Review Article

Stronglyoidiasis Infection: A Review

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ABSTRACT

Strongyloidiasis is a worldwide parasitic disease. Among the diverse species of Strongyloides, only the following are of importance to man: S. Stercoralis, S. Fulleborni and S. Fullerboni-like. Eventhough S. Stercoralis is an intestinal helminth. Strongyloidiasis is a systemic infection that can affect, beside the gastrointestinal tract, lungs, CNS, liver and biliary tract, pancreas, genitourinary tract and skin. Strongyloides stercoralis has a unique and complex life cycle. Recent evidence has suggested a role for the cytokine, IL-22, during helminths infection and in maintaining mucosal barrier function. IL- 22 may therefore play an important role in the relationship between the mammalian immune response, gut microbiota and helminths infections. Death from strongyloidosis can result from hyperinfection or disseminated disease. Diagnosing strongyloidiasis may be difficult, and eventhough the parasitological stool examination is the most used diagnostic test, sometimes larvae cannot be identified. Management of S. Stercoalis infection includes the aim of eradication of the infection. The drug like albendazole, ivermectin, thibenzimdazole use for the treatment. A high index of suspicion should be maintained by clinicians treating patients in endemic area presenting with new onset wheezing, acute respiratory distress and/or gram negative sepsis to prevent the serious complication of strongyloides hyperinfection and dissemination. Strongyloidiasis hyperinfection syndrome carries a high mortality approaching 100 percent; mortality with therapy exceeds 25 percent.

Keywords: Albendazole, ivermectin, larve, strongyloidosis, S. stercoralis, S. fuelleborni

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INTRODUCTION

The helminths are worm-like parasites. The clinically relevant groups are separated according to their general external shape and the host organ they inhabit. There are both hermaphroditic and bisexual species. The definitive classification is based on the external and internal morphology of egg, larval, and adult stages.

Helminth is a general term meaning worm. The helminths are invertebrates characterized by elongated, flat or round bodies. In medically oriented schemes the flatworms or platy helminths (platy from the Greek root meaning "flat") include flukes and tapeworms. Roundworms are nematodes (nemato from the Greek root meaning "thread"). These groups are subdivided for convenience according to the host organ in which they reside, e.g., lung flukes, extra intestinal tapeworms, and intestinal roundworms.

Most natural host populations are exposed to a diverse community of parasites, and co-infection of hosts by multiple parasites is common place across a diverse range of systems [1,2].

S. Stercoralis was first reported in 1876 in the stools of French soldiers on duty in Vietnam who had severe diarrhea, and the disease.

According to Genta (1989), severe diseases may occur in immunocompromised and untreated individuals infected with the intestinal nematode parasite. Strongloides Stercoralis, infection of which may persist for long periods of time [4,5]. Strongyloidiasis is an intestinal infection caused by 2 species of the parasitic nematode *Strongyloides.* The most common and clinically important pathogenic species in humans is *S stercoralis* and also globally

distributed human pathogen of clinical importance.

The genus Strongyloides is classified in the order Rhabditida and most members are soil wellig microbiverous nematodes. Fifty-two species of Strongyloides exist, but most do not infect humans. S. Stercoralis is the most common pathogen for humans.

The adult female worm is very small and almost transparent. It measures approximately 2.2–2.5 mm in length with a diameter of 50 μm; it lives in tunnels between the enterocytes in the human small bowel.

Stronglyoidiasis hyperinfection is defined as an increase in the parasite load whereby the rhabditiform larvae penetrate the bowel mucosa and the organism is confined to the organs normally involved in the pulmonary autoinfection cycle.

The term "hyperinfection" is often used to denote autoinfection, a phenomenon in which the number of worms increases tremendously and the worms are detectable in extraintestinal regions, especially the lungs. Some conditions associated with HIV infection are known to predispose to hyperinfection syndrome, including inanition and the use of steroids.

Distinctive characteristic s of this parasite are its ability to persist and replicate within a host for decades while producing minimal or no symptoms (individuals with an intact immune system) and its potential to cause life-threatening infection (hyperinfection syndrome, disseminated strongyloidiasis) in an immunocompromised host (60-85% mortality rate) [6,7].

When the microenvironment changed to unfavorable circumstances (dry and/or cold temperature), rhabditi form larvae transform to filari form larvae, an infective form to the final host. Upon a contact with the contaminated soil, the filari form larva penetrates into the human skin and takes into superficial veins. In immune competent hosts, the infection by S. Stercoralis is largely confined to the intestinal tract and is asymptomatic or induces nonspecific complaints such as moderate abdominal pain, nausea and diarrhea.

