Review

A review of female genital schistosomiasis

Eyrun F. Kjetland[1,2], Peter D.C. Leutscher[3] and Patricia D. Ndhlovu[4]

[1] Centre for Imported and Tropical Diseases, Department of Infectious Diseases, Ullevaal University Hospital, Oslo, Norway
[2] School of Biological and Conservation Sciences, University of KwaZulu-Natal, Durban, South Africa
[3] Department of Infectious Diseases, Aarhus University Hospital/Skejby, DK-8200 Aarhus, Denmark
[4] Imperial College London, Claybrook Centre, London, UK

In a review of the studies on genital schistosomiasis, the cervix, the Fallopian tubes, and the vagina are the most common gynaecological sites to harbour *Schistosoma haematobium*. Lesions are caused by host responses to dead or viable schistosomiasis eggs and may render women with genital schistosomiasis susceptible to HIV. The typical genital changes, such as sandy patches and pathological blood vessels may make women susceptible to super-infection, cause contact bleeding, decreased fertility, abortions, discharge and bleeding. Further research is needed to find simple, low-tech diagnostic methods, treatment for chronic lesions, and to explore the preventive effects of mass drug administration on symptoms, sandy patches, HPV and the HIV epidemic.

Domestic necessity and recreation

In recreational, domestic and professional freshwater contact, people in endemic areas may acquire schistosomiasis (Bilharzia). There are several types of schistosomiasis which are associated with infection by *Schistosoma haematobium*, *Schistosoma mansoni* and the other types of schistosomes, and these have similar transmission cycles but different predilection sites and egg morphologies (Figure 1, Box 1). *S. haematobium* was originally termed urinary schistosomiasis, reflecting key symptoms such as bloody urine, pain on urination, and an increased risk of bladder cancer. However, *S. haematobium* also commonly causes severe egg-induced pathology and symptoms in the genitals of both women and men. The World Health Organization (WHO) has therefore recommended that *S. haematobium*, urinary schistosomiasis, should henceforth be referred to as 'urogenital schistosomiasis' (www.who.int/neglected_diseases/integrated_media_urogenital_schistosomiasis/en/). Recent studies have substantiated the biologic plausibility that female genital schistosomiasis may make women and men more susceptible to HIV [1–4]. Furthermore, reports on the severe effects of urogenital schistosomiasis on human cognition, economy and symptoms have emerged [5]. These findings coincide with the expiry of the drug patent for praziquantel; several companies have now commenced production of the drug and mass drug administration (MDA) has been successfully implemented in some African countries for several years [6]. The prospect of MDA for the prevention of HIV, sexually transmitted diseases and other reproductive tract morbidity has renewed interest in research and individual therapy for patients with female genital schistosomiasis.

Distribution of schistosome eggs in the genital tract

Many case reports indicate that *S. mansoni* and *S. japonicum* may affect the genital tract [7]. However, only two community-based studies have explored this via biopsy of the uterine cervix [8,9]. Both studies were carried out in low-endemic areas, and further investigations are required. Blood vessel anastomoses between the pelvic organs are probably responsible for 'spill-over' of eggs into the genital tract, and the cervix has been suggested to be the predilection site for trapped eggs (Figure 2). In clinical practice, the cervix, the Fallopian tubes, and the vagina are the most common gynecological sites found to contain *Schistosoma* eggs (Figure 3). However, eggs appear to be almost equally distributed between the different pathophysiologically important pelvic areas. Figure 3 shows that, in autopsy specimens of the genital tract, eggs are relatively common both in the ovaries and in the uterus, and are therefore probably under-diagnosed in clinical practice [7,10–21]. Community-based studies have shown prevalences from 33% to

Glossary

Ascites: intraperitoneal fluid induced by severe liver disease, ovarian disease, or other significant medical problem.
Colposcope: equipment used in gynecology for magnification and source of white and green light.
FGS: female genital schistosomiasis.
Katayama fever: febrile illness caused by schistosomiasis some weeks after infection. Patients may also have fatigue, diarrhea, abdominal pain, cough, high eosinophil granulocyte cell count, enlargement of both the liver and the spleen.
Myometrium: the muscular part of the uterus.
Rubbery tubercles: firm smooth beige to yellow lesions with pustuloid but firm 'pinhead' protrusions 1–3 mm in diameter. Using colposcope micro-focusing, the blood vessels stand out like small spirals under the surface. The finding was described in the bladder already in 1946 [17,80]. To date these have only been seen intravaginally in Madagascar.
STDs: sexually transmitted diseases.
Type 2 error: studies with too few studied events may fail to detect a significant difference between groups.
Ureter: tube that conducts urine from the kidney to the urinary bladder. The ureter is normally 25–30 cm long and 3–4 mm in diameter. Ureters may become blocked by *S. haematobium*, and may therefore cause kidney failure.

