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Women's health in developing countries

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Healthcare priorities are different in developing and developed countries. A more effective resource allocation, complemented by efforts to implement only those practices that are effective, should be a priority for improving reproductive health services in developing countries. A large burden of gynaecological disease exists in developing countries and it is difficult to envisage serious reforms and improvements without an increase in public-sector spending. However, communities themselves could assume some responsibility for women's health in ways that prioritize women's own perceptions and primary needs. In this chapter we have compiled existing evidence regarding various gynaecological problems faced by women in developing countries. To name a few: sexual health issues, abortion, subfertility, cancer, and genital fistulae. We believe that there is a large knowledge gap in the area of women's health in developing countries, and there is an urgent need to conduct appropriately designed studies.

Key words: developing countries; gynaecological problems; morbidities; reproductive health; women's health.

Questions and Literature Sources

Questions

- Population: women in developing countries
- Problems: various gynaecological problems (sexual health issues, abortion, subfertility, cancer, genital fistulae)
- Outcomes: epidemiology, effectiveness of interventions

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Literature sources

We searched for only synthesized sources; no systematic attempt was made to search the published literature outside the following sources:

- The Reproductive Health Library, Issue 8, 2005. Oxford: Update Software Ltd. Available from: <http://www.rhlibrary.com>
- The Cochrane Library, Issue 1, 2006. Chichester, UK: John Wiley & Sons, Ltd. Available from: <http://www.cochrane.org>
- Clinical evidence. Available from: <http://www.clinicalevidence.com>
- NICE Guidelines. Available from: <http://www.nice.org.uk>
- Green Top Guidelines. Available from: <http://www.rcog.org.uk>

As there is a knowledge translation gap between existing information and its availability to users, a significant part of this chapter is based on the available synthesized information in the Reproductive Health Library. We have compiled best-practice interpretations of the available information on various women's health problems for their application in developing countries.

INTRODUCTION

Developing countries bear a large burden of gynaecological disease and it is difficult to imagine how serious reforms and improvements could take place without increases in public-sector spending. It is possible, however, that the responsibility for women's health could be assumed by communities in such a way that prioritizes women's own perceptions and primary needs.¹ Healthcare priorities differ between developing and developed countries. Yet in many developing countries the allocation of resources for healthcare, as well as healthcare practices, remains modelled on those of developed countries. A more effective resource allocation, complemented by efforts to implement only those practices that are effective, is a priority if reproductive health services in developing countries are to improve.² Initiatives to change practice and improve healthcare outcomes often require programmes that integrate systems and organizational change, as well as interventions to target individual clinicians. To develop and sustain the achievements already made in evidence-based reproductive health, providers should focus on behaviour-change methods that are relevant to the locality.³ Systematic reviews are now widely accepted as a prerequisite for making decisions on clinical interventions and health policy. However, although clinicians, programme managers and policy-makers need equally comprehensive and reliable information on a variety of other healthcare areas in which research designs other than randomized controlled trials (RCTs) are used, there is an absence of such systematic reviews.⁴

This chapter specifically targets women in developing countries. Various gynaecological problems are faced, including: sexual health issues, abortion, subfertility, cancer and genital fistulae. These problems are presented below in the context of their epidemiology and effectiveness of various interventions.

SEXUAL HEALTH ISSUES

Sexually transmitted infections (STIs), including HIV, are extremely common in many developing countries, particularly in sub-Saharan Africa. In some areas of Africa (e.g. Botswana), between 40 and 50% of women attending antenatal care clinics are HIV positive.⁵ Surveys in more general populations in Kisumu, Kenya, and Ndola, Zambia, also report relatively high HIV prevalence rates of 30 and 32%, respectively, in women of reproductive age.⁶ In other areas of Africa, however, the HIV prevalence rates are lower in women of reproductive age, although they are still quite high. For example, in Yaoundé, Cameroon, the HIV prevalence rate in women of reproductive age is 8%.⁷

STIs remain a major public health problem worldwide. They are a leading cause of morbidity, with far-reaching health, social and economic consequences.⁷ Rates of STIs are increasing in some regions, especially in people aged 15–25 years. Although the best means of dealing with the spread of the infections continues to be elusive⁸, the HIV/AIDS pandemic, which has had particularly devastating effects in sub-Saharan Africa, has focused attention on the urgent need to control STIs. The presence of STIs substantially increases the risk of sexually acquired HIV infection.⁸

Trichomonas vaginalis is particularly frequent among women of developing countries, who have limited access to medical care. Prevalence rates of 15% or higher are common among women in developing countries, which makes this one of the most common STIs.