In developing countries of the tropics, subtropics and temperate areas, Strongyloides stercoralis infection is a common cause of morbidity and mortality. A high index of suspicion should be maintained by clinicians treating patients in endemic areas presenting with new-onset wheezing, acute Respiratory distress and/or Gram-negative sepsis to prevent the serious complications of Strongyloides hyperinfection and dissemination.

On the other hand, disseminated strongyloidosis is characterized by the migration of larvae to organs not usually involved in the normal life-cycle of the parasite, such as the brain and skin.

Recent studies in vertebrates have indicated that interactions between co-infecting parasites can be pronounced and have important consequences for disease development, severity and transmission dynamics [8,9] .

Thus for any given parasite, understanding how it interacts with other parasites infecting the same host may be crucial for a deeper understanding of its biology and epidemiology, as well as effective disease control. Two of the most prevalent types of human infection in the developing world, malaria and helminthiases, overlap extensively in their epidemiological distributions and frequently co-infect the same individuals [2,10-12].

Inflammatory bowel diseases (IBD) are conditions of unknown cause that usually start in people during the second or third decade of life. The patients frequently experience continuous or intermittent diarrhoea, abdominal pain, rectal bleeding and fatigue due to aberrant intestinal inflammation, probably resulting from inappropriately vigorous immune responses to components of our natural intestinal faecal stream [13].

Gastrointestinal helminths have coevolved with the mammalian immune system similarly to the gut microbiota. Just as commensal bacteria can shape mammalian immunity, helminthes exert immune regulatory effects on their mammalian hosts. However, the relationship between helminths and gut microbiota is still unclear.

Treatment with helminths is now in clinical trials for IBD but the mechanism by which they may improve the symptoms of IBD is not well understood. Recent evidence has

suggested a role for the cytokine, IL-22, during helminths infection and in maintaining mucosal barrier function. IL-22 may therefore play an important role in the relationship between the mammalian immune response, gut microbiota and helminths infections.

EPIDIMIOLOGY:

Strongyloidiasis is endemic in tropical and subtropical regions and occurs sporadically in temperate areas. In tropical and subtropical regions the overall regional prevalence may exceed 25 percent. The highest rates of infection in the United States are among residents of the southeastern states and among individuals who have been in endemic areas (including immigrants, refugees, travelers and military personnel) [14,15]. A Canadian study of newly arrived Southeast Asian refugees identified strongyloidiasis seroprevalence among Kampucheans, Laotians, and Vietnamese (76, 56, and 12 percent, respectively) [15]. In another study, over 40 percent of Cambodian immigrants to Australia had positive or equivocal strongyloides serology indicating possible infection [15].

LIFE CYCLE:

Helminths have different and complex life cycles and ideal living environments. Helminths' life cycle is very different from that of bacteria and protozoan, which are well-known microbes in the sanitary field.

- stages for Roundworms and whipworms:

1. Eggs mature in the soil over a period of 2–4 weeks.
2. Eggs are ingested -by humans.
3. Larvae travel to the small intestine where they mature into adult worms.

Adults lay eggs which are passed in human faeces.

- stages for Hookworms:

1. Eggs hatch into larvae which rest in the soil.
2. Larvae penetrate skin and enter the bloodstream.
3. Larvae travel to the small intestine where they mature into adult worms.

Adults lay eggs which are passed in human faeces.

The infection begins when human skin contacts filariform larvae (the infective larval stage) of S. Stercoralis, which are found in soil or other materials contaminated with human feces [15,16]. The filariform larvae penetrate the skin and migrate hematogenously to the lungs where they penetrate into the alveolar air sacs. The larvae then ascend the tracheobronchial tree and are swallowed.

The larvae mature into adult worms that burrow into the mucosa of the duodenum and jejunum. Adult worms may live for up to five years. The adult female produces eggs, from which noninfectious larvae (rhabditiform larvae) develop within the lumen of the gastrointestinal tract. The rhabditiform larvae are generally passed in the feces.

The cycle from dermal penetration to appearance of larvae in the stool requires approximately three to four weeks. Strongyloides spp. Larvae penetrate the human host and reach the intestine where they mature into adults and produce eggs; the eggs hatch in the gut lumen and yield larvae that are evacuated in faeces. The peculiarity of this worm is that some larvae are not excreted but reinvade the intestine or perianal skin to perpetuate the infection ("autoinfection cycle").

