Confronting parasite resistance: The power of One Health strategy

Review Article

Amira Ismail

Department of Medical Parasitology, Faculty of Medicine, Mansoura University, Mansoura Egypt

ABSTRACT

Antiparasitic resistance is recognized as one of the most serious global health challenges of the 21st century. A continued focus on parasitic diseases is essential for improving strategies to preserve the efficacy of existing antiparasitic medications and to reduce the global burden posed by these diseases. This review explores the One Health perspective on antiparasitic resistance, emphasizing the interrelationship of human, animal, and environmental health. It also analyzes the primary categories of antiparasitic drugs, the parasitic organisms exhibiting resistance, the mechanisms by which resistance is acquired. Additionally, it evaluates current control and surveillance methods, strategies to fight resistance, and offers insights into future research directions.

Keywords: anthelmintics; antiprotozoals; drug resistance; One Health; parasites.

Received: 22 May, 2025; **Accepted:** 27 June, 2025.

Corresponding Author: Amira Ismail, **Tel.:** +20 1116700240, **E-mail:** a.alazab@live.com

Print ISSN: 1687-7942, **Online ISSN:** 2090-2646, **Vol. 18, No. 2, August, 2025.**

INTRODUCTION

The expansion of globalization and biological changes signified the linkages between human, animal and ecosystem health , increasing the urgency for focusing on the impact of parasitic diseases on global health[1]. Bacterial antimicrobial resistance has been extensively reported; however, the emergence of drug-resistant parasites presents an equivalent threat with global implications[2]. These parasites represent a huge burden of morbidity and mortality, especially for vulnerable subjects in low- and middle-income countries, where they facilitate the transgenerational transmission of poverty and impede socioeconomic development[3]. In addition, the health and productivity of livestock, critical to global food security and income, is increasingly threatened by anthelmintic-resistant parasites[4]. Understanding the complex interrelation between human, animal and environmental health is crucial for addressing this accelerating crisis[5].

The evolution of new therapeutics to combat parasitic infections has been characterized by remarkable periods of progress followed by the predictable emergence of drug resistance[6], from the early dependence on plant-derived preparations to the synthesis of recent chemotherapeutic agents[7-9]. In contrast to bacteria, the eukaryotic nature of parasites, with their elaborate cellular machinery and in many cases also complex life cycles spanning several hosts and environmental stages, presents unique challenges in drug design and resistance management[10,11]. The extreme diversity of the parasitic kingdom, including unicellular protozoa as well as multicellular helminths, requires diverse solutions to elucidate and manage resistance against all these different taxa[12].

The increasing threat of parasites resistance to antiparasitic therapies demonstrates the flaws of inadequate fragmented approaches to animal and human health[13]. It requires a comprehensive view that considers interactions between drug use in various sectors and the environmental reservoirs where resistance can propagate[14,15]. Implementation of the One Health concept, the associated integrated approaches and the appreciation of these interrelated domains[5,16], are required for the analysis of this complicated matter[17].

This review aims to provide a broad analysis of antiparasitic resistance in parasites, focusing on the principal drug classes, the spectrum of target parasites, the resistance mechanisms involved, and the key drivers of resistance in human, animal and environmental contexts. Additionally, it evaluates current control and surveillance methods, strategies to combat resistance, and offers insights into future research directions.

One Health framework in antiparasitic resistance

The One Health concept recognizes that the health of human is inseparably linked to the health of animals and the shared environment[5,18]. This interdependence becomes very clear in parasites, where the resistance to one domain may have a great impact on other domains[16]. For example, anti-parasitic drug use in livestock can lead to the emergence of resistant parasites that may be transmitted to human. Similarly, drug release into the environment can exert selective pressure on parasites, accelerating resistance development during their free-living larval or egg stages[14,15,19].

 DOI: 10.21608/puj.2025.387466.1296

Historical development: The concept of One Health goes back to the 19th century when Rudolf Virchow presented the term zoonosis to explain animal infections that are transmissible to human[20]. The idea expanded to consider environmental health in addition to human and animal health[21]. This concern increased after growth of global concerns over the highly pathogenic avian influenza at the start of the century, drawing attention to the inter-sectoral or cross-sectoral approach[10].

The fundamental rules of One Health include understanding the connection phenomenon relating to human, animal and environment; supporting transdisciplinary efforts; and systems thinking; highlighting a preventive approach; and appreciating that local culture can significantly influence health[22]. These concepts are especially relevant to antiparasitic resistance in parasites whose life cycles may occur in multiple hosts with a variety of environmental stages.

Global health context: Antiparasitic resistance is one of the challenges that demonstrates the need and advantage of One health[13,23]. This resistance serves as an example of how human, animal and environmental health are interconnected, since resistant microorganisms (including the resistance genes themselves) are transferred relatively easily between these domains[2,24]. Promotion of antiparasitic resistance is based on all three domains of One Health: human health (misuse in prescribing and/or lack of adherence to treatment), animal health and agriculture (antiparasitic for growth promotion, prophylaxis), and environmental (drug pollution from manufacturing, hospital waste, agricultural runoff)[25-27].

In 2015, the World Health Organization published the 'Global Action Plan on Antimicrobial Resistance' in conjunction with the Food and Agriculture Organization (FAO) and World Organization for Animal Health (WOAH), that explicitly takes One Health into account. This realization was reached in 2016, when the United Nations (UN) General Assembly held a high-level meeting on antiparasitic resistance, which led to the adoption of a political declaration committing the world's countries to a comprehensive, coordinated response across multiple sectors[28].