Population-based interventions for reducing STIs and HIV infection

STIs and the prevalence of HIV are considered to be interdependent. Similar attitudes and practices have been observed among people with these infections, and this places people at high risk for both types of infection. As the presence of STI increases the shedding of HIV, the probability of HIV transmission is increased. The fact the treatment of STIs reduces HIV shedding further enforces the concept that population-based interventions of STI control might significantly prevent HIV.

A Cochrane review⁹ of five RCTs found limited evidence to support STI control as an effective strategy to prevent HIV. It was also seen that STI treatment services, when accepted by the community (and along with use of condoms), substantially improve outcomes. In areas with an emerging HIV epidemic, where treatment services for STIs are poor and STIs are highly prevalent, improving STI treatment services can reduce HIV transmission by as much as 40%; experience from Tanzania shows that such an intervention is feasible in a developing country.

The randomized trial in Mwanza, United Republic of Tanzania, found STI treatment intervention to be beneficial in reducing the incidence of HIV. The intervention comprised a set of four activities: (1) training health workers in syndromic STI case management as recommended by the World Health Organization (WHO); (2) providing inexpensive but effective drugs; (3) making regular supervisory visits to health facilities; and (4) conducting village campaigns to improve treatment-seeking behaviour. The Mwanza intervention was designed to be sustainable and affordable. Indeed, the investigators implemented an intervention that was pragmatic and adapted to circumstances in sub-Saharan Africa. The costs were not exorbitant and the provision of syndromic case management fitted into the cultural and educational milieu. That the investigators were able successfully to implement this intervention in Tanzania validates its feasibility for other parts of sub-Saharan Africa.

A different intervention, used in Rakai, Uganda, involving repeated rounds of mass treatment for STIs was not to be as feasible as the Tanzanian experience. Operational implementation difficulties, excessive drug costs and the potential for development of resistant organisms all limited the feasibility of this mass treatment option. Had this project been effective, these concerns might have been overcome. However, the mass treatment arm was found to be ineffective, at least in the rather high HIV-prevalence environment that characterizes Rakai, and this renders the question of the feasibility of this intervention irrelevant.

Success in the Mwanza intervention depended on: (1) training health workers in the syndromic case management of STIs; (2) having sufficient healthcare facilities to provide treatment; and (3) maintaining adequate supplies of effective STI therapy. Training the health workers in syndromic case management is critical but syndromic treatment should not be introduced without first determining the key STIs in the population to be covered by the services. Thus, syndromic case management depends on determining the prevalence of STIs and then training health workers in the implementation of the syndromic approach. Presumably, additional STI control will improve case-management services, screening or periodic presumptive treatment of STIs but these approaches, particularly case management based on laboratory results, might not be feasible in many under-resourced settings. The caveat, again, is that the reduction in HIV transmission brought about by control of STIs might be limited to settings characterized by: (1) an emerging HIV epidemic; (2) inadequate STI treatment services; and (3) a high prevalence of STIs.

Partner notification strategies for reducing transmission of STIs

Notification of the partner about the diagnosis of STI has been considered an effective strategy in reducing its spread. A Cochrane review¹⁰ of 11 RCTs found moderately strong evidence in its favour. However, only two of these trials were conducted in developing countries and all of the trials had some risk of bias. Patients with STIs are likely to have partners who are infected. To prevent the further transmission of infection, or reinfection, of index patients, sexual partners should be referred for diagnosis and treatment. This is particularly important for female partners of male patients with STIs, because the female partners are frequently asymptomatic and thus might not recognize the need for treatment. The Cochrane review compared three main referral strategies: provider referral (partner notification by healthcare personnel), contract referral (health personnel notifying partners who fail to visit the health clinic by an agreed date) and patient referral (the index patient notifying his or her partner or partners).

