Chapter 39

Traditional Methods and Alternative Strategies for the Control of Neglected Helminthic Zoonoses

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ABSTRACT

Neglected diseases are those absent from the global health agenda, although they could be a source of health damage that is associated with economical losses and suffering. They are mainly prevalent in poor hygienic conditions that are located in different areas, and some have a larger geographical distribution. Many exhibits different life cycles, require a vector for transmission or need animal reservoirs, which makes them difficult to control. Most parasitic diseases are somehow neglected, especially in low-income countries. Zoonoses are defined as diseases transmitted by animals to humans or vice versa. Here, the generalities of zoonoses are presented with emphasis on their epidemiology, aspects of basic biology including morphology and physiology, and a critical and reflective analysis of traditional control methods is continued. This chapter focuses on the importance of three zoonotic diseases: Dipylidiasis, Ancylostomiasis, and Taeniasis. Drug resistance is exposed as an important problem in the treatment of infectious diseases, which gives rise to the need for a constant search for therapeutic alternatives. Alternative control strategies are based mainly on the use of natural products, and we present proposals for the use of *Bacillus thuringiensis* applied on different life stages of the parasites as an alternative strategy in the control of parasitosis, based on scientific evidence.

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INTRODUCTION

Zoonotic Diseases

Zoonotic diseases are naturally acquired by humans, comprising a large percentage of long existing and new diseases. Even though some of them are 100% preventable through vaccination or other methods, several of these diseases are considered public health problems worldwide, to some extent due to the close coexistence that animals have with humans in various domestic, agricultural and wildlife settings. Zoonoses have an impact on the marketing and production of products intended for consumption, which together represent a threat to food security and a burden on government health systems (Rahman et al., 2020). The most important zoonoses caused by parasites have a variable distribution in the world, since parasitosis depends on various factors that are highly variable in different areas of the globe. The methods of spread can be variable and will depend on animals, climate, human migration, water cleanliness, etc. to determine these diseases is through diagnostic and control methods (Pisarski, 2019). Also, many diseases tend to be endemic mainly in regions where the infrastructure, economy, social environment and health conditions are characterized by poverty.

Human-animal interaction has increased with domestication, and over the past 70 years, several diseases totaling 250 have been classified as both re-emerging and emerging zoonoses, and their distribution patterns, frequency and geographic location have spread throughout the world. A wide range of factors have been identified as essential, including climate, greater human-animal interaction, degree of adaptation of pathogens, animal production systems, vectors, urbanization, and climate change, among others. In this regard, zoonoses account for 61% of the total number of pathogens affecting humans and the potential of zoonoses to contribute to the appearance of new emerging or re-emerging diseases in humans has also been pointed out (Salyer et al., 2017). The amplification of pathogens occurs when domestic animals that are closer to people interact with wild animals, thus establishing a circle in which different animals participate such as cats, ruminants, dogs, horses, among others that can be carriers or reservoirs of the pathogen. Thus, habits such as allowing pets to sleep with their owners, a situation that occurs between 14-62% worldwide, are potential triggers in the development and emergence of zoonotic diseases (Chomel and Sun, 2011). Both pet and stray dogs may act as reservoirs of zoonotic parasites that cause significant veterinary, medical, and economic problems. The point at which human, animal and environmental health come together is where the concept of "one health" is applied and restricted to mainly zoonotic diseases (Torres-Velez et al., 2019). The occurrence of signs such as diarrhea in humans is associated with the consumption of food containing pathogens, thus the group of pathologies known as foodborne diseases arises and some of them are classified as zoonoses.

Taeniasis-cysticercosis

Taenia solium taeniasis-cysticercosis transmitted between pigs and humans, is between the most important foodborne transboundary parasitic infections. Taeniasis are cyclozoonoses diseases, as their transmission requires more than one vertebrate. According to worldwide estimates, 2.6 to 8.3 million people have neurocysticercosis and its mortality rate is 28,000, which is considered one of the most important food-borne zoonotic diseases. (Havelaar et al., 2015; Hallal-Calleros et al., 2016). For cysticercosis, both free-roaming pigs with access to human feces form an essential binomial for its transmission dynamics that influence the increase in frequency and are a reason for the existing variability in its frequency. The definitive host of the adult phase (*Taenia*) is the human, (figure 1) and the pig hosts the larval phase in the muscles (cysticercus or metacestode). Pigs become infected by ingesting the microscopic eggs excreted in human feces by *Taenias*. In addition, if a human ingests eggs, he can also develop cysticercosis which can lodge in the muscles, but also in the brain causing neurocysticercosis.

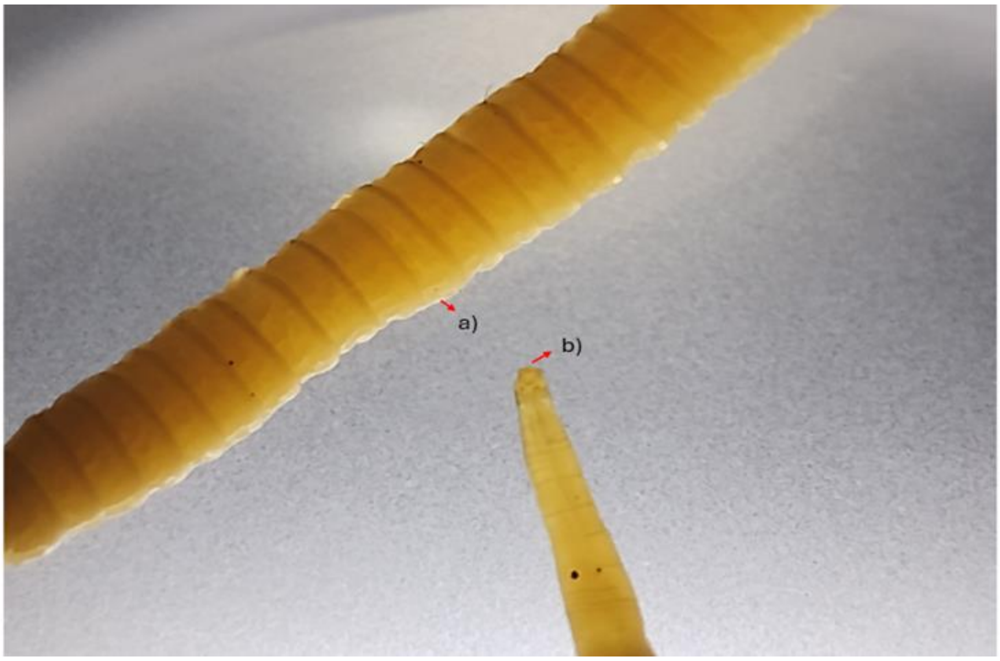

Fig. 1: *Taenia* spp. a) Mature proglottids, b) Scolex.

