Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

Intestinal parasites

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Frequently found intestinal parasites

Protozoa

- *Giardia lamblia*
- *Entamoeba histolytica/dispar*
- *Cryptosporidium spp*
- *Cyclospora cayetanensis*
- *Dientamoeba fragilis*
- *Isospora belli*
- *Microsporidium* spp

- *Blastocystis hominis*
- *Endolimax nana*
- *Entamoeba hartmanni*
- *Entamoeba coli*
- *Enteromonas hominis*
- *Iodamoeba bütschlii*
- *Chilomastix mesnili*

Helminths

- *Ascaris lumbricoides*
- *Enterobius vermicularis*
- *Hymenolepis nana*
- *Hymenolepis diminuta*
- Hookworm
- *Schistosoma* spp
- *Strongyloides stercoralis*
- *Trichuris trichiura*
- *Taenia spp*
- *Fasciola hepatica*
- *Clonorchis sinensis*

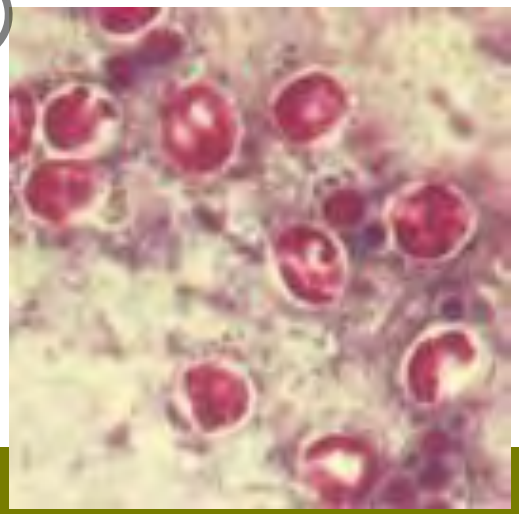
Frequently found intestinal parasites

Protozoa

- *Giardia lamblia*
- *Cryptosporidium spp*

Helminths

Schistosoma spp



Diagnostics intestinal protozoa

- Big differences between countries in methods
  - Microscopy, antigen detection or molecular detection
  - Trained technicians
  - Commercial kits (Ag detection) : some have poor quality – many false positives
  - Molecular detection: multiplex PCR

- QC schemes :
  - Some countries : not available
  - Some: available but expensive

- Are we able to pick up an outbreak?
  - Not only detection but also typing

Do you know what happens in your parasitology lab?

Methods?

Algoritm?

Age	Season	Duration of symptoms	Diagnostic request	GP patients The Netherlands
0-4 yr	Dec-May	1-3 d	→	Rota (52%); NLV (13%)
		4-7 d	→	Rota (22%); Adeno (22%); NLV, SLV, Crypto (7%)
		>7 d	→	NLV (18%); Rota, Adeno (7%)
	June-Nov	1-3 d	→	Rota (27%) ; NLV (13%); Camp., Adeno (7%)
		4-7 d	→	Salm (17%);Camp.(13%); Rota,Adeno, Crypto (4 %)
		>7 d	→	Giardia (9 %); Crypto, Adeno (6%)
>5 yr	Dec-May	1-3 d	→	Camp(16%)NLV(14%)Rota(7%)Astro (6%) Salm (4%)
		4-7 d	→	Camp.(18%);Rota, Crypto (5 %) ; Astro , Salm. (4%)
		>7 d	→	Camp., Giardia (4%)
	June-Nov	1-3 d	→	Camp. (21%); Salm. (7%)
		4-7 d	→	Camp. (20%); Giardia (5 %)
		>7 d	→	Giardia (10 %); Camp. (6%),

Algoritm depends on epidemiology in your country

Clinical presentation *Giardia lamblia*

Intermittend diarrhoea

- Flatulence
- Smelly diarrhoea
- Sticky
  - A toilet brush is needed!
- Bloating
- Fatigue

Therapy: possible but not always necessary

Resistance against metrinodazol: increasing?

See ESCMID library: presentation Hanevik
www.escmid.com

Clinical presentation *Giardia*:

- Can become chronic
- Malabsorption of fat and fat-soluble vitamins.
  - Frequency?
- Mucosal damage and villous atrophy
  - Frequency?
- Failure to thrive in young children
  - Frequency?
- Extra intestinal symptoms
  - Arthritis
  - Urticaria
  - Eosinophilia

Giardia outbreak Bergen 2004

Hanevik K, Wensaas KA, Rortveit G, Eide GE, Mørch K, Langeland N.

Irritable bowel syndrome and chronic fatigue 6 years after giardia infection: a controlled prospective cohort study.

Clin Infect Dis. 2014 Nov 15;59(10):1394-400. doi: 10.1093/cid/ciu629. Epub 2014 Aug 12.

PMID: 25115874 Free PMC Article

Table 1. Description of the Cohorts Available for Analyses of Irritable Bowel Syndrome and Chronic Fatigue 3 and 6 Years After the 2004 *Giardia* Outbreak in Norway

Cohort	Exposed[a]	Controls[b]	Total No.
Target population 2007 [19]	1252 (100.0)	2504 (100.0)	3756
Study population 2007	817 (65.3)	859 (34.3)	1676
Lost to follow-up[c]	13 (1.0)	60 (2.4)	73
Target population 2010	1239 (100.0)	2444 (100.0)	3683
Questionnaires returned 2010	748 (60.4)	888 (36.3)	1638
Giardia during outbreak		7 (0.3)	
Incomplete/ambiguous response		3 (0.1)	
Study population in 2010	748 (60.4)	878 (35.9)	1626
Responded in 2007 and in 2010	601 (48.5)	559 (22.9)	1160

Data are presented as No. (%).