Although all three strategies for partner notification should be feasible in under-resourced settings, special challenges exist. Provider referral might be more challenging and costly to implement than the others. Where health services are overburdened, it might be difficult to ensure adequate privacy for patients to discuss issues of notification of partners. Where healthcare providers are not adequately trained to be sensitive towards patients' needs, there is a risk of some of the providers adopting authoritarian and coercive approaches to partner notification, which are likely to render patients even less willing to share information. Cultural factors must always be considered, as failure to consider issues such as the imbalance of power between men and women could lead to the abandonment of, and violence against, women. In this regard, the importance of confidentiality cannot be emphasized sufficiently. Finally, access to adequate diagnostic and treatment facilities can be difficult in

under-resourced settings. This is especially true for women in rural areas whose partners are treated in the cities where they are employed as migrant workers.

Nonoxynol-9 for preventing vaginal acquisition of STIs by women from men

Among other interventions to reduce the incidence and prevalence of STIs and HIV, the vaginal microbicide, nonoxynol-9, has been used widely. However, a Cochrane review¹¹ of ten RCTs found broadly consistent results against its use. Indeed, there is some evidence that it might actually be harmful because it increases likelihood of genital ulceration. As such, this product cannot be recommended for STI prevention.

The ten RCTs reported outcomes for gonorrhoea, cervical infection, trichomoniasis, bacterial vaginosis, chlamydia and candidiasis, although not all the trials assessed each of these outcomes. Use of nonoxynol-9 did not significantly reduce the risk of any of these infections. The review reports that genital lesions, such as ulcers, are significantly more likely to occur in women using nonoxynol-9, but this result [relative risk (RR) 1.17; 95% confidence interval (CI) 1.02–1.35] is only marginally significant. Almost all the trials included in the Cochrane review were conducted in developing countries, adding weight to the applicability of these results to under-resourced settings.

Trichomoniasis treatment in women

Trichomoniasis is one of the most common STI in women and is thought to facilitate HIV transmission. A Cochrane review¹² of 54 trials showed that nitroimidazole seems to be effective in achieving parasitological cure in short-term follow-up. It was also inferred that partner treatment can be effective in decreasing long-term reinfection. Among varying nitroimidazole drugs available for the therapy of trichomoniasis, tinidazole was more effective than metronidazole, although the quality of the studies comparing the two drugs was not optimal. Identifying women infected with trichomoniasis is often more difficult than treating them.

Short treatment regimens with drugs of the nitroimidazole class (mostly given as a single dose) are as effective in achieving success as longer treatment regimens (of at least 5 days' duration: RR 1.12; 95% CI 0.58–2.16); therapy with any regimen is generally >90%. Failure to treat partners can lead to apparent lack of therapeutic success and, because trichomoniasis is an STI, treatment of male partners must be part of the treatment regimen of infected women. The only trial that compared treatment outcome among women whose partners were not treated versus those whose partners were treated showed that women whose partners were not treated had a significantly higher failure rate (24% versus 5%).

Practice points

- Sexually transmitted infection (STI) services should be easily accessible at the lowest healthcare level available.
- Customized syndromic case management should be encouraged.
- Costly laboratory procedures should be avoided.

- Improve treatment-seeking behaviour and recognition of symptoms.
- Ensure that partner notification does more good than harm.
- Nonoxynol-9 is not recommended for the prevention of vaginal acquisition of STIs by women from men.
- A single oral dose of nitroimidazole can achieve parasitological cure.
- Partners should be treated to prevent reinfection and transmission to others.
- Health education messages that promote safer sex will help prevent trichomoniasis.

Research agenda

- Range of alternative STI control strategies for various settings and measurable endpoints.
- The value of combining provider training and patient education for partner notification of STI.
- Impact of potential harmful effects of partner notification of STI.
- Strategies of effective treatment of partner to prevent reinfections.