Once the eggs reach the stomach, hatch originating the oncosphere, which can be transported by the bloodstream and the metacestodes can develop in the brain, staying mainly in the interior or parenchyma, although they can also be lodged in the subarachnoid space. In some cases, they can lodge in the ventricles, and they are found grouped with a racemose pattern in the extra parenchymatous presentation, which occludes the circulation of cerebrospinal fluid and causes hydrocephalus and other complications. When lodged in the choroid plexus, colloidal metacestodes can be observed, which are characterized by a collagen capsule and by mononuclear inflammatory cells that may be surrounding the parasite in the granular and calcified stages (Del Brutto et al., 2014). The possibility that the metacestode lodges in different parts of the brain causes a wide variety of heterogeneous and non-specific signs and symptoms ranging from headache, increased intracranial pressure, epileptic seizures, among others, making its diagnosis difficult; Furthermore, the number of metacestodes, their state of degeneration, the degree of the inflammatory response, and the difference in susceptibility or resistance of the host, are determining factors in the severity of the disease (Garcia y Del Brutto, 2005; Verma et al., 2010). In the case of taeniasis, humans are the host of the adult parasite. Taenias are cestodes with a structure called scolex with 4 suckers and a crown of hooks, which helps with morphological diagnosis; next, the neck is followed by strobile measuring up to 4 m in length and contains the proglottids, which can have around 50-60x10^3 fertile eggs that they release into the environment, being ingested by pigs which will develop cysticercosis (Gilman et al., 2000). The symptoms reported by carriers are very general and non-specific, such as stomach pain, diarrhea and nausea, and patients may even be asymptomatic. Traditional tools for detecting gastrointestinal parasitosis, such as coproparasitoscopic tests, commonly fail in the diagnosis, being immunological and molecular tests more accurate and reliable for diagnosis.

Dipylidiasis

Dipylidium caninum (figure 2) commonly known as dog tapeworm, can accidentally lodge in the intestines of humans with a cosmopolitan distribution; It has been found in countries such as Germany, USA, Mexico, among others. It has an obligate indirect life cycle, involving arthropods like fleas (*Ctenocephalides felis*, *Xenopsylla cheopis*, *Trichodectes canis*, *Pulex irritans* and *Felicola subrostratus*) and lice (*Trichodectes canis*), in which the phase named metacestoid or cysticercoid is harbored. The adult phase of the parasite is the tapeworm or Taenia, that can be found in dogs, cats and humans, who get infected by accidentally ingesting infected fleas or lice. Flea larvae will feed on eggs found in the environment that were shed in the feces by proglottids of animals infected with *D. caninum*. Taenia can have a variable length between 22 and 48 cm and proglottids are shaped like cucumber or rice seeds, allowing their macroscopic identification in feces. The scolex has an approximate diameter of 0.5mm, with four suckers and a rostellum containing three or four pairs of hooks, whose function is to fix the parasite to the intestinal mucosa. Mature gravid proglottids have two sets of sexual organs, therefore it is a hermaphroditic parasite; within these proglottids there are ovigerous capsules with packages containing 7 to 30 eggs, with a diameter between 34 and 40µm. Although *D. caninum* infections are generally not serious in humans or animals, a high parasite load can cause abdominal pain, flatulence, weight loss, enteritis, diarrhea or constipation, and anal pruritus, guiding the clinical diagnosis in companion animals, since dogs exhibit a behavior known as scooter behavior that consists of rubbing the anus on the floor making traction with the thoracic extremities (Nerissa Ramnath et al. 2009). Clinical manifestations include growth retardation growth retardation, reduced work capacity and general health impairment. These infections occur in humans, mainly in children, as they are at risk of ingesting infected fleas. Diagnosis is mainly based on the observation of proglottids, and eggs found in feces (Narasimham et al., 2013; Saini et al., 2016).

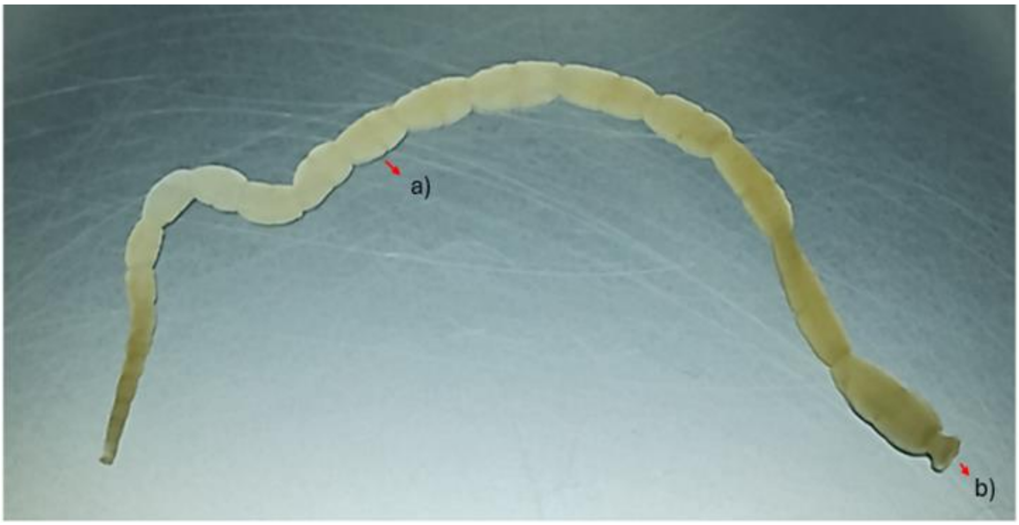

Fig. 2: *Dipylidium caninum*, a) Proglottids, b) Scolex.

