

QUESTIONS & ANSWERS FOR Workshop Female Genital Schistosomiasis MAY 4TH - 11TH, 2021, GENEVA

Version 2, June 06th 2021



Learn about one of the most neglected sexual and reproductive health issues in sub-Saharan Africa

Workshop on Female Genital Schistosomiasis

The workshop on Female Genital Schistosomiasis (FGS) is part of the FGS Accelerating Scale Together (FAST) Project. The training was conducted online from 4th-11th May 2021 as part of the FAST Project. The workshop was led by Bridges to Development in partnership with the Geneva Learning Foundation. More than 100 health care professionals in Sub-Saharan Africa participated. They were trained on improving the Prevention, Diagnosis, and Treatment of FGS. The questions presented in this material emerged from the participants of the workshop. The team of Subject Matter Experts supporting the training provided the answers.

This is a living document, and it is subjected to updates and reviews. For your reference, you are reading version 2 elaborated on June 06th, 2021.

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List of Abbreviations

| FGS | Female Genital Schistosomiasis |
|------|--------------------------------|
| HIV | Human Immunodeficiency Virus |
| HPV | Human Papillomavirus |
| MDA | Mass Drug Administration |
| NTD | Neglected Tropical Diseases |
| PZQ | Praziquantel |
| WASH | Water Sanitations and Hygiene |
| wно | World Health Organization |







1. How is schistosomiasis transmitted?

Schistosomiasis infection and transmission: People become infected when larval forms of the parasite – released by freshwater snails – penetrate the skin during contact with infested water (see Figure 1).

Transmission occurs when people suffering from schistosomiasis contaminate freshwater sources with their excreta (urine, faeces) containing parasite eggs, which hatch in water.

In the body, the larvae develop into adult schistosomes. Adult worms live in the blood vessels where the females release eggs. Some of the eggs are passed out of the body in the faeces or urine to continue the parasite's lifecycle. Others become trapped in body tissues, causing immune reactions and progressive damage to organs.

2. Is FGS sexually transmitted?

No, it is not. The parasite cannot be transmitted through sexual contact. Transmission is only through contact with infected water bodies.

However, FGS increases vulnerability to some sexually transmitted infections. Women and girls with FGS have a three-times higher risk of acquiring HIV and two-times higher risk for HPV – which are both sexually transmitted.

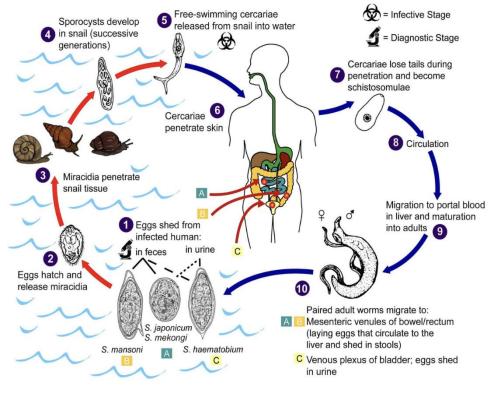


Figure 1: Life Cycle Schistosoma spp.

Source: Schistosomiasis CDC. DPDx - Laboratory Identification of Parasites of Public Health Concern Available at: https://www.cdc.gov/dpdx/schistosomiasis/index.html

3. Is FGS transmitted through contact?

There is no transmission from person to person.

People shed the eggs in urine or feces that then gets into water sources. The eggs hatch in freshwater releasing the parasite to infect snails which then release the cercariae which penetrate human skin to begin the human infection.

4. Do people with FGS need to be quarantined?

There is no need to quarantine. The infection cannot be transmitted from person to person.

5. Is the water infected by urine?

Yes, water is contaminated when an infected individual urinates (or defecates, depending on the species) in fresh water where the vector/snails are present. Eggs in the urine hatch and then infect snails. See transmission cycle as above.

6. If contaminated water is thoroughly boiled before drinking, will chances of schistosoma infection reduce?

Schistosomiasis <u>is not transmitted</u> by drinking contaminated water or food. The parasite penetrates the skin when it comes into contact with water while swimming, bathing, or collecting water - directly infecting the person. 7. If water is taken from a contaminated river infested with *Schistosoma haematobium* is allowed to stay for some time, can someone still be infected with Schistosomiasis?

After 3 days in a bucket (or other container) it is safe to have skin-contact with water. However, a tank which is topped-up with infested water will never be safe.