ABORTION

Unwanted pregnancy poses great threat to woman's health. Despite under-reporting, it is estimated that 36–53 million unwanted pregnancies are terminated by induced abortion every year throughout the world.¹³ Unsafe termination of pregnancy can lead to death or severe morbidities like infection, haemorrhage, uterine injury and toxic effects of interventions. Although termination of pregnancy is quite safe in developed countries, where adequate services are available and abortion is legal, the situation is significantly different when the abortion is performed by unskilled persons, in suboptimal conditions and without a legal back-up. Deaths related to unsafe abortions represent about one-quarter to one-third of the estimated 500,000 maternal deaths that occur each year throughout the world, the vast majority in developing countries.¹⁴ Several international meetings have recommended that governments recognize and deal with the impact of unsafe abortion as a major public health concern as 20–25% of all maternal deaths in Asia, 30–50% of all maternal deaths in Africa and Latin America and 25–30% of all maternal deaths in Russia are believed to be the result of induced abortion.^{15,16}

Surgical methods for first-trimester termination of pregnancy

Termination of pregnancy can be done by dilatation and curettage (D&C), dilatation and electric vacuum aspiration or manual vacuum aspiration (MVA). Surgical abortion at 7–9 weeks of gestation is preferable because it is associated with statistically significantly fewer complications than when performed at 9–14 weeks of amenorrhea or in the second trimester.

A Cochrane review¹⁷ of three trials compared the safety and efficacy of D&C with MVA in the termination of first-trimester pregnancy. This review also evaluated the

use of flexible versus rigid vacuum aspiration cannula. The results of the review need to be interpreted in the context of its several limitations, as the outcomes were based on small sample sizes and the quality of studies is not high. Furthermore, the trials were conducted some 20–30 years ago. There were no reports of maternal deaths and no cases of uterine perforation were recorded. There were no statistically significant differences in excessive blood loss, blood transfusion, febrile morbidity, incomplete or repeat uterine evacuation procedure, rehospitalization, postoperative abdominal pain or therapeutic antibiotic use. Duration of operation was statistically significantly shorter with vacuum aspiration than with D&C in both subgroups [<9 weeks weighted mean difference (WMD): -1.84 min, 95% CI -2.542 to -1.138 ; ≥ 9 weeks WMD -0.600 min, 95% CI -1.166 to -0.034]. In the comparison of flexible versus rigid vacuum aspiration cannulae, there were no statistically significant differences with regard to cervical injuries, febrile morbidity, blood transfusion, therapeutic antibiotic use, or incomplete or repeat uterine evacuation procedure. It should be borne in mind that the clinical trials comparing the surgical methods were small and lacked the power to identify differences between the groups for rare outcomes. The finding that D&C was not clearly superior to MVA in tertiary care settings under trial conditions suggests that the use of MVA could be encouraged at the primary and secondary levels in the healthcare systems in low-income countries.

Medical methods for first-trimester abortion

Various medical methods have been used for first-trimester abortion. Among these, the most widely researched ones are prostaglandins (PGs) alone, mifepristone alone, methotrexate alone, mifepristone with prostaglandins and methotrexate with prostaglandins.

A Cochrane review¹⁸ of 39 trials evaluated many medical interventions either alone or in combination used at various gestational ages via different routes. There is ample evidence that medical methods for first-trimester abortion are both safe and effective. Regimens that combine mifepristone or methotrexate with a prostaglandin such as misoprostol are more efficacious than a prostaglandin alone. In the case of regimens that combine mifepristone with a prostaglandin, the dose of mifepristone can be reduced from 600 mg to 200 mg without affecting efficacy. In combination with mifepristone, vaginally administered misoprostol in an 800- μ g dose appears to be more efficacious than 0.5 mg of a prostaglandin E₁ analogue. When mifepristone is used with misoprostol to terminate pregnancies of up to 63 days' gestation, misoprostol administered vaginally is more efficacious than when administered orally. Oral administration of misoprostol was found to be associated more frequently with nausea and diarrhoea than was vaginal administration.

A WHO multinational study¹⁹ investigated mifepristone combined with three different misoprostol regimens: (1) mifepristone plus 800 μ g misoprostol vaginally on day 3 only; (2) mifepristone plus 800 μ g misoprostol vaginally on day 3 followed by 400 μ g misoprostol orally twice daily for 7 days; (3) mifepristone plus 800 μ g misoprostol orally on day 3 followed by 400 μ g misoprostol orally twice daily for 7 days. The study found that in women with gestation periods ≥ 57 days, the risk of failure was higher in group (3) than in group (2) (RR 2.8; 95% CI 1.3–5.8); there were no significant differences in efficacy in women with gestation periods < 57 days.