For parasitic diseases, the One Health methodology to antiparasitic resistance is important because of the complex lifecycles of many parasites. Furthermore, several antiparasitic drugs are shared among human and veterinary sites offering potential for cross-resistance development. The development of resistance in zoonotic parasites directly challenges human health whereas resistance in livestock parasites challenges food security and livelihoods[29]. Certain studies reported environmental exposure to antiparasitic drugs and to drug-resistant parasites that could impact wildlife and ecosystem health, acting as potential reservoirs for resistance that may affect human and domestic animals later[16,30].

Parasite resistance: A comprehensive overview

Challenges in antiparasitic drug development and design: Treatment of parasitic diseases is based on a variety of drugs, which were developed to specifically destroy parasitic organisms that infect man and animal. Unlike antibiotics that preferentially act against bacterial cell components or processes that are not present in mammalian cells, eukaryotic parasites must be selectively targeted by antiparasitic drugs while minimizing toxicity to the eukaryotic host[7,8]. This represents a major challenge for drug discovery and is a cause of the relative scarcity of antiparasitic drugs compared with antibacterial drugs[31].

Primary classes of antiparasitic drugs

Anthelmintics

Anthelmintics are a group of antiparasitic drugs that expel parasitic worms (helminths) and other internal parasites from the body by either stunning or killing them and without causing significant damage to the host. Benzimidazole compounds (BZs) are broad-spectrum anthelmintics that interfere with a number of crucial biological functions, such as mitosis and intracellular transport through the inhibition of microtubule polymerization by targeting parasite β-tubulin[10]. This class of compounds comprises albendazole and mebendazole, the so-called reference drugs and World Health Organization drugs of choice, to treat and control human soil transmitted helminth infections in mass drug administration programs[32-34].

Macrocyclic lactones (MLs) molecules comprise two main subfamilies: avermectins (*e.g.*, ivermectin) and the milbemycins (*e.g.*, moxidectin). These molecules act on worm nerve and muscle cell glutamate-gated chloride channels GACC to cause paralysis and death of the parasite[28,35]. The MLs are used to control parasitic infections of human and veterinary significance, including those caused by onchocerciasis, lymphatic filariasis and strongyloidiasis in human as well as a range of endo-and ectoparasites infesting livestock and companion animals. Nicotinic acetylcholine receptor agonists, such as tetrahydropyrimidines like Pyrantel and oxantel and imidazothiazoles like levamisole, cause spastic paralysis to nematodes. Levamisole is mainly in livestock and pyrantel in both in human and companion animals[7].

Antiprotozoals

These medications act against a wide range of protozoan parasites, and some are specific to certain groups of organisms. Antimalarials consist of diverse chemical groups with activity against various stages of *Plasmodium* life cycle. The representative artemisinin and its derivatives exert their activity by means of

free radicals' production that, in turn, destroy parasite proteins[36,37]. Quinolines (chloroquine, mefloquine, quinine) block detoxification of heme. Antifolates (pyrimethamine, sulfadoxine) are inhibitors of folate metabolism[38,39]. The drugs above are frequently employed in combination therapy to enhance potency and suppress resistance.

Nitroimidazoles such as metronidazole and tinidazole require reduction of their nitro group to active metabolites that disrupt DNA and other cellular macromolecules. These are active against anaerobic protozoa such as *E. histolytica, T. vaginalis*, and *G. lamblia*[11,40,41]. For many years, antimonials (sodium stibogluconate, meglumine antimoniate) have been the first-line agents in the treatment of leishmaniasis, although their mode of action is not completely known. They seem to act via the inhibition of the parasite's energy metabolism and macromolecular biosynthesis[28,42].

Shared drug classes between human and veterinary medicine

Antiparasitic drugs are administered both to human and animals. This information is crucial in the context of One Health as resistance may develop and spread. Such shared use can lead to cross-resistance and requires coordination across sectors[43]. Benzimidazoles, particularly albendazole, are extensively used in human and veterinary medicine. The same applies to ivermectin, which is used for human onchocerciasis and strongyloidiasis and is one of the most widely used antiparasitic drugs in livestock and companion animals[16,44]. Pyrantel is frequently used against some common gastrointestinal parasites in human and other animals. Against trematodes and cestodes, praziquantel is administered orally to human against schistosomiasis, and to dogs and cats against tapeworm infestations[31,45]. Such dual use of drugs leads to challenging conditions for the emergence and development of resistance. Resistance that arises in one context (*e.g.*, in veterinary medicine) can have efficacy implications in another (*e.g.*, human medicine), especially zoonotic parasites that can alternate between animals and human[10].

Insecticides: As a heterogeneous class of chemical agent, they are used to combat insects harmful to human and animals or are vectors for parasitic diseases. They act on different physiological processes necessary for insect survival, primarily targeting the nervous system, but also metabolism or growth[46]. Various types of insecticides, including organophosphates, pyrethroids, and neonicotinoids, manifest their toxicity via different biochemical modes, such as inhibiting acetyl-cholinesterase or disrupting sodium channels[47]. Most biological mechanisms are directed to produce rapid immobilization or to reduce reproduction of insects in covered areas[48]. They are commonly used in agriculture to protect crop losses from destructive insect populations, in public health to regulate vectors of diseases such as malaria and dengue fever, and in homes to mitigate nuisance pests[47]. The choice of insecticide should be dependent on the target insect species, the environment of use, and considerations for efficacy and possible impacts on non-target organisms[46].