MORBIDITY DATA:

Helminthiases diseases are poorly recorded due to the lack of economical, technical and human resources in places where they are dominant. Data comes mainly from the medical reports of public facilities where helminthiases are identified through the patient's symptoms rather than by using laboratory analysis [17]. Thus, helminthiases are frequently poorly and globally reported (as worm diseases) without indicating the specific type of helminth involved.

SURVIVAL TIME:

According to the available information obtained using a less sensitive helminth ova quantification technique than the one available currently, it was found that helminth eggs live in water, soil and crops for several months and over periods that are much longer than those reported for other microorganisms [18] .

INFECTIVITY:

As mentioned, helminths eggs found in wastewater are not normally infective. To become so they first need to be viable and

second to develop a larva. Viability in wastewater, sludge and faecal sludge is variable and depends on environmental conditions. Unfortunately, there are few data on this, but of 440 samples performed in wastewater viability turned out to be 74 % ± 8.3 and in raw sludge it was 83 ± 21.4 globally (but 90% for Ascaris) [19]. In contrast, in faecal sludge viability is very variable depending on the amount of time the sludge has been stored, the temperature and the material added to the faeces; unfortunately, little data is available on this.

INTERACTION OF HELMINTHS AND HOST:

Helminths must interact through direct contact with host cells or by the release of soluble molecules to alter susceptibility to enteritis. The presence of worm-derived factors that can control disease is supported by the observation that extracts from H. Diminutas adult worms [20] or administration of dead schistosome ova protect mice from IBD [21].

Heligmosomoides polygyrus bakeri and other helminths secrete proteins that can induce T cells to express Foxp3 [22], which have implications for IBD control. Helminths produce a number of products with potential immune modulatory properties.

Intestinal helminths also must overcome the gut epithelial barrier to affect host immunity. Intestinal helminths go through several larval stages before maturing into adults. These larvae live within the epithelial layer of the intestine, closely associated with host intestinal leukocytes. The intestinal epithelial lining can release substances that affect mucosal immune function.

There are a variety of helminthic species that have evolved to live in different regions of the gut. Some helminths attach to the intestinal wall while others move freely without anchoring to the intestinal lining. Still others can reach beneath the epithelial lining.

MECHANISMS RESPONSIBLE FOR THE PROTECTIVE ROLE OF HELMINTHS:

The main approach to dissecting the mode of action of helminthes has been to identify helminthic substances with immune modulatory properties. ES-62 the most studied of the helminth products is ES-62.

ES-62 is a 62-kda phosphorylcholine (PC)–containing glycoprotein secreted by the filarial nematode Acanthocheilonema viteae. 41, 42 ES-62 possesses many immunomodulatory activities that appear to be due mainly to its PC moiety.

It inhibits B-cell activation and the signals that result from it (B-cell proliferation and cytokine secretion) by targeting various components of the signaling pathways downstream of the B-cell receptor.

RESISTANCE:

Helminth eggs are considered to be the most resistant biological particles in the sanitary engineering field. This resistance is due to their shell, which is comprised of several layers (3-4 depending on the genera). There is an external irregular lipoprotein layer bounded by a trilaminate membrane, a middle chitinous variable thick layer formed with proteins and an inner lipoidal layer [23,24]. The middle layer, divided by some authors into several ones, serves to give structure and mechanical resistance to the eggs. The protein layer is an important barrier preventing the passage of material through the shell. The innermost one, which dissolves in organic solvents, is known as the vitelline or ascaroside layer, and also confers resistance. It is particularly resistant to salts and chemicals which are lethal to other microorganisms [25]. This layer is also useful for protecting eggs from desiccation, strong acid and bases, oxidants and reductive agents as well as detergent and proteolytic compounds. The permeability of the shell is limited to the passage of respiratory gases and lipid solvents, although water may move slowly through it. Changes in the permeability of the shell occur during hatching owing to the breakdown of the lipid layer [26,27]. It is at this stage that it is easiest to inactivate helminth eggs.

