Abdominal manifestations of urogenital schistosomiasis in girls

A school based cross-sectional pilot study in Ugu District, KwaZulu-Natal South Africa

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Abstract

Introduction: People in 77 different countries are infected with schistosomiasis. Ninety percent of these live in Africa and 300 million women and girls in Africa are at risk of getting infected. Female genital schistosomiasis is a poverty-related water-transmitted parasitic disease which may create gynaecological symptoms, contact bleeding, friable blood vessels and inflammation. Children have been found to have urinary manifestations such as dysuria, haematuria and increased urinary frequency. Up to 75 % of the women who excrete eggs from *Schistosomiasis haematobium* in the urine may also have eggs in the uterus, cervix, vagina or vulva. It has frequently been hypothesized that the granulomatous inflammation that occurs due to ova deposition in the genitals may be the cause of abdominal pain, lower back pain and dyspareunia. However, it is not known whether children have pain in the abdomen as a consequence of this disease. Our aim was to investigate whether abdominal pain could be a symptom of urogenital schistosomiasis in children.

Materials and methods: This investigation was nested in a larger school based study and included 10-12 year old girls from 3 different primary schools in the Ugu district area. Abdominal palpations were performed in all girls who gave consent. The stool and urine were investigated for schistosomiasis and other helminths, urine dipsticks and bacterial cultures were performed.

Results: There was no significant association between lower abdominal pain and infection with schistosomiasis ($p=0.31$) or with general abdominal pain ($p=0.83$). .

Conlusion: This pilot study did not show that schistosomiasis is associated with abdominal pain. Since there are many reasons for abdominal pain in children, abdominal pain is probably not a useful indicator for urogenital schistosomiasis in children.

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Introduction

Schistosomiasis is a chronic parasitic disease causing illness in more than 230 million people worldwide (1). Ninety percent of the infected live in Africa and poor communities are particularly affected because of poor sanitation and lack of access to clean water (1). It is estimated that 700 million people worldwide are at risk of getting the disease. People become infected with schistosomiasis through contact with contaminated freshwater (2). Children's sanitary and recreational water contact practices may expose them to the cercariae, and in some areas large proportions of school-aged children are infected by the disease (1). The cercariae may penetrate human skin, reach venules surrounding different organs, and create pathology there (3).

S. heamatobium is one of five different species of schistosomiasis. Together with *S. mansoni* and *S. japonicum*, it contributes to the major disease burden. See appendix for more information about life cycle of the parasites and predilection sites.

Eggs from *S. haematobium* may induce urinary tract morbidity and patient symptoms may be characterized by dysuria, pollakisuria and haematuria (1, 3). There is a higher prevalence of urinary ova excretion in infected children and young adults than in an older age groups, possibly due to less water contact in the adults and immunological processes (1, 4).

Infection with *S. haematobium* may also affect the genital organs and has been found in 33 to 75 % of the women with ova from *S. haematobium* in their urine (5).Genital schistosomiasis is associated with an increased intensity of urinary *S. haematobium* infection, but may also be found in cases that do not have urinary schistosomiasis (6, 7). The predilection site for ova has been proposed to be the cervix, however the Fallopian tubes and the vagina are also common sites for genital manifestations of schistosomiasis (8). Histologically, the ova are often surrounded by granulomatous inflammation and the most

common clinical finding is sandy patches (7). A female genital schistosomiasis consensus 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. The lesions are aceto-negative (i) grainy sandy patches, (ii) homogenous yellow sandy patches, or (iii) rubbery tubercles (8). Female genital schistosomiasis has been defined either as sandy patches and/or microscopically proven *S. haematobium* eggs in genital tissue (8). Other findings that are correlated with ova in the genital tract are neovascularisation and contact bleeding (7). Clinical symptoms are thought to be caused by host reactions against ova in the tissues and depending on the site of the lesions different symptoms may arise. It has been hypothesised that the disease may cause lower abdominal pain, bloody cervical discharge, dyspareunia and dysmenorrhoea (8).

It has further been hypothesised that puberty, vascular changes take place in the pelvic vascular system and this may result in anastomoses between external and internal genital organs as well as between rectal and vesical plexii (9). It has also been hypothesized that the increased blood flow during puberty enhances the probability for adult worms to reach and settle in the female genital organs. Other findings suggest that changes in hormone levels during puberty may alter the host's immune response to the parasites (4). Especially, it is thought that a rise in the levels of the hormone dehydroepiandrosteronesulphate may induce a resistance to schistosomiasis infection causing higher intensities of infection before puberty (4, 10). However, unpublished interview data from our group indicates that even pre-pubertal children have genital schistosomiasis (submitted, Hegertun et al)

Since gynaecological investigations are rarely done in virgins, one knows little about the clinical signs of genital schistosomiasis in young girls (6). However, a vaginal polyp was found in a 3 year old girl and a "raised reddened area" in the vagina was found in a 16 year

old. In addition, sandy patches have been found in a 15 year old girl (8). Later in life genital schistosomiasis may make the women more susceptible to infections and female genital schistosomiasis may be associated with a higher risk of having HIV and other sexual transmitted diseases (11, 12). Infertility may also be one of the chronic manifestations (3, 13).