Acaricides: These are a very important class of pesticides used for mite and tick control, as these arthropods are important vectors of parasitic diseases that affect human and animals. Like other pesticides, acaricides are designed to interfere with essential physiological functions in arthropod vectors, ultimately causing the vector to be disabled or killed while ideally causing minimal damage to the host[49]. Acaricides belong to diverse chemical families, including organophosphates, pyrethroids, formamidines, and macrocyclic lactones, with different mechanisms of action[47]. For example, some act as nerve poisons that halt neurotransmission in mites and ticks by targeting receptors like GABA or octopamine receptors, whereas others hinder their development, molting process, or reproductive capabilities. The choice of acaricide usually is based on the target species, the animal host or environment, and on effectiveness and potential toxicity, including the risk of resistance development. Their common application in farming for the control of mite infestations in crops and in veterinary medicine against tick- and mite-borne diseases highlights their relevance for food security and animal health[49].

Major parasites with documented resistance

Protozoan parasites: *Plasmodium* spp., the causative organism of malaria, is responsible for over 200 million new infections annually and approximately 600,000 fatalities each year, predominantly in sub-Saharan Africa[50,51]. This coccidian protozoan parasite poses a significant obstacle to malaria management due to its increasing resistance to antimalarial medications. Chloroquine resistance was first encountered in the late 1950s, and it swept across the globe, leaving this once-effective drug useless in many endemic areas. Later, resistance emerged to sulfadoxine-pyrimethamine, mefloquine, and other antimalarials[2,39]. Of particular importance is the emergence of partial resistance to artemisinin and its companion medications within artemisinin-based combination therapies, which serve as the primary treatment for uncomplicated *falciparum* malaria. The phenomenon of artemisinin resistance, characterized by a slower rate of parasite clearance, was initially reported in the Greater Mekong Subregion and has since been observed in various regions across Africa[22,36]. This resistance is a threat to the global efforts to control and eliminate malaria[51].

Leishmania spp., the causative agents of leishmaniasis, have shown resistance to pentavalent antimonials, the first-line treatment for visceral

*Leishmania*sis in many regions. In some areas, such as Bihar, India, treatment failure rates with antimonials have reached as high as 60%, leading to the adoption of alternative therapies like amphotericin B, miltefosine, and paromomycin. Resistance to these second-line drugs is also emerging, complicating the management of this neglected tropical disease[42]. Besides, *E. histolytica, G. lamblia,* and *T. vaginalis* have shown variable levels of resistance to metronidazole, the primary drug used to treat infections caused by these anaerobic protozoa. Resistance mechanisms include decreased drug activation, enhanced drug efflux, and alterations in metabolic pathways[41].

Helminth parasites: Soil-transmitted helminths, including *A. lumbricoides, T. trichiura*, and hookworms (*N. americanus* and *A. duodenale*), affect over 1.5 billion people worldwide[33]. Additionally, *S. stercoralis* is also a soil-transmitted helminth, affecting an estimated 300-600 million people globally, with transmission primarily occurring through skin contact with contaminated soil[34]. Resistance to benzimidazoles, particularly albendazole and mebendazole, has been reported in these parasites, although the extent and clinical significance of this resistance in human populations remain under investigation[32].

Schistosoma spp., the causative agents of schistosomiasis, have shown reduced susceptibility to praziquantel in some settings. While widespread resistance has not yet been confirmed, there are concerning reports of treatment failures and reduced drug efficacy in areas with intensive praziquantel use, such as in parts of Africa[45].

On the other hand, resistance to anthelmintics in veterinary medicine is widespread and well-documented in gastrointestinal nematodes of livestock, particularly in sheep, goats, and cattle. *H. contortus, T. circumcincta*, and *Trichostrongylus* spp. have developed resistance to multiple drug classes, including benzimidazoles, macrocyclic lactones, and imidazothiazoles. In some regions, these parasites have developed resistance to all available anthelmintic classes, posing a significant threat to livestock production and welfare[32].

Arthropod vectors: *Anopheles* mosquitoes, vectors of malaria, have developed resistance to multiple insecticides used in vector control programs, including pyrethroids, organochlorines, organophosphates, and carbamates. This resistance threatens the effectiveness of insecticide-treated bed nets and indoor residual spraying, key interventions for malaria control[48]. Ticks, vectors of various parasitic diseases, have shown resistance to acaricides used for their control. *R. microplus*, a major cattle tick, has developed resistance to multiple acaricide classes, complicating the management of tick-borne diseases in livestock[50].

Mechanisms of antiparasitic resistance

Antiparasitic resistance occurs at the molecular and cellular levels, enabling survival in the presence of a drug intended to be lethal. Consequently, comprehending these resistance mechanisms is crucial for formulating strategies that not only combat this issue but also stay ahead of emerging resistance. This understanding will help ensure the optimal use of the remaining effective antiparasitic medications[41].

Genetic mechanisms: Resistance to antiparasitic drugs occurs due to various genetic mechanisms that include point mutations, gene amplifications, and changes in gene expression. These genetic changes can be inherited or acquired during a parasite's lifetime. The rate at which resistance develops depends on factors such as the parasite's generation time, the intensity of drug selection pressure, and the fitness cost associated with resistance mutations[52].

In *P. falciparum*, resistance to chloroquine is associated with mutations in the *Pfcrt* gene, which encodes a transporter protein involved in drug efflux from the parasite's digestive vacuole. Resistance to artemisinin is linked to mutations in the *kelch13* gene, which affects the parasite's ability to enter a dormant state and evade drug action[36,37]. In helminths, resistance to benzimidazoles is primarily due to single nucleotide polymorphisms in the gene encoding β-tubulin that alters the drug's binding site. Resistance to macrocyclic lactones involves changes in glutamate-gated chloride channels and P-glycoprotein transporters that affect drug uptake and efflux[32].