RISK FACTORS FOR SEVERE STRONGYLOIDIASIS:

1. Corticosteroid therapy: This is the most important risk factor[28,29] other immunosuppressive agents are also risk factors (eg, chemotherapeutic agents,

tacrolimus, tumor necrosis factor [TNF] modulators)
2. Human T-cell leukemia virus type 1 (HTLV-1) infection [30,31].
3. HTLV-1, the retrovirus associated with adult T-cell leukemia, has a bidirectional relationship with Strongyloides; coinfection with Strongyloides shortens the preleukemic phase of HTLV-1 infection[32] ; the Strongyloides antigen accelerates leukemogenesis, and treatment of the infection may actually decrease HTLV-1 viral load.
4. Human immunodeficiency virus (HIV) infection [33].
5. Hypogammaglobulinemia
6. Malignancy/neoplasms, particularly hematologic malignancies (lymphoma, leukemia): Studies have suggested that Strongyloides infection may be associated with increased incidence of gastrointestinal lymphoma [34].
7. Organ transplantation[35,36,37,38]
8. Malabsorption states and malnutrition
9. Chronic renal failure and end-stage renal disease
10. Diabetes mellitus
11. Advanced age
12. Collagen-vascular disease
13. Chronic alcohol consumption.[39]
14. Chronic renal failure and end-stage renal disease.

HELMINTHS CONTROL:

Understanding the principles and constraints to the control of helminths parasites is of global relevance.Helminth parasites can be controlled conventionally either by evasion, or by suppression primarily involving pharmaceutical treatments of their hosts.

Planned control programmes for sheep nematode parasites in the UK are mainly based on conventional epi-demiological studies that were performed during the 1960sand 1970s.

During recent years, however, suboptimal sheep productivity due to parasitic gastroenteritis has become common place in UK sheep flocks, despite the adoptionof previously highly successful nematode parasite con-trol programmes involving the use of anthelmintic drugs.

These problems have arisen because the epidemiology ofthe parasites has changed [40] due to a combination of interacting factors, including: effects of concurrent disease or management on anthelmintic drug pharmacokinetics; inappropriate timing of anthelmintic treatments as a consequence of parasite evolution inresponse to climate change; and consequences of changes in farm and grazing management resulting from changing economics of sheep production.

The increased prevalence of cestode parasites with sheep as their intermediate hosts may be due in part to regu-lations banning burial of fallen stock, meaning that dead sheep may lie around farm yards for a few days before theycan be uplifted, affording opportunities for scavenging by farm dogs.

DIAGNOSTIC TECHNIQUES:

There are several diagnostic procedures:

- String Tests
- Duodenal aspiration
- Immunodiagnostic tests (IFA, IHA, EIA, ELISA)
- Repeated examination of stool
- Baermann funnel technique (still regarded as the gold standard)
- Directly (dissection microscopy)
- Direct smear of faeces in saline-lugol iodine stain.

DIFFERENTIAL DIAGNOSIS:

There are many conditions producing similar symptoms –

Consider:

- Intestinal Infections (amebiasis, bacterial colitis, shigella, campylobacter, yersinia, clostridium difficile)
- Inflammatory bowel disease
- Irritable bowel syndrome
- Functional abdominal disorders
- Drugs (NSAIDS, gold)

ANALYTICAL TECHNIQUE:

The identification of helminths and helminth eggs in stools are beyond the scope of this chapter but information can be found in Ayres [41]. Environmental samples (wastewater, sludge and faecal sludge) are analysed without using and international standardized technique. Analytical techniques for enumerating helminth ova

can be classified into two: direct and indirect methods [42].

Direct techniques have two general steps. The first one consists of separating, recovering and concentrating helminth ova from the sample. In the second one, the helminth ova are identified and counted visually using a microscope and a Doncaster or a Sedwig-Rafter chamber. Although these techniques are useful for all kinds of helminth eggs, most of the laboratories only report the Ascaris content, not the total helminth ova content indicating the different types of genera observed.

Furthermore, each analytical technique has different recovery percentages [43] and care must be taken to report the values obtained mentioning also the method used to obtain them.

Indirect techniques for measuring helminth eggs are used only in liquid samples. Their principle is based on measuring an alternative parameter that can be correlated to the helminth ova content using a previously established calibration curve.

CHEMOTHERAPY:

These programmes consist of the mass treatment of a large segment of population with drugs. The choice of an appropriate antihelmintic drug depends on (a) its safety record; (b) its therapeutic effect (cure rate or efficacy), (c) its spectrum activity; (d) local health policy; and (e) financial considerations. A key issue for the optimal use of an anthelmintic drug is to decide when and how frequently to treat the population of concern.

From an economic point of view, targeted population chemotherapy programmes are half the price of universal ones[44]. The fact that long-term chemotherapy programmes are not efficient is often overlooked, as when stopped, if proper sanitation systems have not been put in place, individuals' vulnerability to worms increases, both in terms of infectivity (predisposition to catching the diseases) and intensity (number of worms developed per individual) [44].

