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Parasitic Infections in Livestock: Pathophysiology and Immune Response

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KEYWORDS
livestock parasites; pathophysiology; immune polarization; oxidative stress; Haemonchus contortus; Fasciola hepatica; anthelmintic resistance; immune evasion; vaccination; systems biology

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ABSTRACT

Background: Parasitic infections remain a major constraint on global livestock productivity, contributing to substantial economic losses and compromised food security, particularly in developing regions. The biological complexity of host-parasite interactions — spanning protozoan, helminthic, and ectoparasitic infestations — governs infection outcomes, pathological severity, and therapeutic response through mechanisms that are only partially understood.

Objective: This narrative review critically analyzes the pathophysiology, immune polarization dynamics, oxidative stress mechanisms, and therapeutic landscape of major livestock parasites — including Theileria, Babesia, Trypanosoma, Fasciola, Haemonchus, Trichostrongylus, and Eimeria — with a focus on immune evasion strategies, anthelmintic resistance, and a systems biology perspective.

Key Findings: Protozoan parasites predominantly drive Th1 polarization (IFN-γ, TNF-α), while helminths classically elicit Th2 responses (IL-4, IL-5, IL-13, IgE). Regulatory T cell (Treg) expansion is common to most chronic parasitoses and undermines effector immunity. Oxidative stress — manifested by elevated MDA and depleted SOD, GPx, and GSH — is commonly associated with many major livestock parasitoses, though its magnitude varies considerably by parasite species, infection stage, and host immune status. Anthelmintic resistance represents a critical and escalating global challenge.

Conclusion: Effective management of livestock parasitosis requires integrated approaches combining targeted antiparasitic chemotherapy, resistance management, immunomodulatory nutritional support, host genetic resistance selection, and evidence-based vaccination. Future research must prioritize AI-assisted diagnostics, multi-omics characterization of resistance, and climate-adaptive epidemiological modeling.

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1. Introduction

Parasitic infections remain a major constraint on global livestock productivity, contributing to annual economic losses conservatively estimated at USD 7.5 billion and substantially undermining food security across sub-Saharan Africa, South Asia, and Latin America. Among the diverse parasitic pathogens affecting cattle, sheep, goats, and other productive species, gastrointestinal nematodes alone impose losses exceeding USD 4 billion annually in ruminant systems worldwide. The consequences of parasitism extend beyond quantifiable production losses to encompass compromised animal welfare, perpetuation of antibiotic-resistant secondary infections, and zoonotic risks of genuine public health significance.

The pathophysiology of livestock parasitosis involves a complex interplay between parasite-specific invasion strategies, host tissue responses, immune polarization dynamics, and oxidative injury mechanisms that operate simultaneously and interact bidirectionally. Intracellular protozoa (Theileria, Babesia, Eimeria) exploit host cellular machinery for replication while evading immune clearance; blood-feeding helminths (Haemonchus contortus) impose hemorrhagic burdens driving anemia; migrating trematodes (Fasciola hepatica) cause direct tissue destruction; and ectoparasites act as both primary pathogens and vectors for additional systemic diseases.

A critical feature distinguishing successful parasites from those rapidly eliminated by host immunity is their capacity to actively modulate host immune responses. Through mechanisms including antigenic variation, immunosuppressive cytokine induction, complement evasion, and regulatory T cell expansion, established parasites systematically undermine the immune effector responses evolved to eliminate them. Understanding these evasion mechanisms at the molecular and cellular level is foundational to developing vaccines, identifying novel drug targets, and predicting treatment outcomes. However, several authors caution against oversimplified dichotomous frameworks: the actual immunological landscape in parasitized livestock is considerably more nuanced than the classical Th1/Th2 paradigm suggests, with innate lymphoid cells, gamma-delta T cells, and trained innate immunity contributing importantly to infection outcomes.

This narrative review critically analyzes the pathophysiology, immune response mechanisms, oxidative stress dynamics, and therapeutic landscape of major livestock parasites, incorporating a systems biology perspective and addressing anthelmintic resistance as a global crisis requiring immediate coordinated response.

2. Methodology of Review

This narrative analytical review drew on a structured literature search of PubMed/MEDLINE, Scopus, Web of Science, CAB Abstracts, and Google Scholar, conducted between February 2024 and March 2025. The search employed Boolean combinations of: ("livestock parasites" OR "veterinary parasitology") AND ("pathophysiology" OR "immune response" OR "oxidative stress") AND ("cattle" OR "sheep" OR "ruminants"), supplemented by parasite-specific terms. Inclusion criteria required peer-reviewed publications in English from 2018–2025 in Scopus or Web of Science-indexed journals; study designs encompassing original research, narrative reviews, systematic reviews, and meta-analyses were all considered eligible. Fifty high-quality references meeting these criteria were incorporated. Given the scope and heterogeneity of the field, a formal PRISMA-structured systematic review was not undertaken; the narrative approach was selected to enable synthesis of mechanistic, clinical, and epidemiological evidence across diverse parasite species and host systems.