Biochemical and cellular mechanisms: Parasites can develop resistance through various biochemical and physiological adaptations, including: (1) Target site alterations: Changes in the structure or expression of drug targets can reduce drug binding and efficacy. For example, mutations in the genes encoding dihydrofolate reductase and dihydropteroate synthase confer resistance to antifolate antimalarials by altering the enzymes' binding sites[38]. (2) Enhanced drug efflux: Increased expression or activity of efflux pumps, such as P-glycoproteins and multidrug resistance-associated proteins, can reduce intracellular drug concentrations. This mechanism is observed in various parasites, including *Plasmodium*, *Leishmania*, and helminths[52]. (3) Metabolic detoxification: Parasites can develop enhanced ability to detoxify drugs through increased expression or activity of metabolic enzymes. For instance, elevated levels of glutathione S-transferases and cytochrome P450 enzymes can contribute to insecticide resistance in mosquitoes[48]. (4) Reduced drug activation: Some antiparasitic drugs require metabolic activation to exert their effects. Decreased expression or activity of activating enzymes can lead to resistance. This mechanism is observed with nitroimidazoles, which require reduction of their nitro

group to form toxic metabolites[41]. (5) Dormancy and stress responses: Some parasites can enter a dormant or stress-resistant state to survive drug exposure. This mechanism has been implicated in artemisinin resistance in *P. falciparum*, where parasites can temporarily suspend their development during drug exposure[36].

Transmission of resistance

Resistance genes can be transmitted vertically (from parent to offspring) or horizontally (between individuals of the same generation). In some cases, resistance can spread through genetic recombination during sexual reproduction, as observed in *Plasmodium*. Resistance genes can be enhanced by various factors, including high parasite density, frequent drug use, and human and animal movement[51,52]. The spread of resistance can be particularly rapid in parasites with short generation times and high reproductive rates. Additionally, the movement of human and animals can facilitate the geographical spread of resistant parasites. For example, artemisinin-resistant *P. falciparum* has spread from the Greater Mekong Subregion to other parts of Asia and Africa through human movement[37].

Drivers of antiparasitic drug resistance

Human health drivers: Inappropriate anthelmintic use in human healthcare, including incorrect dosages, insufficient treatment, and substandard medications, foster drug resistance[35,53]. Self-treatment in endemic areas, driven by limited healthcare access, often leads to suboptimal drug selection and dosing, promoting resistance emergence and spread[31,54]. While mass drug administration programs are crucial for parasitic disease control[33], their implementation requires careful design to avoid accelerating resistance accumulation. These programs often involve preventive chemotherapy without individual diagnosis[55], and despite their success in reducing diseases like lymphatic filariasis and onchocerciasis, large-scale administration has led to the development of strong parasite resistance[56].

Limited access to diagnostic tools in many resource-limited settings necessitates empirical treatment, which can lead to overuse of medications, inefficient treatment, and resistance development[16,57]. Furthermore, the lack of alternative drugs for many parasitic diseases results in repeated use of the same drugs, despite their diminishing efficacy[58].

Animal health and agricultural drivers: Use of anthelmintics in livestock production is a major driver of resistance[4]. In most parts of the world, these drugs are utilized not only therapeutically but also as prophylactics and growth promoters[59]. The regular, subtherapeutic administration of antiparasitic agents in feed or water increases the likelihood of developing resistance. Intensive farming systems that keep large numbers of animals with few genetic lines are favorable to the fast spread of resistant parasites within herds or flocks[60].

Moreover, through the international trade of livestock and animal products, resistant parasites can be transmitted across borders and influence global resistance dissemination[61]. Poor regulation and control of the sale and use of veterinary antiparasitic drugs in many countries means that these chemicals are sold "over-the-counter" and used without the direction or prescription of a veterinarian[52,62]. This is a potential problem given that poor professional guidance may result in inappropriate selection of drugs, dosing of drugs, and duration of treatment[7]. Additionally, economic challenges faced by farmers may lead them to utilize less expensive, potentially lower-quality products or to apply inadequate dosages as a means of reducing expenses[63].

Environmental drivers: Antiparasitic drugs and their residual metabolites enter the environment through several sources including pharmaceutical wastewater production, hospital effluents, and agricultural runoff[25,64]. Once present, these environmental residues act as selective pressures, promoting the development of drug resistance in free-living parasite stages, and environmental reservoirs in which parasitic stages can survive and potentially multiply[19]. This process is further intensified by the long-term persistence of some of these compounds in soil and water[26,27]. Climate change, through altered temperature and precipitation, influences parasitic disease distribution, abundance, and drug resistance by affecting parasite life cycles, vector distribution, and host-parasite interactions[11,65]. Poor sanitation and waste management further exacerbate transmission, increasing the spread of resistant parasites. Additionally, ineffective water treatment can lead to exposure to drug residues and resistant parasites in drinking water[26].

Socioeconomic and political drivers: Limited access to quality healthcare, clean water, and adequate sanitation significantly contributes to antiparasitic resistance[2], exacerbating parasitic disease burden and hindering accurate diagnosis and treatment[31]. Poor health infrastructure and laboratory resources in endemic regions impede diagnosis, treatment, and monitoring of parasitic infections and resistance[66].

