapine related side effects disappeared. We propose that in HIV clinical trials patients should be monitored more closely for possible neuropsychiatric side effects and that if these side effects appear antiretroviral drug levels should be measured.

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References

- 1 **Prime K**, French P. Neuropsychiatric reaction induced by clarithromycin in a patient on highly active antiretroviral therapy (HAART). *Sex Transm Inf* 2001;**77**:297–8.
- 2 **Abbott Laboratories**. 2000. Clarithromycin: summary of product characteristics. Available from the ABPI compendium of data sheets and SPCs, 1999–2000.
- 3 **Maxwell S**, Scheffer WA, Kessler HA, *et al*. Manic syndrome associated with zidovudine treatment. *JAMA* 1988;**259**:3406–7.
- 4 **Blanch J**, Martinez E, Rousaud A, *et al*. Preliminary data of a prospective study on neuropsychiatric side effects after initiation of efavirenz. *J AIDS* 2001;**27**:336–43.
- 5 **Boehringer Ingelheim International**, April 2000. Viramune: summary of product characteristics. Available from <http://www.eudra.org/humandocs/humans/EPAR/Viramune/Viramune.htm>

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Immune reconstitution eosinophilia due to schistosomiasis

A 21 year old black African heterosexual woman, formerly resident in south east Africa, presented in early October 2000 on arrival in the United Kingdom. Examination revealed hepatosplenomegaly. Investigation showed Hb = 10.2 g/dl, WBC = $2.9 \times 10^9/l$ (neutrophils = 1.5, lymphocytes = 0.8, and eosinophils = $0.3 \times 10^9/l$). Blood urea and electrolytes were normal. Liver function tests showed alkaline phosphatase = 1704 (normal = 45–122) U/l, and alanine transaminase = 65 (normal = 7–63) U/l. Hepatitis A and C serology was negative; hepatitis B serology showed sAg negative and cAb positive. Serum α fetoprotein was negative. An HIV-1 antibody test was positive, plasma HIV-1 RNA level >75 000 copies/ml, CD4 count = $170 \text{ cells} \times 10^9/l$. An abdominal ultrasound confirmed hepatosplenomegaly; there was no intra-abdominal lymphadenopathy and no ascites. A chest radiograph showed micronodular shadowing throughout both lungs. In order to rule out the possibility of tuberculosis, bronchoscopy was performed. Staining and culture of bronchoalveolar lavage fluid was negative for bacteria, mycobacteria, fungi, and parasites. A bone marrow biopsy showed only non-specific reactive changes; culture was negative. A liver biopsy showed portal fibrosis with a moderate chronic inflammatory infiltrate, but no cirrhosis; a schistosomal egg was seen. Schistosomal antibodies were detected by ELISA, positive at level 4 (optical density = 0.767). A diagnosis of schistosomiasis was made.

The patient began highly active antiretroviral therapy (HAART) with stavudine, lamivudine, and efavirenz on 1 December

2000. Four weeks after starting HAART the HIV RNA level had fallen to 25 000 copies/ml, CD4 count remained at $170 \text{ cells} \times 10^9/l$ but the eosinophil count had risen to $0.8 \times 10^9/l$ (normal = $0.04\text{--}0.44 \times 10^9/l$). After 4 months of HAART the HIV level was below the limits of detection, the CD4 count had risen to $230 \text{ cells} \times 10^9/l$, and the eosinophil count had further risen to $1.5 \times 10^9/l$. At this time the patient agreed to treatment of schistosomiasis with praziquantel (40 mg/kg in two divided doses in 1 day). Following praziquantel the eosinophil count fell to $0.5 \times 10^9/l$.

The development of eosinophilia in this HIV infected patient with schistosomiasis occurred in the context of a falling HIV RNA level and an increase of CD4 count, indicating partial immune reconstitution.

Partial restoration of cell mediated immunity induced by antiretroviral therapy, as demonstrated by recovery of partial CD4+ T lymphocyte reactivation to memory antigens,^{1,2} may cause development of an inflammatory response, in this case eosinophilia, in patients latently affected with opportunistic and non-opportunistic pathogens. Reactivation mycobacterial lymphadenitis,³ cryptococcal meningitis,⁴ and cytomegalovirus retinitis⁵ and pneumonitis⁶ have been described. The case described here suggests that development of an eosinophilia to schistosomiasis should be added to the list of immune reconstitution phenomena.