Corresponding author: Kjetland, E.F. (e.f.kjetland@medisin.uio.no)

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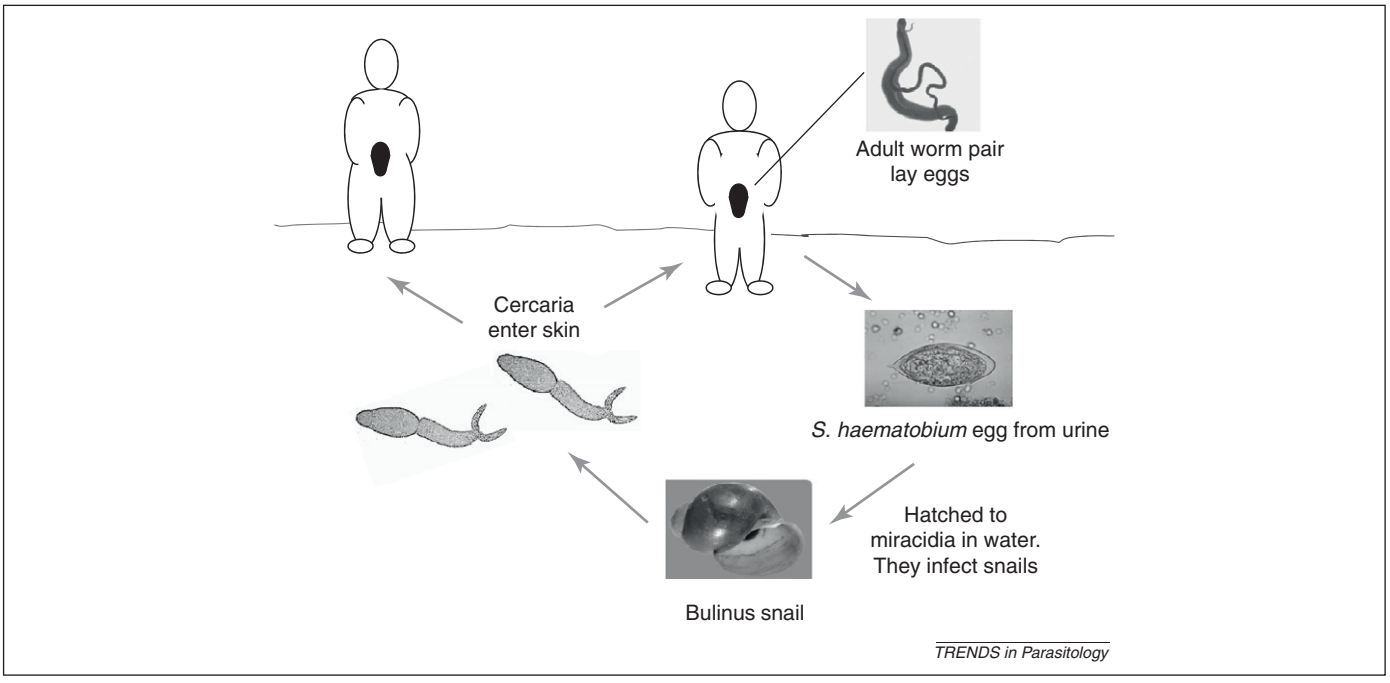

Figure 1. Urogenital schistosomiasis transmission cycle, infection, and reinfection. The cycles for other schistosome types differ with respect to human organ predilection sites, egg shape and snail types.

75% of female genital schistosomiasis in *S. haematobium* endemic areas [22,23].

Histology of genital schistosomiasis

The tissue around both viable and dead *S. haematobium* eggs has increased vascularity and a high density of macrophages, lymphocytes, foreign body giant cells, eosinophils, neutrophils, plasma cells, Langerhans cells, fibroblasts, and multinucleate histiocytes [24,25]. Even calcified eggs may induce the influx of immune cells and blood vessel proliferation, local bleeding and edema [26]. The exact natural history of the local immune reactions to *S. haematobium* eggs in different phases is not known, but should be explored because it will have implications on treatment schedules and in choosing the best target populations for costly interventions (Box 2).