Lack of surveillance and early resistance detection can lead to missed interventions. Low investment in research and development for new antiparasitic drugs, especially for neglected tropical diseases, limits treatment options when resistance emerges[8,31]. To combat antiparasitic resistance, integrated approaches applying the One Health concept are necessary[13,17]. Strategies should focus on better management of existing drugs, improved resistance monitoring, and developing alternative measures to address

socioeconomic and environmental factors driving resistance[67,7].

Monitoring and surveillance of antiparasitic drug resistance

Current surveillance methods: Global surveillance of antiparasitic resistance is less extensive than for bacterial resistance. The WHO's 'Global Antimicrobial Resistance and Use Surveillance System' (GLASS) primarily focuses on bacterial pathogens, with limited coverage for parasites[68]. However, disease-specific surveillance programs exist for some parasitic diseases, such as the WHO's antimalarial drug efficacy surveillance, which tracks resistance to artemisinin-based combination therapies and other antimalarials[31,37]. National and regional surveillance systems exhibit high variability in coverage, methods, and capacities, with high-income countries generally having stronger systems. Conversely, most low- and middle-income countries, that bear the highest burden of parasitic diseases, face significant challenges in establishing and maintaining surveillance. These disparities create gaps in our understanding of global antiparasitic resistance and hinder integrated actions[22]. In veterinary practice, anthelmintic resistance monitoring for parasitic helminths in livestock is more established in regions with significant livestock industries, such as Australia, New Zealand, and parts of Europe, through programs like the Fecal Egg Count Reduction Test (FECRT) network. However, international coverage remains irregular, and methodological standardization is often lacking[10].

Methods of surveillance: Clinical treatment efficacy research serves as the benchmark for identifying resistance in numerous parasitic diseases. Such evaluations imply observation of clinical and parasitological response of infected hosts after treatment. Decreased cure rates or delayed times of parasite clearance can serve as indications of developing drug resistance. However, these studies can be time consuming and expensive, especially in rural areas. Parasitological techniques, *e.g.* microscopic evaluation of blood smears for malaria parasites or stool samples for helminth eggs/larvae, serve as fundamental approaches of diagnosing parasites and monitoring the treatment effect. Quantitative techniques, such as egg counts in feces, can be useful to estimate the degree of infection and the response to therapy; changes in parasite burden may indicate resistance[35].

The use of molecular diagnostics has also become a more relevant approach for identifying and characterizing antiparasitic resistance[67]. Of note, PCR and DNA sequencing are utilized to detect critical gene mutations for drug resistance, contributing to the monitoring of resistance markers. They tend to be both more sensitive and more specific than phenotypic tests, allowing for the identification of resistance prior to the onset of any clinical failure[69,70].

The mapping of drug-resistant parasites and the determination of factors associated with the emergence and spread of resistance have become increasingly reliant upon geographic information systems (GIS) and spatial analysis. They can be used to visualize patterns of resistance, find hotspots and target interventions more effectively. Combining resistance-related data from human, animals and the environment using a GIS approach may contribute to a more holistic One Health perspective of the resistance epidemiology[71].

Challenges in surveillance: Monitoring antiparasitic resistance, especially in low-income countries, is limited by insufficient laboratory capacity, human resources, and funding for sustainable surveillance[72]. Non-standardized diagnostic tests, treatment regimens, and data collection methods complicate the comparison of resistance data across regions and time periods[73].

Complex parasite life cycles, involving multiple hosts and environmental stages, complicate monitoring and necessitate multisectoral collaboration[74]. Asymptomatic or mildly symptomatic infections lead to under-reporting, making drug efficacy assessment difficult[75]. A lack of integrated data sharing mechanisms across human, animal, and environmental health hinders a comprehensive One Health understanding. Addressing these issues requires increased investment in surveillance, capacity building, methodological standardization, and enhanced inter-sectoral cooperation and data sharing[5].

Strategies to combat antiparasitic resistance

Development of new antiparasitic agents: There is a pressing need for enhanced financial support to discover and develop new antiparasitic drugs with new modes of action[8]. Investigating the antiparasitic properties of currently authorized medications that are intended for different uses may yield faster and more economical solutions[7]. Host-independent essential pathways in parasites could be targeted and serve as a basis for novel drugs[9].

Combined One Health interventions: Communication and cooperation among healthcare professionals, veterinarians, agricultural stakeholders, and environmental scientists is required for tackling the interrelated factors that contribute to resistance[5]. Actions to decrease environmental contamination with anti-parasitics and resistant parasites, *e.g.*, improved wastewater treatment or agricultural runoff control, can reduce the selection, and further spread of resistance[15].

There is an urgent need to increase awareness among healthcare staff, animal keepers, farmers and the general public on the consequences of non-responsible use of antiparasitic drugs and the development of resistance in order to foster behavior change[63]. Development and enforcement of regulations on the

production, distribution, and use of antiparasitic drugs in human and veterinary medicine can help to limit misuse and overuse[27].

Future research directions

While significant progress has been made in understanding molecular mechanisms of resistance, further characterization of species-specific resistance pathways remains critical for developing targeted diagnostics[71]. Insights into the evolutionary histories and patterns of transmission of drug-resistant parasites across human-animal-environmental sectors are essential for predicting and outlining measures to control antiparasitic resistance[4].

The influence of environmental contamination and global warming are not clear in the selection and dispersal of antiparasitic resistance and require further exploration[14]. There is an urgent need for new, fast, and cost-effective detection tools for parasitic infections and for detecting drug resistance markers, especially in low-resource settings[53]. Investigating and applying alternative parasite control options, such as vector control, sanitation improvement and biological control are expected to reduce dependence on antiparasitic drugs and minimize the spread of resistance[52]. Research that reports the burden of resistance encourages increased funding and policy change[40].