Another RCT²⁰ of mifepristone followed 48 h later by either sublingual or vaginal misoprostol (200 mg mifepristone with 800 μ g misoprostol administered 48 h after

the mifepristone) included women with gestation periods up to 63 days. No significant difference in efficacy between the two regimens (sublingual 98.2%; vaginal 93.8%) was found, although women in the sublingual group experienced significantly more nausea, vomiting, diarrhoea, fever and chills.

Medical methods for first-trimester abortion have been demonstrated to be both safe and effective. Regimens that combine mifepristone or methotrexate with a prostaglandin such as misoprostol are more efficacious than a prostaglandin alone.

Practice points

- Use of manual vacuum aspiration could be encouraged where surgical method of abortion is chosen.
- Combination of mifepristone or methotrexate with misoprostol is more efficacious.

Research agenda

- Provider's and women's satisfaction with the instrument and procedure.
- Provider's and women's satisfaction with the drug and route.
- Optimal dose of misoprostol administered via the sublingual or oral routes.

SUBFERTILITY

Primary subfertility rates vary widely between countries, ranging from 10% in Africa to about 6% in North America and Europe.²¹ It is expected that approximately 25% of health young couples will conceive in a single cycle. The per-cycle fecundity falls to 10% after seven cycles and to 3% in the twelfth cycle. One-third of subfertility cases are unexplained; the rest are caused by ovulatory failure (27%), low sperm count or quality (19%), tubal damage (14%), endometriosis (5%) and other causes (5%).²²

Medical therapies and adjuncts for subfertility associated with anovulation

In a Cochrane review of 12 RCTs²³, clomiphene was shown to be effective in increasing pregnancy rate compared with placebo [fixed odds ratio (OR) 5.8; 95% CI 1.6–21.5]. No evidence of a difference in effect was found between clomiphene and tamoxifen (fixed OR 1.0; 95% CI 0.5–2.1) or between clomiphene and clomiphene plus bromocriptine (fixed OR 1.0; 95% CI 0.3–3.0) rates. However, clomiphene plus dexamethasone treatment resulted in a significant improvement in the pregnancy rate (fixed OR 11.3; 95% CI 5.3–24.0) compared with clomiphene alone. From these findings it can be inferred that, currently, clomiphene citrate is effective as the first-line treatment for subfertility and that the use of dexamethasone as an adjunct to clomiphene therapy appears promising.

Accuracy of hysterosalpingography in the diagnosis of tubal pathology

A Centre for Reviews and Dissemination (CRD) review appraised a meta-analysis²⁴ that assessed the value of hysterosalpingography (HSG) in diagnosing tubal patency and peritubal adhesions compared to laparoscopy with chromopertubation as a gold standard. Of the 20 studies included in the meta-analysis, 19 were included in the analysis of tubal patency and 13 in the analysis of peritubal adhesions. Due to heterogeneity, these studies could not be combined. Three trials that made independent judgements of HSG and laparoscopy were combined in a subgroup analysis that calculated an overall summary estimate of sensitivity and specificity and involved weighting by study size. Based on these three studies, the point estimate for sensitivity was 0.65 (95% CI 0.50–0.78) and for specificity 0.83 (95% CI 0.77–0.88). It was concluded that HSG is of limited use in the detection of tubal patency because of its low sensitivity, that it might be useful in the detection of tubal obstruction because of its high specificity and that it is not reliable for detection of peritubal adhesions.

Normality of the postcoital test

A review of observational studies²⁵ evaluating the postcoital test (PCT) for predicting conception failure was critically appraised. The results obtained for sensitivity and specificity varied widely and this fact, combined with the poor predictive value of test results, meant that the discriminating ability of the PCT is poor. It was suggested that to avoid over-treatment of the poorly defined condition known as 'cervical factor infertility', the cut-off point of normality should be set at at least one motile spermatozoon per high power field (HPF). The sensitivity of the PCT ranged from 0.10 to 0.90 in different studies; its specificity ranged from 0.30 to 0.97. The predictive value of a normal test ranged from 0.37 to 0.92, whereas the predictive value of an abnormal test ranged from 0.58 to 0.85. There is a marked increase in sensitivity with increasing strictness of diagnostic criteria. The marked heterogeneity of results and the limitations of studies raise serious doubts about evidence for the value of the PCT.