[a] *Giardia* exposed.

[b] Age- and sex-matched individuals from the general population in Bergen, Norway.

[c] Emigrated or died between 2007 and 2010, or address not found in 2010.

Chronic Fatigue and persisting IBS

CF

251 exposed individuals with CF in 2007

146 (58.2%) still had CF in 2010

16 of 58 (27.6%) of controls.

RR Giardia exposure - persisting CF : 2.13 [95% CI,1.55−2.64]

RR Increasing age - risk for CF (ref 20−39 years) age group :

40−59 years 1.43 (95% CI, 1.14−1.69)

60−97 years 1.57 (95% CI, 1.12−1.91)

262 exposed with IBS in 2007,

164 (63.1%) still reported IBS in 2010.

25 of 64 (39.1%) controls with

Giardia exposure was significantly associated with persisting IBS in 2010 (RR, 1.64 [95% CI, 1.29−1.95]), whereas age and sex were not.

Bruijnesteijn van Coppenraet LE ea
Case-control comparison of bacterial and protozoan microorganisms associated with gastroenteritis: application of molecular detection.
Clin Microbiol Infect. 2015 Jun;21(6):. 7 592.e9-592.e19. Epub 2015

TABLE 4. Positivity for all target organisms by age category

	Case								Control								p (case vs. control)*			
	<5 (n = 152)		5–20 (n = 313)		21–50 (n = 557)		>50 (n = 493)		<5 (n = 104)		5–20 (n = 208)		21–50 (n = 445)		>50 (n = 428)					
Organism	No. positive	%	No. positive	%	No. positive	%	No. positive	%	No. positive	%	No. positive	%	No. positive	%	No. positive	%	<5	5–20	21–50	>50
Giardia lamblia	14	9.2	24	7.7	24	4.3	23	4.7	4	3.8	15	7.2	10	2.2	4	0.9	0.135	1.000	0.081	0.001
Cryptosporidium parvum/hominis	12	7.9	9	2.9	21	3.8	4	0.8	5	4.8	2	1.0	2	0.4	1	0.2	0.446	0.213	0.000	0.380

Age difference detection *Giardia* in controls ;
5-20 yr old cases: 7.7 %; controls 7.2 %
>50 yrs cases 4.7 %; only 0.9% in controls

Clinical presentation *Cryptosporidium*:

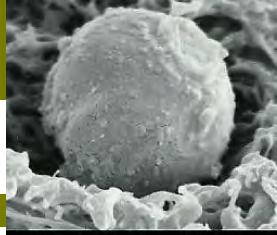

Cryptosporidium Oocyst

Non-immunocompromised individuals:

- Self-limiting diarrhea (watery)
- Vomiting
- Nausea, decreased appetite, weight loss, flatulence
- Abdominal pain and cramps.
- Recurrent gastrointestinal symptoms (30 -40 % of cases).
- Malabsorption: frequency?

Therapy: not required

Clinical presentation *Cryptosporidium*


Cryptosporidium Oocyst

Immunocompromised individuals:

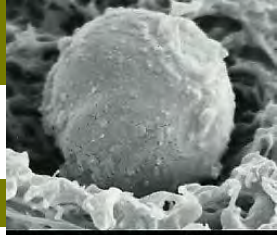
CD4 Tcell-count <200 mm3

- persistent diarrheal infection >30 days
- severe illness.

Therapy: The most effective therapy in patients with AIDS is highly active antiretroviral treatment (HAART) of HIV.

Role nitazoxanide : very debatable

Clinical presentation & genotyping


Cryptosporidium Oocyst

- Sporadic cases :
  - 35 % at least one nongastro-intestinal symptom
    - joint pain, eye pain, recurrent headaches, dizzy spells, and fatigue
    - 14.5% two or more
  - different clinical symptoms *C. hominis* and *C. parvum*.
    - *C. hominis* infections more non-gastro symptoms: 44.3% and 27.9%
    - *C. parvum* infections 28.0% and 4.0%;
    - controls 15.1 and 5.2 % .
  - Duration of symptoms shorter in *C.parvum*
  - Age difference Adults > children.

Hunter P.et all: Clinical Infectious Diseases 2004; 39:504–10

Increase Cryptosporidium 2012

RAPID COMMUNICATIONS

Simultaneous increase of *Cryptosporidium* infections in the Netherlands, the United Kingdom and Germany in late summer season, 2012

N Fournet[1,2,3], M P Deege[3,4,5], A T Urbanus[1], G Nichols[6], B M Rosner[7], R M Chalmers[8], R Gorton[9], K G Pollock[10], J W B van der Giessen[1], P C Wever[11], J W Dorigo-Zetsma[12], B Mulder[13], T G Mank[14], I Overdevest[15], J G Kusters[5], W van Pelt[1], L M Kortbeek (Titia.Kortbeek@rivm.nl)[1]