Progression of the Disease

1. Is there a case definition for FGS?

Yes, and it is included in the WHO Atlas. See below:

WHO Library (2015) Female genital schistosomiasis: a pocket atlas for clinical health-care professionals.

Available at: https://apps.who.int/iris/handle/10665/180863

2. Is FGS a risk factor to any of the genital or other cancers?

It is a HIV risk factor and risk of more severe progression with HPV and cervical cancer.



RESEARCH AHEAD: So far, no confirmatory evidence. The relationship and association are still being investigated

3. Is there an ovarian or fallopian signs or complications of FGS?

Eggs can be implanted in ovaries or fallopian tubes.

- **Symptoms**: Pain might be a symptom (confirmed by bimanual palpation) but studies have not been large enough to show this.

- <u>Signs</u>: Case reports (using ultrasound scan or laparoscopy) have shown swelling of the Fallopian tubes and tumours of the ovaries
- **<u>Complications</u>**: secondary infertility or ectopic pregnancy from blockage of the Fallopian tubes.

It is important to note that FGS is an important cause of ectopic pregnancy which is a leading cause of maternal deaths.



4. Do the eggs that are being excreted cause the blisters and patches at the vaginal region during FGS. Do the eggs also lodge in the tissue around the vaginal region to cause the observed ugly patches?

FGS does NOT cause blisters.

Yes, FGS causes patches.

A. If yes, how would one remove the lodged eggs?

The eggs cannot be removed manually. The body's natural inflammation processes make attempts to shed or dissolve the eggs, with little success. This means that even after treatment all the lesions will not resolve especially if diagnosed late.

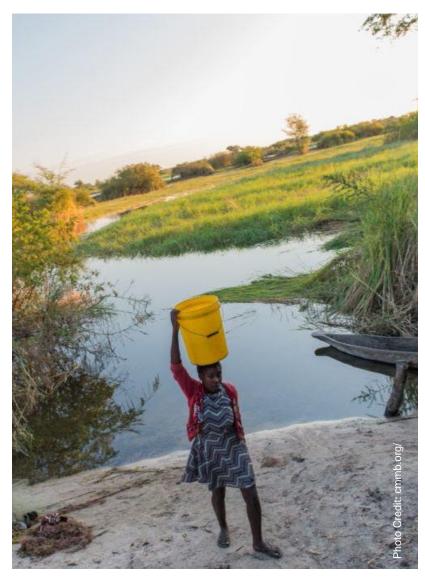
Patients respond better to early treatment.

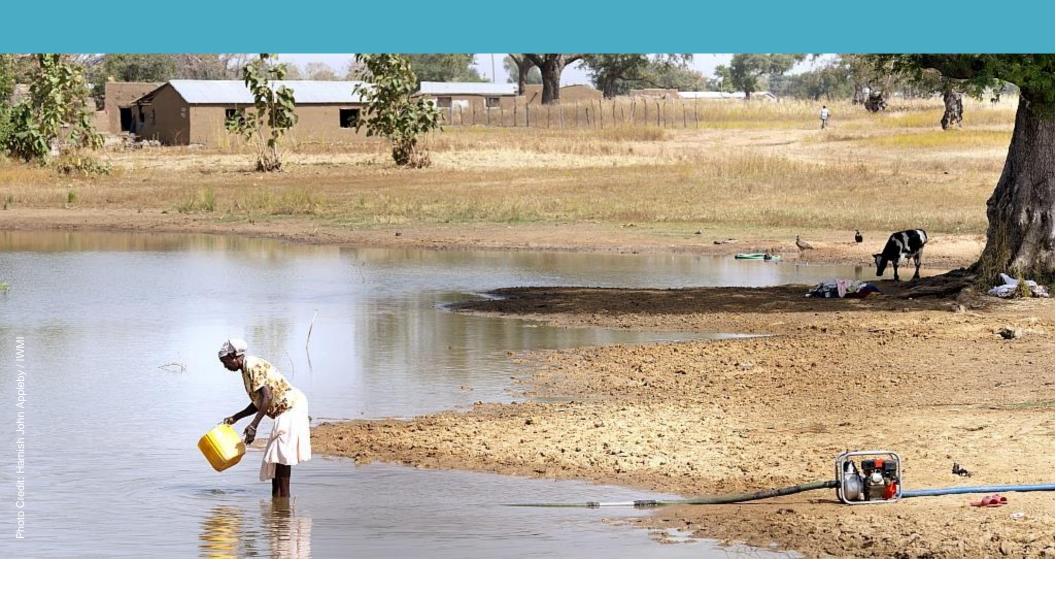
B. What are the causes of the blisters and grainy patches during FGS?

