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ORIGINAL ARTICLE

Detection of *Enterobius vermicularis* in greater Berlin, 2007–2017: seasonality and increased frequency of detection

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Abstract

The pinworm (*Enterobius vermicularis*) causes mostly mild infections characterised by nocturnal anal pruritus, mainly in children. Still, the infection is stigmatising and sleep disturbances may lead to lack of concentration. For Germany, no epidemiological data are available. Laboratory data of all patients for whom detection of *E. vermicularis* by cellulose tape test had been requested between 2007 and November 2017 were analysed retrospectively. *E. vermicularis* was detected in 971/5578 (17.4%) samples collected from 3991 patients. The detection rate increased significantly within the period of investigation. It was higher in male than in female patients (20.0 vs. 15.4%). Children 4 to 10 years old and, if also examined, their relatives were most frequently affected. Control investigations at an interval of at least 1 month, which could indicate insufficient therapy or re-infection, were performed in 90/714 patients (12.6%). While parasite detection in children < 6 years was evenly distributed throughout the year, in older patients, it peaked between October and December. In conclusion, in the area of investigation, the frequency of *E. vermicularis* is higher in males than in females and is subject to a hitherto undescribed seasonality. The causes of the increased frequency of parasite detection warrant further investigations.

Keywords *Enterobius vermicularis* · Cellulose tape test · Epidemiology · Seasonality · Enterobiasis

Introduction

The nematode, *Enterobius vermicularis* (pinworm), shows a worldwide distribution due to its direct transmission without intermediate hosts [1]. Transmission occurs by ingestion of fertile eggs. In the intestine, larvae hatch and adult worms develop following moulting. In contrast to other intestinal nematodes, e.g., *Ascaris lumbricoides* or hookworm, pinworm larvae and adults usually do not transmigrate through the intestinal wall. Following mating, the female pinworms, which measure around 1 cm, migrate at night to the perianal area where they attach their eggs to the skin, and within only a few hours, the eggs contain infectious larvae. This causes perianal pruritus and the patients contaminate their fingers with eggs by scratching. These eggs may cause autoinfections, and finger sucking is a known risk factor for infections and relapses [2]. The eggs also may be passed to other humans or the environment. Further risk factors for the transmission of *E. vermicularis* in children, although with various relevance in different age groups, comprise leaving hands unwashed after closet use or before dinner, sucking toys or biting pencils as well as playing on the ground [3–5].

Due to the peculiar perianal deposition of the eggs, enterobiasis is diagnosed by the cellulose tape test [6]. The sensitivity of the method of detection rises with the number of specimens examined; four tosix specimens collected at various days are necessary to exclude the infection. Analysis of stool specimens is not recommended for the diagnosis of enterobiasis because of its low sensitivity (5–15%) [1].

The infection is treated with mebendazole, in pregnant women and young children with pyrvinium embonate. In order to also cover worms that may have developed after cessation of therapy, repeat treatments are recommended. Drug resistance of the parasites has not been reported.

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Thus, detection of eggs following treatment is due to either insufficient therapy or re-infection.

The cause of the infection usually is mild and asymptomatic in around one-third of the patients. Still, the nocturnal pruritus may cause sleep disturbances followed by difficulties in concentration on the following day. Rare complications may occur by the invasion of the parasite, e.g., in vagina and cervix, fallopian tubes, ovaries or the peritoneal cavity [1]. *E. vermicularis* also was detected in 7% of paediatric patients with appendicitis [7], although the uncomplicated infection is not associated with abdominal pain [8]. In addition, there may be mental stress as helminth infection may stigmatise [9].

Enterobiasis is among the most frequent parasitoses worldwide and not associated with socioeconomic or cultural peculiarities [1]. Tomaso et al. [10] detected *E. vermicularis* in 167 (0.12%) of 142,426 samples (e.g., stool, worms/worm segments, tape tests, urine) collected between 1990 and 2000 in the Tyrol, i.e., the parasite was present in almost every second helminth-positive sample. In 1997, 11.4% of 9.597 tape tests from 35 US states were positive [11].

Since for Germany, only a small epidemiological study on enterobiasis in children and nursery school teachers has been published [12], the present study aimed at collecting first epidemiological data for all age groups over a larger period of time.

Materials and methods

Patients' data All data regarding detection of *E. vermicularis* by tape test between January 2007 and November 2017 were extracted from the laboratory information system. Stool samples with incidental detection of *E. vermicularis* eggs were excluded. In total, 5578 of 5941 data sets retrieved (belonging to 3991 patients) were included in the study; the remaining 363 data sets were excluded for incompleteness. Family members were defined by identical surnames and addresses.