To our knowledge, the assumption that urogential schistosomiasis gives abdominal pain has never been investigated by systematic clinical or epidemiological studies. This study therefore aims to examine if there is any association between abdominal pain and urogenital schistosomiasis in prepubertal girls. If urogenital schistosomiasis gives abdominal pain in children it could be used diagnostically as an indicator for infection.

Materials and methods

Study participants and area

Girls at 10-12 years of age were recruited from three different rural schools in the Ugu district in KwaZulu-Natal, South Africa. The schools were situated below the altitude of 300 metres and were located in an area endemic for schistosomiasis (figure 1). This is one of the poorest areas in South Africa and it is thought to be similar to other schistosomiasis endemic areas in Africa {Kvalsvig, 1988 #41

Figure 1. A map showing the position of Ugu district (red) in KwaZulu-Natal (white) and in South Africa. *Source: en.wikipedia.org*

Ethical considerations

Three ethics' committees had granted permissions. Ethical clearances were received from Biomedical Research Ethics Administration, University of KwaZulu-Natal (KZN) February 20th 2009, and Ref BF029/07 and from Department of Health, Pietermaritzburg,

KZN, February 3rd 2009, Reference HRKM010-08. REK Øst-Norge, the Norwegian ethics committee, gave ethical clearance Ref 469-07066a1.2007.535, September 17th 2007. The Departments of Health and Education in Ugu district, KwaZulu-Natal have given permissions.

Prior to starting the study at each school, project representatives held parents meeting where they gave information about the background for the study and a summary about which investigations that were supposed to be done. After they had received the information the guardians were asked for permission, and girls with written consent from their guardian were invited to the study. All the children were also given the information that they had the right not to participate and that they could withdraw at any moment. After assent from the girls specimens collected were given identification numbers not traceable to the individuals. All children in the endemic schools, whether part of the study or not, were offered free treatment for schistosomiasis through the school health nurses in accordance with the WHO recommendations, and were informed about the side effects of this treatment.

Faces pain scale

Faces pain scales were used to measure self-reported pain in children. The tool shows faces expressing increasing intensity of pain. Studies have shown that children, nurses and parents prefer the use of faces pain scales above other self-report measures, such as the visual analogue scale, and that children may find it difficult to translate their pain experience into numerical values (14). A faces pain scale called the Faces Pain Scale-Revised (FGS-R) was chosen for this investigation (figure 2), freely available on www.painsourcebook.ca (15). It consists of six faces and has no smiling or tearful faces. The six faces are translated into

numerical values (0-2-4-6-8-10) starting from the left. It has been found to be reliable in children aged 4 to 16 years (14).

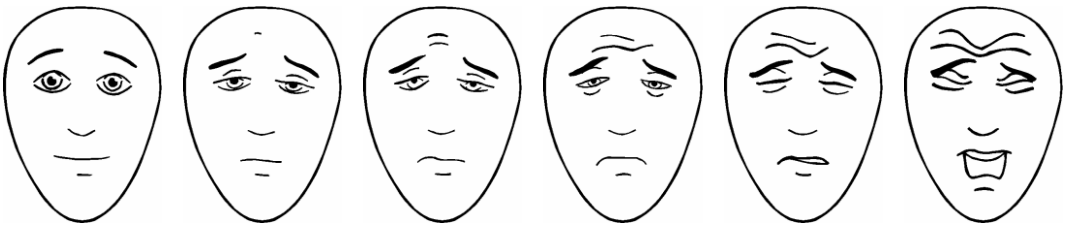


Figure 2. The faces pain scale used in this study. *Source: www.painsourcebook.ca*

Before use, the following information was given to the child in Zulu (the local language): "These faces show how much something may hurt. This face [point to left-most face] shows no pain. The faces show more and more pain [point to each from left to right] up to this one [point to right-most face] – it shows very much pain. Point to the face that shows how much you hurt right now" (14). Only the faces (not the numbers) were shown to the children, while the numerical value was recorded by the examiner.

Clinical examination

The clinical examinations were performed in class rooms behind a screen out of hearing range from others. The child was given the following information in Zulu before starting the examination:"I am now going to massage your stomach, and it is very important that you tell me to stop if it hurts anywhere, even if it only hurts a little bit". After the instructions were given, all the nine quadrants of the abdomen were examined for pain by pressing once in every quadrant in the following order: right hypochondrium, epigastrium, left hypochondrium, right lumbar, umbilical, left lumbar, right iliac fossa, hypogastrium and left

iliac fossa. Abdominal pain was defined as having pain in at least one quadrant, while lower abdominal pain was defined as pain in one of the three most caudal quadrants.

For the first 13 cases the child´s abdomen was palpated by both examiners in order to reveal discrepancies. The girl was also asked if palpations had been similar. The ensuing abdomens were only palpated alternately by one examiner while the other was looking on. If the child did not express any pain during the examination she was asked afterwards if she was sure she had not felt any pain during the investigation, and if the answer was no, then the number 0 was recorded for all quadrants. However, if a child expressed pain during the palpation, the examiner stopped and the six graded faces pain scale was used. If the child reported pain in more than one quadrant, the faces scale was used to grade the pain in each one separately. Then the examination continued until all quadrants were palpated.