The mucosal remains of childhood infection

Female genital schistosomiasis (FGS) has been defined as having sandy patches and/or microscopically proven

Box 1. The freshwater transmission cycle

Schistosomiasis (Bilharzia) is a parasitic infection caused by the *Schistosoma* blood fluke. In endemic regions the larvae (cercaria) released from the *Bulinus* snail (the intermediate host) penetrate the skin upon water contact (Figure 1). The parasite is then transported through the lymphatic system and the lungs to the liver, where the final maturation into dimorphic worms takes place (male and female adult worms 1.2 to 2 cm in size). Further migration of the adult worm pair to the different organs, mesenteric venous plexus, is specific for each *Schistosoma* subspecies: *Schistosoma haematobium* affects the pelvic organs, whereas for example *S. mansoni* affects the intestines. The schistosome eggs, following penetration of the mucosal membrane, are excreted in urine, feces or vaginal discharge into freshwater where miracidia reach the *Bulinus* snail to complete the life cycle of the parasite.

Worms may cause venous obstruction where they reside. However, the disease is predominantly caused by the daily trapping of numerous eggs released by the female worms after mating, resulting in localized inflammatory host responses that may lead to extensive tissue damage in the urogenital or intestinal tracts, in the liver, and at other so-called ectopic sites [20].

Box 2. Outstanding questions

Gynecological investigations of women who may have lived with their problems for decades require cultural insight and communication skills. Furthermore, rural research is demanding. In the opinion of the authors, future studies on genital schistosomiasis are not warranted unless they test extensively for differential diagnoses.

(i) Indirect, non-invasive and syndromic diagnostic methods should be explored.
(ii) A multi-center study should be carried out using standardized diagnostic methods controlling for sexually transmitted diseases and confounders.
(iii) What is the ideal timing of treatment for prevention of genital lesions and HIV?
(iv) How many treatments must be done?
(v) How do we treat adults and young women with chronic, calcified lesions and severe inflammation?
(vi) What are the clinical and histological courses of genital *S. haematobium* infection? What does an early lesion look like? And a late?
(vii) What is the impact of *S. haematobium* and *S. mansoni* upon fertility and cancer?
(viii) Do the different lesions pose different risks of acquiring HIV or other super-infections? What is it about the lesions, the reactions around the Bilharzia eggs, immunoactive cells and substances, that may make women susceptible to HIV? Can these reactions be prevented?
(ix) Do HIV-positive women with FGS have increased vaginal HIV load? In other words, are men who have intercourse with infected women at higher risk of HIV infection?
(x) An atlas of genital schistosomiasis should be made freely available online.

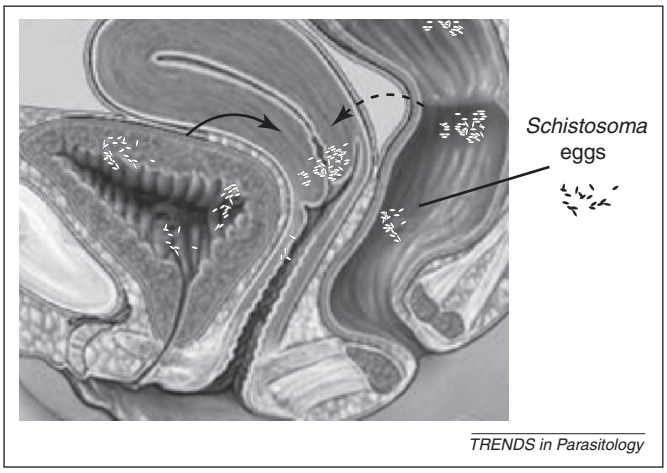

Figure 2. Urinary, genital and intestinal tracts of a schistosomiasis-infected woman. Schistosomiasis eggs are transmitted to the genital tract through blood vessel anastomoses in the pelvic organs. It is possible to have genital *S. haematobium* without involvement of the urinary tract, probably due to individual blood vessel patterns, blood flow and worm localization [27,81]. *S. mansoni* (intestinal schistosomiasis) is sometimes also found in the genital tract.

S. haematobium eggs in genital tissue (Figure 4). The largest clinical studies in adult women living in endemic areas have found that the prevalences of women with sandy patches, contact bleeding, or eggs in genital tissue seem to be fairly constant in adulthood [27,28].

Mucosal and stromal lesion severities do not follow the same characteristic decline with age as urinary egg excretion [27,28]. It is well known that urinary *S. haematobium* egg excretion rises steadily to a peak in the early teenage years, falling to relatively low levels in adulthood [29,30]. The trend is almost independent of duration of exposure, fuelling the theory that the onset of puberty might offer some protection against the worm [31]. Urinary egg excretion is significantly correlated with urinary tract morbidity in the young, but there is no such correlation in adults [32]. Although egg count in urine (currently interpreted as intensity of infection) is used as an overall proxy for *S. haematobium* worm burden, the genital involvement seems to be associated with the presence of eggs in urine but not with the intensity of infection [14,27]. Lesions have been found to be more persistent in adults, possibly because many lesions now constitute calcified dead eggs and chronic immunological reactions [24,26,32,33].