Ancylostomiasis

Is a common gastrointestinal helminthic zoonoses (figure 3); The development of cutaneous infections requires contact with the infective stages of *Ancylostoma caninum*, which will lead to eosinophilic enteritis (Landmann and Prociv, 2003). *Ancylostoma* spp. infections have been reported to be 37.19%, followed by *Toxocara* spp. (24.79%), *Taenid* spp. (20.66%), *Diphyllobothrium latum* (1.65%), and lastly *Dipylidium caninum* (1.65%) to name a few. Male dogs have been shown to have a higher prevalence (27.3%) than female dogs (18.91%) of zoonotic parasites (Suganya et al., 2019).

Control Methods against Zoonoses

For disease control, the general principles must be applied, as well as the application of vaccines for sick people, in the case of animals that are healthy they must be placed in restriction, as well as avoiding any movement of healthy animals to control the population, carry out diagnostic methods, disinfection, eliminate vectors and carry out adequate surveillance methods. If the corresponding preventive methods were implemented, zoonotic diseases would be preventable, however, failure to do so would become a threat to public health. The principles of the "One Health" policy should be put into practice. This concept is based on the collaboration of multiple disciplines working together locally, nationally and globally to maintain the health of animals, people and the environment (AMVA, 2008).

Effective control of zoonoses must bring together different areas such as research, economics, sociology, government and citizens, especially those related to animal and public health (Murphy et al., 2019); also, other activities that must be carried out to control zoonoses are strict isolation and quarantine, public awareness, health education and training, as well as the implementation of biosecurity on farms, mass vaccinations, testing and if necessary the culling of animals. Training and education must also be provided for those groups of people who are at risk of zoonotic diseases, and methods of prevention and control of emerging and re-emerging diseases must be established in order to improve health, prevent morbidity and avoid the death of people and animals.

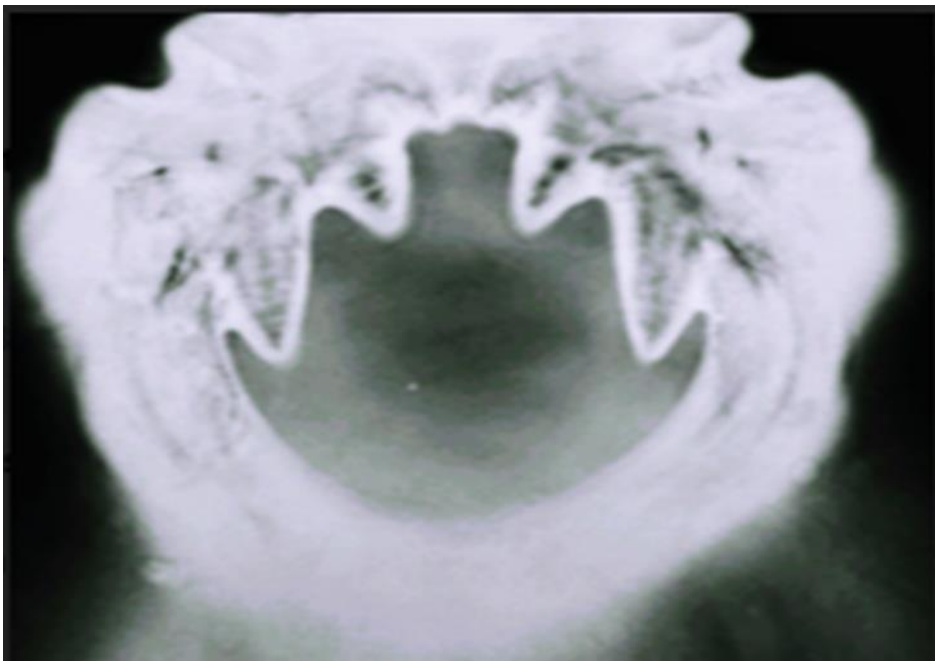

Fig. 3: *Ancylostoma caninum,* a) The buccal capsule of the helminth, b) dorsal teeth are observed 40x (Dunstan-Guzmán, 2020).

When proper nutrition is carried out, the immune system of humans and animals is prevented from fighting off serious parasitic infections. It is important to control animals such as dogs and cats from hunting wild animals such as birds, reptiles and some mammals as they play an important role as intermediate hosts for many parasites that end up causing zoonoses.

The high prevalence of vector-borne diseases (mainly ticks) has developed the use of products with repellent effects, as well as those that completely eliminate these parasites (Otranto and Dantas-Torres, 2013).

It is also important to control other vectors such as lice and fleas as they also have a great impact on human health. It is important to avoid these diseases by applying certain cleaning routines such as collecting and eliminating pet excrement, cleaning children's areas, avoiding contact between people and faeces, washing hands before and after playing, eating and when in direct contact with animals; hygiene is fundamental for the control of zoonotic diseases. However, when infections are identified, appropriate treatment should be given with certified medicines that guarantee the safety, efficacy and quality control of the manufacturing laboratory.

Anthelmintic Drugs

Most countries that have high incidence rates of tropical diseases have insufficient financial resources to invest in the development and production of drugs to control these diseases. However, there is, albeit in smaller quantities, a repertoire of drugs that are used in research that has previously been carried out in animals and are subsequently used in veterinary and human use. In addition, most anthelmintics have limited action among trematodes, cestodes and nematodes. The treatment commonly used to control trematodes or cestodes in humans is praziquantel, although it lacks activity against nematodes, the benzimidazoles have activity between phyla and are more active against nematodes than against cestodes or trematodes. Moreover, for more than thirty years, ivermectin has been used and this has been a disincentive for the discovery of new anthelmintic drugs. The classification of anthelmintics is based on their chemical structure and mode of action. For some of the world's major zoonoses, the main registered drugs are used: blood parasites (schistosomiasis) are treated mainly with oxamniquine or praziquantel; cestodiasis (taeniasis), with benzimidazoles, albendazole, niclosamide and praziquantel; parasites such as fascioliasis with triclabendazole; intestinal roundworms (nematodes) mainly with avermectins, benzimidazoles, pyrantel, levamisole, milbemycins, tribendimidine, to mention a few; tissue roundworms (filariasis)are treated with diethylcarbamazine, albendazole, ivermectin (Holden-Dye and Walker, 2018).