After examining all quadrants for pain, the abdomen was palpated again with focus on finding possible tumours, enlargement of the liver or enlargement of the spleen. However, the most painful areas were avoided to not inflict unnecessary pain on the children. Other relevant clinical findings such as bruises or wounds were also registered. Height and weight of the children were also registered in order to calculate the BMI.

Sample collection and analyses

Three urine samples were collected between 10 and 12 am from each girl on three consecutive days (16). The total volume of urine was collected and stored in clean, honey jars. One faeces sample was collected. The faeces were laid out on non-stick paper by the girls and the research assistants collected a part of it with a spatula and placed it in a small jar. Samples were stored in cooler boxes until examined in the afternoon.

S. haematobium was explored by urine microscopy, and infection was defined as having one or more ova present. One of the urine samples from each girl was tested with a urine dipstick (Macromed), and if positive the urine was cultured using UriCult. A urinary tract infection was defined as a bacterial growth of at least 10 in the power of 5 CFU/ml on the CLED-agar. The stool was investigated by using the Kato Katz method for *Ascaris lumbricoides, Taenia solium, Schistosomiasis mansoni* and *Trichuris sp*..Urine and stool examinations for helminths are described further in the appendix.

Interview

All the girls were interviewed individually by a research assistant in an isolated part of the classroom. The interview was performed in Zulu (the local language) and lasted about 45 minutes. They were asked questions on a number of subjects. For the purpose of this investigation they were asked for signs of puberty, water contact patterns, signs of urinary tract infection (UTI), HIV infection and sexual activity, previous history of schistosomiasis, and feelings of sadness and hopelessness.

If a girl disclosed she was HIV infected, had discomfort in her private parts, or had been sexually abused, she was offered further consultations at a clinic or with a psychologist as appropriate. At the end of the interview, all girls were asked if they wanted participate in the follow-up.

Statistical methods

Statistical Package for the Social Science (SPSS) version 18 was used to perform the statistical analyses. All the frequencies were calculated using SPSS. Crosstabs and chi-square tests were used to study the association between laboratory results and clinical findings.

Results

Description of population frequencies

A total of 325 girls from three different schools were included in the study. The mean age was 11.2 years with a standard deviation (SD) of 0.8. Forty eight percent had signs of having reached puberty such as having undergone menarche, started growing breasts or having hair under their arms. The prevalence of *S. haematobium* in urine was 24.1 % (78/324), and 49.2 % (160/325) reported having risk water contact and could possibly be infected. There were 19 girls with visible bruises, wounds or scars on the abdomen, these areas were not palpated. Abdominal pain was detected in 47.4 % (154/325). Figure 3 shows the location of and the prevalence of abdominal pain for each of the nine quadrants. Of the nine regions, pain was most commonly found around the umbilicus (19.4% (63 / 325)) and in the epigastric region (16.0% (52/325)). Lower abdominal pain was reported by 19.1 % (62/325) and in addition, 61.3 % (190/310) answered yes to the question if they had abdominal pain frequently.

Right Hypochondrium 7,1 %	Epigastrium 16,0 %	Left Hypochondrium 3,7 %
Right Lumbar 4,6 %	Umbilical 19,4 %	Left Lumbar 5,5 %
Right Iliac Fossa 4,3 %	Hypogastrium 12,9 %	Left Iliac Fossa 4,0 %

Figure 3. The frequencies of abdominal pain in each of the nine quadrants.

Associations

Of those with schistosomiasis in the urine 23.1 % (18/78) had lower abdominal pain whereas this was found in 17.9 % (44/246) of the ones without schistosomiasis (p= 0.31). Of those with schistosomiasis in their urine, 46.2 % (36/78) had abdominal pain in one or more of the nine quadrants. Similarly, 47.6 % (117/246) of those with no schistosomiasis in the urine had general abdominal pain (p=0.83). We did a multivariate analysis controlling for BMI, age, UTI, sexual abuse and infection with other helminths, is did not change the above. In order to detect a significant difference, 1968 young girls would have had to undergo investigation (EpiInfo, statcalc).

Other possible causes of pain

Intestinal parasitic infections were found in 22.8 % (74/325) of the girls. *Ascaris lumbricoides* was the most common affecting 15.7 % (51/325 of the girls). Of the 51 girls who were infected with *Ascaris lumbricoides*, 22 experienced abdominal pain in one or more of the nine quadrants (p=0.51). In 110 girls the urine dipstick was positive for leukocytes and six of these had positive culture for bacterial urinary tract infection (1.8%). Only three of the girls with urinary tract infection had abdominal pain in one or more of the nine quadrants (p=0.90).

Of the girls 27.4 % (81/325) felt they had a dark and hopeless future and/or had been so sad and hopeless almost every day, for two weeks or more in a row, that they had stopped doing some usual activities, but this was not associated with abdominal pain (p=0.77). Six of the girls reported sexual abuse; amongst these three had abdominal pain.