Although in children urinary tract lesions reportedly resolve within 2–6 months of treatment, some reports in adults have found that lesions remain even though urinary egg excretion ceases or decreases [32,33]. Thus the effects of schistosomiasis may be revealed long after puberty, and the intensity of egg excretion in the urine cannot be used to assess the degree of genital morbidity [5,32].

Genital changes are breaches in the mucosal surface, open wounds, perhaps susceptible to superinfection by bacteria and viruses such as human papillomavirus (HPV) or other sexually transmitted diseases (STDs; see Glossary) [17,34,35]. The coexistence of *S. haematobium* eggs with other diseases such as STDs may make it difficult to single-out the causes of lesions or discharges, and only one community-based study has controlled extensively for confounders [27]. *S. haematobium* in the genitals is strongly associated with clinically observed sandy patches, pathological vessel morphology and contact bleeding (Figure 4; Table 1) [27,28,36]. Furthermore, Table 1 shows that *S. haematobium* eggs were found in conjunction with a range of lesions morphologically similar to the different reproductive tract diseases including malignant-looking lesions [23–25,27,28,34,36–48].

Symptoms, suffering and chronicity in adult women

All community-based studies on FGS to date have been performed in pre-menopausal adults aged 15–49 years

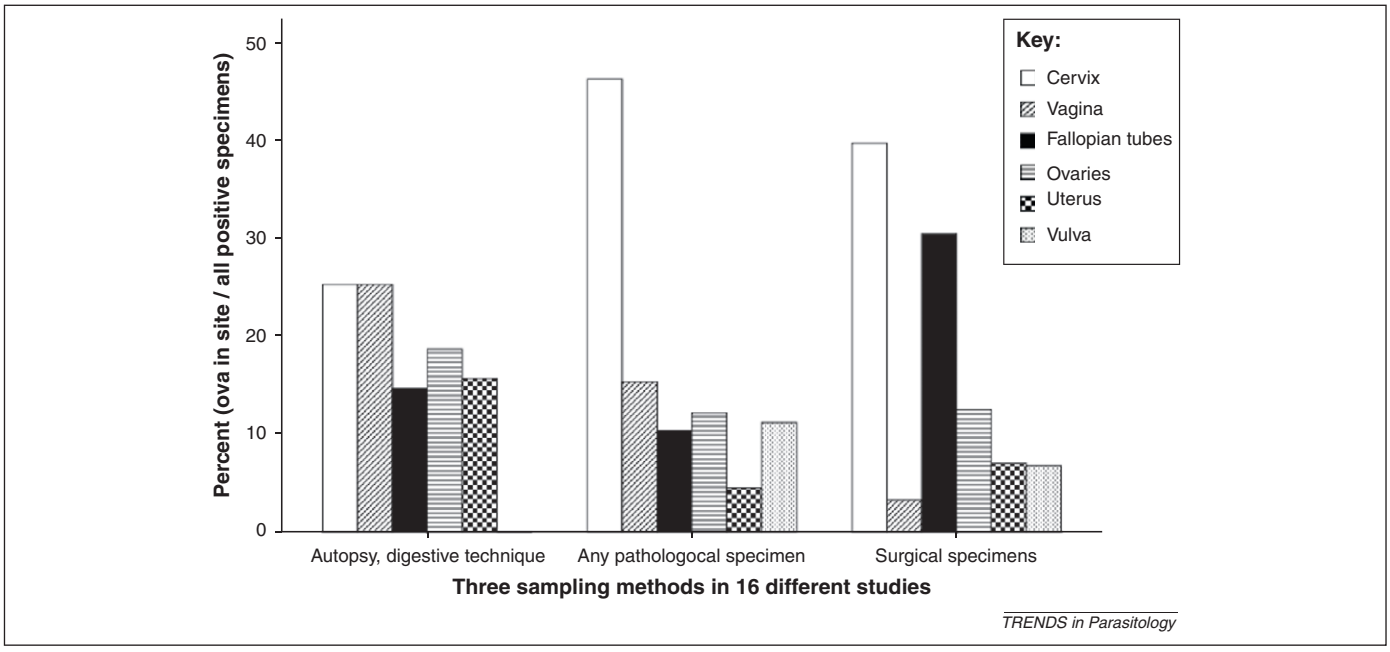

Figure 3. Gynecologic predilection sites for schistosomiasis. Schistosomiasis-positive gynecological specimens: systematic investigations of organs at autopsy, presented together with results from pathological, surgical or cytological specimens from schistosomiasis endemic areas are shown [7,10–18,20,21,23]. Data for the vulva have not been presented in most of the autopsy studies.