To treat mixed infections such as nematode and trematode infections, drug combinations have been used to achieve a broad-spectrum effect with activity against parasites of the same phylum.

Resistance to Anthelmintic Drugs

Pharmacoresistance or drug resistance is the development of the ability to withstand the effect of a drug designed to cure a disease or to mitigate symptoms, by the cells against which the drug acts, be it microorganisms, parasites, or tumor cells; therefore, drugs that were usually effective against certain organisms are no longer capable of eliminating or inhibiting them. Drug resistance is generally the result of evolution and develops in response to selective pressures exerted on living organisms. Resistance is produced by various mechanisms, among which the four best known are: inactivation or modification of the drug rendering it ineffective; the alteration of the target element preventing the action of the drug; the alteration of the metabolic pathway in which the drug interferes, using alternative pathways; reduction in the bioavailability of the drug, either by decreasing its absorption or by increasing efflux. Resistance to anthelmintics has presented itself in various forms even with different formulations. That is, when a parasite population shows a change where the susceptibility to a compound across population generations decreases, this can be defined as resistance (Geary et al., 2012). Due to the difficulty to monitor the anthelmintic resistance, the use of molecular markers for anthelmintic resistance is convenient.

Alternative Approaches to Drugs based on Botanical Medicine

Proposals for the use of plant products of natural origin as an alternative to conventional anthelmintics have gained momentum, however, they have been used previously in developing countries with problems of parasitic diseases in humans and animals. Research has shown that these natural alternatives have activity against parasites and are mostly readily available and accessible. It is important to identify the active components present in the extracts as this information is important to be able to develop and design new synthetic actives that have the same properties, as well as to consider using phytochemicals that are present for a combined strategy with commercial anthelmintics (Lanusse et al., 2018). It is also important and necessary to rigorously identify the active components, which must then be evaluated and tested before their true effect on parasite control can be adequately determined in the future. For example, one treatment used against malaria and against human schistosomiasis are artemisinins, which are originally extracted from the wormwood plant (*Artemisia absinthium*), another example is the myrrh preparation (Mirazid), which is obtained from the *Commiphora molmol* plant that is commonly used as a fasciolicidal treatment and is for human as well as animal use, also reported to have properties against protozoa and helminths (Abdelaal et al., 2017).

Alternative Approaches to Medicines based on the use of Nematophagous Fungi

A number of micro-organisms have been studied that may be useful for the biological control of zoonotic parasites and parasites of human medical importance. In 1888 it was described for the first time that the fungus *Arthrobotrys oligospora* was capable of capturing nematodes (Zopf, 1888); From there, different studies were performed on fungi where they were identified and classified according to their capacity as nematode traps, endoparasites, egg or adult parasites or toxin producers. Likewise, the nematophagous fungus *Trichoderma virens* has been evaluated against embryonated eggs of *Toxocara canis* (De Souza, 2017), causing a decrease in the number of larvae found in mice; *Paecilomyces lilacinus*, *T. harzianum* have also been tested in the hatching of *Ancylostoma* eggs; against *T. canis* eggs, *Pochonia chlamydosporia* and *P. lilacinus* have shown strong activity (Carvalho et al., 2011); *Purpureocillium lilacinum* has also been reported to be most effective in reducing the number of *T. canis* larvae (Maia et al., 2019); *P. chlamydosporia* is effective *in vitro* against *T. saginata* eggs (Araujo et al., 2009; Araujo et al., 2012); For the capture of *Ancylostoma* spp. *in vitro*, *Arthrobotrys cladodes, A. oviformis, A. oligospora, A. conoides, Duddingtonia flagrans, Monacrosporium appendiculatum, A. robusta, M. thaumasium, A. bronchophaga, and Nematoctonus robustus* have been reported to be successful (Carvalho et al., 2009), *Pleurotus eryngii in vitro* reduced the number of *A. caninum* larvae, *P. chlamydosporia and Paecilomyces lilacinus* showed ovicidal activity against *Dipylidium caninum* (Araujo et al., 2009). Thus, nematophagous fungi can be considered a promising tool for parasites of zoonotic importance when used as a biological control.

Alternative Approaches to Drugs based on the use of Bacteria

The use of beneficial and harmless microorganisms has been used as biological control of animal parasites, they have an effect depending on the stage of the parasites' life cycle and are capable of inducing death and non-viability or decreased movement. It has been reported that the use of the bacterium *Bacillus thuringiensis* has been effective for the control of pests affecting crops and even the mechanism of action that the bacterium has on some pests has been proposed and determined. There is a diverse group of *B. thuringiensis* proteins (Cry and Cyt) that have activity against invertebrates (nematodes), as well as insects (Diptera, Lepidoptera and Coleoptera). The main target site is with midgut epithelial cells as it smoothes them to insert itself into the membrane to form pores (Bravo et al., 2007). However, its use in the control of parasites that are considered zoonotic and affect both animals and humans is more recent. These bacteria have shown activity against ectoparasites such as *P. cuniculi* mite, which mainly affects rabbits. In this parasite, the histological damage caused by BT has been studied and its effects has been tested in naturally infected rabbits (Dunstand-Guzmán et al., 2015; Dunstand-Guzmán et al., 2017).

In the search for new alternatives, strains of the bacteria *B. thuringiensis* have been evaluated against some parasites; Cappello et al. (2006) reported a 90% reduction in egg excretion of *Ancylostoma ceylanicum* in mice; Dunstand-Guzman et al. (2023) evaluated *in vitro B. thuringiensis* GP526 strain on *T. pisiformis* eggs, showing macroscopic damage and loss of integrity in the eggshell; Also, *B. thuringiensis* confronted with *Dipylidium caninum* inhibited motility, demonstrating the antiparasitic effect that this bacteria has against public health diseases (Table 1).

Biological Alternatives for the Control of *Taenia* spp.