CONCLUDING REMARKS

1. **Ongoing challenge:** Drug resistance in parasites is a growing serious threat, compromising the control of significant parasitic diseases of human and animals worldwide.
2. **One Health perspective:** Tackling this problem demands a universal One Health strategy, that recognizes the deep interconnection of drug use and the emergence of resistance across human, animal, and environmental health.
3. **Multifaceted drivers:** Resistance may be emerging and spreading because of several issues, including inappropriate usage of the drugs, contamination of the environment, and socio-economic factors.
4. **Fragile therapeutics:** Effectiveness of modern antiparasitic drugs may be threatened leading to major losses in health and food security.
5. **Knowledge gaps:** There are many large gaps regarding resistance mechanisms and the ecological dynamics affecting resistance development.
6. **Immediate action is required:** Researchers, policymakers and stakeholders across sectors should act in a joint and coordinated manner.
7. **Sustaining the efficacy of antiparasitic treatments:** To preserve the efficacy of antiparasitic treatments and protect global health, strong antiparasitic programs, responsible drug use, surveillance, and investment in new therapeutics are essential.

Competing interests: None.
Funding statement: None.

REFERENCES

1. De Gaetano S, Ponzo E, Midiri A, Mancuso G, Filippone D, Infortuna G. Global trends and action items for the prevention and control of emerging and re-emerging infectious diseases. Hygiene 2025; 5(2):18.
2. World Health Organization. Global report on antimicrobial resistance. Geneva: WHO; 2023.
3. Torgerson PR, Devleesschauwer B, Praet N, Speybroeck N, Willingham AL, Kasuga F. World Health Organization estimates of the global and regional disease burden of 11 foodborne parasitic diseases, 2010: A data synthesis. PLoS Med 2015; 12(12):1001920.
4. Woolhouse M, Ward M, van Bunnik B, Farrar J. Antimicrobial resistance in humans, livestock and the wider environment. Philos Trans R Soc Lond B Biol Sci 2015; 370(1670):20140083.
5. Amuasi JH, Walzer C, Heymann D, Carabin H, Huong LT, Haines A. Calling for a COVID-19 One Health Research Coalition. Lancet 2020; 395(10236):1543-1544.
6. Baker RE, Mahmud AS, Miller IF, Rajeev M, Rasambainarivo F, Rice BL. Infectious disease in an era of global change. Nat Rev Microbiol 2022; 20(4):193-205.
7. Qu Z, Luo Y, Jiang Y, Guo Y, Jiang J, Yan Y. Impact of dual climatic and socioeconomic factors on emerging infectious diseases. Sci Rep 2025; 15(1):1-12.
8. Sibley LD. Campbell S, Soman-Faulkner K. Antiparasitic drugs. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. Available online at https://www.ncbi.nlm.nih.gov/books/NBK544251.
9. Invasion and intracellular survival by protozoan parasites. Immunol Rev 2015; 240(1):72-91.
10. Oliveira PA, Ferreira I, Santos C. An overview of the recent advances in antimicrobial resistance. Microorganisms 2024; 12(9):1920.
11. Liao H, Xiao J, Li Y, Zheng S, Xu W, Yang H. Climate change, its impact on emerging infectious diseases, and the need for novel surveillance approaches. Emerg Microbes Infect 2024; 13(1):2356143.
12. Wiethoelter AK, Beltrán-Alcrudo D, Kock R, Mor SM. Global trends in infectious diseases at the wildlife–livestock interface. Proc Natl Acad Sci USA 2015; 112(31):9662-9667.
13. Hernando-Amado S, Coque TM, Baquero F, Martínez JL. Defining and combating antibiotic resistance from One Health and Global Health perspectives. Nat Microbiol 2019; 4(9):1432-1442.
14. Bengtsson-Palme J, Kristiansson E, Larsson DGJ. Environmental factors influencing the development and spread of antibiotic resistance. FEMS Microbiol Rev 2018; 42(1):53.
15. Berendonk TU, Manaia CM, Merlin C, Fatta-Kassinos D, Cytryn E, Walsh F. Tackling antibiotic resistance: The environmental framework. Nat Rev Microbiol 2015; 13(5):310-317.
16. Organization for Economic Co-operation and Development. Embracing a One Health framework to fight antimicrobial resistance. Paris: OECD Publishing; 2023. Available online at https://www.oecd.org/en/