FGS does NOT cause blisters.

FGS patches are caused by the inflammatory response to the eggs implanted in the tissues. After treatment with praziquantel the adult worms die and are no longer biologically active, so there will be no

more shedding of new eggs and symptoms will improve. However, lesions due to existing eggs may not resolve until fresh tissue grows where possible.







1. What about invasive interventions /investigations for young girls/virgins?

Pelvic examination of young girls / virgins is not necessary as preemptive treatment.

Preventive treatment is standard care.

Examination should follow local standard practice but is not required to confirm FGS for treatment.

The following facts will help you decide on **syndromic** diagnosis:

- Water contact any time in their lifetime in an endemic area
 AND
- ✓ Abnormal discharge or
- ✓ Bloody discharge or
- ✓ Burning sensation in genitals or
- ✓ Lower abdominal pain or
- ✓ Genital ulcer (in children)
- ✓ Obviously red urine,
- ✓ Dysuria

RESEARCH AHEAD The PCR-method is being developed, sensitivity is 57-67%. In virgins, a vaginal PCR-self-swab can be done (in older children who are sure of which "hole" to put the swab in). There are studies published and it can aid with diagnosis, but it is still under development and not commercially available.

cont.



RESEARCH AHEAD cont.: The vaginal PCR-self swab may be very useful in hard to reach areas especially where there are religious /stigmatization issues.

2. What age category can we not do the pelvic examination?

The patient must be willing to have a pelvic exam. Anyone can be investigated externally. Sexually active women can be investigated internally.





3. Do I need to confirm the diagnosis of FGS before treatment? Or can I do preemptive treatment?

Preemptive treatment is **appropriate and prudent** in most cases. The syndromic diagnosis of FGS is based on the following facts:

- Water contact any time in their lifetime in an endemic area
 AND
- ✓ Abnormal discharge
- ✓ Bloody discharge
- ✓ Secondary infertility
- ✓ Burning sensation in genitals
- ✓ Secondary infertility

Mass drug administration (MDA) with Praziquantel (PZQ) in endemic communities is treatment without confirming diagnosis. **The drug is very safe!**

The drug is also safe in pregnancy.

A **history of previous treatment** is an important part of the history. Previous treatment means that the patient has either been infected or lived or travelled in an area that was endemic and put them at risk.

Reinfection is rampant and previous treatment does not mean that a person is not infected currently.



RESEARCH AHEAD

- Effect of schistosomiasis on primary infertilityPain on intercourse (dyspareunia)
- 4. How reliable are laboratory tests to diagnose FGS?

Unfortunately, you will miss many cases if you rely only on lab tests.

You can diagnose presumed FGS without microscopic examination of the eggs based on symptoms and history.

FGS can be present even without eggs found.



Treatment

1. How approved is this drug [PRAZIQUANTEL] for FGS? Considering FDA approval in Ghana? And is it only prescribed or in healthcare centers?

Praziquantel is routinely delivered to all school aged children without a prescription or a diagnostic test in mass drug administration programs supported by the Ministry of Health, Ghana Health Services and in other endemic countries.

Praziquantel is on the WHO essential medicines list and is approved for use by national ministries of health.

2. I would like to know if Praziquantel is the only medication for the treatment of FGS?

Yes, currently praziquantel is the only drug available for treatment of FGS.

3. Can pregnant women get treatment with praziquantel? In which trimester can a pregnant woman take Praziquantel?

Yes, praziquantel is safe in pregnancy. Current WHO preventive chemotherapy treatment strategy T2 **does not exclude any pregnancy trimester** of treatment.

See page 23 on:

WHO, 2006. Preventive chemotherapy in human helminthiasis : coordinated use of anthelminthic drugs in control interventions : a manual for health professionals and programme managers.

Available at:

http://apps.who.int/iris/bitstream/handle/10665/4 3545/9241547103_eng.pdf;jsessionid=F9DE72A 605853AC6C478867D9FBBE5CF?sequence=1

4. Is the dose for praziquantel (PZQ) the same for a child as in an adult?

The dose of praziquantel is 40mg/kg (weight dependent). In some countries for mass drug distribution (MDA) they use a height pole where the number of tablets given is based on height to calculate PZQ dose for children.

