Perianal verrucous epidermal naevus mimicking perianal warts

A case of perianal verrucous epidermal naevus mimicking perianal warts in a 2-year-old boy is described. Verrucous epidermal naevi are circumscribed hamartomatous lesions composed almost exclusively of keratinocytes. The typical linear configuration, and histological features may help in the differential diagnosis of perianal wartlesions, particularly when they are present since birth or appear during childhood.

CASE REPORT

A 2-year-old boy was referred by a paediatrician for the evaluation of a perianal verrucous lesion which looked like perianal warts. The condition was first noticed by the child’s mother when he was 9 months old as a raised velvety area around the anal orifice. The lesions had remained stable thereafter.

Figure 1 Perianal warty papules.

Detailed systemic examination failed to reveal any abnormalities.

A provisional diagnosis of verrucous epidermal naevus was made and a punch biopsy specimen was obtained. Histological examination corroborated the clinical diagnosis by showing hyperkeratosis, acanthosis, and papillomatosis without any evidence of vascular change in the keratinocytes or any dermal pathology. Virological study for human papillomavirus (HPV) could not be done owing to lack of facilities. The parents declined any immediate treatment for the asymptomatic condition and during a follow-up period of 1 year, the child has remained healthy with the lesions remaining unchanged in appearance.

COMMENT

Verrucous epidermal naevi are circumscribed hamartomatous lesions composed almost exclusively of keratinocytes. Most epidermal naevi usually occur at birth or infancy but rarely their appearance may be delayed until puberty. The lesions typically consist of closely set warty papules that coalesce to form well defined keratotic plaques usually in a linear fashion. Verrucous epidermal naevi may be almost of any size, may be single or multiple, and can occur at more or less any site. Since these lesions closely mimic viral warts, their occurrence in the perianal region during childhood or adolescence may raise the suspicion of perianal warts as in the present case. Onset of the lesions early in life, their stable nature, typical linear configuration, and histological features may help in the differential diagnosis. Usually only of cosmetic importance, the skin lesions may be treated by cryotherapy, surgical excision, or carbon dioxide laser ablation. Verrucous epidermal naevi are almost of any size, may be single or multiple, and can occur at more or less any site. Since these lesions closely mimic viral warts, their occurrence in the perianal region during childhood or adolescence may raise the suspicion of perianal warts as in the present case. Onset of the lesions early in life, their stable nature, typical linear configuration, and histological features may help in the differential diagnosis. Usually only of cosmetic importance, the skin lesions may be treated by cryotherapy, surgical excision, or carbon dioxide laser ablation. Verrucous epidermal naevi are circumscribed hamartomatous lesions composed almost exclusively of keratinocytes. The typical linear configuration, and histological features may help in the differential diagnosis of perianal warts, particularly when they are present since birth or appear during childhood.

References


Investigating the microbial aetiology of pelvic inflammatory disease

An effort to elucidate a subject which is laden with difficulties is noteworthy, so that it was interesting to read the report by Simms et al. on the associations between Mycoplasma genitalium, Chlamydia trachomatis, and pelvic inflammatory disease (PID). The difficulties are at least threefold. Firstly, a diagnosis of PID based on symptoms and clinical signs, as in the study reported, is acknowledged, both generally and by the authors, to be imprecise. Clinical observations often do not tally with laparoscopic findings, laparoscopy being a fundamental diagnostic requirement in research investigations. Secondly, it is obvious that specimens cannot be taken from the inflamed site in question without laparoscopy. Indeed, it is axiomatic that this should be done if there is to be any chance of unravelling the microbial aetiology. Taking specimens from the cervix is very much second best as the results of microbiological testing may bear no relation to the pathological changes in the tubes. Thirdly, and no less relevant, is the question of an adequate control group. It seems that this should not comprise women undergoing tubal ligation. Although a source of normal tubes would seem sensible, the women were not in the same cohort as those with disease and, in any event, for comparative purposes specimens were taken from the cervix. Surely, an examination of specimens from women without symptoms and signs of PID but who were otherwise comparable to those who did have symptoms and signs would have been more appropriate? In future investigations, controls should be women within a laparoscopically based study who are found not to have PID on laparoscopy. Even then, the situation may be clouded because, in one study, C. trachomatis was detected as often in the tubes of women who did not have PID as visually as in those of women who did. Certainly, however, finding M. genitalium in the cervix of women with ill-defined PID significantly more often than in the cervix of women who did not have PID and who, in other ways, appeared not to be comparable may mean nothing in relation to the pathological changes in the tubes. It is a far cry from unravelling the role of M. genitalium to tubal pathology. It is a far cry from unravelling the role of M. genitalium to tubal pathology. It is a far cry from unravelling the role of M. genitalium to tubal pathology.

