



IPPF Medical Bulletin

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Rapid diagnostic tests for sexually transmitted infections

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At the International Conference on Population and Development in Cairo in 1994, a call was made for the integration of services for the diagnosis and treatment of sexually transmitted infections (STIs) into programmes for family planning and maternal health, as part of a comprehensive reproductive health care package.¹ There are few countries in which this objective has yet been achieved; and, even in those where it has, there is little evidence that it has had any impact on the prevalence or incidence of STIs. There are both political and technical reasons for this.

Politically, STI control remains low on the list of public health priorities in most countries, and there is a lack of public awareness about STIs and their consequences, even among those responsible for family planning programmes. Moreover, family planning programmes have tended to focus almost exclusively on women, whereas it is not possible to control STIs unless the male partners of infected women are also treated.

Syndromic management

One possible approach is "syndromic" management: when symptoms could be due to one of several infections that cannot be distinguished without laboratory tests, treatment is given that covers all the causes. Syndromic management generally works well in men, but in women it has proved less effective than was hoped. Studies in several developing countries have shown that syndromic management of women with the common complaint of vaginal discharge is neither sensitive nor specific in identifying women who have an STI.^{2,3} It is not sensitive because most women with STIs have no symptoms.⁴ It is not specific because most women who complain of vaginal discharge are not suffering from an STI but from a derangement of the normal vaginal bacterial flora, such as bacterial vaginosis or thrush (candidiasis). Low specificity, resulting in over-treatment on a massive scale, is a particular drawback in populations with a low prevalence of STIs but a high prevalence of symptomatic vaginal discharge, as is often found in Asia.^{5,6} In addition to the costs and possible side-effects resulting from over-treatment, the over-diagnosis of STIs in women may carry a heavy personal and social cost – especially when women are encouraged to refer their husbands or other sexual partners for treatment. Attempts to improve the performance of the syndromic management flowchart for vaginal discharge by use of simple laboratory tests, such as microscopy and the leucocyte esterase dipstick, which detects pus cells in urine, have not been very successful.⁷

Point-of-care testing

A wide range of tests for the diagnosis of STIs are now on the market.⁸ Nucleic acid amplification tests such as the polymerase chain reaction and ligase chain reaction assays are commercially available for the diagnosis of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection.⁹⁻¹¹ These amplification tests are highly sensitive and specific, and have become the "gold standard" for laboratory diagnosis of *C trachomatis* infection. With their high sensitivity, they allow use of non-invasive specimens such as first-catch urine or self-administered vaginal swabs for diagnosis. This has led to the design of innovative approaches to screening outside of clinic settings, such as the use of vaginal or vulval swabs collected by the patient and sent in by mail.¹²

Although nucleic acid amplification tests are cost-effective in high-prevalence settings, they are expensive and technically demanding. Since many clinic attenders have difficulty in returning to the clinic for results, less sensitive tests that can be done rapidly at the point of care, allowing immediate treatment, may have a greater impact than more sensitive tests that require samples to be sent to a distant laboratory.¹³⁻¹⁵ In addition to enabling treatment to be given immediately – so preventing the development of long-term complications such as pelvic inflammatory disease and infertility – near-patient or point-of-care tests make it possible to initiate partner notification with confidence at the first clinic visit. Widespread testing, if accompanied by sound reporting systems, will draw the attention of health workers and policy makers to the high prevalence of STIs in some populations and allow for the rational design of appropriate intervention programmes.

Although many near-patient tests for the diagnosis of STIs can now be purchased, their performance has not been widely evaluated.^{8,15} Panel 1 lists the tests available and their estimated performance characteristics. Most rapid tests are based on the principle of immunochromatography, where antigen-antibody reactions are trapped on the strips and appear as coloured lines or spots on membrane strips. For genital chlamydial and gonococcal infections the diagnostic target is antigen, and for syphilis and viral STIs the target is antibody. Most rapid tests are designed for room-temperature storage, can be performed in less than 30 minutes with minimal training, and require little or no equipment.