The mean BMI was 19.5. However, it ranged from 13.9 (underweight) to 34.7 (obese), and 4.3 % (14/159) of the girls were overweight. There was no significant association between pain and BMI (p=0.27).

Discussion

In this population of primary school girls urogenital schistosomiasis infection was not significantly associated with the clinical detection of lower abdominal pain or with pain in any of the areas of the abdomen. Abdominal pain has been hypothesised to be a symptom in adult patients with schistosomiasis in several case studies, but none of the studies have to date found a significant association (8). Since studies suggest that early treatment may prevent long term damage to the genital organs, it is important to further investigate clinical signs and symptoms so that a diagnosis can be made at an early stage (17).

Comparison to other studies

To our knowledge no other studies have explored the association between abdominal pain and schistosomiasis infection. However, Swai et al. published an article in 2006 where the age of the females ranged from 5 to 61 years, with 10 of the females in the age group 5 to 19 years. It was a retrospective descriptive histopathological study performed in 111 patients with female genital schistosomiasis in Tanzania. Eleven percent of the infected women had reported lower abdominal pain (18). The fact that this study included both children and adults makes it one of the most comparable to our study. However they only investigated self-reported pain and not pain during palpation, furthermore there were no schistosomiasis negative groups for comparison.

Studies have found that other symptoms are associated with schistosomiasis, and this suggests that when mapping symptoms of schistosomiasis in children one should look for other symptoms than abdominal pain. In 2011 Buowari published a cross-sectional study of 35 adult patients in Nigeria with urinary schistosomiasis, of these, only four individuals

reported abdominal pain. Haematuria and dysuria were described as the two most common complaints, in respectively 13 and 12 of the patients (19).

In 2012 Kjetland and collegues wrote a review article about female genital schistosomiasis, in which they conclude that schistosomiasis is not associated with abdominal pain. However, this is regarding women of reproductive age (8).

Alternative explanations to results

Abdominal pain in children is the most common type of pain in younger children and it markedly worsens quality of life (20). Studies have found that the prevalence of abdominal pain show two peaks of age, one at 4-6 years and the next at 7-12 years of age, the latter is the age group in our study (21). The most common cause of chronic abdominal pain in children is so-called functional abdominal pain, that is, without objective underlying evidence of organic cause (22). Functional abdominal pain includes functional dyspepsia, irritable bowel disease, abdominal migraine and functional abdominal pain. Organic causes of abdominal pain may be food intolerance, celiac disease, dysmenorrhoea, gastro-esophageal reflux disease, diseases of the urinary tract (for example infection), chronic inflammatory bowel disease, peptic ulcer, anatomical malformations, amongst others (20). Hence, there are several alternative explanations for why there was a high prevalence of abdominal pain in this study. To better understand the underlying causes of abdominal pain, the organic causes looked for in this study were urinary tract infection, palpable liver or spleen and infection with other helminths. Yet, there are more factors regarding functional abdominal pain and organic causes of abdominal pain that could be looked for specifically in future studies.

Little is known about the association between chronic abdominal pain in children and sexual abuse. However, some studies which suggest that abused children report more

functional disorders than control groups (21). Depression and other stressful life events are difficult to relate to abdominal pain, because it is often difficult to determine whether the pain causes depression or if depression causes pain (21). The association between abdominal pain and overweight should also be investigated further.

Limitations

The study group might have been too small to detect a significant association between abdominal pain and schistosomiasis ova in the urine (Type 2 error). The urinary-negative girls may have had genital schistosomiasis and hence the real differences between the groups may have been larger than we were able to detect. Further, there were two different people palpating the abdomens. Even though the first girls were palpated by both examiners and for all the subsequent cases the examiners observed each other while palpating to assure that the same technique was used, there might have been some slight differences.

Some of the girls included in our study were overweight and this may have influenced the quality of our examination. In addition, the BMI was measured using percentile charts published for American standards, and the use in South African children may therefore have created a prevalence bias (23).

A faces pain scale has been validated in South African children between the ages 4 to 12 years during a study that explored postoperative pain (24). However, the current faces pain scale had not been used in a South African population previously and that may have created a communication problem. There are several different types of faces pain scales and they differ in the number of faces used and in the way the faces are presented. Some scales use smiling faces and some use neutral faces as baseline (25). The smiling face may be mistaken for the child's mood instead of level of pain and might therefore overestimate pain ratings (26). The

Faces Pain Scale-Revised however did not contain any smiling or tearful faces. The use of a translator and lack of standardised information may have given rise to interpretation problems and differences in the explanation to each girl. Further, the setting in which the examination was performed was not ideal. The classroom was full of other waiting girls and it was difficult to get complete privacy around the examination table. The girls seemed a bit tense when it was their turn. All these factors may have influenced the results and may therefore have caused over-or even under-reporting of abdominal pain.