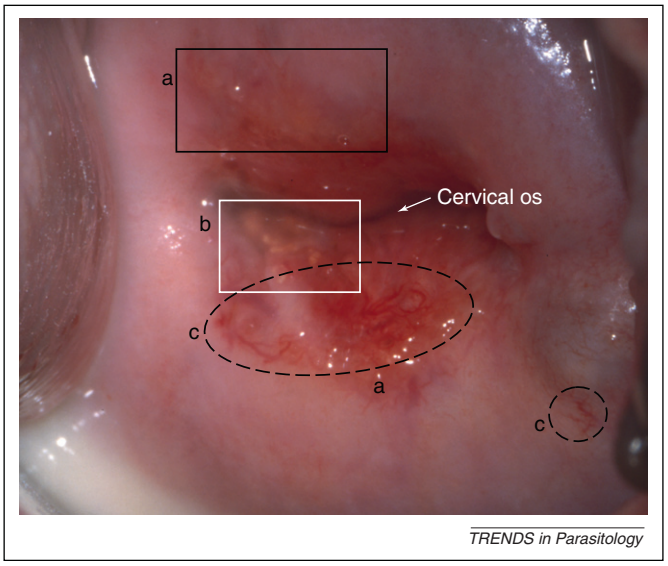

Figure 4. Sandy patches and abnormal blood vessels typical of female genital schistosomiasis. Sandy patches are visible by colposcopy and sometimes by the naked eye. The cervical os (mouth) is the opening of the cervix into the uterine cavity. Sandy patches and abnormal blood vessels may be situated both within and outside that transformation zone, they are aceto-negative and they are not enhanced by green light, common diagnostic techniques used by colposcopists to explore for (pre-)cancerous lesions of the cervix. **(a)** Homogenous yellow sandy patches (HYSP): sandy areas with no distinct grains using 15× magnification. **(b)** Grainy sandy patches (GSP) constitute oblong yellow to white grains, approximately 0.05 × 0.2 mm in size. They are deeply or superficially situated in the mucosa. With a metal spatula the movable distinct minuscule crust-like superficial protrusions can be felt and sometimes even heard [27]. **(c)** Abnormal blood vessels or 'neo-vascularization' are pathological convoluted (corkscrew), reticular, circular and/or branched and uneven-calibered blood vessels that are visible (under 15× magnification) on the mucosal surface.

[27,28,36,38,49]. Women with genital sandy patches have significantly more genital itch and perceive their discharge as abnormal [34]. Genital schistosomiasis is associated with stress incontinence and increased frequency of urination. There are case reports of severe acute disease such as ascites with ovarian schistosomiasis, ectopic pregnancy, and heavy egg infestation of the uterus in pregnancy [45,48].

Several case reports indicate decreased fertility and abortions in women with FGS, but this has only been explored in two community-based studies and needs further investigation [36,43]. A direct effect on hormones or ovarian function is controversial [34,36]. It is likely that the women with fatal complications, such as extra-uterine pregnancies, may have died or recovered receiving neither diagnosis nor adequate care [43]. The largest study to date, in Zimbabwe, did not find any association between abortion or menstrual irregularities with *S. haematobium*. In Madagascar, however, an association was found with abortion (Table 1). There are reports of soft cervices by bimanual palpation as usually found in pregnancy, although the clinicians in the community-based studies have not discussed this [17].

Manifestations of genital schistosomiasis in the young

Because intravaginal inspection is usually not performed before the onset of sexual activity, the normal and pathologic characteristics of the prepubertal tissue have not been studied. Furthermore, adolescents are often too shy to come for gynecological investigations during the first few years after sexual debut. Case reports on girls below the age of 15 are therefore most commonly from the vulval regions [10,13,17,50]. A vaginal polyp was found in a 3 year old [18], a 4 × 4 cm 'raised, reddened area' in the upper third of the vagina was found in a 16 year old [51], and sandy patches have been found in the cervix of a 15 year old [36]. Furthermore, there are reports of stunting and late pubertal development, suggesting hormonal disturbances, confirmed in animal models with decreased fertility and arrested development of corpora lutea [52]. One study suggests that mucosal changes are present in children even before sexual debut (I.E.A. Hegertun, unpublished).

Traveling women and genital schistosomiasis

Travelers, defined as coming from non-endemic areas, are often exposed for a limited time. Unfortunately schistosomiasis, and in particular genital schistosomiasis, has been neglected in travelers despite increasingly common travel activities such as rafting and other forms of so-termed ecotourism [53,54]. Eighteen percent of asymptomatic travelers to Africa, exposed to infested freshwater and subsequently screened at the Hospital for Tropical Diseases in London over the period 1993–1997, were found to have schistosomiasis [55]. Katayama fever, fatigue, and pain on urination were the commonest presentations in symptomatic travelers. There are, however, a few case reports where clinically important genital schistosomiasis has been found, sometimes years after relatively short exposure [56,57]. The symptoms are similar to those of women with chronic manifestations (Table 1). The authors suggest it is likely that a long duration of exposure increases the risk of severe disease. However, the unpredictable micro-localization of the egg deposition is likely to be a key determinant of whether the eggs affect health or fertility.