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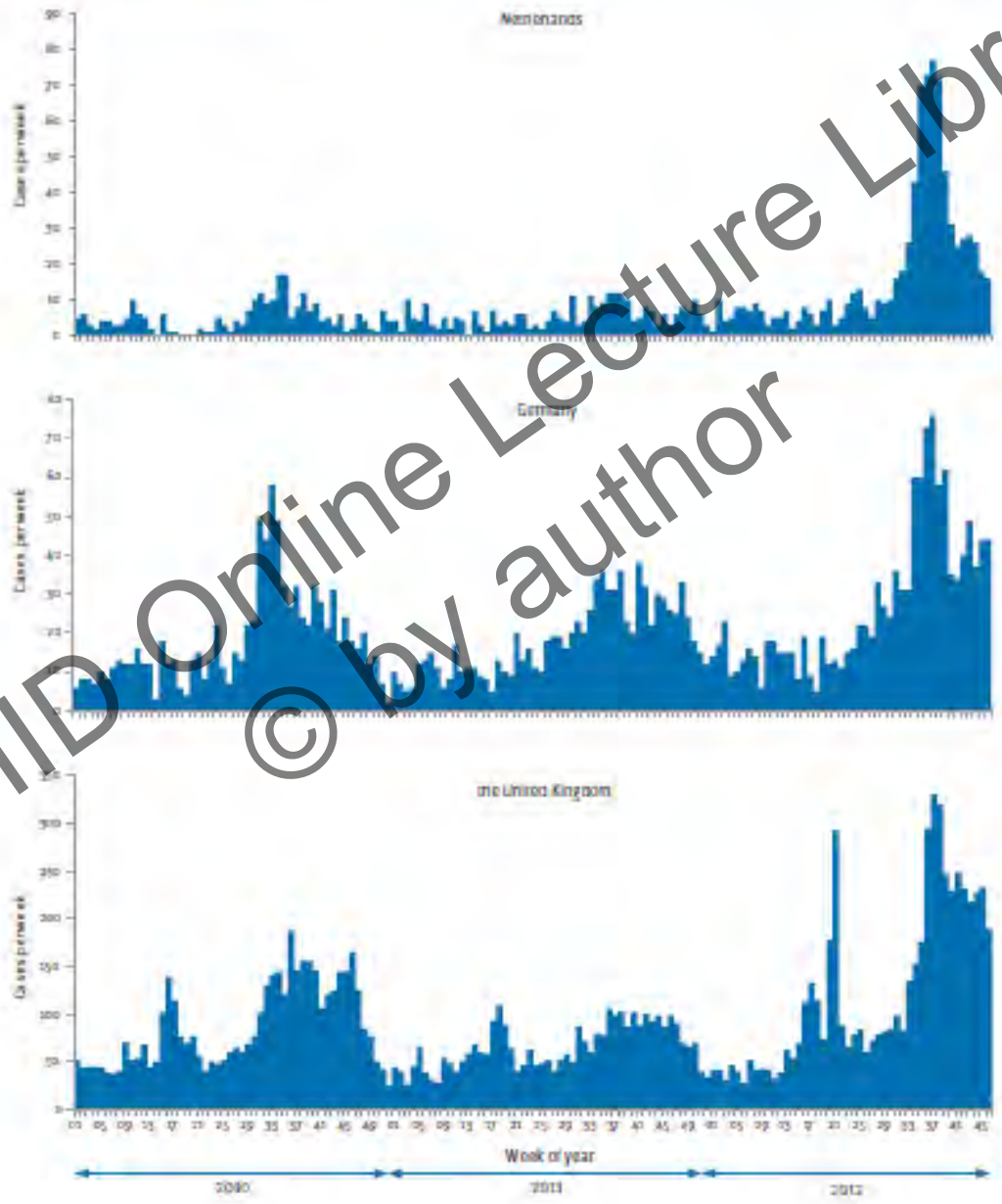
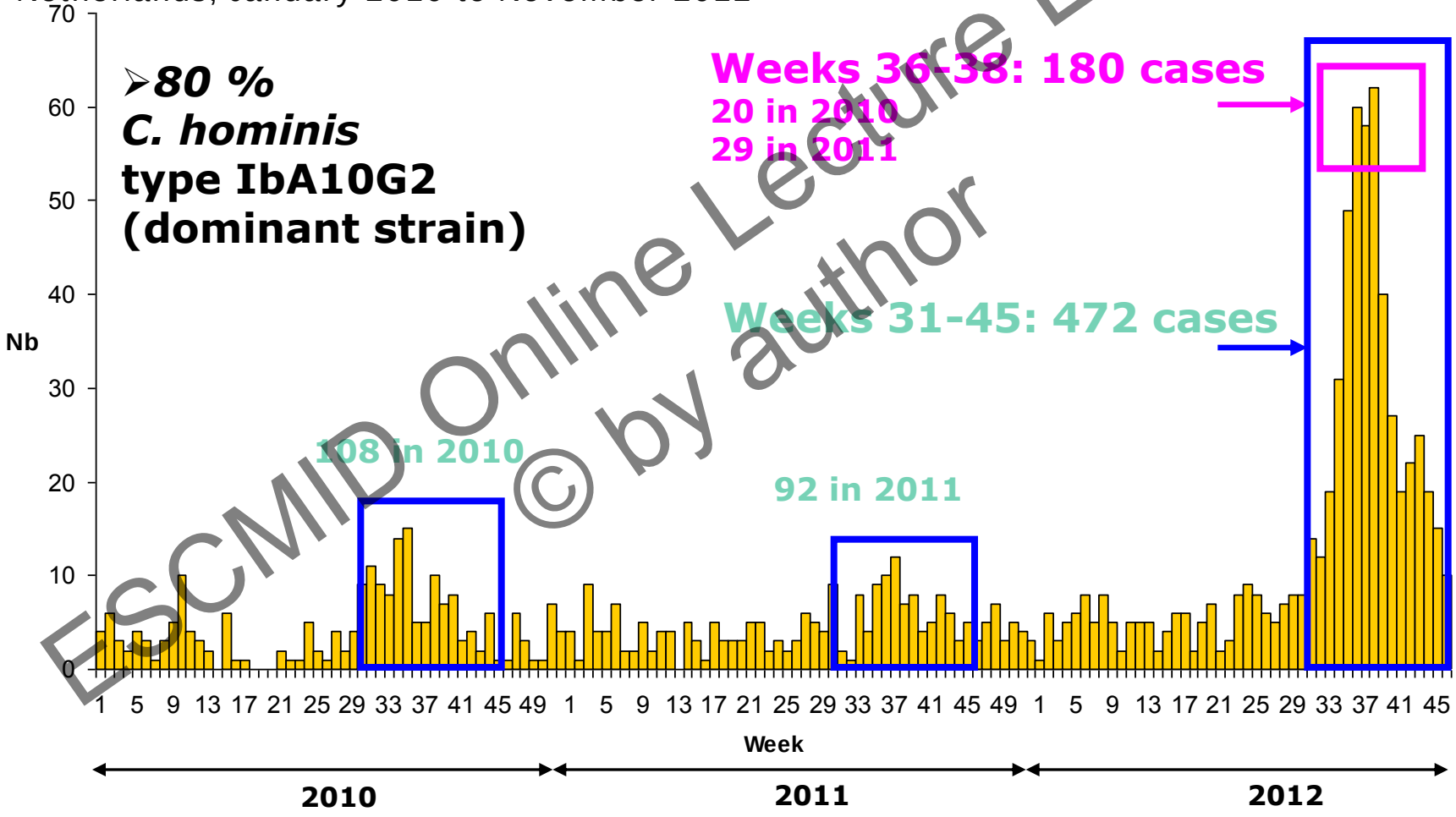
Euro Surveill. 2013;18(2):pii=20348. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20348