The use of nematophagous fungi has been reported to control viability in *Taenia* spp. eggs. Ovicidal activity has been described for fungi *Pochonia chlamydosporia* and *Duddingtonia flagrans*, considered lethal on eggs of *T. saginata* and the fungus *Monacrosporium thaumasium* on *Taenia taeniaeformis* eggs. The mechanism of penetration of the fungus into tapeworm eggs is not yet fully known, but it is postulated that enzymatic activity is the main route of attack for the penetration of the fungus into the eggs (Araújo et al, 2012). Also, to control the adult cestode, the use of botanical extracts has been reported. An example is the hydroalcoholic extract of the *Tamarindus indica* seed at 25, 50 and 100 mg/ml. The treatments induce paralysis and death of the cestode *T. solium* in less than one hour (Bhadoriya et al., 2011). The drupe extract of *Melia azedarach* in *T. solium* cestode at doses of 0.1% y 0.2% induces a lethality with a LT_{50} of 52 y 32 minutes respectively (Szewczuk et al., 2006). For the control of cysticercosis due to *Taenia* spp., the use of recombinant vaccines based on parasite antigens has been referred, with the most effective vaccines being those using antigens obtained from oncospheres, demonstrating high effectiveness in various animal models such as rodents, pigs, sheep and cattle (Flisser et al., 1979; Lightowlers, 2003).

Table 1: Antiparasitic effect of *Bacillus thuringiensis* on different species of parasites

Parasite	Host	*B. thuringiensis* strain or protein	Dose/mortality (Ref.)
Rhipicephalus microplus	Bovine	GP123, GP138, GP130, GP140	1.25 mg/ml 79-96% (Fernández -Ruvalcaba et al., 2010)
Dipylidium caninum eggs	Dogs	GP526	10 mg/ml 100% 600 µg/ml 75%. (Peña et al., 2013)
Ancylostoma ceylanicum larvae	Human, Hamsters	Cry 5B protein	200 µg/ml 100% (Cappello et al., 2006)
Haemonchus contortus	Ruminants	Cry5B protein	60mg/kg 91% (Sanders, 2020)
Trichostrongylus colubriformis eggs and larvae	Ruminants	*Bt* subspecies *Kurstaki*	0.38 ng/ml 50% 1.1µg/ml 50% (Bottjer et al., 1985)

To reduce the parasite load of *T. solium* in community-reared pigs, synthetic peptides have been used to make vaccines based on protein sequences of *T. crassiceps* (Huerta et al., 2001). Information on the anthelmintic activity of bacteria to break the biological cycle of *Taenia* spp. is limited to date; however, there are studies that suggest that proteins produced by bacteria may be a potential alternative for the control of this parasitosis. Cry 5B was administered *in vivo* in mice as an anthelmintic against *Heligmosomoides bakeri* (Hu et al., 2010) and against *Haemonchus contortus* in its adult and larval stages (O`Grady et al., 2007).

Bacillus thuringiensis against Zoonotic Parasitosis

B. thuringiensis is one of the few safe bacterial alternatives with therapeutic potential against cestodiasis; GP526 strain demonstrated efficacy against *Dypilidium caninum in vitro*, where a concentration of 1,000 µm/ml of the crystal-spore extract was lethal in 82.75% of the ovigerous capsules in 3.5 hours (Figure 4).

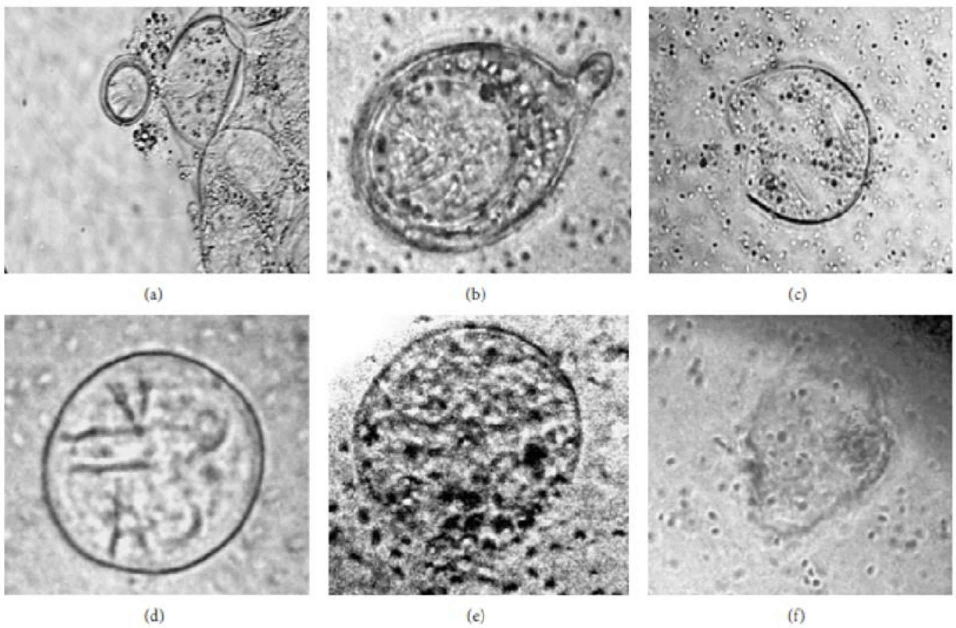

Fig. 4: Lethal effect on *Dipylidium caninum* eggs caused by the GP526 protein of *Bacillus thuringiensis,* (a) Lysis of the ovigerous capsule, (b)Eggshell with fracture, (d) Exit of the embryo, (e-f) destruction of hexacanth embryo (initial and final stages) (Peña et al., 2013).

Bacillus thuringiensis against *Taenia*

Several species of the genus *Taenia* are susceptible to death by *B. thuringiensis*. In *in vitro* studies with *Taenia pisiformis*, the spore-crystal complex of GP526 strain alters the structure of the integument surrounding the genital pore of mature gravid proglottids, which is reflected in a decrease in its size, and a decrease by 60% in the number of eggs released 3 hours after incubation (Dunstand-Guzmán et al., 2021). The effect that *B. thuringiensis* has on the structure and size of the genital pore of *Taenia pisiformis* could be attributed to apoptotic cell death, since has been reported that PS2Aa1 toxin of *B. thuringiensis* was able to induce the expression of caspases on tumor cells (Brasseur et al., 2015).