DRUG USED FOR TREATMENT:

The treatment of strongyloidiasis is difficult because in contrast with other helminthic infections the strongyloides worm burden must be eradicated completely. Complete eradication is difficult to ascertain because of the low worm load and irregular larval output. A true cure cannot be pronounced on the basis of negative follow-up stool examination alone. A single stool analysis for Strongyloides stercoralis was found to be negative in up to 70% of known cases with strongyloides infection.

Over the past 10–20 years, the worldwide problem of anthelmintic resistance has steadily increased in parasites of horses and small ruminants, and more recently also in parasites of cattle. Many populations of parasites have developed resistance to multiple anthelmintics, and cases of total anthelmintic failure are being reported with increasing frequency.

It is now well recognized that anthelmintic drugs cannot continue to be used as they have been in the past. Ivermectin, thiabendazole and albendazole are the most effective medicines for treating the infection. Common drugs used are albendazole, pyrantel, mebendazole, tiabendazole, niclosamide, pyrantel pomoate and lavamisole.

1. ALBENDAZOLE:

The first patients were treated with ABZ in s1981, using an empirical dose based on what little was known of the pharmacokinetics and human dose tolerance when used in intestinal helminthic diseases since it was introduced and licensed for use in man.

In late 2010 WHO pledged to donate an additional 400 million treatments of albendazole to fight STH infections in school-age children.

Albendazole causes a series of biochemical alterations in susceptible nematodes, although how it effectively does so is not completely understood. The drug might act by selectively and irreversibly reducing or blocking the glucose uptake in parasites sensitive to its action, affecting various stages of its development[45,46].

Mechanism of Action [47]

Blocks the glucose uptake by the larvae

Depletes glycogen storage of the adult worm,

Decreases the formation of ATP

-as a result the parasite is immobilized and dies.

Dose-

Single dose of 400mg in the morning.

800 mg/day (single or divided dose) for 30 days in case of hydatid cyst.

2. IVERMECTIN:

It is the drug of choice in Strongyloidiasis and Onchocerciasis (Onchocerca volvulus). It is also an alternative drug for scabies. May prove useful in treatment of other forms of Filariasis and cutaneous larvae migrans. The era of effective new modern broad spectrum anthelmintic classes, the last being the avermectins in 1981 (ivermectin), spanned the period of the 1960s–1990s. Ivermectin has proved highly effective against S. stercoralis [48-50].

Mechanism of Action-

Ivermectin appears to paralyze nematodes and arthropods by intensifying GABA mediated transmission of signals in the peripheral nerves.

In Onchcerciasis, Ivermectin is microfilaricidal and affects embryogenesis.

Dose:

Use a single dose of Ivermectin 200 μg /kg to treat strongyloidiasis.

3. PYRANTEL PAMOATE:

- Used if the patient is allergic to Albendazole or Mebendazole.
- Broad spectrum
- If orally given 15% absorbed
- Excreted in the unchanged form (no metabolism)

Mechanism of Action-

Causes depolarizing type of paralysis (spastic paralysis) of the helminthes. So, cannot retain original position and comes out through stool with normal peristalsis.

Dose-

11mg/kg body weight (not more than 1gm at a time)

4. PRAZIQUANTEL:

Praziquantel is the drug of choice of all forms of schistosomiasis (S. Haematobium, S. Mansoni & S. Japonicum). Praziquantel is effective in the treatment of Schistosomiasis and Most flukes.

MOA:

Praziquantel has a selective effect on the tegument of trematodes and increases permeability of calcium.

Praziquantel is rapidly absorbed after oral administration & distributes into the CSF. High levels occur in the bile. The drug is extensively metabolized & excreted through the urine & bile.

Praziquantel appears to increase the permeability of trematode & Cestode cell membrane to calcium, resulting in paralysis, dislodgement & death. Also used against Taeniasis, Diphyllobothriasis, and neurocysticercosis. It rapidly absorbed, bioavailability is about 80% after oral administration.

The drug increases cell membrane permeability to calcium resulting in vacuolization, marked contraction, paralysis, dislodgement and death.

Adverse effects are headache, dizziness, lassitude, nausea, loose stool, pruritus, abdominal pain, urticaria and Arthralgia.

5. AMINO-ACTEONITRILE DERIVATIVES AND SPIROINDOLES:

We are fortunate that two new anthelmintic classes have been introduced, the Amino-Acetonitrile Derivatives (aads) and the spiroindoles, with monepantel (Zolvix®) and a derquantel/abamectin combination (Startect®), as the initial products. It is important that strategies be developed to ensure that the anthelmintics available (old and new) remain effective as long as possible and livestock producers must recognize the need for both parasites control a sustainability of production.