FIGURE

Cryptosporidium cases reported from eight laboratories in the Netherlands and cases notified in Germany and the United Kingdom, January 2010–November 2012



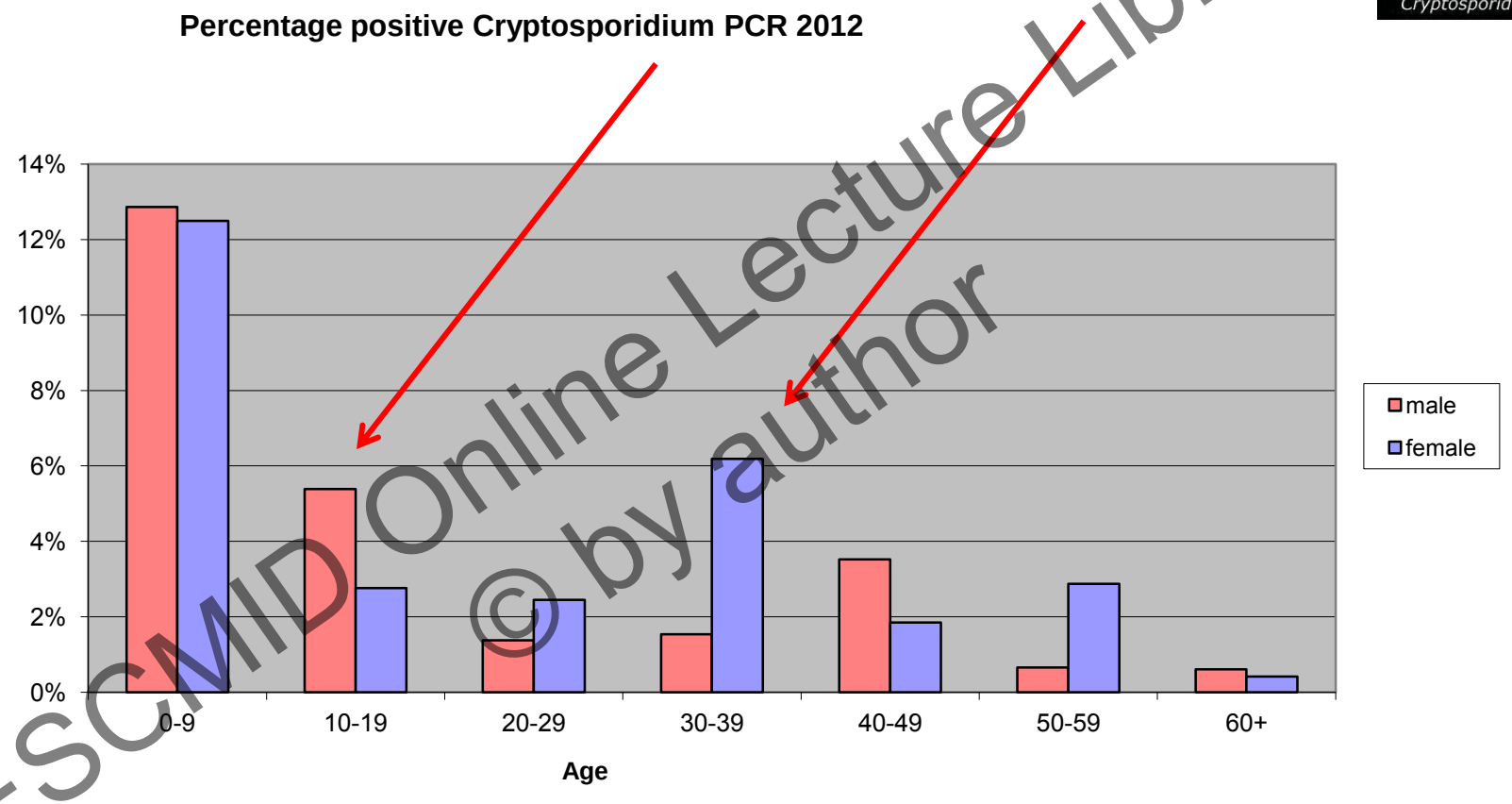
Number of *Cryptosporidium* positive faecal samples by week of confirmation in 4 laboratories*, Netherlands, January 2010 to November 2012