Genital schistosomiasis and the susceptibility to HIV

Public health interventions against the HIV epidemic have been implemented based on the evidence that sexually transmitted genital ulcers, Chlamydia, and gonorrhea may increase the susceptibility of women to HIV infection [58]. Currently, the syndromic management of STDs, based on concepts of etiology, has been a central strategy for HIV prevention in developing countries. In a given area, the impact of different STDs upon HIV transmission depends upon the relative frequencies of the different STDs.

The cervix is the suggested site of most HIV acquisition, and the relative frequencies of the mucosal immune cells are crucial determinants of HIV transmission [59]. Calcified *S. haematobium* eggs in genital tissue have been found to increase the density of HIV-receptive CD4 cells [26]. Compared to healthy tissue, ulcers caused by Herpes simplex virus, and primary or secondary syphilis, had significantly higher numbers of neutrophils and macrophages (CD14-positive cells) expressing HIV coreceptors on the cell surfaces, crucial for primary HIV transmission [60]. Peripheral blood mononuclear cells in *S. mansoni* infected individuals also express higher levels of HIV coreceptors [3]. This may indicate that the lesion(s) around the eggs in genital mucosa provide an entry point for the HIV virus [26].

Table 1. Findings in community-based studies of genital schistosomiasis in women of reproductive age[a]

	Zimbabwe[b] [27,34,43]	Madagascar II [38]	Tanzania [28]	Madagascar I [36]	Malawi [37]	Refs.[c]
Number of participants	*n* = 527	*n* = 254	*n* = 434	*n* = 116	*n* = 52	
Symptoms						
Vaginal discharge[d]	S	NS	NS	S	-	[23]
Genital itch	S	-	-	NS	-	[42]
Pain (abdominal / back)	NS	-	NS	-	NS	[39,41]
Pelvic discomfort	-	S	-	S	-	
Pain during sex[e]	NS	-	-	NS[f]	NS	
Bleeding after vaginal sex	NS	-	S	NS	NS	[16]
Spot bleeding	*P* = 0.063	-	NS	-	NS	
Irregular menstruation	NS	-	S	S	NS	[16]
Heavy bleeding	NS	-	S	NS	NS	
Menstrual pain	NS	-	-	NS	-	
Stress incontinence	S	-	-	-	-	
Urge incontinence	NS	-	-	-	-	
Reproductive history						
Primary infertility[f,g]	NS	-	-	NS	NS	[43,44]
Secondary infertility[h]	S	-	-	NS	S	[43,45]
Subfecundity[i]	S	-	-	-	-	
Abortion[j]	NS	-	-	S	NS	[45–48]
Gynecological findings						
Sandy patches in mucosa[k]	S	-	S	-	NS[f]	[10,41]
Abnormal blood vessels[l]	S	-	S	-	NS[f]	[24,39,40]
Contact bleeding	S	-	S	-	NS	[10,16,17]
Edema	S	-	S	-	NS	[17,23]
Erosion	S	-	S	-	NS	
Genital ulcer[g]	NS[m]	-	S	NS	NS	
Malignant-looking lesion	S[m]	-	-	-	NS	[10,16,17,23]
Genital tumor	NS[n]	-	-	-	P=0.08	[10,16,17,42]
Petechiae	NS	-	S	-	-	
Pain on bimanual palpation	NS	-	-	-	NS	

[a]Abbreviations: S, significant association with *S. haematobium* infection; NS, non-significant; -, not discussed.

[b]The only study that controlled for confounders: sexually transmitted diseases (syphilis, *Chlamydia trachomatis*, gonorrhea, bacterial vaginosis, *Trichomonas vaginalis*, Chancroid, herpes simplex virus type II, human papillomavirus), cell atypia and/or HIV where applicable.

[c]Case reports and supporting references.

[d]In Madagascar II, when cases had been treated for STDs, there was no association between *S. haematobium* and discharge. Whether the discharge is a sign of FGS itself or a super-infected mucosal area must still be explored (Box 2).

[e]Pain during intercourse was found at very different prevalences in the different studies (7–31%).

[f]The findings are rare and a lack of significant association may represent a type 2 error.

[g]No children, sexually active for a minimum of 4 years, husband has children.