Detection of *E. vermicularis* Perianal tape tests were performed in the morning by the patients or their parents/legal guardians. Slides with tapes were sent in mailing tubes to the laboratory where they were analysed microscopically (magnification, × 100–400), and results were entered in the laboratory information system.

Statistical analyses Data were analysed by GraphPad Prism Version 6.0a for Mac OS X and 95% confidence intervals (95% CI) calculated. Statistical significance was determined by Fisher's exact test, and P values < 0.05 were considered significant.

Results

E. vermicularis was detected in 971 of 5578 samples (17.4%; 95% CI, 16.4–18.4%); while adult worms were detected in only nine samples, the characteristic eggs were seen in the remaining 962 samples. Positive test results were more frequent in male than female patients (20.0%; 95% CI, 18.5–21.6% vs. 15.4%; 95% CI, 14.2–16.7%; $P < 0.0001$). The majority of positive patients were children of 4 to 10 years (68.3% 95% CI, 65.3–71.1%; Fig. 1); the median age of all patients with positive test result was 7 years (range, < 1 to 75 years). A similar age pattern was seen when only the age at time of the first positive result was considered excluding following positive results (data not shown). Family members, if also examined, were infected frequently (Table 1). When only fathers or mothers were examined, there was a weak trend towards more frequent parasite detection in mothers ($P = 0.145$; Table 1). The bimodal age pattern (Fig. 1) identifies the two populations at risk of acquiring enterobiasis, i.e., children and their parents.

Since re-infections or insufficient treatment of infections may lead to repeat detection of the parasites, we next analysed the data regarding positive single patients ($n = 714$) and repeat parasite detection within a period of > 1 month. The life cycle of *E. vermicularis* lasts 2 to 4 weeks, and it takes 4 to 6 weeks before eggs may be detected [13]. Only one positive test results was recorded for the vast majority of patients (526; 73.8%; 95% CI, 70.4–76.9%). In 75 patients (10.5%; 95% CI, 8.4–13.0%), *E. vermicularis* was detected twice within ≥ 1 month, and only in 15 patients (2.1%; 95% CI, 1.3–3.5%), the parasite was detected three times or more often within ≥ 1 month. In the remaining 98 patients (13.7%; 95% CI, 11.4–16.5%), repeat parasite detection occurred within less than 1 month.

Comparing the boroughs of Berlin, the frequency of positive test results was 7.4 to 20.6% without major differences between former Western and Eastern boroughs. There was a trend towards more frequent parasite detection in patients with statutory health insurance than in patients with private health insurance (778/4357; 17.9%; 95% CI, 16.8–19.0% vs. 193/1221; 15.8%, 95% CI, 13.9–18.0%; $P = 0.096$). This trend was not discernible, however, when the data were analysed regarding single patients independently of the number of samples submitted (private insurance, 14.1%; 95% CI, 12.0–16.4%; statutory insurance, 15.5%; 95% CI, 14.3–16.7%; $P = 0.291$).

Since absolute numbers of positive samples increased over time within the period of investigation (2007: 32; 2010: 47; 2013: 106; 2016: 159 positive samples), we next determined the frequency of positive test results for the years 2007 to 2016 in initial examinations excluding

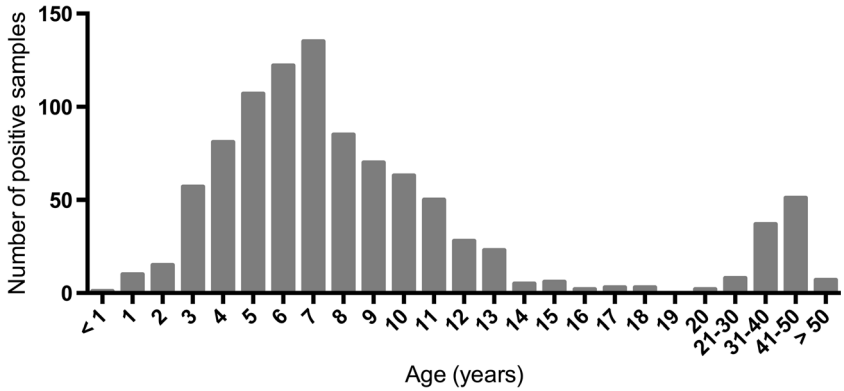

Fig. 1 Age distribution of individuals tested positive between January 2007 and November 2017

