

Phlyctenular eye disease in association with *Hymenolepis nana* in Egypt

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SUMMARY It had been previously noticed that infection with parasites was common in children suffering from phlyctenulosis. In the present study the stools of 471 patients suffering from phlyctenular disease were examined and it was found that 62.6% of them had *Hymenolepis nana* ova in their stools as compared with 10.8% of the controls. All patients had *Hymenolepis nana* immune sera. Many of these patients had abdominal symptoms. *Hymenolepis nana* is a cestode parasite discovered by Bilharz in Cairo in 1851. Infections with it have the same age incidence and geographical distribution as phlyctenular eye disease. It has a tissue stage responsible for a state of hypersensitivity which is thought to be responsible for the phlyctenules.

Phlyctenular keratoconjunctivitis is a disease occurring mainly in children, with a slight preponderance of males. In Egypt it is very common, constituting about 20% of cases of acute conjunctivitis (Al-Hussaini and Saoudi, 1968). It is known to be an allergic response of the corneal and conjunctival epithelium to an endogenous toxin. The most accepted theory was that this toxin is a tuberculo-protein. In 1968 Al-Hussaini and Saoudi found that tuberculo-protein does not seem to be a factor in phlyctenular eye disease in Egypt. Bakly (1929) attributed a high incidence of phlyctenular eye disease in Port-Said, Egypt, to ascariasis. Jeffery (1955) found that *Ascaris lumbricoides*, *Ancylostoma duodenale*, *Enterobius vermicularis*, and *Entamoeba histolytica* are responsible for a number of eye diseases, phlyctenulosis being the most common.

Al-Hussaini *et al.* (1977) found that phlyctenular eye disease in Egypt is often associated with intestinal infection with *Hymenolepis nana* (the dwarf tape worm). A careful examination of the stools of 155 cases of phlyctenular eye disease showed that 57.4% of them had *H. nana* ova in their stools. In cases of multiple or recurrent phlyctens the eggs were found in 73.4% of cases.

That preliminary study, pointing to *H. nana* having an important role in the aetiology of

phlyctenular eye disease, suggested the need for more evidence. The stools of a larger number of cases were therefore examined, the serum was tested for antibodies, and a specific anthelmintic drug was given to some patients.

Material and methods

This study includes 471 cases of phlyctenular eye disease, while 157 cases in the same age groups were used as controls. The age and sex, the social condition, and the presence of any abdominal symptoms were noted. The stools of both groups were examined by both the direct and the more sensitive flotation methods (Faust *et al.*, 1975).

In addition to the examination of stools of another 64 cases of phlycten their sera were tested for any circulating antibodies. The sera of 16 controls were also tested. About 2 ml of blood were taken into a closed sterile test-tube. This was left in the slanting position until serum was separated. With sterile Pasteur pipettes serum was pipetted into sterile small vials, which were preserved at -4°C until being used.

Living *H. nana* worms were obtained from the small intestines of laboratory white rats or mice. The test was done after leaving the sera to warm at room temperature. Serum of every case was added separately to few segments of the living strobila of the worm. Immune sera affect adult worms by

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Table 1 Incidence of different parasites in phlycten cases and controls

	Total number of cases of phlyctenular disease (471)				Controls (157)			
	Male	Female	Total	%	Male	Female	Total	%
<i>Hymenolepis nana</i>	179	116	295	62.63	10	7	17	10.82
<i>Ancylostoma duodenale</i>	14	4	18	3.8	3	0	3	1.91
<i>Enterobius vermicularis</i>	8	17	25	5.8	2	1	3	1.91
<i>Strongyloides stercoralis</i>	0	0	0	0.0	0	0	0	0.0
<i>Ascaris lumbricoides</i>	0	1	1	0.21	0	0	0	0.0
<i>Trichostrongylus colubriformis</i>	0	1	1	0.21	0	0	0	0.0
<i>Giardia lamblia</i>	2	1	3	0.63	1	0	1	0.63

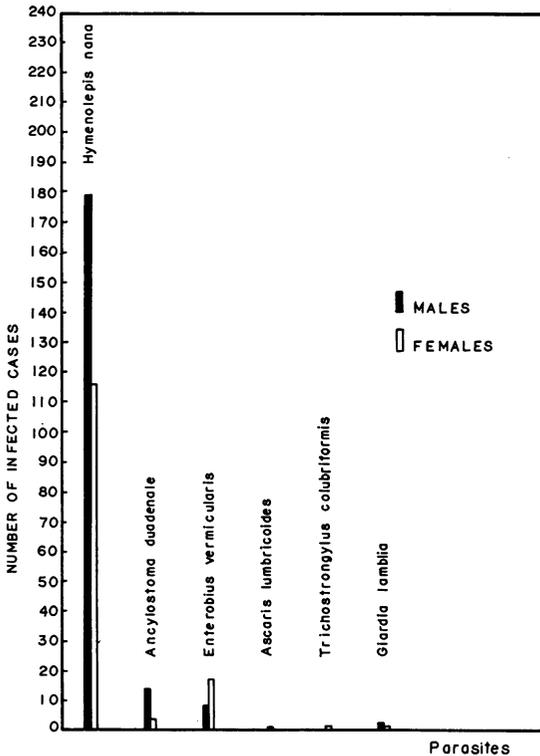


Fig. 1 Incidence of different parasites in phlycten cases

completely enveloping them in a layer of precipitate and rupturing the cuticle (Heyneman and Welsh, 1959).