[h]No children the last 4 years, sexually active in the period with a husband who has other children.

[i]Unwanted intermission of 4 years between children while having an active sexual life with same husband.

[j]Extra-uterine pregnancies are a diagnostic challenge in remote rural areas.

[k]There are two types: homogenous yellow and grainy sandy patches (Figure 4).

[l]Figure 4.

[m]Controlled for cell atypia and human papillomavirus by PCR.

[n]Tumors have been analyzed separately or together as warts, papillomatous, polypous, or papules, mucosal or vulval.

STD treatment studies have been marred by the lack of effect on the incidence of HIV infection [58]. These studies have generally been performed in schistosomiasis endemic areas. In the opinion of the authors, these investigations should have taken genital schistosomiasis into consideration [2,4,58]. FGS may be a cofactor for HIV transmission in endemic areas, and the association between schistosomiasis and HIV has been corroborated by several scientific groups [1–4,61,62]. The two diseases, HIV and schistosomiasis, meet in migrating populations, travelers, commuting spouses, roadside villages, and in prostitutes, who are often newcomers to urban areas [63,64].

A dangerous liaison: genital schistosomiasis and HIV

Dually infected women and men, with schistosomiasis and HIV, may pose an additional risk of HIV transmission to their partners [38]. Increased HIV levels have been demonstrated in genital ulcers compared to neighboring normal tissue in the same women; this may also hold true for schistosomal lesions [38,60]. Genital HIV RNA excretion increases in the presence of reproductive tract diseases in women and men alike [65]. Similarly, *S. haematobium* infection has been hypothesized to cause increased virus shedding into the semen of HIV-infected men as a result of egg-induced inflammation in the seminal vesicles and prostate [66].

Diagnosis of genital *S. haematobium*

An FGS consensus meeting held in Copenhagen in October 2010 considered clinical and laboratory results from several African studies (http://www.ivs.life.ku.dk/English/Sections/SPHD/Research/Research Projects/VIBE Project Female Genital Schistosomiasis.aspx). The meeting concluded that, in patients from *S. haematobium* endemic areas, one of three clinical findings, by visual inspection, may serve as an adequate diagnosis for genital schistosomiasis (Figure 4). The lesions are aceto-negative (i) grainy sandy patches, (ii) homogenous yellow sandy patches, or (iii) rubbery tubercles. Before this meeting, the crushed biopsy of genital tissue was deemed to be the gold standard for the parasitological diagnosis of genital *S. haematobium* [67]. However, the eggs are located in highly focal clusters and can be missed during histological analysis of biopsy sections [11,25,36]. Moreover, taking a biopsy for the diagnosis of genital *S. haematobium* remains an HIV transmission risk for the patient and her partner until the wound has healed, raising due ethical concern [68].

Where funds are available, an alternative to biopsy is *Schistosoma* real-time PCR, which is sensitive and specific in urine and stool. However, in a pilot study on FGS the sensitivity in vaginal lavage was only 53%. The sensitivity was better in younger women (67%), suggesting that *Schistosoma* DNA from eggs (that have a limited life span) is perhaps more likely to be present in recent lesions [68].

Wet smears and Pap smears may serve as a contribution to the diagnosis of FGS, but their sensitivity is low [27,67]; Pap smears have a sensitivity below 15%. Tanzanian and Zimbabwean studies have shown that 23–41% of women with negative urine tests had FGS [28,34]. Urinary filtration or dipsticks are hence insensitive indicators for diagnosis of genital *S. haematobium* [69]. Increased levels of eosinophil cationic protein, Neopterin or IgA in cervicovaginal lavage have only limited value in the diagnosis of female gynecological schistosomiasis [67]. Furthermore, *S. haematobium* eggs may be found in almost every organ of the body and there may sometimes be no inflammatory reaction [12,25,70]. The presence of *S. haematobium* eggs in a lesion or discharge may not always be the cause.

Studying FGS in an endemic area is a logistic and cultural challenge requiring disproportionate amounts of funding for fundamental requirements such as water and electricity, but also for the colposcope (required for visual diagnosis) and extensive training in identification [27,68]. Further research to find more appropriate diagnostic tools is long overdue (Box 2).