the data of possible follow-up examinations ($n = 3442$). Here, positive test results were significantly more frequent in 2012–2016 (19.3%; 95% CI, 17.7–21.0%) than in 2007–2011 (12.9%, 95% CI, 11.2–14.8%; $P < 0.0001$; Fig. 2). To exclude the possible impact of fluctuations within the group of physicians submitting samples, we repeated this analysis for only those physicians who had submitted at least one sample in either one of the two 5-year periods ($n = 88$), and observed a similar increase in test positivity (2007–2011, 12.9%, 95% CI, 11.1–14.9%; 2012–2016, 19.0%, 95% CI, 17.2–21.1% $P < 0.0001$; Fig. 2). In fact, also the numbers of samples increased similarly (2007–2011, 1198 samples; 2012–2016, 1544 samples), and the frequency of positive results almost doubled (2007, 12.7%; 2016, 23.6%).

Finally, we analysed the annual distribution of parasite detection. Here, we detected considerable differences between the various age groups, i.e., highest frequencies of positive test results were observed in October to December in individuals ≥ 6 years whereas the frequency of positive results did not vary considerably in individuals < 6 years (Fig. 3a). When we analysed these data regarding sex, this seasonality was present in female patients ≥ 6 years (IV vs. I, $P = 0.0009$; IV vs. II, $P = 0.0001$; IV vs. III, $P = 0.0026$; Fig. 3b). In male patients ≥ 6 years, there was no significant difference between the second and fourth quarter of the year ($P = 0.1620$), but more frequent parasite detection was observed in the fourth than in the first ($P = 0.0224$) or third quarter ($P = 0.0075$).

Table 1 Infection status of co-examined family members

Degree of relationship	Infected	Uninfected	Infected/ uninfected
1 Brother/sister	43	81	0.53
> 1 Brother/sister	16*	19	0.84
Mother	15	15	1
Father	2	8	0.25
Mother and father	2	9	0.22

*At least one brother/sister infected

Discussion

Enterobiasis apparently was no seldom event within the period of investigation, and the relatively low number of individuals tested positive after more than 1 month indicates a sufficient therapy for the vast majority of patients.

In Estonia, 24.4% of 954 nursery school children tested were positive, and also boys more often infected than girls [3]. In Myanmar, the prevalence in 761 school children 5–7 years of age was even 47.2% [14]. In contrast, only 1.1% of 353,106 children 1–7 years of age examined were cellulose tape positive in 2013/2014 in Bulgaria where annually more than 90% of all children in childcare facilities were examined [15]. The prevalence of enterobiasis in this age group was higher than that in the total population (0.81%); in the latter, however, it was still around double as high as the prevalence of *Giardia duodenalis* (0.34%). A representative nationwide survey performed in 2004 in Korea revealed an average prevalence of 0.6% in both rural and urban areas, again detecting the highest prevalence (2.8%) in children of 0–9 years [16].

Interestingly, while single patients with statutory and those with private health insurance did not differ regarding the frequency of positive results, there was a trend towards a higher frequency of detection in patients with statutory insurance when considering all results. This can only be explained by more tests performed, and thereby also more tests with negative results in patients with private insurance. Still, this observation does not permit conclusions regarding over- or undersupply in those patients.

We cannot easily explain the increased frequency of detection over time. We can, however, exclude a possible increased sensitivity through changes within the laboratory, e.g., staff- or instrument-based changes. The increase also in those physicians who had requested examinations

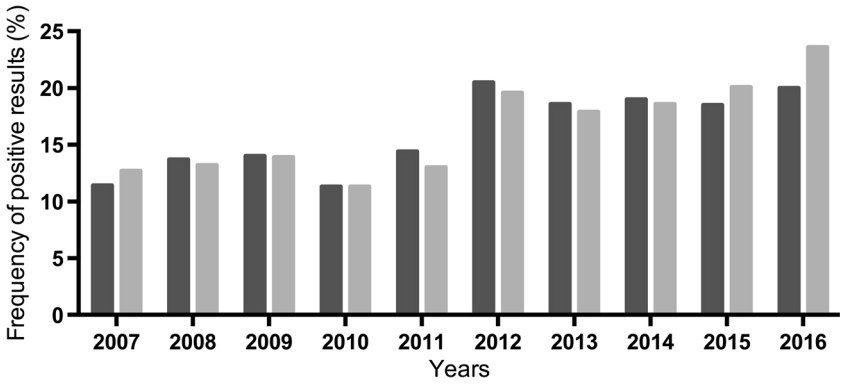

Fig. 2 Frequency of positive test results from 2007 to 2016. Data for all initial examinations ($n = 3442$; dark grey bars) as well as for initial examinations requested by physicians who had submitted at least one sample in 2007–2011 as well as in 2012–2016 ($n = 2742$; light grey bars)

in the entire period of investigation together with an increased number of tests requested by them may indicate a real increase of infection and simultaneously an improved sampling by the parents. Future studies should address this aspect.