Timed intercourse versus intrauterine insemination for subfertility in men

A Cochrane review of the results of 13 trials showed that, in natural cycles, intrauterine insemination (IUI) significantly improved the probability of conception compared with timed intercourse (TI) (combined OR with 95% CI 2.43, 1.54–3.83). In cycles with controlled ovarian hyperstimulation (COH), IUI significantly improved the probability of conception also compared with TI (combined OR with 95% CI 2.14, 1.30–3.51). It was inferred that IUI offers couples with male subfertility benefit over timed intercourse, both in natural cycles and in cycles with COH. In the case of a severe semen defect, IUI in natural cycles should be the treatment of first choice.

Practice points

- The discriminating ability of the postcoital test, which measures numbers of motile spermatozoa per high-power ($\times 400$) field, is poor.
- Hysterosalpingography is of limited use in detecting tubal patency.

Research agenda

- Establish usefulness of sonographic saline test for tubal patency in developing countries.
- Develop effective and efficient low cost protocols for assisted reproductive techniques (ART) [in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI)].

CANCER

Cervical cancer is the second most common cancer in women worldwide, but the most common in developing countries. Annual global estimates in the year 2000 were for 470,600 new cases and 233,400 deaths from cervical cancer annually.²⁶ It has been estimated that the prevalence of human papillomavirus (HPV) in cervical cancer is 99.7%²⁷, and that two subtypes of the virus — HPV16 and HPV18 — are present in more than 80% of invasive cervical cancers. The level of protection women gain as a population by regular screening, and the number of tests they will need in a lifetime, have been calculated by WHO.²⁸ Annual screening smears provide a 93.5% reduction, a smear every 2 years provides a 92.5% reduction, 3-yearly smears provide a 90.8% reduction, 5-yearly smears provide a 83.6% reduction and a smear test every 10 years has a benefit with a 64.1% reduction in incidence of cervical cancer.

Interventions targeted at women to encourage the uptake of cervical screening

A Cochrane review²⁹ of 35 clinical trials, including 27 RCTs, found that invitations and educational interventions appeared to be the most effective methods of increasing the absolute uptake of cervical screening. As there was heterogeneity between the studies, this resulted in limiting the statistical pooling of data. In addition, the number and quality of included studies further limited the evidence regarding the effectiveness of other interventions, such as economic incentives, procedural interventions, counselling and risk-factor assessment. It was also noted that no studies examined the effectiveness of interventions at increasing the informed uptake of cervical screening.

Nineteen studies in this Cochrane review evaluated the effectiveness of invitation letters. The studies were subdivided according to the invitation type (i.e. GP letter, letter from another authority source, face-to-face invitation, open invitation and invitation with fixed appointment). Comparison groups included different types of invitation or a control group (usually consisting of usual care or no intervention). All but one of the studies favoured invitation letters. Two studies looked at invitations from different authority sources. Both reported a significant increase in uptake for GP invitation letters versus invitation letters from health clinics (RR = 1.84; 95% CI 1.21–2.81) and invitation letters from screening programme co-ordinators (RR = 1.13; 95% CI 1.05–1.21).

Six studies in the same Cochrane review evaluated the effectiveness of different educational interventions. Although five of the six found these interventions to be beneficial compared with controls, the benefit was neither statistically nor clinically significant.

At the present time, cervical cytology is considered to be the only way to reduce the incidence of cervical cancer. However, it is effective only in developed countries because a reliable health infrastructure is a prerequisite for this approach. Central to the success of any screening programme is its ability to identify, reach and screen the defined target population.

Cytological screening in middle-income countries

It is generally agreed that high-quality cytology has specificity of the order of 95–99%. Recent meta-analyses of studies^{30–32}, conducted in different settings, have estimated cytology sensitivity to be of the order of 50% or even less. Several of these studies evaluated cytology cross-sectionally as a diagnostic test rather than a screening test. Few studies assessed the sensitivity of cytology longitudinally, using cancer as the end-point. All of these studies were conducted several years ago in developing countries with high-quality laboratories, they produced estimates of sensitivity ranging from 60 to 90%.^{33,34}

The major advantages of cytology screening are the considerable experience accrued worldwide in its use and the fact that it is so far the only established screening test for the precursors of cervical cancer that has been shown to reduce the incidence of mortality of the disease. But cytology has its limitations: it is incompatible with some women's beliefs and it is impossible to abolish the disease with screening.³⁵

Visual inspection with acetic acid application: an alternative in low-income countries?