*CBSL (Hilversum), Haarlem, Saltro (Utrecht) and Labmicta (Enschede)

Increase Cryptosporidium 2012


Cryptosporidium Oocyst



- Significantly more women 20-39 yr
- More boys 10-20 years

Are the mothers infected by their children? Or vice cersa?

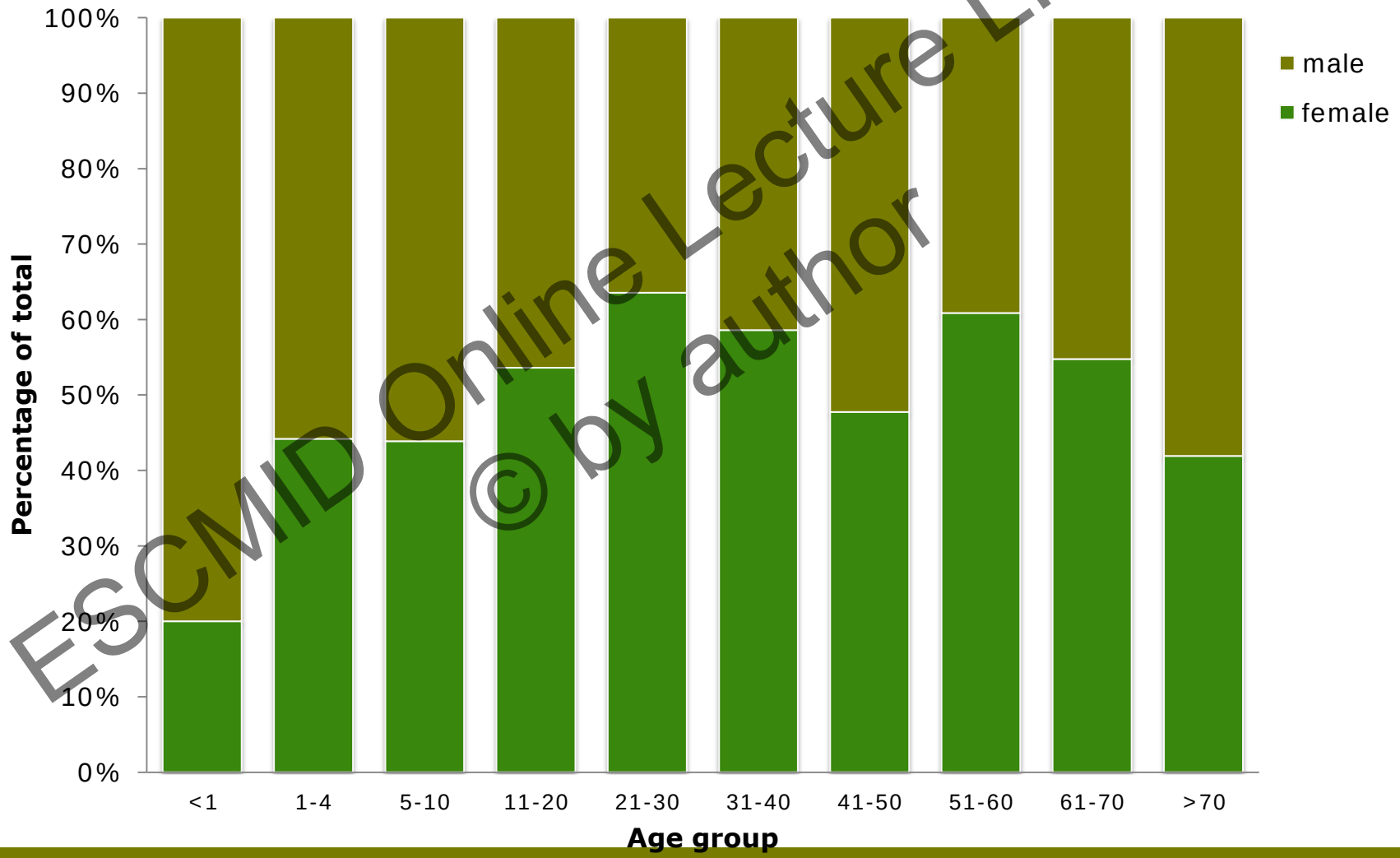
Cryptosporidium in GP patients in the Netherlands
Crypto study april 2013-2015

- Patients visiting GP; diagnostic request by GP
- Positive results (Cryptosporidium positive): questinonnaire send to patient
- Age and sex matched controls