Chlamydia

The Clearview Chlamydia test (Unipath, UK) is a simple, rapid, near-patient test with a visual endpoint that requires either a urethral swab or centrifuged urine pellet in men, or a cervical swab in women. It has a heating step and therefore needs electricity, although a heat block is supplied with the kit. The Chlamydia Quickvue (Quidel, USA) and OIA (ThermoBiostar, USA) tests are similar to the Clearview test but do not require heating, and a filter device is available for concentrating *C trachomatis* in urine specimens. In limited evaluations, these tests have been found to have sensitivities of 50-75% and specificities of 98-99% (when compared with nucleic acid amplification tests) in symptomatic and high-prevalence populations.¹⁶⁻¹⁸ Their utility in screening asymptomatic or low prevalence populations requires further study.

PANEL 1. RAPID TESTS FOR THE DIAGNOSIS OF SEXUALLY TRANSMITTED INFECTIONS AND VAGINOSIS

Condition	Type	Target	Specimens	Sensitivity	Specificity	Comments
<i>Chlamydia trachomatis</i> infection	Immuno-chromatographic strips	Antigen	Urethral, cervical swabs	50-75%	98-99%	Performance compared with NAAT and/or culture. Some kits can be used with concentrated urine from men
<i>Neisseria gonorrhoeae</i> infection	Gram stain	Morphology	Urethral, cervical swabs	>90% M 45-65% F	>95% M 90-95% F	Performance compared with culture. Requires microscope and technical expertise
	Immuno-chromatographic strips	Antigen	Urethral, cervical swabs	50-70%	98-99%	Performance compared with culture. Some kits can be used with concentrated urine from men
<i>Trichomonas vaginalis</i> infection	Wet mount	Motile trichomonad	Vaginal secretions	50-70%	99-100%	Performance compared with culture. Requires microscope
Bacterial vaginosis	Gram stain	Gram-ve rods	Vaginal swab	?*	?*	Requires microscope; scoring standardised (Nugent score)
	Wet mount	Clue cells	Vaginal secretions	38-70%	90-95%	Performance compared with Nugent score; requires microscope
	Card test	Proline amino-peptidase	Vaginal swab	93%	93%	Performance compared with Nugent score
Syphilis	Non-treponema-specific tests	Antibody	Serum	90-98%	90-95%	Requires centrifuge and rotator
	Treponema-specific tests	Antibody	Serum, plasma or whole blood	90-99%	99-100%	Do not distinguish between current and past infection
	Dark field microscopy	Motile spirochaete	Lesion material	<50%	95-100%	Requires microscope; low sensitivity due to prior application of antiseptic or antibiotic treatment. Not useful in latent syphilis
Herpes simplex virus type 2	Immuno-chromatographic strips	Antibody	Serum	96%	98%	Performance compared with culture for sensitivity and immunoblot for specificity

NAAT=nucleic acid amplification test

*Performance uncertain in the absence of consensus reference standard

Vaginal infections

Relatively simple tests, requiring only a microscope and a trained microscopist, are available for the diagnosis of vaginal infections. These include wet mount for *Trichomonas vaginalis* or for the identification of clue cells (suggestive of bacterial vaginosis). Bacterial vaginosis can also be diagnosed by use of the Nugent score, which is based on the proportion of lactobacilli in vaginal flora seen on a gram-stained smear. A few rapid near-patient tests that detect bacterial enzymes or antigen agglutination on a card format are now commercially available for the diagnosis of vaginal infections. Although easy to use, they are costly and have not been widely validated. In the absence of clear-cut control strategies, and in view of the uncertain significance of bacterial vaginosis in asymptomatic women, the cost-effectiveness of such tests is not clear.