Non-magnified visual inspection of uterine cervix with 3–5% acetic acid (VIA) appears to fulfil the basic criteria of a satisfactory alternative screening test for cervical cancer. The current consensus is that well-defined, demarcated, densely opaque acetowhite lesions located in the transformation zone (TZ) close to the squamocolumnar junction define a positive VIA test. A negative test would include one or more of: no acetowhite lesions; faint, ill-defined, translucent acetowhite lesions; endocervical polyps; nabothian cysts; dot-like acetowhite lesions and a prominent squamocolumnar junction.

A recent WHO consultancy report²⁶ concluded that, in cross-sectional study settings, the sensitivity of VIA for detecting high-grade precancerous lesions ranged from 66 to 96% and specificity ranged from 64 to 98%; whereas positive predictive value ranges from 10 to 20% and negative predictive value ranges from 92 to 97%. The major strengths of VIA are its simplicity and low cost, real-time availability of results and easy training of care providers.

HPV tests in cervical cancer screening programmes

Existing evidence from epidemiological and molecular studies strongly suggest that most of the cases of cervical cancer occurring worldwide are caused by some type of human papillomavirus (HPV). Currently available HPV testing systems can detect the presence of viral markers in close to 100% of invasive cervical cancer specimens, 75–90% of precursor lesions [low-grade squamous intraepithelial lesion (LSIL)/cervical intraepithelial neoplasia (CIN I), CIN2/3, high-grade squamous intraepithelial lesion (HSIL)] and in 50% of borderline cytology lesions [atypical squamous cells of undetermined significance (ASCUS)].²⁷ Current best evidence suggest that HPV testing is an

acceptable, safe and effective procedure for detecting cervical cancer precursors at a sufficiently early stage to permit intervention.

Collection devices for obtaining cervical cytology samples

A Cochrane review³⁶ of 36 trials and six observational comparative studies found the Ayre spatula to be less effective than the extended-tip spatula for collecting endocervical cells in eight trials (OR 2.25; 95% CI 2.06–2.44). It was also shown that the use of an extended-tip spatula with the cytobrush was more effective than a spatula alone at collecting endocervical cells (OR 3.33; 95% CI 3.05–3.63). Health workers will need training in the form of a 1-day workshop to implement this intervention. The extended-tip spatula plus the cytobrush was also more effective for adequate smear rates (OR 1.51; 95% CI 1.19–1.92). Compared with the traditional spatula, extended-tip spatulas were also superior for the detection of dyskaryosis in seven trials (OR 1.21; 95% CI 1.10–1.33). Two trials and three observational studies inferred that smears containing endocervical cells were more likely to detect dyskaryosis, particularly in severe disease. With increasing severity of the disease, the proportion of smears with endocervical cells present also increased.

Surgery for cervical intraepithelial neoplasia

Cervical intraepithelial neoplasia (CIN) can be treated by local ablative therapy or by excisional methods. Before colposcopy was introduced, all lesions were treated by knife excisional cone biopsy or by ablative radical point diathermy. These latter techniques are usually performed under general anaesthesia and are no longer the treatment of choice as other, more conservative, local ablative and excisional therapies can now be performed in an outpatient setting. The effectiveness and morbidity of the various forms of treatment have been generally evaluated by uncontrolled observational studies.

In a Cochrane review³⁷ of 28 RCTs, seven surgical techniques were tested in various comparisons. No significant difference in disease eradication was shown, other than between laser ablation and loop excision. This was based on one trial in which the quality of randomization was doubtful. Large loop excision of the transformation zone appeared to provide the most reliable specimens for histology with the least morbidity. Morbidity was lower than with laser conization, although the five trials did not provide data for every outcome. There were not enough data to assess the effect on morbidity compared with laser ablation. In conclusion, no single technique emerged as superior to others.