References

1. Simms I, Eastick K, Mullinax H, et al. Associations between Mycoplasma genitalium,
Lack of evidence for sexual transmission of hepatitis C virus in patients attending STD clinics in Pune, India

The presence of hepatitis C virus (HCV) RNA in semen among two of six (33%) HIV negative and six of 15 (40%) HIV infected males, reported recently suggests that HIV may facilitate genital shedding and subsequent sexual transmission of HCV.1 We determined HCV prevalence and examined evidence for its sexual transmission in a cohort of STD patients with observed HIV prevalence of 21.2%. Consecutive serum samples (n = 9141) collected between January 1994 and December 1999 were batched, pooled, and positive pool were screened. Samples from positive pools were then tested individually. Positive sera were tested by HCV RNA polymerase chain reaction (PCR) using standard primers.2 HIV antibody status of each sample was ascertained using the algorithm described previously.3 Data were analysed using statistical package SPSS version 10.0. This study was a part of a prospective cohort study that was approved by ethics committee/institutional review boards of the collaborating organisations and blood samples were collected after counseling and informed consent.

Overall prevalence of anti-HCV antibodies was 0.68% (62/9141, 95% CI 0.52 to 0.87). The prevalence among HIV infected individuals (1.5%, 95% CI 1.0 to 2.1) was higher (p = 0.01) than that in those not infected (0.44%, 95% CI 0.3 to 0.6). The annual anti-HCV antibody prevalence rate between 1994 and 1999 was 0.57%, 0.46%, 1.10%, 0.81%, 0.37%, and 0.61%, which did not change significantly over time (table 1). Of the 35 anti-HCV antibody positive sera tested, 27 (49%) were HCV RNA PCR positive.

Univariate analysis revealed that history of past or current STD was not associated with HCV, whereas female sex (OR = 2.07, 95% CI 1.17 to 3.66), prevalent HIV infection (OR = 3.38, 95% CI 2.05 to 5.58), history of tattoo (OR = 1.28, 95% CI 1.31 to 3.63), and being a sex worker (OR = 2.35, 95% CI 1.27 to 4.35) were significantly associated with presence of anti-HCV antibody. However, multivariate analysis revealed that prevalent HIV infection and tattooing increased the likelihood of presence of anti-HCV antibodies by 3.08-fold (AOR 3.08, 95% CI 1.86 to 5.11, p = 0.001) and 1.87-fold (AOR 1.87, 95% CI 1.12 to 3.13, p = 0.017), respectively (table 1).

A rapid spread and high HCV prevalence of 80% has been reported recently among a cohort of injecting drug users from Kolkata, India.4 In contrast, we observed a low and stable prevalence of anti-HCV antibody among STD clinic attenders over the past 6 years in an urban setting where HIV transmission was predominantly sexual. Given that a high HIV prevalence was reported among female sex workers (FSWs) in this population and about 70% of males attending STD clinic had visited FSWs in the past 3 months, stable HCV prevalence over 6 years suggests that HCV is not efficiently transmitted sexually. Additionally, no association was found between past or current STD and HCV prevalence, and a high prevalence and incidence of HBV, a known sexually transmitted infection, have been reported in this population.5 Our analysis failed to identify any evidence that could support sexual transmission of HCV.

References

Monosymptomatic hypochondriacal psychosis

Dr O’Mahony illustrates in his literary and graphic way the difficulties associated with dealing with this condition (from which his patient was almost certainly suffering).6 It is good to know that his hospital is taking seriously the issue of actual or threatened violence to staff. Having had several similar cases over the past couple of years, including one who eventually committed suicide, I have been able to make appropriate arrangements with a psychiatrist who was unequal to his advice that he should be in on a subsequent consultation right from the start and be introduced to the patient as a double consultation. The ethics of this include the fact that such delusional prevalences are, of course, psychotic and unable to bring rational decision making processes to the problem.