Syphilis

The priority for syphilis diagnostics is a test for screening of pregnant women, and of men and women at high risk of infection. Rapid non-treponemal tests, such as the rapid plasma reagin (RPR) test, are widely used for screening in high prevalence settings. Although simple to perform and inexpensive, RPR tests require electricity to operate a rotator and possibly a centrifuge for separating serum. Reagents for RPR that can be stored at room temperature are now obtainable, as are rotators driven by solar energy. Non-treponemal tests are prone to false positives, especially in pregnant women. Ideally, results should be confirmed with a treponema-specific test. These confirmatory tests are technically demanding and may only be available in reference laboratories. Over twenty companies now manufacture rapid simple treponema-specific tests that can

be used on whole blood, serum, or plasma. The tests can be used in primary health care settings as they are stable at room temperature for months, require no equipment, and give a visual readout in 8-15 minutes. Limited evaluations suggest that some have comparable performance to laboratory-based tests.¹⁹ Rapid near-patient treponema-specific tests will be useful for syphilis screening in low-prevalence settings, but will be less useful in high-prevalence settings since they do not distinguish between past and current infection.

Genital herpes

For genital herpes infections, rapid tests for the detection of antibody to *Herpes simplex* virus type 2 are available but they are expensive.²⁰ In view of the lack of control strategies for genital herpes infection in most countries, the lack of curative treatment, and the low feasibility of long-term suppressive treatment, the utility of such tests in disease control is uncertain.

Further evaluation

The Sexually Transmitted Diseases Diagnostics Initiative at the World Health Organization has initiated a programme to evaluate simple, affordable, rapid tests for syphilis and genital chlamydial and gonococcal infections appropriate for use in primary health care settings in developing countries. Since over forty rapid tests are commercially available for these three diseases and field trials are costly, tests will first be evaluated in laboratory sites in diverse geographic locations. The most promising of these will be selected for further evaluation, not only of test performance but also of feasibility and acceptability in field settings. Several funding agencies – for example, the Wellcome Trust, USAID, and the US National Institutes of Health – have supported the development of rapid STI tests. The Sexually Transmitted Diseases Diagnostics Initiative is planning to develop a framework for collaborative effort with these and other agencies to further test development and to assess the impact of rapid STI tests on disease control.

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The mention of specific companies and products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature.

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Behaviour change among youth: reproductive health and HIV

Nancy E Williamson

The lifelong health and wellbeing of the world's 1.7 billion youth (aged 10-24) will be enhanced if they practise a handful of behaviours – if they delay sexual experience, avoid smoking and substance abuse (alcohol and drugs), take exercise, and practise safe sex when they become sexually active. The World Health Organization estimates that 70% of premature deaths now occurring in adults are due to behaviours that began during adolescence. For prevention of these deaths, information and skills are needed – but a much greater challenge is to change behaviour. That this can be done in the context of HIV is shown by trends in Uganda¹ and Zambia,² where youth, especially girls, have begun sexual activity later, reduced their number of sexual partners, and increased condom use – with an associated decline in HIV prevalence. In Thailand, a behavioural intervention in young military conscripts has similarly reduced the incidence of sexually transmitted infections including HIV.³ "Success stories" of this sort are very important for convincing policy-makers and donors to put resources into youth programmes, which so far have received a pittance of development funds.

The behaviour of young people is hugely diverse, being influenced particularly by age, sex, marital status, whether they are in or out of school, and whether they live in an urban or rural area; so the task of reaching large numbers with information, skills, and services is daunting. Until lately, most youth programmes were small, isolated, and unable to document either the process or the impact of their interventions. Nevertheless, some general conclusions can now be drawn on what works and what does not.

HIV and reproductive health

An issue of *Population Reports*,⁴ on youth and HIV/AIDS, is subtitled 'Can we avoid catastrophe?'. 12 million youth are now infected with the virus, and half the new infections are in people aged 15-24. Six African countries are projected to lose 42-88% of their current 15-year-olds to AIDS.