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References

- 1 **Autran B**, Garcelain G, Li TS, *et al*. Positive effects of combined antiretroviral therapy on CD4+ T cell homeostasis and function in advanced HIV disease. *Science* 1997;**277**:112–16.
- 2 **Komanduri DV**, Wiswanathan MN, Wieder ED, *et al*. Restoration of cytomegalovirus-specific CD4+ T-lymphocyte responses after ganciclovir and highly active antiretroviral therapy in individuals infected with HIV-1. *Nat Med* 1998;**4**:953–6.
- 3 **Race EM**, Adelson-Mitty J, Kriegel GR, *et al*. Focal mycobacterial lymphadenitis following initiation of protease-inhibitor therapy in patients with advanced HIV-1 disease. *Lancet* 1998;**351**:252–5.
- 4 **Woods ML**, MacGinley R, Eisen DP, *et al*. HIV combination therapy: partial immune reconstitution unmasking latent cryptococcal infection. *AIDS* 1998;**12**:1491–4.
- 5 **Jacobson MA**, Zengans M, Pavan PR, *et al*. Cytomegalovirus retinitis after initiation of highly active antiretroviral therapy. *Lancet* 1997;**349**:1443–5.
- 6 **Miller RF**, Shaw PJ, Williams IG. Immune reconstitution CMV pneumonitis. *Sex Transm Inf* 2000;**76**:60 (letter).

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Cost effectiveness analysis of a population based screening programme for asymptomatic Chlamydia trachomatis infection in women

With reference to the article by van Valkengoed *et al*,¹ we would like to express our views.

We agree with the authors' statement that systematic screening of all women aged 15–40 years for asymptomatic *Chlamydia trachomatis* infection is not cost effective, especially when the prevalence of infection in Amsterdam is low (2.2%–2.8%). Not all countries have achieved such low levels. Even in England and Wales where the prevalence of the infection is higher it is not cost effective to screen all women. However, computer modelling performed for the chief medical officer's expert advisory group on *Chlamydia trachomatis*² in the United Kingdom and other countries^{3,4} has shown that it is cost effective to screen populations where the prevalence is 3%–6%. The Chlamydia Pilot Study, which was conducted in Wirral and Portsmouth in 1999–2000, detected a prevalence of chlamydial infection of approximately 10% in women aged between 16 and 25.⁵ There is, therefore, a strong argument for screening this age group in the United Kingdom at the present time and not above 25 years as prevalence above this age is low.

One must be careful when extrapolating data from a different country with a different population. However, it would be wise to consider that in the future in the United Kingdom, when screening is established, the prevalence may fall and the cost effectiveness may be reduced.

Although it is not cost effective to screen men, as there are only minor sequelae to be prevented, one shouldn't forget that they are the major reservoir of infection. We should aim not to reinforce existing inequalities by sparing them their share of responsibility for sexual health. Screening men as well will not only decrease the prevalence but also reduce the psychosocial impact of screening for genital chlamydia in women.

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References

- 1 **Van Valkengoed IGM**, Postma MJ, Morre SA, *et al*. Cost effectiveness analysis of a population based screening programme for asymptomatic *Chlamydia trachomatis* infections in women by means of home obtained urine specimens. *Sex Transm Inf* 2001;**77**:276–82.
- 2 **Turner H**, Townshend J. Cost effectiveness: modelling for chlamydia screening. In: Chief Medical Officer's Expert Advisory Group. *Main report of the CMO's Expert Advisory Group on Chlamydia trachomatis*. London: Department of Health, 1998.
- 3 **Paavonen J**, Puolakkainen M, Paukku M, *et al*. Cost-benefit analysis of screening for chlamydial infection in low prevalence population. Proceedings Third Meeting of the European Society for Chlamydia Research, Vienna, Austria, 11–14 September 1996.
- 4 **Genc M**, Mardh P-A. A cost-effectiveness analysis of screening and treatment for *Chlamydia trachomatis* infection in asymptomatic women. *Ann Intern Med* 1996;**124**: 1–7.
- 5 **Tobin JM**, Harindra V, Tucker LJ. The future of chlamydia screening. *Sex Transm Inf* 2000;**76**:233–4.