Table 1 Characteristics of study participants and association with prevalent anti-HCV antibody

<table>
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<th>Variable</th>
<th>No</th>
<th>Anti-HCV antibody positive (%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>p Value</th>
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<tr>
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*Multivariate analysis was done using binary logistic regression by forward LR method. OR = odds ratio.
A population based dynamic approach for estimating the cost effectiveness of screening for Chlamydia trachomatis

We read the recent paper in STI on cost effectiveness for Chlamydia trachomatis screening by Honey et al with great interest.1 We concur with their conclusion that more data derived from clinical trials are needed for policy making, particularly when considering the evidence on the subsequent risk of pelvic inflammatory disease (PID) in women who test positive for Chlamydia trachomatis.

Our paper was included and discussed in this review. As our approach was rather complex, we note that some parts of our design and results may have been misinterpreted. Honey et al note that our study was focused on screening both men and women in general practice with an age range for evaluation of 15–64 years. Although this information is correct, it does not reflect that screening for women only was considered separately and that women older than 34 years were not included in the screening programme. This misinterpretation by Honey et al formed the basis for exclusion of our study from further systematic review.2

Our approach differs from others1 in that we investigate cost effectiveness by employing a population based dynamic model (Monte Carlo simulation).2 This approach enables us to simulate the C. trachomatis transmission, the impact of prevention measures on the C. trachomatis incidence and prevalence, and the risk for C. trachomatis infection in a population. As a result, indirect effects (for example, future partners of current partners) over a period of several years can be considered using rates of partner change, mixing patterns, and transmission probabilities. We chose to analyse the screening programme over a period of 10 years. In our baseline analysis we assessed screening of men and women aged 15–24 years. However, in the scenario analysis we evaluated several other screening strategies, including screening of women aged 15–24, 15–29, and 15–34 years.

Despite the restriction of C. trachomatis screening to the age groups labelled as “young” women, an evaluation of the transmission dynamics of C. trachomatis in the population as described by our dynamic model requires the inclusion of men and older women in the model. For example, it may well be that C. trachomatis is transmitted from a young woman to a man, from this man to an older woman, etc. Such transmission chains may occur over a period of years and may involve men and women of all ages. So, to adequately evaluate screening of women aged 15–24, a model is required that considers all sexually active age groups. Therefore, sexual activity was modelled for both men and women aged up to 64 years, using assumptions based on a Dutch Sex Survey.

Application of our model to the Netherlands showed that screening women aged 15–24, 15–29, and 15–34 years over a period of 10 years would result in net cost savings to society. When including (excluding) indirect costs, cost savings were reached after 2.8 (3.8) years, 3.1 (4.3) years and 3.3 (5.0) years, respectively. This evaluation considered the costs of screening (polymerase chain reaction testing, azithromycin treatment, GP fee) and partner referral as well as direct (medical) savings as a result of averted health care and indirect savings as a result of averted productivity loss.

We think that our dynamic approach leads to more realistic assessments of cost effectiveness in this area as it appropriately considers the highly infectious character of C. trachomatis. At this time, our approach is being used to evaluate the cost effectiveness of C. trachomatis screening programmes in two other European countries.

Contamination of environmental surfaces by genital human papillomaviruses (HPV): a follow up study

In a previous study we investigated the contamination of environmental surfaces with human papillomavirus (HPV) DNA in two genitourinary medicine (GUM) clinics.3 This study was intended to review the GUM clinic in which HPV DNA was found to be present. Cleaning with “general purpose neutral liquid detergent” (detergent) (Youngs Detergents, Lancatre Ltd, UK) and water, or 2% Cisarsol (disinfecting detergent, 40% VV Tar Acids; Coventry Chemicals Ltd, Coventry, UK) in 70% methylated spirits (Cisarsol) was performed following the results of the previous study.

Twenty samples were collected from two treatment rooms and patients’ toilets at each time of sampling. Samples were tested and typed as described previously.4 Surfaces sampled, and accumulation of HPV DNA during a single day, are listed in table 1.
Sampling was performed at 08.30 on two consecutive days and a third set of samples was collected at 16.30, the end of the clinic hours, on day 2.

Following cleaning with detergent and water at the end of the working day (sampling 1), nine of the 20 surfaces tested were contaminated. It was decided to clean surfaces with a more stringent agent. After subsequent cleaning with Cleasol solution HPV DNA was present on one surface at the beginning of the day, and on four at the end of the day.