Conclusion

In this small pilot study of pre-pubertal girls we could not show that there was an association between lower or other abdominal pain and urinary schistosomiasis. However, further analyses should be conducted. The pain should be explored against behavioural risk factors and multivariate analyses should be run to control for confounders. Since there are many reasons for abdominal pain in children, it is probably not useful as an indicator for urogenital schistosomiais.

List of references

1. WHO. Factsheet No 115 Schistosomiasis. World Health Organisations Media Center: World Health Organisation; 2012 [cited 2010]; Available from: http://www.who.int/mediacentre/factsheets/fs115/en.
2. Eddleston M DR, Brent A, Wilkinson R. Oxford Handbook of Tropical Medicine. 3rd ed. New York: Oxford University Press; 2008.
3. Gryseels B, Polman K, Clerinx J, Kestens L. Human schistosomiasis. Lancet. 2006;368(9541):1106-18. Epub 2006/09/26.
4. Fulford AJ, Webster M, Ouma JH, Kimani G, Dunne DW. Puberty and Age-related Changes in Susceptibility to Schistosome Infection. Parasitol Today. 1998;14(1):23-6. Epub 2006/10/17.
5. Kjetland EF, Kurewa EN, Ndhlovu PD, Midzi N, Gwanzura L, Mason PR, et al. Female genital schistosomiasis--a differential diagnosis to sexually transmitted disease: genital itch and vaginal discharge as indicators of genital Schistosoma haematobium morbidity in a cross-sectional study in endemic rural Zimbabwe. Tropical medicine & international health : TM & IH. 2008;13(12):1509-17. Epub 2008/12/06.
6. Poggensee G, Kiwelu I, Weger V, Goppner D, Diedrich T, Krantz I, et al. Female genital schistosomiasis of the lower genital tract: prevalence and disease-associated morbidity in northern Tanzania. The Journal of infectious diseases. 2000;181(3):1210-3. Epub 2000/03/18.
7. Kjetland EF, Ndhlovu PD, Mduluza T, Gomo E, Gwanzura L, Mason PR, et al. Simple clinical manifestations of genital Schistosoma haematobium infection in rural Zimbabwean women. The American journal of tropical medicine and hygiene. 2005;72(3):311-9. Epub 2005/03/18.
8. Kjetland EF, Leutscher PD, Ndhlovu PD. A review of female genital schistosomiasis. Trends in parasitology. 2012;28(2):58-65. Epub 2012/01/17.
9. Feldmeier H, Poggensee G, Krantz I. Puberty and Age-intensity Profiles in Schistosome Infections: Another Hypothesis. Parasitol Today. 1998;14(10):435. Epub 2006/10/17.
10. Abebe F, Birkeland KI, Gaarder PI, Petros B, Gundersen SG. The relationships between dehydroepiandrosterone sulphate (DHEAS), the intensity of Schistosoma mansoni infection and parasite-specific antibody responses. A cross-sectional study in residents of endemic communities in north-east Ethiopia. APMIS : acta pathologica, microbiologica, et immunologica Scandinavica. 2003;111(2):319-28. Epub 2003/04/30.
11. Kjetland EF, Mduluza T, Ndhlovu PD, Gomo E, Gwanzura L, Midzi N, et al. Genital schistosomiasis in women: a clinical 12-month in vivo study following treatment with praziquantel. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2006;100(8):740-52. Epub 2006/01/13.
12. Mosunjac MB, Tadros T, Beach R, Majmudar B. Cervical schistosomiasis, human papilloma virus (HPV), and human immunodeficiency virus (HIV): a dangerous coexistence or coincidence? Gynecologic oncology. 2003;90(1):211-4. Epub 2003/06/25.
13. Kjetland EF, Kurewa EN, Mduluza T, Midzi N, Gomo E, Friis H, et al. The first community-based report on the effect of genital Schistosoma haematobium infection on female fertility. Fertility and sterility. 2010;94(4):1551-3. Epub 2010/02/13.
14. Huguet A, Stinson JN, McGrath PJ. Measurement of self-reported pain intensity in children and adolescents. Journal of psychosomatic research. 2010;68(4):329-36. Epub 2010/03/24.