In total: 1008 positive cases

- 513 Female
- 495 Male

Cryptosporidium in GP patients in the Netherlands
Crypto study 2013-2015

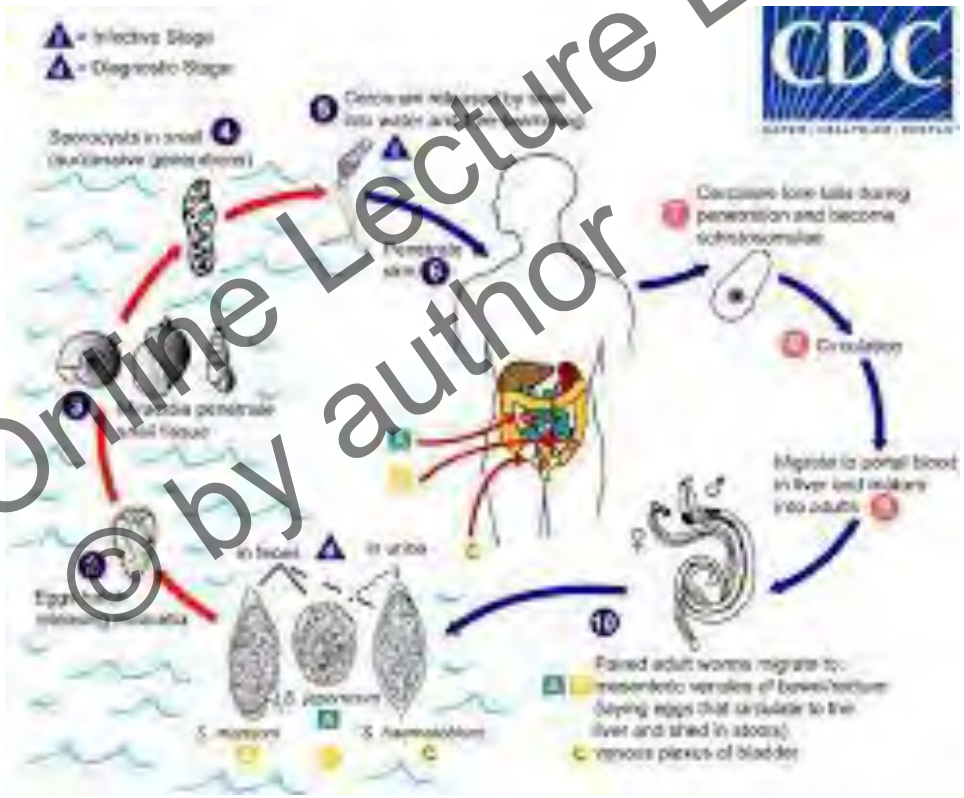


- Overall there is no indication for different risks for sex
- Differs per age group
- We also see cases in elderly

- Transmission within families ? difficult to tell
  - GPs are hesitant to send in samples for testing; only for YOPIs
  - (Young,Old,Pregnant,Immunocompromised)
  - changes in finances : insurance company only pays after patients pay first 250 euro (or more)

- Transmission within family study (G&G study): not enough cases of Cryptosporidium to tell.
- After 3 years: also more information about extra-intestinal sequela

Schistosoma



Schistosoma

- affects almost 240 million people worldwide,
- 700 million at risk: tropical and sub-tropical areas
- Poverty ; without potable water and adequate sanitation.

Transmission : via contaminated water with snails

- skin contact with infested fresh water.
- The adult worms lays eggs – partly they are trapped in organs;
  - some eggs are excreted.
  - adult worms live in the blood vessels
    - bladder or intestines.

Treatment with praziquantel

Schistosoma

	Species	Geographical distribution
Intestinal schistosomiasis	*Schistosoma mansoni*	Africa, the Middle East, the Caribbean, Brazil, Venezuela, Suriname
	Schistosoma japonicum	China, Indonesia, the Philippines
	Schistosoma mekongi	Several districts of Cambodia and the Lao People's Democratic Republic
	Schistosoma guineensis and related *S. intercalatum*	Rain forest areas of central Africa
Urogenital schistosomiasis	*Schistosoma haematobium*	Africa, the Middle East

pathology schistosomiasis

Morbidity	S. mansoni/S. japonicum	S. haematobium
General	Acute schistosomiasis	Acute schistosomiasis
	Anaemia	Anaemia
Organ specific pathology	Hepatomegaly	Vesicular wall hardening
	Splenomegaly	Bladder cancer
	Ectopic egg granulomas	Ectopic egg granulomas
	Altrenative venous circulation	Kidney malfunction
	Genital schistosomiasis	**Genital schistosomiasis**
Developmental impairment	Cognitive dysfunction	Cognitive dysfunction
	Delayed growth/stunting	Delayed growth/stunting

Symptoms

- Haematuria

- In women Female genital schistosomiasis (FGS).

  - lesions of the cervix and vagina,
  - vaginal bleeding,
  - pain during sexual intercourse and nodules in the vulva.

  - a risk factor HIV transmission to women.

- Genital schistosomiasis also affects men, inducing pathology of the seminal vesicles, prostate and other organs.
- Long-term irreversible consequences, including infertility.

Symptoms

- Bladder and ureteral fibrosis and hydronephrosis are common findings in advanced cases, and bladder cancer is also a possible late-stage complication.

- Intestinal schistosomiasis
  - nonspecific clinical picture
  - abdominal pain,
  - diarrhoea,
  - blood in the stool.

Advances cases:

  - Liver enlargement
  - ascites a
  - other signs of increased portal pressure. In such cases there may also be splenomegaly.