β Globin DNA was detected in all HPV DNA positive samples, indicating HPV was cell associated, and in a further five samples taken at the end of the day from HPV DNA negative surfaces.

Compared to our previous study a 50% reduction in surface contamination with HPV DNA was found after cleaning with detergent and the number of types detected was reduced. Only HPV types 6, 11, 16, and 58 were detected on the nine different surfaces. This is also a 73% reduction in the number of types detected in our previous study. Only HPV types 6, 11, and 16 were still the most efficacious than antiseptic soaps.

Comparing our study with previous reports, we found a 65% reduction in the number of HPV DNA positive samples, indicating a HPV 50% reduction in the number of types detected was.

HPV types 6, 11, and 16 were still the most common types found (all types in table 1).

Three of the samples positive for β globin DNA but negative for HPV DNA were from the patients’ toilets and/or the male clinic examination coach. On the examination couch switch and the edge of the examination couch in the patients’ toilet, DNA was probably from the doctor’s gloves, whereas β globin DNA detected on the surfaces sampled in the patients’ toilets was probably the result of cells shed naturally.

Cleasol with ethanol was more effective then cleaning with a detergent, which was more effective than no cleaning, but not sufficient.

Early in the 20th century Ignaz Philipp Semmelweis showed that hand washing with normal strength alcohol was the best method to prevent puerperal fever. It has also been shown that alcohol based disinfectants have a better effect than cleansing with soap. Different antiseptics and decontaminants, whether water or alcohol based, may have different viricidal efficiencies. There are few data on environmental decontamination; however, this study suggests cleaning with Cleasol solution with a more stringent spirit is reasonably effective at decontaminating environmental surfaces, but contamination will recur unless cleaning is performed regularly.

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Issues associated with the introduction of circumcision into a non-circumcising society

A team lead by Kebaabetswe propose the introduction of infant circumcision in Botswana, based on:

- a survey of its acceptability to Batswana (people of Botswana)
- its practice in certain Western nations, and
- its alleged value in preventing HIV infection.

There are several medical, psychological, sexual, social, ethical, and legal problems with this proposal.

Medical effects

Male neonatal circumcision is not an innocuous procedure. There are many complications ranging from trivial to life threatening. Complications generally include bleeding, infection, and surgical accident, including penile necrosis and penile amputations. Bleeding or infection can progress to death. It is difficult to control complications with mass circumcisions. Circumcision excises significant amounts of nerve bearing skin and mucosa, especially the ridged band structure near the mucocutaneous boundary. The protective effects of circumcision against HIV remain controversial. UNAIDS has not accepted circumcision as a useful public health measure.

In neighbouring South Africa, many children are infected with HIV. This is attributed to unsafe health care.

Circumcision creates an open wound through which infection may proceed. It is not clear that mass circumcision can be delivered in Botswana. It is possible that mass circumcision may worsen the epidemic.

Psychological effects

Psychological manifestations of circumcision have been an area of study at Bond University.

Neonatal circumcision is an intensely painful, traumatic, and stressful operation. General anaesthesia is unsafe in the newborn. Available methods of anaesthesia are only partially effective. Circumcised infants show hypersensitivity to pain suggestive of post-traumatic stress disorder (PTSD). Our study of the incidence of PTSD in the Philippines found extensive PTSD in circumcised boys. PTSD secondary to neonatal circumcision has been identified in adult males. Victims of trauma tend to re-enact their trauma either on themselves or others in a cycle of violence. Circumcised males may rely on psychological defence mechanisms such as rationalisation and denial, and strongly avoid thoughts, feelings, or conversations about circumcision.

There are additional concerns. The state of the phallus is closely related to a man’s sense of wellbeing. Men who were circumcised neonatally may feel unhappy about being circumcised, experience significant anger, sadness, feeling incomplete, cheated, hurt, concerned, frustrated, abnormal, and violated. In addition, circumcised men may suffer from resultant low self esteem, which frequently can result in a host of disordered behaviours.