15. Bieri D, Reeve RA, Champion GD, Addicoat L, Ziegler JB. The Faces Pain Scale for the self-assessment of the severity of pain experienced by children: development, initial validation, and preliminary investigation for ratio scale properties. Pain. 1990;41(2):139-50. Epub 1990/05/01.
16. Doehring E, Vester U, Ehrich JH, Feldmeier H. Circadian variation of ova excretion, proteinuria, hematuria, and leukocyturia in urinary schistosomiasis. Kidney international. 1985;27(4):667-71. Epub 1985/04/01.
17. Kjetland EF, Ndhlovu PD, Kurewa EN, Midzi N, Gomo E, Mduluza T, et al. Prevention of gynecologic contact bleeding and genital sandy patches by childhood anti-schistosomal treatment. The American journal of tropical medicine and hygiene. 2008;79(1):79-83. Epub 2008/07/09.
18. Swai B, Poggensee G, Mtweve S, Krantz I. Female genital schistosomiasis as an evidence of a neglected cause for reproductive ill-health: a retrospective histopathological study from Tanzania. BMC infectious diseases. 2006;6:134. Epub 2006/08/25.
19. Buowari YD. Clinical presentation and management of schistosomiasis at a hospital in a rural area in Nigeria. Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria. 2011;20(1):61-4. Epub 2011/10/06.
20. Bufler P, Gross M, Uhlig HH. Recurrent abdominal pain in childhood. Deutsches Arzteblatt international. 2011;108(17):295-304. Epub 2011/06/02.
21. Berger MY, Gieteling MJ, Benninga MA. Chronic abdominal pain in children. BMJ. 2007;334(7601):997-1002. Epub 2007/05/12.
22. Chronic abdominal pain in children. Pediatrics. 2005;115(3):812-5. Epub 2005/03/03.
23. Prevention CfDCa. Children's BMI. Atlanta: CDC; 2012; Available from: http://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html.
24. Bosenberg A, Thomas J, Lopez T, Kokinsky E, Larsson LE. Validation of a six-graded faces scale for evaluation of postoperative pain in children. Paediatric anaesthesia. 2003;13(8):708-13. Epub 2003/10/11.
25. Chambers CT, Giesbrecht K, Craig KD, Bennett SM, Huntsman E. A comparison of faces scales for the measurement of pediatric pain: children's and parents' ratings. Pain. 1999;83(1):25-35. Epub 1999/10/03.
26. Chambers CT, Craig KD. An intrusive impact of anchors in children's faces pain scales. Pain. 1998;78(1):27-37. Epub 1998/11/20.
27. Gill G BN. Tropical Medicine. 6th ed. West Sussex: Wiley-Blackwell; 2009.
28. Leder K WP. Ascariasis. Up to Date; 2012; Available from: http://www.uptodate.com/contents/ascariasis?source=search_result&search=ascaris&selectedTitle=1.
29. Hotez PJ, Arora S, Bethony J, Bottazzi ME, Loukas A, Correa-Oliveira R, et al. Helminth infections of children: prospects for control. Advances in experimental medicine and biology. 2005;568:135-44. Epub 2005/08/20.
30. Weller PF LK. Hookworm infection. Up To Date; 2012; Available from: http://www.uptodate.com/contents/hookworm-infection?source=search_result&search=hookworm&selectedTitle=1
31. Leder K WP. Intestinal tapeworm. Up To Date; 2012; Available from: http://www.uptodate.com/contents/intestinal-tapeworms?source=search_result&search=Intestinal+tape+worm&selectedTitle=1
32. Leder K WP. Enterobias and trichuriasis. Up To Date; 2012; Available from: http://www.uptodate.com/contents/enterobiasis-and-trichuriasis?source=search_result&search=enterobius+and+trichiura&selectedTitle=1.

Appendix

Life cycle of the parasite

Schistosomal eggs are excreted through human urine or faeces into freshwater. Each egg contains a miracidium, an immature larval form that will be released when the egg gets into contact with the water. The miracidium is able to penetrate and infect a freshwater snail. Snails in ponds, rivers, dams and lakes are the intermediate hosts for the schistosome parasite. Different schistosomiasis species use different snail genus. *Schistosomiasis haematobium* use snails of the *Bulinus* genus as their intermediate host, and these snails mainly exist in Africa and on the Arabian Peninsula. *S. mansoni* is transmitted by the genus *Biomphalaria* which live in Africa, on the Arabian Peninsula and in South America. In this way the distribution of the different snail genera will decide the distribution of the schistosomiasis species (3).

After infecting a snail the miracidium will reproduce asexually. First it will transform into a multi-cellular sporocyst and later into a cercarial larva. 4-6 weeks after the snail has been infected it may shed thousands of cercarial larvae each day, and this may go on for months. Shedding is provoked by sunlight and therefore peaks at daytime. Each larva may survive up to 72 hours in the water, and it will by this time try to penetrate the skin of a definitive host (3).At one end the cercaria has got two suckers which make it possible to penetrate human skin. At the other end it has got a bifurcatial tail that it sheds during the penetration, and then becoming a schistosomule. Inside the human body the schistosomule will reach the bloodstream and travel via the lungs to the portal vein and the liver. Once in the liver it will mature into an adult worm and this takes about 1-3 months. Adult worms are cylindrical and 7 to 20 mm long and they mate sexually. The male has a gyneacophoric channel used by the female during mating. After mating, the schistosomulae will migrate to

venous plexuses surrounding different organs (3, 27). Different species of schistosomiasis prefer different venous plexuses when inside the human body. *S. haematobium* will migrate to the peri-vesical and genital venules and give disease related to the urogenital organs, while *S. mansoni* will migrate to mesenteric venules and cause intestinal disease. Adult worms live as a couple in the venules and have an average life span of 3-5 years; however, recordings have been made of worms living in the human body for up to 30 years (3, 27). While in the human body, the parasite doesn't reproduce, but the fertilized female worm may produce hundreds of eggs per day. The eggs penetrate the bladder wall / the genital tract wall (*S. haematobium*) and the intestine wall (*S. mansoni*) by secreting proteolytic enzymes, and the eggs then reach the urine or faeces (3). If contaminated urine or faeces reach freshwater with snails the disease will spread and a cycle will maintain.