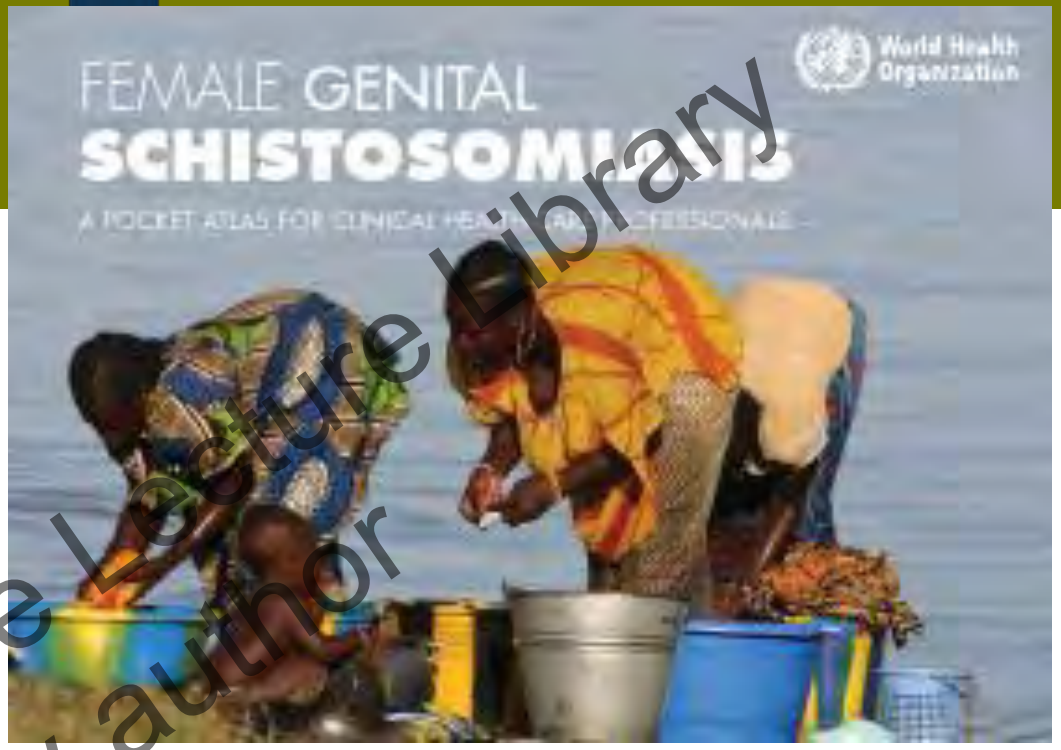
FGS

- common complication of schistosomiasis (bilharziasis, a worm infection)
- can be present without urinary schistosomiasis.

- FGS may be the most common gynaecological condition in schistosomiasis-endemic areas.
- FGS remains undiagnosed in most cases.

- FGS is associated with a risk of HIV and human papillomavirus infections.

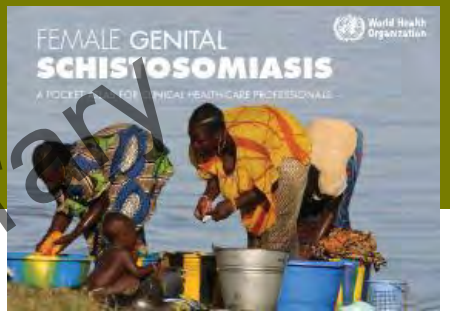
Pocket manual



- *Female Genital Schistosomiasis Pocket Atlas*

http://apps.who.int/iris/bitstream/10665/180863/1/9789241509299_eng.pdf

Symptoms FGS



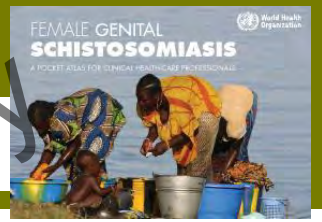
- Vaginal discharge
- Bloody discharge
- Bleeding after intercourse or spotting
- Genital itching or burning sensation
- Pelvic pain or pain during or after intercourse

Girls may present with some of the above symptoms.

Some patients may also have bloody urine.

http://apps.who.int/iris/bitstream/10665/180863/1/9789241509299_eng.pdf

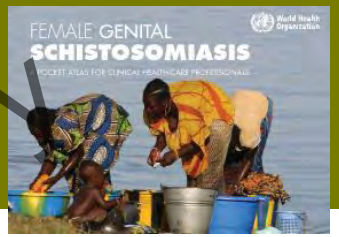
Complications



- Bleeding during examination (contact bleeding)
- Infertility
- Abortion or ectopic pregnancy
- Involuntary urination when coughing, laughing or jumping, etc.
- Genital ulcers
- Tumours or swelling (vulva, vagina, cervix)

Other complications of schistosomiasis include anaemia, stunted growth, abdominal cramps,learning difficulties and school absenteeism.

Diagnosis FGS

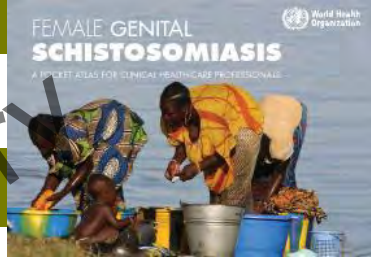


- Visual inspection of characteristic lesions on the cervix and vaginal wall. Visualization can be improved by using a digital camera or a colposcope.