Practice points

- Invitation letters to promote uptake of cervical screening in primary healthcare clinics in developing countries are not feasible.
- Educational interventions, such as distribution of brochures, audiovisual materials or interpersonal contact, might not be feasible in developing countries.
- Cervical screening has been effective in reducing the incidence of and mortality from cervical cancer in developing countries.

- The sensitivity of non-magnified visual inspection of uterine cervix with 3–5% acetic acid (VIA) to detect cervical intraepithelial neoplasia is the same as that of cervical cytology, but the specificity is lower.
- The Aylesbury device should replace the Ayre spatula.
- Cervical cancer screening should be performed at the primary healthcare level.
- Non-magnified visual inspection of uterine cervix with 3–5% acetic acid (VIA) or human papillomavirus (HPV) DNA screening might offer attractive alternatives to cytology-based screening programmes.

Research agenda

- Identification of cost-effective screening tool and intervention to increase up-take of screening in developing countries.
- Longitudinal evaluation of smear testing in developing countries.
- Feasibility of introducing VIA-based cervical screening programmes on a population-wide basis in developing countries.
- Evaluation of one-stop, VIA and cryocautery treatment strategies.
- Data on cost–benefit balance of screening programs that adopt HPV as a stand-alone screening test.

GENITAL FISTULAE

There is a paucity of research articles with high-level evidence pertaining to the management and treatment of genital fistulae. The prevalence of fistulae has fallen remarkably in the industrialized nations of Asia and Latin America but has remained high in Africa and in less developed regions of Asia and Oceania. Furthermore, no standardized classification system exists, a fact that also complicates evaluation of the successful repair of fistulae. No accurate estimate of the fistula burden exists; a rough way to evaluate the extent of the problem could be to look at the proportion of labours that become obstructed and to try to extrapolate the incidence of potential fistulas from this data.

A recent report prepared by United Nations Population Fund (UNFPA)³⁸ reviews the current state of knowledge regarding obstetric fistulae in the developing world and discusses the challenges presented by this condition. The UNFPA found an extreme paucity of reliable scientific data in the existing world literature. If approximately 2% of women in developing countries experience obstructed labour, and there are 33,748,000 estimated births per year in Africa, then there could be as many as 674,060 cases of obstructed labour each year. If 10% of these women develop fistulae, there would be approximately 67,000 new fistula cases each year in Africa alone.

Surgical technique for fistula closure

The traditional approach has been to defer the repair of fistula for 3 months. This is based on the presumption that delay allows full manifestation of the injury and an

adequate time for the insulted tissues to heal spontaneously. Regardless of whether a fistula is repaired early or late, antibiotics and vigorous local care of the injured tissue have been advocated as soon as such patients are seen.³⁹

Contrary to this approach, encouraging results of spontaneous healing of small fistulae (≤ 2 cm) have been demonstrated in 50–60% of cases when prompt prolonged bladder drainage was started within 3 months of the initial injury.⁴⁰ In cases in which a fistula failed to close spontaneously, early surgical closure was done with 92% successful closure and 94% continence rates. These results need to be replicated before this approach can be recommended.

The first operation provides the best chance of successful fistula closure. In a large series of 2484 fistula patients, successful fistula closure was reported in 82.8% of patients at first attempt, whereas only 65% of those patients who required two or more operations experienced a successful closure.⁴¹ Traditional fistula repair techniques are still used and there is a big gap in quality evidence. Only one prospective RCT⁴² from a developing country and one comparative study⁴³ on surgical technique is available. Currently, wide mobilization of surrounding tissues and absolute watertight closure of fistula in multiple layers is recommended, along with prolonged drainage of bladder postoperatively for 14 days or more.

Practice points

- Small fistulae can heal spontaneously if the bladder is drained with a catheter.
- The first operation stands the best chance of successful fistula closure.
- Fistula repair should be done in layers and should be tension free, with free drainage of bladder postoperatively.

Research agenda

- Optimal timing of repair for genital fistulae.
- Optimum duration of bladder drainage following fistula repair.
- Need for closure of fistula in multiple layers.
- Role of flaps and grafts in fistula closure surgery.
- Treatment of urinary incontinence after successful closure of fistula.

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