Bacillus thuringiensis* against *Ancylostoma caninum

The nematicidal effect of various *B. thuringiensis* strains was evaluated in the adult stage of *A. caninum* males and females, as well as its ovicidal and nematicidal effect. The GP526 strain was capable of inducing lethality in 81.47% of *A. caninum* eggs with 135 µg/mL after 72 h. It also killed 65% of adult *Ancylostoma caninum* nematodes at 60 µg/mL of spore-crystal complex. Also, DG03 strain was effective against the adult nematode by inducing a mortality of 71.66%, while the ovicidal effect was 36.7% with 60 µg/mL. GP526 strain caused tissue damage in the adult and egg phases of the nematode, and the crystal spore complex of the same strain induced uterine prolapse, altering the cuticle and intestine 24 h post incubation; It also caused the paralysis and death of the adult parasite. In gravid females it causes the loss of continuity of the cuticle and exteriorization of the uterine tubes accompanied by uterine detachment; this finding was not observed in non-gravid females; In the case of eggs, vacuolization and an alteration of internal cell division were observed (Dunstan-Guzmán, 2020).

Biological Alternatives for the Control of *A. caninum*

Among the alternative control methods for *A. caninum*, there is a history of the use of botanical extracts, some recombinant vaccines, the use of nematophagous fungi and bacteria that produce powerful toxins against nematodes (Carvalho et al., 2009; Shaziya and Goyal, 2012). Considering the feasibility history of the use of biological agents for parasite control, the bacterium *B. thuringiensis* is an excellent candidate due to its safety and *in vitro* and *in vivo* effect on nematode larvae and eggs (Meadows et al., 1989).

Conclusion

Zoonoses are caused by a strongly interrelatedness among animals, humans and the environment. epidemiological control shows that there are currently endemic areas and free areas that have been controlled with a unique approach. Currently, the best way to control any disease is to use strategies that combine the vectors, the pathogen and the reservoir as an integrated approach, with hygiene and education being essential factors. Early and accurate detection of zoonotic pathogens are convenient to apply effective control measures. For a unified approach, adequate surveillance is important, prevention or control, as well as one health focused research for intervention steps in the transmission of zoonotic pathogens. It is important to have knowledge of the region or zone, but also about the animal population, the local ecology and the parasites that affect local animals in order to be able to correctly manage parasitic infections in the tropics and thus be adapted for better management. Also, there is an urgent need for alternative strategies for parasitic control in view of the growing threat that anthelmintic resistance poses to animals and humans when using pharmaceuticals, it is important to consider toxicity and tolerance to the host as the presence of residual chemicals in tissues that are used for commercial supply, as well as the wastes that are disposed of and cause toxicity to the environment that have effects on non-target organisms that are important for the ecosystem. Based on its effectiveness and safety, *B. thuringiensis* is proposed as a potential broad-spectrum anthelmintic treatment in animals, allowing the interruption of the biological cycle of several zoonotic parasites.

REFERENCES

Abdelaal, M. M. O., Brennan, G. P., Hanna, R. E. B., Abdel-Aziz, A., and Fairweather, I. (2017). Disruption of egg production by triclabendazole-resistant *Fasciola hepatica* following treatment with a commercial preparation of myrrh (Mirazid). *Acta Parasitology*, 62, 336-347.

Araujo, J. M., Braga, F. R., de Araujo, J. V., and Carvalho, R. O. (2009). Activity of nematophagous fungi *Pochonia chlamydosporia* and *Paecilomyces lilacinus* on *Dipylidium caninum* egg capsules. Revista do Instituto Adolfo Lutz, 68(3), 488-91.

Araujo, J. M., Araújo, J. V., Braga, F. R., Araújo, D. M., Ferreira, S. R., Soares, F. E., and Benjamin, L. D. A. (2012). Survival of *Pochonia chlamydosporia* in the gastrointestinal tract of experimentally treated dogs. *Research in Veterinary Science*, 93(2), 803-806.

Araújo, J. M., Araújo, J. V., Braga, F. R., Carvalho, R. O., Silva, A. R., and Campos, A. K. (2009). Interaction and ovicidal activity of nematophagous fungus *Pochonia chlamydosporia* on *Taenia saginata* eggs. *Experimental Parasitology*, 121(4), 338-341.

American Veterinary Medical Association. AVMA, (2008), One Health: A New Professional Imperative, One Health Initiative Task Force: Final Report. http://www.avma.org/onehealth/.

Bhadoriya, S. S., Uplanchiwar, V., Mishra, V., Ganeshpurkar, A., Raut, S., and Jain, S. K. (2011). *In vitro* anthelmintic and antimicrobial potential of flavonoid rich fraction from *Tamarindus indica* seed coat. *Pharmacologyonline*, *3*, 412-420.

Brasseur, K., Auger, P., Asselin, E., Parent, S, Côté, J.C., and Sirois, M. (2015). Parasporin-2 from a New *Bacillus thuringiensis* 4R2 Strain Induces Caspases Activation and Apoptosis in Human Cancer Cells. *PLoS ONE*, 10(8): e0135106.

Bottjer, K. P., Bone, L. W., and Gill, S. S. (1985). Nematoda: susceptibility of the egg to *Bacillus thuringiensis* toxins. *Experimental Parasitology*, *60*(2), 239-244.

Bravo, A., Gill, S. S., and Soberon, M. (2007). Mode of action of *Bacillus thuringiensis* Cry and Cyt toxins and their potential for insect control. *Toxicon: Official Journal of the International Society on Toxinology*, 49:423-435.

Cappello, M., Bungiro, R. D., Harrison, L. M., Bischof, L. J., Griffitts, J. S., Barrows, B. D., and Aroian, R. V. (2006). A purified *Bacillus thuringiensis* crystal protein with therapeutic activity against the hookworm parasite *Ancylostoma ceylanicum. Proc. Natl. Acad*.

Carvalho, E. A., and Rocha, R. L. (2011). Toxocariasis: visceral larva migrans in children. *Journal Pediatr* (Rio J) 87(2): 100-110. doi: 10.2223/JPED.2074.

Carvalho, R. O., Araújo, J. V., Braga, F. R., Araujo, J. M., Silva, A. R., and Tavela, A. O. (2009). Predatory activity of nematophagous fungi on infective larvae of *Ancylostoma* sp.: evaluation *in vitro* and after passing through the gastrointestinal tract of dogs. *Journal of Helminthology*, *83*(3), 231-236.