Treatment

In the urinary tract, the effect of praziquantel has largely been determined by resolution of lesions detectable by ultrasound scan and decreased egg excretion in urine [71]. Praziquantel kills the egg-laying worms; however, lesions may remain and develop around eggs already deposited in the tissues [32,33]. Once egg deposition has induced lesions in the genital tract, egg excretion and lesion development are two independent processes, with praziquantel affecting the former almost immediately, but not the latter [32,33,70]. After less than two years, treatment has been described to resolve schistosomal infertility (with pregnancy) in six of 13 infertile women [72,73]. However, only one study has followed gynecological lesions after treatment [74]. It showed no significant change in the adult sandy patches and contact bleeding over a 12 month period, even though urinary egg excretion ceased. The outcome of treatment in the urinary tract has been found to be variable, depending on four factors: (i) the age of the patient, (ii) the pre-treatment intensity of infection, (iii) the degree of fibrosis or calcification, and (iv) the site of the lesion. In younger patients, the urinary tract lesions are more responsive to treatment; this may also be the case in the genital tract [32]. However, given the same age group and exposure rates, lesions in the bladder decrease faster than do lesions in the upper ureters after treatment.

To prevent long-term morbidity, the World Health Organization (WHO) has recommended treatment for women and school-based mass-treatment of children in schistosomiasis endemic areas [75]. MDA frequency is recommended at 6 month to 3 year intervals depending on whether there is a continuous high or low seasonal transmission, respectively. Moreover, studies have found that the prevalence of schistosomiasis is higher in non-enrolled children [76]. Furthermore, girls are often under-represented in schools. In an area of Egypt, only 18% of infected girls were reached through school-based programs.

Based on a number of reports, the WHO decided to recommend praziquantel to pregnant and lactating women [75]. Treatment for urinary schistosomiasis has been found equally effective in both HIV-positive and -negative individuals and does not seem to influence plasma HIV load significantly [77]. Studies indicate that some worms remain alive after treatment and that treatment should be repeated [75]. Moreover, even though treatment is efficient and the worms die, lesions may remain for years after correct use of praziquantel [32,33,70]. For the time being, praziquantel should be given as a single oral dose of 40 mg/kg, or 60 mg/kg in two divided doses, with food and drink to minimize gastrointestinal side effects [75]. Reinfection rates are rampant, and the suggestion that treatment creates immunity against reinfection in the individual is disputed [78]. There are several imperfect ways to reduce reinfection rates: (i) remove the vegetation along the shorelines where the snails reside, (ii) kill the snails (and fish) with various substances such as endod and others, (iii) reduce the pressure of infection of the snails by preventing urination and defecation in or near the body of water (e.g. establish latrines and community instruction programs), or (iv) mass-treat the human host population. The latter method has been found to have a dual effect in both reducing short- and long-term morbidity [6]. MDA is feasible, and several countries have achieved countrywide coverage. Praziquantel only kills adult worms, and worms mature in the course of approximately 6 weeks after entry into the human body. Praziquantel therefore should be given in the low-transmission season or at least 6–8 weeks after transmission, ideally as mass- or group treatment, encompassing all who will continue to use the same water bodies and who may urinate or defecate therein. The interval between the treatments should follow WHO recommendations.

Public health implications of genital schistosomiasis in girls and women

Of all parasitic infections, schistosomiasis is second only to malaria in terms of public health impact and has been estimated to affect at least 200 million people – equivalent to one in 30 people being affected worldwide [5]. Urogenital schistosomiasis is endemic in 53 countries in Africa and the Middle East [79]. The control groups in all studies to date are women who had been exposed to the same water sources [28,32,36]. The differences between exposed and unexposed groups are therefore probably larger than the reported figures. It has been estimated that 16 million women will acquire the genital manifestations of *S. haematobium* infection and that, if cured, 120 000 new cases of HIV could be averted through regular praziquantel treatments in the next decade [22,61]. However, the optimal timing for curative treatment for girls and novel treatment of adults remains to be explored (Box 2) [32].

Clinical action

Depending on the local panorama of diseases in a community and individual risk factors, *S. haematobium* may be the most likely cause of genital morbidity [27,38]. However, in *S. haematobium* endemic areas women currently receive neither correct advice nor treatment for the majority of their lower reproductive tract symptoms and findings. Based on the current knowledge of FGS, the information provided to adult women must be sober. The treatment kills the worm, but may have no effect on the lesions [32], and resolution of the clinical problem may therefore be slow or lacking. Women with symptoms of STDs should be given the information that symptoms may be caused by schistosomiasis and may possibly be irreversible [27,38]. Many women cannot choose to abstain from vaginal intercourse. Taking this into consideration, for those who already have genital schistosomiasis, they may be at higher risk for HIV acquisition and should be informed thereof in a sensitive manner by a professional [2].

Praziquantel must still be recommended because there is only meager documentation on treatment of genital schistosomiasis [32,33]. Furthermore, even though current lesions may be refractory to treatment by praziquantel, egg-laying worms may induce new lesions which must be prevented. Moreover, the opportunity should be used to trace and treat young female family members. Praziquantel should be provided as a prophylactic measure against future egg-induced genital lesions.

References

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