- Lesions:
  - Grainy sandy patches
  - Homologenous yellow sandy patches
  - Abnormal blood vessels
  - Rubbery papules

Current laboratory techniques are inadequate for diagnosing FGS.

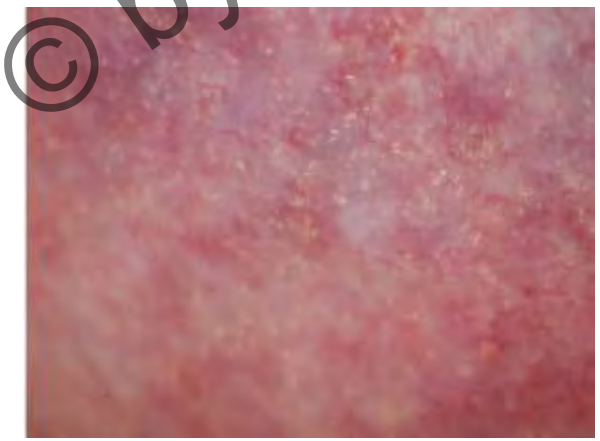
Pocket manual :



Normal cervix

SCHEMATIC OF LESIONS WITH REAL-LIFE EXAMPLE

Grainy sandy patches. Widespread abnormal blood vessels. The discharge shown is candidiasis



Grainy sandy patches

Diagnosis FGS

Recent publications :

Sigve Dhondup Holmen et all

Am. J. Trop. Med. Hyg., 93(1), 2015, pp. 80–86

The First Step Toward Diagnosing Female Genital Schistosomiasis by Computer Image Analysis

Bodo Sahondra Randrianasolo ea

JID 2015:212 (15 July)

Gynecological Manifestations, Histopathological Findings, and Schistosoma-Specific Polymerase Chain Reaction Results Among Women With Schistosoma haematobium Infection: A Crosssectional Study in Madagascar

Treatment

The WHO-recommended treatment for schistosomiasis is:

- **PRAZIQUANTEL 40 MG/KG AS A SINGLE DOSE**

- Treatment kills the adult worms and prevents the development of new lesions. Treatment can improve reproductive health and diminish some FGS symptoms.

- one FGS case = more cases

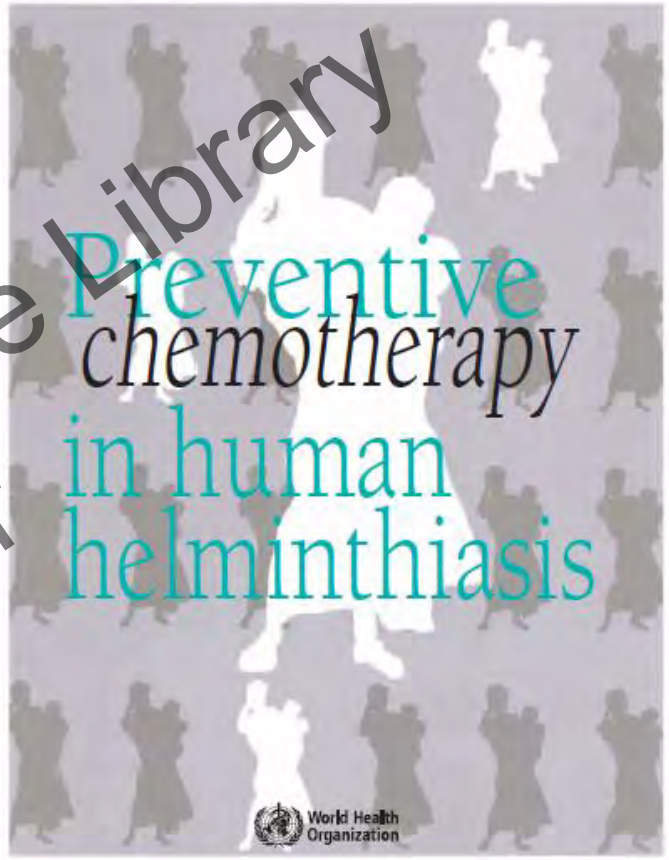
- Early detection in children can preventg chronic disease schistosomiasis.

- mass drug administration programmes in endemic aereas

- Http://www.who.int/schistosomiasis/en/

- WHO coordinated strategy
  Preventive chemotherapy in human helminthiasis

  This manual and its dose-poles provide health professionals and programmes managers with the latest recommendations.
  Ref: ISBN 92 4 154710 3



Conclusion

- Research often does not present detailed sex-disaggregated data
  - Wrong both from a biological and gender perspective

- Dynamics of the social relationship and interactions with other critical social, cultural and environmental determinants of health

- Intestinal protozoa are important for all age groups and not only for children

- Genital schistosomiasis should be considered in endemic aeras

Thanks to

National institute Public Health

- Laura Nic Lochlainn (EPIET)
- Barbara Schimmer
- Wilfrid van Pelt
- Jeroen Roelfsema

- Lisette van Lieshout Leiden University Hospital
- Theo Mank Regional Lab Haarlem

Medical Microbiology Laboratories in the Netherlands

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

ESGCP

ESCMID STUDY GROUP FOR CLINICAL PARASITOLOGY

European Society of Clinical Microbiology and Infectious Diseases

You can **join ESGCP** Chairperson: Titia Kortbeek
Criteria: membership ESCMID (58 euro/year; incl CMI);

www.escmid.org/research_projects/study_groups/