Carrada-Bravo T. (2007). Monografías ilustradas de patología clínica. Uncinariasis: ciclo vital, cuadros clínicos, patofisiología y modelos animales. *Review Mex Patol Clinical Medicine Lab*, 54(4):187-199.

Chomel, B. B., and Sun, B. (2011). Zoonoses in the bedroom. *Emerging Infectious Diseases*, *17*(2), 167-172.

De Souza Maia Filho, F., da Silva Fonseca, A. O., Persici, B. M., de Souza Silveira, J., Braga, C. Q., Pötter, L., and Pereira, D. I. B. (2017). *Trichoderma virens* as a biocontrol of *Toxocara canis: In vivo* evaluation. *Revista iberoamericana de Micología*, 34(1), 32-35.

Del Brutto, O. H. (2014). Neurocysticercosis. Neurologic Aspects of Systemic Disease Part III, 1445–1459. doi:10.1016/b978-0-7020-4088-7.00097-3.

Dunstand-Guzmán, E., Hallal-Calleros, C., Morales-Montor, J., Hernández-Velázquez, V. M., Zárate-Ramos, J. J., Hoffman, K. L., Peña-Chora, G., and Flores-Pérez, F. I. (2017). Therapeutic use of *Bacillus thuringiensis* in the treatment of psoroptic mange in naturally infested New Zealand rabbits. *Veterinary Parasitology*, 238:24-29.

Dunstand- Guzmán, E., Hallal-Calleros, C., Hernández -Velázquez, V.M., Canales- Vargas, E.J., Domínguez-Roldan, R., Pedernera, M., and Flores-Pérez, I., (2020). Nematicidal and ovicidal activity of *Bacillus thuringiensis* against the zoonotic nematode *Ancylostoma caninum*. *Experiment Parasitology*, 218, 107982.

Dunstand-Guzmán, E., Hallal-Calleros, C., Lina-García, L. P., Hernández-Velázquez V. M., Vega-Salazar, A. V., Flores-Pérez, F. I., and Peña-Chora, G. (2021). *In vitro* effect of *B. thuringiensis* on the eggs release by proglottids of *Taenia pisiformis*. *Acta Agrícola y Pecuaria*. 7: E0071017.2021.

Dunstand-Guzmán, E., Hallal-Calleros, C., Hernández-Velázquez, V. M., Dominguez-Roldan, R., Peña-Chora, G., and Flores-Pérez, F. I. (2023). Potential control of the infective stage of *Taenia pisiformis* using *B. thuringiensis* GP526 strain. *Experimental Parasitology*, *249*, 108522.

Dunstand-Guzmán, E., Peña-Chora, G., Hallal-Calleros, C., Pérez-Martínez, M., Hernández-Velazquez, V. M., Morales-Montor, J., and Flores-Pérez, F. I. (2015). Acaricidal effect and histological damage induced by *B. thuringiensis* protein extracts on the mite *Psoroptes cuniculi*. *Parasit Vectors*. 8:285. doi: 10.1186/s13071-015-0890-6. *Erratum in: Parasit Vectors*. 2015; 8:427.

Fernández-Ruvalcaba, M., Peña-Chora, G., Romo-Martínez, A., Hernández-Velázquez, V., de la Parra, A. B., and De La Rosa, D. P. (2010). Evaluation of *Bacillus thuringiensis* pathogenicity for a strain of the tick, *Rhipicephalus microplus*, resistant to chemical pesticides. *Journal Insect Science*, 10:186.

Flisser, A., Pérez-Montfort, R., and Larralde, C. (1979). The immunology of human and animal cysticercosis: a review. *Bulletin of the World Health Organization*, *57*(5), 839.

Garcia, H. H., and Del Brutto, O. H. (2005). Neurocysticercosis: updated concepts about an old disease. *Lancet Neurol*, 4:653-66.

Geary, T. G., Hosking, B. C., Skuce, P. J., von Samson-Himmelstjerna, G., Maeder, S., Holdsworth, P., Pomroy, W., and Vercruysse, J. (2012). World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) guideline: anthelmintic combination products targeting nematode infections of ruminants and horses. *Veterinary Parasitology*, 190, 306-316.

Gilman, R. H., Del Brutto, O. H., Garcia, H. H., and Martinez, M. (2000). Prevalence of taeniosis among patients with neurocysticercosis is related to severity of infection. *Neurology*, 55:1062.

Hallal-Calleros, C., Morales-Montor, J., Orihuela-Trujillo, A., Togno-Peirce, C., Murcia-Mejía C., Bielli, A., Hoffman, K. L., and Flores-Pérez, F. I. (2016). *Taenia pisiformis* cysticercosis induces decreased prolificacy and increased progesterone levels in rabbits. *Veterinary Parasitology*, 229:50-53.

Havelaar, A. H., Kirk, M. D., Torgerson, P. R., Gibb, H. J., Hald, T., Lake, R. J., Praet, N., Bellinger, D. C., de Silva N. R., and Gargouri, N., (2015). World Health Organization Global estimates and regional comparisons of the burden of foodborne disease in 2010. *PLoS Medicine,* 12:e1001923.

Holden-Dye, L., and Walker, R.J. (2014). Anthelmintic drugs and nematicides: studies in *Caenorhabditis elegans*. In: WormBook: The Online Review of *C. elegans* Biology [Internet]. Pasadena (CA): WormBook; 2005-2018. Available from: https://www.ncbi.nlm.nih.gov/books/NBK116072/ Imperative, One Health Initiative Task Force: Final Report. http://www.avma.org/onehealth/ (Accessed online 7/05/2010).

Huerta, M., De Aluja, A.S., Fragoso G., Toledo, A., Villalobos, N., Hernández, M., Gevorkian, G., Acero, G., Díaz, A., Alvarez, I., Avila, R., Beltrán, C., Garcia, G, Martinez, J. J., Larralde, C., and Sciutto, E. (2001). Synthetic peptide vaccine against

Taenia solium pig cysticercosis: successful vaccination in a controlled field trial in rural Mexico. *Vaccine*, 12;20(1-2):262-6.