The data on reproductive health are also very disturbing. 15 million young women (age 15-19) give birth every year and many of these pregnancies are unplanned. Young mothers have higher mortality rates than mothers in their 20s and 30s; their infants fare less well than those of older mothers; and those who are unmarried have less access to contraceptives and are less likely to use them in sexual encounters.

Programmes to encourage behavioural change

Several large programmes are now underway. Probably the biggest, the first global campaign directed to HIV in youth, will be launched at the AIDS meeting in Barcelona this summer. The six-month programme, initiated by MTV, will include public service announcements, a video, rock concerts, and publicity for local youth services, hotlines, and relevant organisations. The 6-year FOCUS programme⁵ reviewed thirty-nine high-quality studies from the developing world. Current data indicate that four activities deserve special attention. *Community-based programmes*, including youth development, peer promotion, and distribution of contraceptives, "can be successful in improving youth reproductive behaviors." *School-based programmes* are "nearly universally effective in improving young people's knowledge of sexual and reproductive health." *Use of the media*, including television, radio, hotlines, and the Internet, holds promise – especially social marketing approaches directed at making regular condom use more socially acceptable. On *youth-friendliness*, surprisingly, there was no conclusive evidence that this attracts young people to clinical services. Sometimes the evidence rests on just a few studies, an example being youth-friendly services. Negative results are also important. On existing information, youth centres are not cost-effective venues for delivering reproductive health services. There is a crying need to measure the processes and impact of youth programmes, including their costs.

In another review paper, based largely on work in North America, Kirby⁶ lists ten common characteristics in the curricula of the most effective sex and HIV education programmes. These programmes:

- Concentrate on one or more sexual behaviours that lead to unintended pregnancy or sexually transmitted infection
- Are based on approaches that have been shown to influence other health-related behaviour and target specific sexual antecedents
- Deliver and constantly reinforce message about abstaining from sexual activity or, alternatively, about use of condoms and other forms of contraception
- Provide accurate information on the risks of teenage sexual activity and ways to avoid intercourse or to protect against pregnancy and infection
- Include activities that address social pressures influencing sexual behaviour
- Provide practice with communication, negotiation, and refusal skills

- Employ teaching methods that involve participants and personalise
- Incorporate behavioural goals and teaching methods appropriate to age, sexual experience, and culture
- Last more than a few hours; short-term curricula (whether abstinence-only or sexuality education) have negligible impact
- Select peer leaders and teachers who believe in the programme, and provide them with adequate training.

Conclusion

None of the approaches outlined here is sufficient to achieve the desired results. Youth themselves are the solution, since it is they who must take the billions of small actions to protect themselves. None will work without the participation and leadership of young people. Application of such programmes in developing countries is particularly challenging. For example, participatory teaching methods are uncommon in many school systems, and teachers themselves may be unclear about what messages should be conveyed. The "biology teacher", for example, is not always the best person to teach about sexuality or refusal skills. Some large randomised trials of education interventions, soon to emerge, will produce valuable information – whether the results are positive or negative.

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News

Emergency contraception is not abortion

In the UK, the emergency contraceptive levonorgestrel can now be supplied by pharmacists to women of 16 years or older. Opposing this liberalisation, the Society for the Protection of the Unborn Child (SPUC) claimed that, because this method prevents implantation of a fertilised egg, the supply of pills by pharmacists amounts to "procuring a miscarriage" – a criminal offence. Arguing that emergency contraception should be subject to the legislation governing abortion, SPUC sought a review by the High Court. This case was comprehensively rejected on April 18. Mr Justice Munby pointed out that SPUC's argument could be applied to any form of contraception that discourages implantation of a fertilised egg – for example, the intrauterine device or the mini-pill. After hearing expert evidence, he was satisfied that the term "miscarriage" applies only after implantation. He was particularly critical of SPUC's attempt to criminalise methods used by vast numbers of people: "I cannot see that it is any part of the responsibilities of public authorities, let alone the criminal law, to be telling adult people whether they can or cannot use contraceptive devices of the kind which I have been considering."