Two phlyctenular cases who were found to be strongly infected with *H. nana* were admitted to hospital. They were given Niclosamide (Yomesan), which is the anthelmintic drug specific for *H. nana*, without the use of steroids or any other topical application to the eyes. In the period of study only these 2 patients accepted admission to hospital; treatment as outpatients is unreliable.

Results

Table 1 and Fig. 1 show the result of stool examination of 471 patients suffering from phlyctenular eye disease and 157 controls. Out of 471 cases 295 had *H. nana* ova in their stools, or 62.63%, as compared with 17 out of 157 controls, or 10.82%. There was no significant difference between the incidence of other parasites in phlyctenular eye cases and controls (Figs. 1 and 2). Of 295 cases of phlycten 260 had

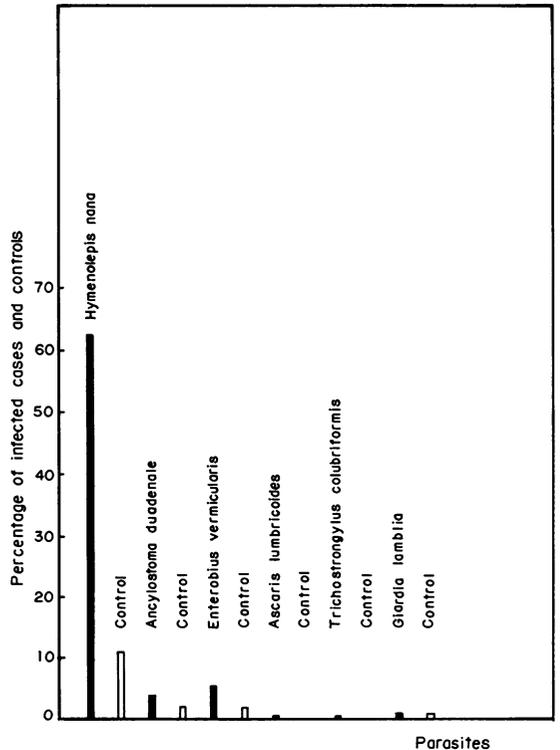


Fig. 2 Percentage of infection with different parasites in phlycten cases and controls

Table 2 Incidence of *Hymenolepis nana* ova in cases with multiple phlyctens

	+ ve <i>H. nana</i>	- ve <i>H. nana</i>	Percentage
Multiple phlycten (84)	63	21	75

Table 3 Age incidence of cases of phlycten

Age (years)	Number of cases	Percentage
1-10	266	56.48
11-20	149	31.63
Over 20	56	11.89
Total	471	

Table 4 Age incidence of cases of *Hymenolepis nana*

Age (years)	Number of cases	Percentage
1-10	189	60.58
11-20	96	30.77
Over 20	27	8.65
Total	312	

H. nana ova only in their stools; the remaining 35 had mixed infection mostly with *Ancylostoma duodenale* and *Enterobius vermicularis*.

Multiple infection with phlyctenules was found in 84 cases; 63 of them had *H. nana* ova in their stools, or 75% (Table 2).

The age incidence of patients with phlyctenular eye disease is shown in Table 3, and that of patients with *H. nana* eggs in their stools in Table 4 and Fig. 3.

Both stool and serum examinations were done on 64 phlyctenular cases. The ova of *H. nana* were found in the stools of only 38 of these patients, while a serum test for circulating antibodies showed that all the patients had *H. nana* immune sera. Within a few minutes an enveloping layer was formed round the living segments, which sooner or later ruptured. Although the test was not done quantitatively, it was noticed that the reaction was more powerful and occurred more rapidly in cases of multiple phlyctenules. As a control the sera and stools of 16 phlycten-free cases were tested in a similar manner. Although one control case was harbouring ova of *H. nana* in the stools, the serum of all the 16 controls failed to give any reaction round the living segments of worms (Table 5).

The 2 inpatients who were given niclosamide (Yomesan) for treatment of *H. nana* were cured of

the symptoms of phlyctenular keratoconjunctivitis within a few days without the use of any other systemic or topical remedies.

Many patients gave a history of vague abdominal symptoms in the form of diarrhoea and colic.