Parasitology and microbiology

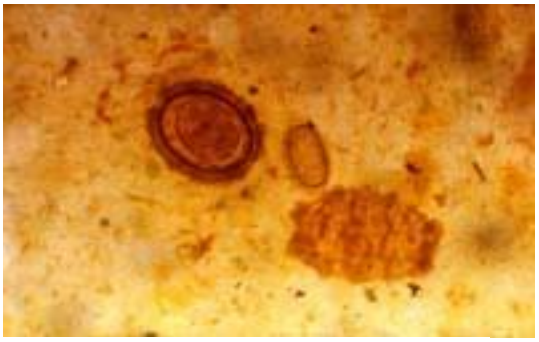
Ascaris lumbroicoides is one of the most common helminthic infections in the world, and it is estimated that 25 % of the world's population is infected (figure 4). It is the largest intestinal roundworm of man and is most common in children. Transmission occurs via water or food contaminated with ascaris eggs. Most infections are asymptomatic, and subtle but with a high worm load the infection may produce symptoms from the lungs and intestine, including hepatobiliary and pancreatic symptoms (28). The worm may cause abdominal pain, fatigue and malnutrition (29).

Hookworm infects humans by penetrating the skin, and this may produce a pruritic maculopapular eruption at the site of penetration (figure 4). After entering the body the worm migrate to the lungs and this phase is most often asymptomatic. Sometimes the infection

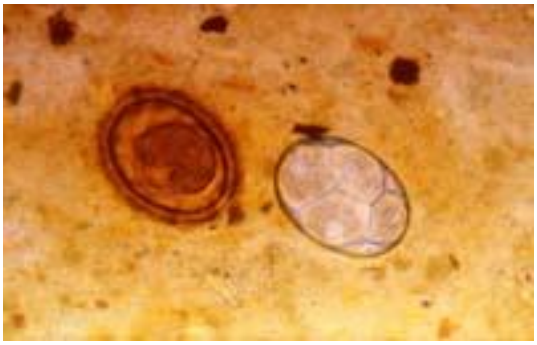
produce acute gastrointestinal symptoms, but the most common clinical manifestation is chronic nutritional impairment and anaemia(30).

Taenia solium is an intestinal tapeworm or cestode and may live as adult parasites in the human gastrointestinal tract, usually in the jejunum (figure 4). People get infected by eating contaminated undercooked meat. The infection is normally asymptomatic, but during the release of adult worms in the stool the person might feel nausea, anorexia or pain in the epigastrium. Anxiety, headache, dizziness and urticaria may also appear (31).

Trichuris trichiuria is also called whipworm and it is estimated that 25 % of the world's population carry this parasite (figure 4). Infection is associated with poor hygiene and may give rise to loose stools, dysentery and rectal prolapse, as well as also impaired growth and impaired cognition in children. But, most common it is asymptomatic (32).



A. lumbricoides, fertile and infertile eggs with a *T. trichiura* egg in the middle.



A. lumbricoides and hookworm eggs.

Figure 4. Show microscopic images of other helminths looked for. *Source: WHO*.

Urine and faeces analyses

UriCult Trio is primarily used to look for *Escherichia coli* infection in urine. It consists of three types of agars. Almost all types of bacteria may grow on the first agar, the

CLED-agar. It may therefore be used to see how many types of colonies the urine contains and for determining the concentration of colony-forming units (CFU/ml). On the McConkey-agar only gram negative bacteria and a few enterococci may grow. The third agar is the *E. coli*-agar for detection of gram negative *E. coli* bacteria. In an asymptomatic person, the cut off limit for a significant infection with *E. coli* is 10^5 CFU/ml, and with symptoms the cut off is 10^4 CFU/ml.