6. BENZIMIDAZOLE COMPOUND [51-53]

1. THIABENDAZOLE [54]:

MOA: The benzimidazole drugs bind selectively to beta-tubulin of nematodes, cestodes and fluke, and inhibit microtubule formation.

Thiabendazole is effective against

- strongyloidiasis
- cutaneous Larva Migrans
- Trichinosis. Thiabendazole affects microtubular aggregation.

It's readily absorbed on oral administration & is hydroxylated in the liver & excreted in the surine. It may cause.

Among the anthelminthics available for the

treatment of human strongyloidosis, the benzimidazole compound, thiabendazole is considered effective in 75–96% of cases, although with considerable adverse effects [4] ; while its therapeutic alternative, albendazole has a cure rate of 42–100%, depending on the dose schedule and length of follow-up. At this stage there was little knowledge of the mechanisms of action of the benzimidazoles in echinococcosis, and experimental work was limited. The therapeutic arsenal available at present for the treatment of human strongyloidosis is limited to thiabendazole and its alternative, albendazole. Thiabendazole therapy is however, frequently associated with considerable adverse reactions. This has necessitated the need for better and safer therapeutic alternatives.

2. MEBENDAZOLE:

Together with the 200 million doses of mebendazole (another deworming medicine) donated by Johnson & Johnson, this will have huge impact on treating the more than 600 million children targeted by the World Health Organization (WHO). Relatively toxic drug.

Mechanism of Action [55]

It inhibits the microtubule formation. So the parasite loses its cytoskeleton and motility and dies.

It also impairs glucose uptake and ↓ ATP formation.

-in stool worm is not seen because the clearance of the dead worm is very slow.

Dose

2 tab of 100mg daily for 3 days

In case of pinworm a single dose can be given

Can be given for 1 month in hydatid cyst or neurocysticercosis

PREVENTION:

- Safe disposal of faeces
- Avoid contact with contaminated soil
- Good personal hygiene
- Adequate sanitation
- Avoid bare footed walking
- Control measures for mosquitoes and flies
- Mass public awareness
- Have a house with a cement floor rather than an earth floor.
- Use a privately owned bathroom rather than a public bathroom.
- On an individual level, wearing shoes in risk-areas is strongly advised and will significantly lower one's likelihood of becoming infected.
- Examine and treat all infected dogs, cats, and monkeys that are in contact with people. Practice strict personal hygiene.
- Adequate public health services and sanitary facilities

PROGNOSIS:

Acute and chronic strongyloidiasis carry a good prognosis in immunocompetent hosts. However, untreated infection can persist for the remainder of the patient's life because of autoinfection. Most immunocompetent individuals who develop strongyloidiasis have asymptomatic chronic infections that result in negligible morbidity. A patient's prolonged absence from an endemic area is no guarantee of freedom from infection.

Severe strongyloidiasis (hyperinfection syndrome and disseminated strongyloidiasis) carries a high mortality rate (up to 80%) because the diagnosis is often delayed. This relates to its nonspecific presentation and the host's immunocompromised status. Death from *Strongyloides* infection is typically iatrogenic and frequently occurs after an asymptomatic infected person is treated with immunosuppression [56]. Gram-negative sepsis is a common consequence of hyperinfection and carries a 50% mortality rate [57]. Disseminated strongyloidiasis may be relatively common in high-risk populations and may be frequently misdiagnosed as isolated gram-negative sepsis or acute respiratory distress syndrome.

Summary:

The anthelmintic drugs currently available are still relatively few in number. Many of them are limited in their usefulness because of narrow spectrum of action, safety, high cost or impractical delivery systems. Some of these will be discontinued because of unforseen problems such as occurrence of drug resistance which needs more attention than it presently receives. Drug development is costly and time consuming and requires exacting interdisciplinary

interactions between researchers using the most stringent quantitative tests to determine toxicity, safety, mode of action and pharmacokinetics before a drug is ever used in clinical trials. A system of universal testing standards accepted by all involved in drug-development should be established. Scientists are beginning to apply rational design to the development of new compounds and this approach can be expected to be exploited more in the future. From the clinical standpoint, the future is beginning to look brighter for the millions of persons suffering from helminth diseases as a result of available broad spectrum compounds which can be used in clinics and mass-treatment programs.

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