Discussion

Hymenolepis nana was discovered by Bilharz in 1851 in the small intestine of a native boy at necropsy in Cairo, Egypt. It affects 10% of children in Egypt and Sudan (Belding, 1952). 62.63% of patients with phlyctenular eye disease had *H. nana* ova in their stools. This incidence rises to 75% among patients with multiple phlyctens. The eggs of other parasites were significantly fewer than those of *H. nana*. The ova of *H. nana* are not easily detected microscopically. Hence the most careful search should be done

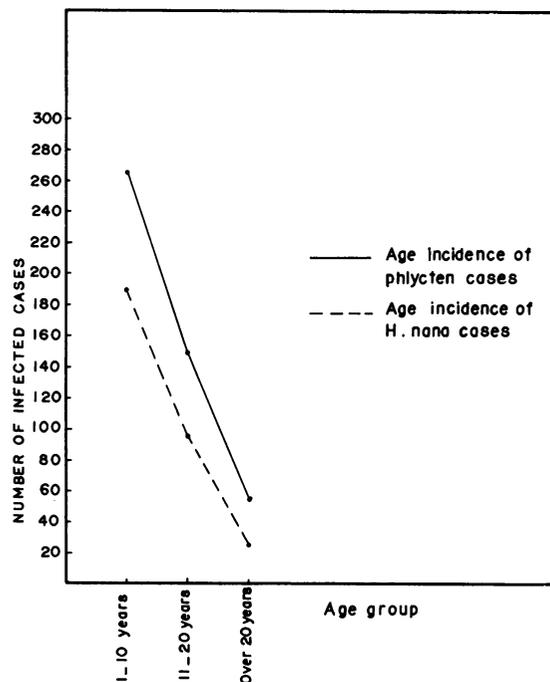
Fig. 3 Age incidence of phlycten cases and *H. nana* cases

Table 5 Results of serum and stools examination of phlycten and control cases

	Number of cases	Positive stools	%	Positive serum	%
Phlycten	64	38	53.1	64	100
Control	16	1	6.2	0	0

by a trained observer by both the direct and flotation methods.

The life cycle of *H. nana* in the human body was described in our preliminary report (Al-Hussaini *et al.*, 1977). Most important in this respect is the presence of a tissue stage of the parasite. The larval stages (cysticercoids) penetrate into the villi of the small intestine, where they complete their maturation for about 7 days before they return into the lumen of the intestine. As the parasite is not restricted to the gut, the degree to which it comes into contact with tissue fluids and serum of the host is increased. The development of helminths from the embryonic and larval stages to the sexually mature forms must include biochemical and physiological changes, all of which make the antigenic mosaic increasingly complex (Sinclair, 1970). Several workers have shown that different stages of the worms can elicit different types of antibodies in the host which are to some degree stage-specific, but it is also known that, at least for some helminths, 1 stage is as efficient as another in stimulating immune bodies.

Sinclair (1970) stated that little is known about enzymes which might help the parasite in its invasion of the host tissue, and consequently even less is known about the antibodies which these might stimulate. However, Bogitsh (1967) demonstrated esterases and an alkaline phosphatase in *H. nana* cysticercoids. As more is learnt about the type and location of these enzymes in the parasite and the sequence in which they are found in the life cycle, their effect on the immunological status of the host will become better understood.

Although little success has been obtained in vaccinating animals with dead helminthic material, Coleman *et al.* (1968) found that *H. nana* homogenate when injected into mice confers a strong immunity. This is further evidence that *H. nana* is an antigenically strong parasite.

The absence of ova in the stools of some patients with phlyctenular eye disease can be explained by intermittent passage of eggs and by the fact that an allergic response to helminths may persist for a long time after disappearance of the parasite from the body. Moreover, helminths may enhance allergic reactions to unrelated antigens (Ershov *et al.*, 1974). The determining factor for the development of phlyctens is not the presence of ova in the stools but the state of hypersensitivity induced by the cysticercoid stage of the parasites. On the same grounds we can explain why some controls have had eggs of *H. nana* in their stools although they did not complain of eye phlyctenules.

The eggs of *Ascaris* were found in only 1 case during the present study. Bearing in mind that the eggs of *Ascaris* are easily seen in the stools because

of their great number and their conspicuous appearance and knowing that *Ascaris* is a parasite that has no tissue stage, we consider that *Ascaris* plays no role in phlyctenular eye disease.

Ancylostoma was found in 3.8% of cases and in 1.91% of the controls. The general incidence is low, and the difference between the cases and controls is insignificant. Moreover, *Ancylostoma* was often associated with *H. nana* in the same patient.

Enterobius vermicularis is best diagnosed by a perianal swab and not by stool examination. In view of the fact that it is a very widely spread parasite among Egyptian children as compared with the incidence of phlyctens among them, and that it is an intestinal parasite that has no tissue stage, it is very unlikely to be responsible for the development of phlyctens.

Amoebiasis is excluded as a factor because it is not associated with eosinophilia or any allergic manifestation (Chandler, 1970).

Abdominal complaints were common among children with phlyctenular eye disease, though accurate statistical data of symptoms definitely related to *H. nana* were impossible because of the prevalence of bowel disturbances of various origins among Egyptian children.

Conclusions

All cases of phlyctenular eye disease had *H. nana* immune sera. Most of them have *H. nana* ova in their stools. Phlyctenules and infection with *H. nana* have the same age incidence and geographical distribution. Abdominal symptoms are common in patients with phlyctens. Two cases of phlycten eye disease responded dramatically to specific anthelmintic treatment. Other parasites are excluded. It is therefore obvious that the state of hypersensitivity caused by the cysticercoid stage of *H. nana* is responsible for the development of phlyctenules in Egypt.

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