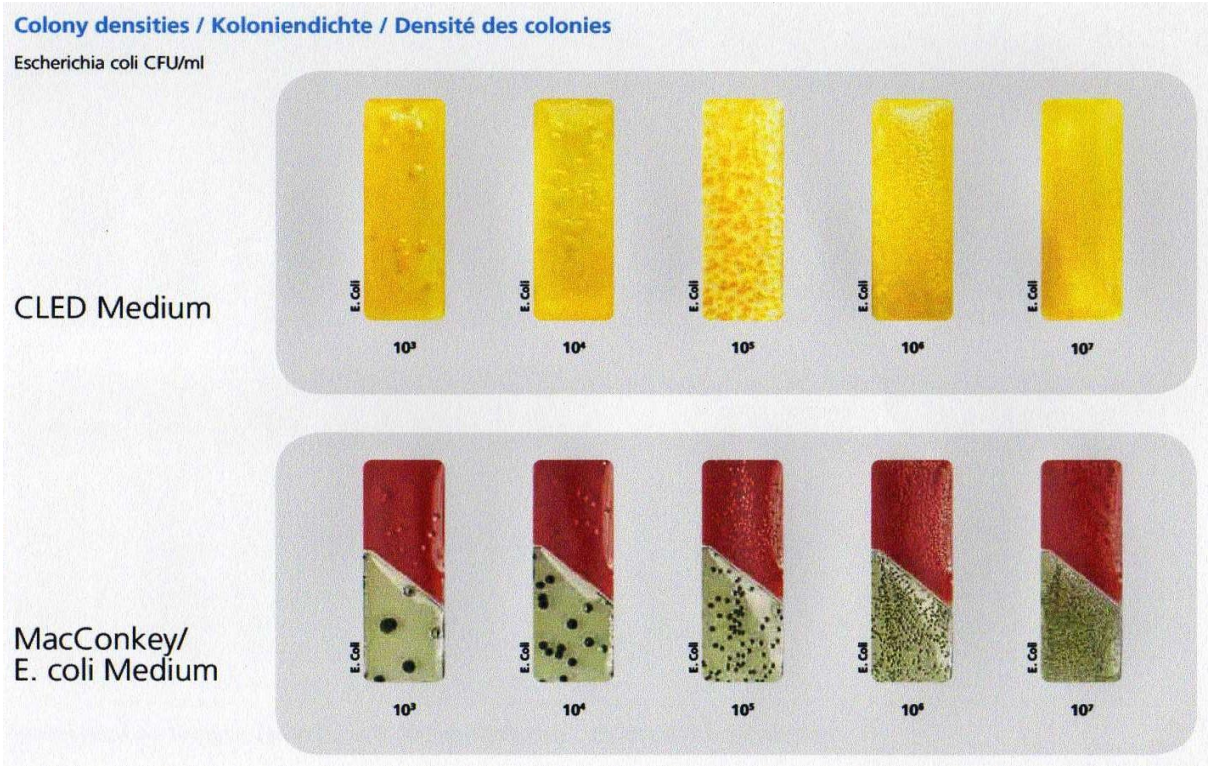


Figure 5. How to read the UriCult agars. *Source: Brochure from Orion Diagnostica.*

Ten ml of urine was placed in 15 ml test tubes with 1 ml of 2 % tincture merthiolate in 5 % formalin solution (ratio 10:1). The sample was then centrifuged at 4000x rpt for 5 minutes and then the supernatant was discarded and the pellet resuspended in small remaining droplets of supernatant. The wet smears were then microscoped for *S. haematobium* eggs and the amount of eggs was counted up to a 1000 eggs.

The stool samples were added drops of 5 % formalin solution before it was thoroughly mixed and stored at four degrees Celsius. Then the stool was prepared using the Kato-Katz technique and microscoped by two different technicians. The eggs looked for were from *Ascaris lumbricoides; Taenia solium, Trichuris trichiura, S. haematobium* and *S. mansoni*. Ova from hookworm species are only visible during the first 30-60 minutes after collection, while ova from the other species remain visible for months.

Body mass index

This score may be used in children from 2 to 20 years, but unlike measuring in adults the norms for BMI in children vary with age and sex and they follow a growth chart. Centres for Disease Control (CDC) have published BMI percentiles, and overweight is defined as BMI between the 85th and 95th percentile. A BMI over the 95th percentile is described as obesity (23).

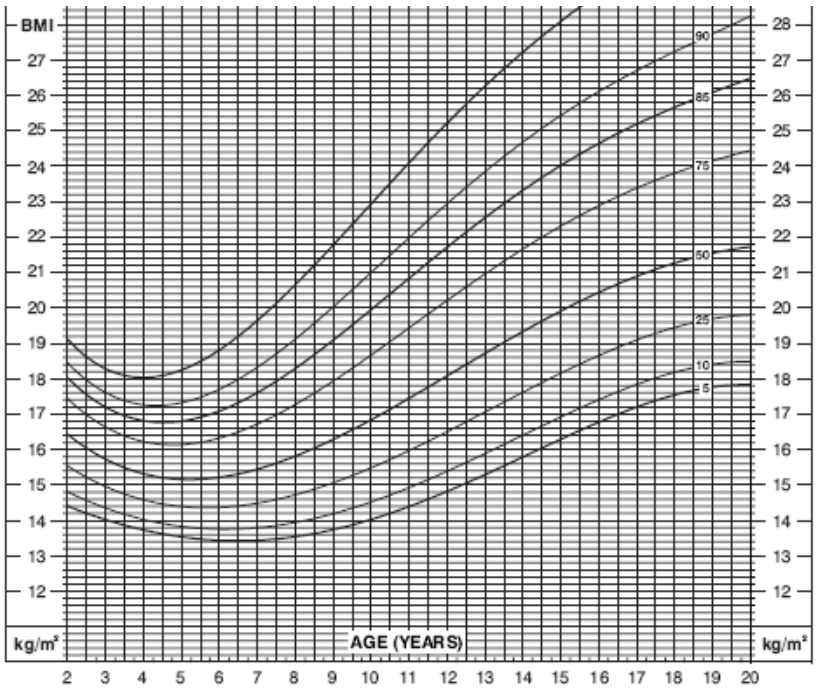


Figure 6. BMI table for children. *Source: www.cdc.gov/growthcharts.*