publications/embracing-a-one-health-framework-to-fight-antimicrobial-resistance_ce44c755-en.html
17. Aarestrup FM, Bonten M, Koopmans M. Pandemics: One Health preparedness for the next. Lancet Reg Health Eur 2021; 9:100210.
18. McEwen SA, Collignon PJ. Antimicrobial resistance: A One Health perspective. Microbiol Spectr 2018; 6(2):0009-2017.
19. Huijbers PM, Blaak H, de Jong MC, Graat EA, Vandenbroucke-Grauls CM, de Roda Husman AM. Role of the environment in the transmission of antimicrobial resistance to humans: A review. Environ Sci Technol 2015; 49(20):11993-12004.
20. Musicha P, Morse T, Cocker D, Mugisha L, Jewell CP, Feasey NA. Time to define One Health approaches to tackling antimicrobial resistance. Nat Commun 2024; 15:8782.
21. Ahmad N, Joji RM, Shahid M. Evolution and implementation of One Health to control the dissemination of antibiotic-resistant bacteria and resistance genes: A review. Front Cell Infect Microbiol 2022; 12:1065796.
22. Ahmed S, Khan MA, Rahman M. Antimicrobial resistance: Impacts, challenges, and future prospects. J Antimicrob Res 2024; 12(1):34-49.
23. Mouiche MMM, Moffo F, Akoachere JTK, Okah-Nnane NH, Mapiefou NP, Ndze VN. Antimicrobial resistance from a one health perspective in Cameroon: A systematic review and meta-analysis. BMC Public Health 2019; 19(1):1135.
24. Hernandez-Vargas EA, Velasco-Hernandez JX. In-host mathematical modelling of COVID-19 in humans. Annu Rev Control 2020; 50:448-456.
25. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: One Health approach. Vet World 2022; 15(3):743-749.
26. Chen Q, An XL, Li H, Su JQ, Ma YB, Zhu YG. Long-term field application of sewage sludge increases the abundance of antibiotic resistance genes in soil. Environ Int 2017; 92-93:1-10.
27. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. Lancet 2022; 399(10325):629-655.
28. Ming Z. Antimicrobial resistance in parasitic diseases: understanding mechanisms and implications for treatment strategies. J Parasit Dis Diagn Ther 2023; 8(3):148.
29. Vercruysse J, Charlier J, Van Dijk J, Morgan ER, Geary T, von Samson-Himmelstjerna G. Control of helminth ruminant infections by 2030. Parasitology 2018; 145(13):1655-1664.
30. Kraemer MUG, Reiner RC, Brady OJ, Messina JP, Gilbert M, Pigott DM. Past and future spread of the arbovirus vectors *Aedes aegypti* and *Aedes albopictus*. Nat Microbiol 2019; 4(5):854-863.
31. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: A global multifaceted phenomenon. Pathog Glob Health 2015; 109(7):309-318.
32. Vineer RH, Morgan ER, Hertzberg H, Bartley DJ, Bosco A, Charlier J. Increasing importance of anthelmintic resistance in European livestock: creation and meta-analysis of an open database. Parasite 2020; 27:69.
33. Chen J, Bergquist R, Li R, Li X, Yin F, Zeng X. Global burden of soil-transmitted helminth infections, 1990-2021: A systematic analysis for the Global Burden of Disease Study 2021. Infect Dis Poverty 2024; 13(1):40.
34. World Health Organization. Guideline on preventive chemotherapy for public health control of strongyloidiasis. Geneva: WHO; 2024.
35. Sangster NC, Cowling A, Woodgate RG. Ten events that defined anthelmintic resistance research. Trends Parasitol 2018; 34(7):553-563.
36. White NJ, Ashley EA, Fairhurst RM. Artemisinin-resistant malaria. Clin Microbiol Rev 2024; 37(3): e00109-24.
37. Uwimana A, Legrand E, Stokes BH, Ndikumana JM, Warsame M, Umulisa N. Emergence and clonal expansion of *in vitro* artemisinin-resistant *Plasmodium falciparum kelch13* R561H mutant parasites in Rwanda. Nat Med 2020; 26(10):1602-1608.
38. Cui L, Mharakurwa S, Ndiaye D, Rathod PK, Rosenthal PJ. Antimalarial drug resistance: Literature review and activities and findings of the ICEMR network. Am J Trop Med Hyg 2015; 93(3 Suppl):57-68.
39. Haldar K, Bhattacharjee S, Safeukui I. Drug resistance in *Plasmodium*. Nat Rev Microbiol 2018; 16(3):156-170.
40. Dadgostar P. Antimicrobial resistance: Implications and costs. Infect Drug Resist 2019; 12:3903-3910.
41. Argüello-García R, Leitsch D, Skinner-Adams T, Ortega-Pierres MG. Drug resistance in *Giardia*: Mechanisms and alternative treatments. Adv Parasitol 2020; 107:201-282.
42. Burza S, Croft SL, Boelaert M. Leishmaniasis. Lancet 2018; 392(10151):951-970.
43. Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH. Antibiotic resistance: A rundown of a global crisis. Infect Drug Resist 2018; 11:1645-1658.
44. Doyle SR, Bourguinat C, Nana-Djeunga HC, Kengne-Ouafo JA, Pion SDS, Bopda J. Genome-wide analysis of ivermectin response by *Onchocerca volvulus* reveals that genetic drift and soft selective sweeps contribute to loss of drug sensitivity. PLoS Negl Trop Dis 2017; 11(7): e0005816.
45. Bergquist R, Zhou XN, Rollinson D, Reinhard-Rupp J, Klohe K. Elimination of schistosomiasis: The tools required. Infect Dis Poverty 2017; 6(1):158.
46. Araújo MF, Castanheira EMS, Sousa SF. The buzz on insecticides: A review of uses, molecular structures, targets, adverse effects, and alternatives. Molecules 2023; 28(8):3641.
47. US Environmental Protection Agency (EPA). Insecticides. In: Causal Analysis/Diagnosis Decision Information System (CADDIS). Washington, DC: EPA; 2022. Available online at https://www.epa.gov/caddis/insecticides
48. Sparks TC, Nauen R. IRAC: Mode of action classification and insecticide resistance management. Pestic Biochem Physiol 2015; 121:122-128.
49. Obaid MK, Islam N, Alouffi A, Khan AZ, Vaz IdS Jr, Tanaka T. Acaricides resistance in ticks: selection, diagnosis, mechanisms, and mitigation. Front Cell Infect Microbiol 2022; 12:941831.