Circumcision may be difficult to eradicate from a society once it is introduced. In addition, to the re-enactment described above, Goldman reports that circumcised men tend to defend the practice. Circumcised doctors tend to develop intellectual arguments to support genital cutting. Fathers who are circumcised may adamantly insist on a son’s circumcision in an emotional defence against their own painful feelings of grief for a lost body part and reduced sexual function. Kebaabetswe et al (p 217) reported that, “Being circumcised was the only significant predictor for a man who would definitely or probably circumcise a male child.”

Sexual effects

As noted above, circumcision excises large amounts of skin and mucosa from the penis. The removal of the prepucce tightens the remaining skin and makes it relatively immobile. Since stimulation of the sex nerves normally occurs by movement of the mobile skin, this further desensitises the penis, perhaps even more than the removal of the ridged band of erogenous nerves noted by Taylor. Excision of sexual nerve endings necessarily reduces sensory input. A decrease in sensation may therefore decrease the sexual response.

Male circumcision also may adversely affect female sexual response. A survey of women found that they were markedly less likely to have an orgasm with a circumcised partner.

Social effects

There has been little study of social problems that may occur when entire cohorts of males are circumcised and consequently most of the men in a society bear physical and psychological wounds associated with circumcision.

We might expect more dependence on alcohol to relieve the symptoms of PTSD. Low self esteem may generate a feeling of shame. Shame may generate problems with...
relationship dissatisfaction, poorer health, depression, drug use, and loneliness. Increased sexual incompatibility and marital problems. Inhibited sexual experiences may not be expected as a result of reduced penile sensory input, increased sexual dysfunction, PTSD, and low self esteem among circumcised men. Increased antisocial behaviour may also be expected. Thus, we might expect to see higher levels of domestic violence, rape, child sexual abuse, suicide, and theft.

Human rights

The fight against HIV/AIDS requires the careful protection of human rights. Among these human rights one finds the rights to security of the person and protection from degrading treatment. The unnecessary infliction of normal human tissue from circumcision or for other reasons is an obvious violation of the security of the person.

Through amputation of erogenous tissue, circumcision necessarily diminishes sexual sensation and function as described above and may constitute degrading treatment.

Ethics

Doctors have a duty of care to behave in an ethical fashion. Among other requirements, they are expected to respect the human rights of their child patients. Circumcision has been shown to be a violation of the child’s human rights and, clearly, many ethical doctors are unwilling to carry out destructive circumcisions on normal, healthy boys. The British Medical Association recognises the right to conscientious objection to the performance of circumcision.

Law

Male circumcision is not unlawful, but valid consent must be obtained. This may be a problem in the case of circumcision performed on unconscious minors, in the absence of any medical indication.

Cases involving the right of parents to consent to the non-therapeutic surgical sterilisation of a child have been heard in several nations. Cases agree that, in the absence of any medical indication, parents are not empowered to consent to the non-therapeutic, irreversible, surgical alteration of their child’s genitalia.

In the absence of a valid consent, a circumcision may constitute an assault.

Conclusion

The value of male circumcision in preventing HIV infection remains unclear. Non-sterile circumcisions may increase the risk.

The proposal by Kebaabetswe and colleagues for the introduction of circumcision into Botswana is seriously flawed, and is irreversibly damaging to security of the person and protection from torture. The unnecessary infliction of normal human tissue from circumcision per-
mind. These are missing. But a direct comparison of the treatment of a common condition, such as vaginal discharge, between the two books points up considerable differences. Whereas *Sexually Transmitted Diseases* tackles in admirable detail the microbiology, epidemiology, diagnosis, management, and complications of the various infections, I looked in vain in the atlas to find out whether sexual partners of women with bacterial vaginosis should be treated. There are however novel aspects of the atlas that should be applauded. I especially liked the opening chapter on genital and dermatological examination that brings together the normal and the abnormal in a particularly useful way, especially for physicians with a limited knowledge of dermatology.

Clearly, the general attractiveness of this atlas will ensure its place on the bookshelves of most specialist departments. As an introduction to the specialty, it fills an important niche and might be an ideal purchase for trainees. It cannot however replace as a resource for serious trainees. It cannot however replace as a resource for serious trainees.

In a book this compact the authors clearly acknowledged this to some extent, by the use of “evolving” references in many instances (p 151 UNAIDS website; www.aidsmap.com for HIV treatment).