Hu, Y., Georghiou, S. B., Kelleher, A. J., and Aroian, R. V. (2010). *Bacillus thuringiensis* Cry5B protein is highly efficacious as a single-dose therapy against an intestinal roundworm infection in mice. *PLoS Neglected Tropical Diseases*, *4*(3), e614.

Landmann, J. K., and Prociv, P. (2003). Experimental human infection with the dog hookworm, *Ancylostoma caninum*. *Medical journal of Australia*, *178*(2), 69-71.

Lanusse, C., Canton, C., Virkel, G., Alvarez, L., Costa-Junior, L., and Lifschitz, A. (2018). Strategies to optimize the efficacy of anthelmintic drugs in ruminants. *Trends Parasitology*, 34, 664-682.

Lightowlers, M. W. (2003). Vaccines for prevention of cysticercosis. *Acta Trop*, Jun;87(1):129-35.

Maia, F. S., Fonseca, A., Valente, J., Baptista, C. T., Moreira, A., Botton, S. A., Pötter, L., and Pereira, D. (2019). Exposure of *Toxocara canis* eggs to *Purpureocillium lilacinum* as a biocontrol strategy: an experimental model evaluation. *Review Bras Parasitology Veterinary*, 28(1): 91-96.

Meadows, J., Gill, S. S., and Bone, L. W. (1989). Factors influencing lethality of *Bacillus thuringiensis kurstaki* toxin for eggs and larvae of *Trichostrongylus colubriformis* (Nematoda). *The Journal of Parasitology*, 191-194.

Murphy, S. C., Negron, M. E., Pieracci, E. G., Deressa, A., Bekele, W., Regassa, F., Wassie, B. A., Afera, B., Hajito, K. W., and Walelign, E., (2019). One Health collaborations for zoonotic disease control in Ethiopia. *Review Science Technology*, 38, 51-60.

Narasimham, M. V., Panda, P., Mohanty, I., Sahu, S., Padhi, S., and Dash, M. (2013). *Dipylidium caninum* infection in a child: a rare case report. *Indian Journal Medicine Microbiology*, 31(1):82-4.

Nerissa, Ramnath, K. M. (2009). Behavioral Effects of Parasitism in Animals. *Journal of Exotic Pet Medicine*, 18(4), 254-265.

O'Grady, J., Akhurst, R. J., and Kotze, A. C. (2007). The requirement for early exposure of *Haemonchus contortus* larvae to *Bacillus thuringiensis* for effective inhibition of larval development. *Veterinary Parasitology*, *150*(1-2), 97-103.

Otranto, D., Dantas-Torres, F., Brianti, E., Traversa, D., Petrić, D., Genchi, C. and Capelli, G. (2013). Vector-borne helminths of dogs and humans in Europe. *Parasit. Vectors*, 6(1):16.

Peña, G., Aguilar Jiménez, F. A., Hallal-Calleros, C., Morales-Montor, J., Hernández-Velázquez, V. M., and Flores-Pérez, F. I. (2013). *In vitro* ovicidal and cestocidal effects of toxins from *Bacillus thuringiensis* on the canine and human parasite *Dipylidium caninum*. *BioMed Research International*, *2013*.

Pisarski, K. (2019). The Global Burden of Disease of Zoonotic Parasitic Diseases: Top 5 Contenders for Priority Consideration. *Tropical Medicine Infection Disease*, 4(1):44.

Rahman, M. T., Sobur, M.A., Islam, M. S., Ievy, S., Hossain, M. J., El Zowalaty, M. E., Rahman, A. T., Ashour, H. M. (2020). Zoonotic Diseases: Etiology, Impact, and Control. *Microorganisms*, *8*, 1405.

Ribeiro, Braga, F., Araújo, J. V., Silva, A. R., Araujo, J. M., Carvalho, R. O., and Tavela A. O., (2009). Biological control of horse *cyathostomin* (Nematoda: Cyathostominae) using the nematophagous fungus *Duddingtonia flagrans* in tropical southeastern Brazil. *Veterinary Parasitology*, 163:335-40.

Saini, V. K., Gupta S., Kasondra, A., Rakesh, R. L., and Latchumikanthan, A. (2016). Diagnosis and therapeutic management of *Dipylidium caninum* in dogs: a case report. *Journal Parasitology Disease*, 40(4):1426-1428.

Salyer, S. J., Silver, R., Simone, K., and Barton Behravesh, C. (2017). Prioritizing Zoonoses for Global Health Capacity Building-Themes from One Health Zoonotic Disease Workshops in 7 Countries, 2014-2016. *Emerging Infectious Diseases*, *23*(13), S55–S64.

Shaziya, B.I., and Goyal, P.K. (2012). Anthelmintic effect of natural plant (*Carica papaya*) extract against the gastrointestinal nematode, *Ancylostoma caninum* in mice. *International Research Journal Biology Science,* 1(1): 2-6.

Suganya, G., Porteen, K., Sekar, M., and Sangaran, A. (2019). Prevalence and molecular characterization of zoonotic helminths in dogs. *Journal of parasitic diseases: official organ of the Indian Society for Parasitology*, *43*(1), 96-102.

Sanders, J. P. (2020). *The anthelmintic effect of Bacillus thuringiensis Cry5B on Haemonchus contortus in sheep* (Doctoral dissertation, Virginia Tech).

Szewczuk, V. D., Mongelli, E. R., and Pomilio, A. B. (2006). *In vitro* anthelmintic activity of Melia azedarach naturalized in Argentina. *Phytother Research*, 20(11):993-6.

Torres-Velez, F., Havas, K. A., Spiegel, K., and Brown, C. (2019). Transboundary animal diseases as re-emerging threats - Impact on one health. *Semin Diagn Pathology*, 36(3):193-196.

Verma, A., Prasad, K. N., Gupta, R. K., Singh, A. K., Nyati, K. K., Rizwan, A., Pandey, C. M., Paliwal, V. K. (2010). Toll-like receptor 4 polymorphism and its association with symptomatic neurocysticercosis. *Journal Infection Disease*, 202:1219-1225>

Zopf, W. (1888). Zur Kenntnis der Infektions-Krankheiten neiderer Thiere. Nova Acta Leop *Acad Naturf Halle*, 52:7