In clinical settings, adults should be weighed where possible otherwise a dose-pole should be used to determine the dosage for treatment.

5. How many times can one be treated?

There is **no limitation** to the number of times you can be treated. In community or school-based programs MDA treatment is given 1 or 2 times a year.

In the case of repeating treatment: time interval should permit of PZQ clearance of adult mature worms (as it doesn't act on other forms/stages of the worms). Allowing time for the worms to mature (e.g. period of 6-8 weeks) would be most impactful.

Therefore, a time interval of at least 8 weeks could be proposed.



RESEARCH AHEAD

There are studies looking at more frequent treatment and longer treatment (more than the single dose) to see if it is better at resolving FGS lesions and breaking transmission of schistosomiasis. 6. Is there any specific time between the first dose and reinfection?

Even though re-infection may occur after treatment, the risk of developing severe disease is diminished and even reversed when treatment is initiated and repeated in childhood.

A woman can be reinfected the day after AND she might also have juvenile worms which survive PZQ.

It takes 6 to 8 weeks for worms to develop so treatment. Therefore, at the **individual level**, treatment does not need to be done more frequently than this period.

For **communities**, the frequency of treatment is determined by the prevalence of infection in school-age children. In hightransmission areas, treatment may have to be repeated every year for a number of years.

Monitoring is essential to determine the impact of control interventions.

For more information, please refer to:

WHO, 2020. Key Facts Schistosomiasis.

Available at: <u>https://www.who.int/news-room/fact-</u> <u>sheets/detail/schistosomiasis</u> 7. Can you prophylactically administer praziquantel to infertile couples?

Yes, if the individual(s) have been to an endemic area it would be good to give praziquantel.

The drugs are safe, and it is not invasive.

However, you cannot administer praziquantel (PZQ) to people who have never been **exposed to fresh water** with schistosomiasis, so it is not really correct to call it "prophylactically". Rather call it "**preemptive**".

8. How do we address the psychosocial aspects of FGS infection?

Some research has shown that there can be important psychosocial aspects from the impact of FGS infection on sexual and reproductive health. Consider: counselling, follow up, **involvement of male partners** for support. **Improved sensitization** within the community will also help to address stigma and social isolation as appropriate in the local socio-cultural contexts.

9. When can preemptive treatment be done?

Straight away if FGS is suspected based on symptoms and history. See <u>question 3</u> of diagnosis section.







1. Can you please highlight how the vector control is carried out?

Vector control is difficult and costly. It can be helpful in some settings and WHO has guidance on how to use vector control of snails and where and when it can be most helpful.

For more information, please refer to:

WHO, 2017. Field use of molluscicides in schistosomiasis control programmes: an operational manual for programme managers.

Available at:

https://apps.who.int/iris/bitstream/handle/10665/254 641/9789241511995-eng.pdf?ua=1

2. Is it possible to identify an infected water body before a community starts showing signs of infection?

There is no simple way to test water to see if it is infected.

3. Why can't we just fix the water source?

Safe uncontaminated running water for all people is the best solution to many health challenges. Until that is available, we will continue to have transmission of schistosomiasis.

Water, sanitation and hygiene goes hand in hand with Neglected Tropical Diseases (NTDs) - without proper WASH it is almost impossible to control, eliminate and eradicate NTDs, including FGS.

4. Should we ask about the history of treatment?

Reinfection is rampant and previous treatment does not mean that a person is not infected currently. Any history of previous treatment is an important part of the history.

Previous treatment means that the patient has either been infected or lived in an area that was endemic and put them at risk and they should be considered at risk.



Awareness

1. Is there a global day on FGS?

There is a World NTD day celebrated on January 30th. It would be encouraged to use this day as an opportunity to focus on FGS as an important and neglected area.

There are other world health days for reproductive and sexual health, into which messages for FGS should be integrated as part of advocacy, awareness raising and health promotion activities.

 How do we prevent women working in freshwater for longtime as rice transplanters, clothes cleaners, etc. especially in endemic areas?

The key is to provide treatment and stop the contamination of water to break transmission. This is linked to general community development efforts led by local governments and administration. We do not want to take away people's employment, but we do want to keep them safe. Uncontaminated piped water and areas to wash clothes outside of contaminated water sources can decrease risk.





Challenging Questions & Policy

CHALLENGING QUESTIONS

 A situation where a clinician sees a virgin/young girl with symptoms like FGS, and does not have access to praziquantel for preemptive treatment. What should the health provider do for the person? What is your advice?