Long term utility of this kind of book depends, among other things on how well it is researched and written, but also crucially on the pace of further progress in the field and thus how often it needs revision. Progress is bound to continue in many areas of STI epidemiology and clinical practice. It would seem that web based books in a state of perpetual revision (for example, www.hopkins-aids.edu/publications/book/book_toc.html) may go some way to addressing the question of whether a book survives as a useful text.

This book may not be the last word on the subject of STIs but it is certainly a good place to start.

Sylvia Ojoo

Clinical Practice in Sexually Transmitted Infections


This book, aimed at doctors in training in genitourinary medicine, is highly readable and manages to pack in a lot more material than one would guess from its size. It is largely successful in this goal, combining clarity of language and excellent clinical photographs where these are used.

In a book this compact the authors clearly did not intend to address comprehensively all the subjects raised, as indicated by the widespread referral to reviews and specialist books and use of up to date references for those inclined to seek further information. The length I think is more a strength than a weakness although it must have been difficult to decide what aspects of these disparate infections to include and what to leave out. However, perhaps because of the wider audience, when discussing certain pathological states some information on, or illustrations of, normal state or function would have been helpful. For the same reason legends explaining some of the abbreviations used (for example, for recently defined cytokines and cellular molecules) would not have been remiss.

It is a brave person who sets upon the task of writing a medical textbook, not least because it is such hard work, but also because the accelerating pace of change in the biomedical sciences can make an author seem more like an historian. Even in this up to date book there is information that needs revision already, in view of recent changes (for example, p 158 Management of *Pneumocystis jiroveci*. *Arch Intern Med* 2001;161:1529–33) The authors have acknowledged this to some extent, by the use of “evolving” references in many instances (p 151 UNAIDS website; www.aidsmap.com for HIV treatment).

In the STI supplement 1 this year, 80th MSSVD Spring Meeting held jointly with the 19th STI Congress of IUSTI Europe, the following abstract was omitted from the printed abstract book, with apologies to the authors.

**Incidence and causes of peripheral eosinophilia in HIV-1 infected individuals attending a district general hospital**

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**Objectives:** To determine the incidence of eosinophilia in a cohort of HIV-1 positive individuals and to compare the prevalence of positive parasitic serology between African cases and controls.

**Methods:** Patients attending an inner city HIV clinic with peripheral eosinophilia (>0.5 x 109/l) on two or more occasions were identified as cases from a retrospective review of haematological records from October 1999 to August 2001. Controls (Africans without eosinophilia) were obtained from an ongoing prospective study. Demographic and clinical data were ascertained by case notes review and patient questionnaire. Investigations for parasitic infections were undertaken (schistosomal, filarial, and strongyloides serology).

**Results:** 295 patients had haematological tests during the observation period, of which 67 (23%) had peripheral eosinophilia. 60/67 (90%) of the cases were of African origin, the mean nadir CD4 count was 195 and 25% were <50. Controls (n = 45) were broadly similar. To date, 26/45 (58%) African cases had positive serological screens for parasites (23 schistosomal, 4 strongyloides, and 2 filarial infections), compared with 4–45 (9%) of controls (4 schistosomal infections) (p<0.001, χ² test). There was no positive serology in 3/7 non-African cases screened.

**Conclusions:** Although previous studies have demonstrated a low incidence of parasitic infection in HIV-1 positive patients with eosinophilia, we have identified a high number of treatable parasitic causes. No cause has been identified in 42%, suggesting that for a proportion of these HIV may be the cause. Despite this, routine screening for parasitic infection, guided by geographical exposure, is recommended in HIV-1 infected Africans with eosinophilia.

The following acknowledgement was omitted from the original article entitled Chlamydial infection: an accurate model for opportunistic screening in general practice, by M Luchhe, C. C. Harris, N. B. G. Verhoeven, M. M. Altenburg, M. S. M. Leenaars, and W. P. A. J. Vos (MSSVD Spring Meeting held jointly with the 19th STI Congress of IUSTI Europe, *Sex Transm Infect* 2003;79:313–317): We would like to thank Eddy Van Dyck and Hilde Smet from the Prince Leopold Institute of Tropical Medicine, Antwerp, for their help with setting up the diagnostic protocol and for performing confirmation tests. Jost Weyler of Antwerp University for his statistical advice, and all participating GPs in the field. This work was partly supported by Eurogenerics, the Scientific Organisation of Flemish GPs (WVVH), and the Local Health Promotion Organization (LOGO) of Antwerp. The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.