Our observations regarding a seasonality of the disease are highly interesting. Previously, a seasonality of enterobiasis has only been described for Jordan, also with a peak of infections in October [17]. Nevertheless, socioeconomic and climate differences between the two countries together with detection of *E. vermicularis* in stool samples in that study question the comparability of the data. A seasonality has been observed before for other parasitoses in Germany, i.e., cryptosporidia and head lice, but not for *G. duodenalis* [18, 19]. Whereas the increased detection of cryptosporidia in the second half of the year could possibly be explained by travelling and altered spare time activities in the summer, e.g., swimming in lakes, the increased detection of head lice and also *E. vermicularis*, which both are transmitted by direct contact, in autumn could be due to the concentration of the population at risk following summer vacation. In fact, numbers of children in kindergartens has been identified as one environmental risk factor associated with transmission of *E. vermicularis* in Korea [20]. Further studies addressing this aspect with the aim of establishing control measures are warranted. These could include increasing of parents' knowledge as well as providing health care education on the disease to schoolchildren [21, 22]. For instance, China could decrease the prevalence of enterobiasis from 12.75% in 2003 to 5.13% in 2013 by

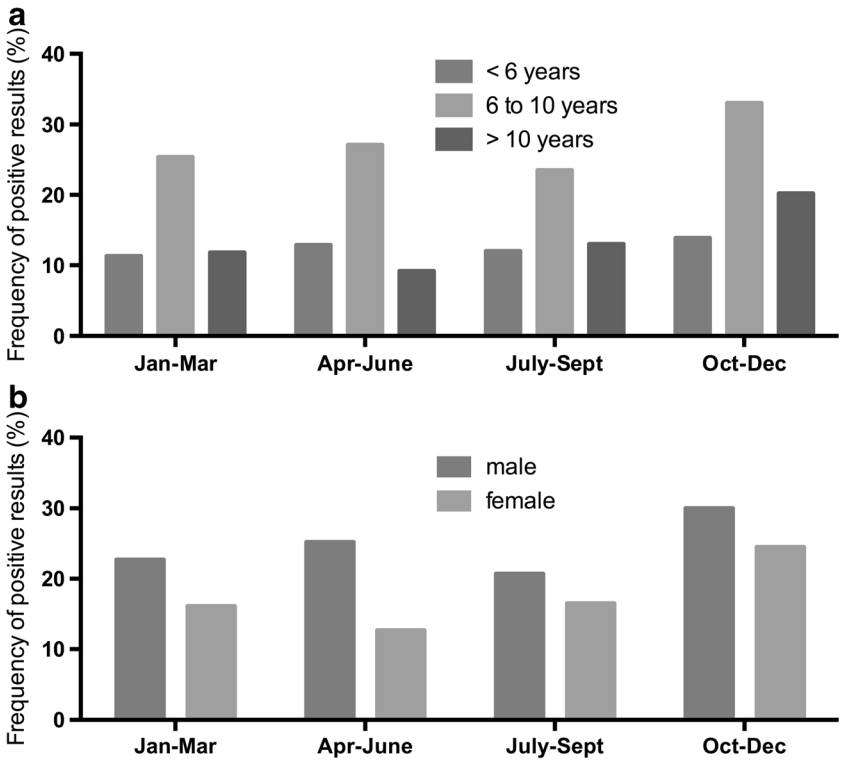

Fig. 3 Frequency of detection of *E. vermicularis* in relation to the season of the year when the sample was examined. Seasonal variation of the frequency of positive findings regarding age (**a**) and sex (**b**)

implementation of control projects, improving of the infrastructure of kindergartens, e.g., sanitation and play grounds, as well as by reducing the average number of children per class [5].

In conclusion, (i) enterobiasis was frequent in Berlin in the period of investigation, (ii) mainly children of school age were affected, (iii) family members were frequently also infected and should possibly be treated without previous confirmation by laboratory diagnosis, and (iv) the increased frequency of parasite detection together with the observed seasonality of the disease should be further investigated in epidemiological studies.

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Compliance with ethical standards

Since the study was a retrospective analysis of laboratory data collected within 10 years and no additional investigations were performed with submitted specimens, no ethical approval was applied for.

Conflict of interest The authors declare no conflict of interest.

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