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NOTICES

International Herpes Alliance and International Herpes Management Forum

The International Herpes Alliance has introduced a website (www.herpesalliance.org) from which can be downloaded patient information leaflets. Its sister organisation the International Herpes Management Forum (website: www.IHMF.org) has launched new guidelines on the management of herpesvirus infections in pregnancy at the 9th International Congress on Infectious Disease (ICID) in Buenos Aires.

Pan-American Health Organization, regional office of the World Health Organization

A catalogue of publications is available online (www.paho.org). The monthly journal of PAHO, the Pan American Journal of Public Health, is also available (subscriptions: pubsvic@tsp.sheridan.com).

Second International Conference on Sexual Health

To be held in Bangkok, Thailand on 23–28 February 2002

Further details: European Secretariat, Dr Richard Burack (tel: +44 (0) 20 8599 8029; email: siamcare@aol.com).

7th Congress of the European Society of Contraception, "Changing attitudes to contraception and reproductive health"

Genoa, Italy, 10–13 April 2002

Further details: ESC Central Office, Orga-Med, Essenestraat 77, B-1740 Ternat, Belgium (tel: +32 2 582 08 52; fax: +32 2 582 55 15; email: orgamed@village.uu.net.be).

MSSVD course in STIs and HIV, Module 1, Epidemiology of STIs and Bacterial Infections

At the Institute for Materials, 1 Carlton House Terrace, London, 22–25 April 2002.

Further details: Sue Bird, MSSVD STIs and HIV Course Secretariat, PO Box 77, East Horsley, KT24 5YP (tel: 01372 454210).

MSSVD course in STIs and HIV, Module 2, Sexual Health and Sexuality

At the Institute for Materials, 1 Carlton House Terrace, London, 26 April 2002.

Further details: Sue Bird, MSSVD STIs and HIV Course Secretariat, PO Box 77, East Horsley, KT24 5YP (tel: 01372 454210).

MSSVD course in STIs and HIV, Module 3, Viral Infections other than HIV

At the Institute for Materials, 1 Carlton House Terrace, London, 20–21 May 2002.

Further details: Sue Bird, MSSVD STIs and HIV Course Secretariat, PO Box 77, East Horsley, KT24 5YP (tel: 01372 454210).

MSSVD course in STIs and HIV, Module 4, HIV Infections

At the Institute for Materials, 1 Carlton House Terrace, London, 22–24 May 2002.

Further details: Sue Bird, MSSVD STIs and HIV Course Secretariat, PO Box 77, East Horsley, KT24 5YP (tel: 01372 454210).

10th International Symposium on Human Chlamydial Infection

16–21 June 2002, in Antalya, Turkey

The scientific programme will encompass the breadth of chlamydial research from clinical and epidemiological studies to molecular and cell biology of all species of *Chlamydia*. Further details: Professor A Demir Serter, Department of Clinical Microbiology and Infectious Diseases, Ege University, Faculty of Medicine, 35100 Bornova, Izmir, Turkey (fax: 90 232 343 71 30; e-mail: ISHCIX@itsa.ucsf.edu).

10th International Congress on Behçet's Disease

Berlin 27–29 June 2002

Further details: Professor Ch Zouboulis (email: zoubbere@zedat.fu-berlin.de).

20th World Congress of Dermatology

Paris, 1–5 July 2002

Further details: P Fournier, Colloquium, 12 rue de la Croix St Faubin, 75011 Paris, France (tel: +33 1 44 64 15 15; fax: +33 1 44 64 15 16; email: p.fournier@colloquium.fr; website: www.derm-wcd-2002.com).

18th Congress on Sexually Transmitted Infections IUSTI–Europe 2002

12–14 September 2002, Hofburg Center, Vienna

Further details: Angelika Stary, M.D., c/o Administrative and Scientific Secretariat, Vienna Academy of Postgraduate Medical Education and Research, Alser Strasse 4, A-1090 Vienna, Austria (tel: +43 1 405 13 8313; fax: 43 1 407 82 74; email: iusti2002@medacad.org).