It is important to rule out other issues especially sexual abuse and cancer. Syndromic treatment is warranted without a pelvic exam if schisto-exposure is possible.

A history of bloody urine should trigger the administration of praziquantel even without other symptoms.

Visual inspection of external genitalia may also provide some indication of pathology or trauma. In younger children, FGS pathology can present on external genitalia (e.g. as polyps) which may be biopsied/scrapped and eggs detected by microscopy.

 Relying on donations for mass drug administration is not sustainable. We need government commitment and plan on how to finance FGS management.

This is an excellent project to work on.

The current global donations are both limited in quantity and time. They are not sustainable for the long-term. National government commitments are essential to take up the role of ensuring access to and availability of praziquantel in national health systems.

If there is no praziquantel and there is schistosomiasis in your area or amongst your patients please document this and immediately report it to the health authorities in your country.

POLICY

3. Addressing the lack of PZQ available in the treatment of FGS.

There is a committed donation treatment for school-aged children. The WHO NTD roadmap says that all at risk groups should be treated. Who provides this treatment?

Governments should buy PZQ for adults, and in some cases, implementing partners do provide funds for purchase for adults. PZQ is on the essential medicines list. If not on the list, then it can cost \$2/tablet.

We need to treat everyone in the community, not just schools, however the donation is not sufficient.

Addressing the assumption that PZQ may be paid in integration with other conditions. If there is no praziquantel and there is schistosomiasis in your area or amongst your patients, please document this and immediately report it to the health authorities in your country.



Notes & Further Resources

NOTES:



Physicians and nurses who use speculum and have a source of light /colposcope:

Are you interested in an online course in FGS manifestations? Eyrun Kjetland will try to put something together towards the end of the year. If yes, please send a letter of interest to <u>e.f.kjetland@gmail.com</u>

We have piloted self-sampling in women in Zambia and results revealed that self-sampling was as good as clinician obtained. It was also welcomed by women that preferred this to attending clinic. More work needs to be done for this to be more widely available.

For more information: <u>Amaya.Bustinduy@lshtm.ac.uk</u>

Further Resources

Websites and Resources:

Female Genital Schistosomiasis Training Competencies available in English, French and Portuguese (click <u>here</u>)

WHO FGS pocket atlas (click here)

COUNTDOWN (click here and here)

FAST package (click here) or www.fastpackage.org

Further Reading:

Engels, D., Hotez, P. J., Ducker, C., Gyapong, M., Bustinduy, A. L., Secor, W. E., ... Malecela, M. N. (2020). Integration of prevention and control measures for female genital schistosomiasis, HIV and cervical cancer. *Bulletin of the World Health Organization*, *98*(9), 615–624. https://doi.org/10.2471/BLT.20.252270

Julie Jacobson, Anastasia Pantelias, Megan Williamson et al. Addressing a Silent and Neglected Scourge in Sexual and Reproductive Health in Sub-Saharan Africa by Development of Training Competencies to Improve Prevention, Diagnosis, and Treatment of Female Genital Schistosomiasis (FGS) for Health Workers, 31 March 2021, PREPRINT (Version 1) available at Research Square https://doi.org/10.21203/rs.3.rs-363043/v1

Pragna Patel, Charles E. Rose, Eyrun F. Kjetland, Jennifer A. Downs, Pamela Sabina Mbabazi, Keith Sabin, Wairimu Chege, D. Heather Watts, W. Evan Secor, Association of schistosomiasis and HIV infections: A systematic review and meta-analysis, International Journal of Infectious Diseases, Volume 102, 2021, Pages 544-553, https://doi.org/10.1016/j.ijid.2020.10.088

About the FAST Package

The FGS Accelerated Scale Together (FAST) project is dedicated to a holistic approach that combines diagnosis and treatment, training, prevention through mass drug administration and community awareness and empowerment.



The FAST Package combines a diverse partnership of global and national partners. Funded by Grand Challenges Canada with matched funding and support from the NTD Support Center, Merck Global Health Institute, WHO Expanded Special Project for the Elimination of Neglected Tropical Diseases and the Schistosomiasis Control Initiative Foundation.

Our research partnership includes:

Bruyère Research Institute, Canada Bridges to Development, USA University of Health and Allied Sciences, Ghana Association K'olo Vanona, Madagascar NTD Program, Ghana Health Service, Ghana NTD Program, Ministère de la Santé, Madagascar

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