50. Chaccour C. Veterinary endectocides for malaria control and elimination: prospects and challenges. Philos Trans R Soc Lond B Biol Sci 2021; 376(1824):20190810.
51. Huang Y, Geng J, Li Y. Trends of global, regional, and national incidence, mortality, and disability-adjusted life years for malaria in 204 countries and territories from 1990 to 2019: A systematic analysis for the Global Burden of Disease Study 2019. Available online at https://www.dovepress.com/article/download/84722.
52. Raheel S, Shahid A, Shah B, Ahmad M. Drug resistance in parasitic diseases. Vet Parasitol 2024; 330, 108157.
53. Kotze AC, Prichard RK. Anthelmintic resistance in *Haemonchus contortus*: history, mechanisms and diagnosis. Adv Parasitol 2016; 93:397-428.
54. Charlier J, Vercruysse J, Van Dijk J, Höglund J, Torgerson PR, Taylor MA. Initial assessment of the economic burden of major parasitic helminth infections to the ruminant livestock industry in Europe. Prev Vet Med 2020; 182:105103.
55. Chaccour C, Hammann F, Rabinovich NR. Ivermectin to reduce malaria transmission I. Pharmacokinetic and pharmacodynamic considerations regarding efficacy and safety. Malar J 2017; 16(1):161.
56. Picot J, Vingataramin L, Cissokho M, Marcombe S, Chandre F, Dupont S. Insecticide resistance in mosquito vectors of arboviruses: mechanisms, monitoring, and public health consequences. Front Physiol 2022; 13:904344.
57. Ayala A, Domínguez-Bernal G, Becerra-Díaz M, Terrazas LI, Satoskar AR, Martínez-Labat P. Advances in *Leishmania* vaccines: Current development status, challenges, and future prospects. Front Immunol 2024; 15:1252087.
58. Salam MA, Al-Amin MY, Salam MT, Pawar JS, Akhter N, Rabaan AA. Antimicrobial resistance: A growing serious threat for global public health. Healthcare 2023; 11(13):1946.
59. Šlapeta J, Vande Velde F, Martínez-Valladares M, Canton C, Claerebout E, Gilleard JS. Towards precision parasite management for livestock gastrointestinal nematodes in 2030. Trends Parasitol 2024; 40(10):86-895.
60. Efstratiou A, Ongerth JE, Karanis P. Waterborne transmission of protozoan parasites: review of worldwide outbreaks: An update 2011-2016. Water Res 2017; 114:14-22.
61. Rousham EK, Unicomb L, Islam MA. Human, animal and environmental contributors to antibiotic resistance in low-resource settings: Integrating behavioral, epidemiological and One Health approaches. Proc R Soc B 2018; 285(1876):20180332.
62. Saha M, Sarkar A. Review on multiple facets of drug resistance: A rising challenge in the 21st century. J Xenobiotics 2021; 11(4):197-214.
63. Dickin SK, Schuster-Wallace CJ, Qadir M, Pizzacalla K. A review of health risks and pathways for exposure to wastewater use in agriculture. Environ Health Perspect 2016; 124(7):900-909.
64. Fairlie T, Kariuki S, Chiller T, Okoth P, Nyambane G, Ochieng D. Antibiotic resistance in *Escherichia coli* from humans and food animals, Kenya, 2012-2016. Emerg Infect Dis 2019; 25(9):1738-1741.
65. Short EE, Caminade C, Thomas BN. Climate change contribution to the emergence or re-emergence of parasitic diseases. Infect Dis 2017; 10. DOI: 1178633617732296.
66. Hotez PJ, Pecoul B, Rijal S, Boehme C, Aksoy S, Malecela M. Eliminating the neglected tropical diseases: Translational science and new technologies. PLoS Negl Trop Dis 2016; 10(3):0003895.
67. Kotze AC, Gilleard JS, Doyle SR, Prichard RK. Challenges and opportunities for the adoption of molecular diagnostics for anthelmintic resistance. Int J Parasitol 2020; 14:264-273.
68. World Health Organization. Global antimicrobial resistance and use surveillance system (GLASS) report: 2021. World Health Organization; Geneva.
69. Raheemi H, Afsheen Z, Naeem MA, Fareed S, Chen X, Tyagi R, *et al*. Molecular methods for detecting antiparasitic resistance. In: Rizwan HM, Naeem MA, Younus M, Sajid MS, Chen X (Eds), Antiparasitic Resistance. CABI Digital Library, Wallingford, UK, 2024; 95-110.
70. Ting H, Zhou B. Clinical use of molecular methods for *Trypanosoma cruzi* infection in endemic and non-endemic countries: Benefits, limitations and challenges. Front Parasitol 2025; 3, 1397095.
71. Shuaib YA, Elhag AME, Brima YA, Abdalla MA, Bakiet AO, Mohmed-Noor SET. Transforming surveillance and control of infectious diseases in the era of climate change and globalization. One Health 2022; 15:100438.
72. Roberts LS, Janovy J, Nadler SA, Schmidt GD. Foundations of Parasitology, 10th ed. 2019; McGraw-Hill Education, New York, USA.
73. Garba B, Saidu B, Mohammed A, Suleiman N, Yahaya MS, Umar AA. Prevalence and intensity of intestinal and soil-transmitted helminth infections among primary school children in Sokoto, Nigeria. Sci Rep 2025; 15(1):1-9.
74. Bloom DE, Cadarette D. Infectious disease threats in the twenty-first century: Strengthening the global response. Front Immunol 2019; 10:549.
75. Molyneux DH, Savioli L, Engels D. Neglected tropical diseases: Progress towards addressing the chronic pandemic. Lancet 2017; 389(10066):312-325.