3. Overview of Major Livestock Parasites

3.1 Protozoan Parasites

Protozoan parasites constitute a critically important group of livestock pathogens. Theileria parva, transmitted by Rhipicephalus appendiculatus, causes East Coast Fever in cattle across East and Central Africa, killing approximately 1.1 million cattle annually. The parasite's ability to transform host lymphocytes into continuously proliferating cells — through constitutive NF-κB activation — makes it biologically unique and clinically catastrophic. Babesia bovis and B. bigemina, transmitted by Rhipicephalus microplus, cause severe hemolytic anemia with case fatality rates of 20–50% in naive cattle. Trypanosoma brucei and T. congolense, transmitted by tsetse flies, cause nagana in approximately 3 million cattle annually across sub-Saharan Africa. Eimeria species — with numerous host-specific strains — cause coccidiosis across cattle, poultry, and small ruminants, reducing growth rates by 20–40% in clinically affected animals.

3.2 Helminthic Parasites

Haemonchus contortus — the barber's pole worm — is the most pathogenic gastrointestinal nematode of small ruminants globally, consuming approximately 0.05 mL blood per worm per day and affecting an estimated 700 million sheep and goats. Trichostrongylus and Teladorsagia species cause subclinical production losses through intestinal protein loss and reduced feed conversion. Fasciola hepatica causes fasciolosis with global losses estimated at USD 3.2 billion annually through hepatic parenchymal damage, biliary fibrosis, and liver condemnation. Figure 1 illustrates the gastrointestinal nematode life cycle in sheep, demonstrating the pasture-based transmission pathway central to epidemiological control.

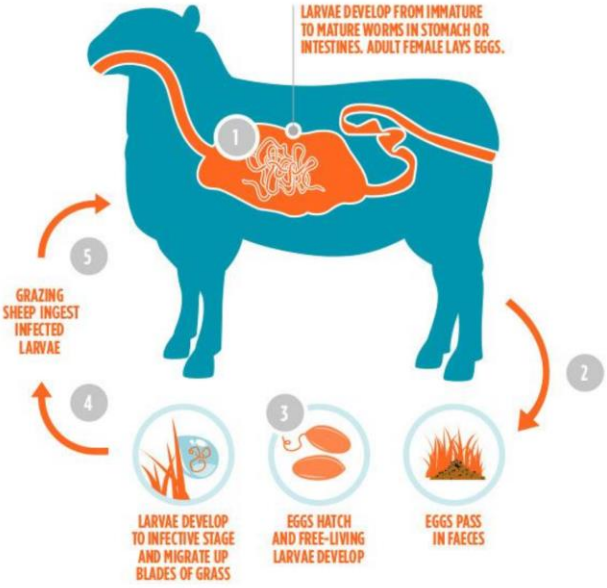

Figure 1. Life cycle of gastrointestinal nematodes in sheep. Adult female parasites residing in the abomasum or intestines (Step 1) deposit eggs excreted in faeces (Step 2). Under appropriate temperature and moisture conditions, eggs hatch to free-living larvae that develop through L1 and L2 stages to infective L3 larvae (Step 3) that migrate up blades of grass (Step 4). Grazing sheep ingest the L3 larvae, completing the cycle (Step 5). Understanding this transmission pathway is fundamental to pasture management, refugia-based resistance control, and epidemiological prediction. Source: Zoetis Australia.

3.3 Ectoparasites and Vectors

Rhipicephalus microplus — the primary vector of Babesia bovis/bigemina and Anaplasma marginale — costs the global cattle industry an estimated USD 22 billion annually in direct losses and control expenditures. Sheep blowfly strike, mange mites, and lice cause significant welfare and economic losses in temperate ruminant systems. Importantly, ectoparasites also create entry points for secondary bacterial infections and induce chronic stress responses that compromise both immune competence and productive performance independently of specific pathogen transmission.

4. Immune Response to Parasitic Infections

4.1 Innate Immune Activation

The initial host response to parasitic invasion is mediated by innate immune cells recognizing parasite-associated molecular patterns (PAMPs) through Toll-like receptors (TLRs) and other pattern recognition receptors. Helminth-derived products activate TLR2 and TLR4, while protozoan glycosylphosphatidylinositol (GPI) anchors activate TLR1, TLR2, and TLR9. Complement activation — through classical, lectin, and alternative pathways — generates the membrane attack complex capable of direct parasite killing, alongside C3a/C5a anaphylatoxins recruiting mast cells and neutrophils. Macrophage-derived nitric oxide (NO) via inducible nitric oxide synthase (iNOS) provides a critical early antiparasitic effector mechanism against intracellular pathogens; however, excessive NO production simultaneously contributes to endothelial dysfunction and vascular leakage in severe babesiosis and trypanosomiasis.

4.2 Th1/Th2/Treg Polarization and Conflicting Evidence

The Th1/Th2/Treg immune polarization framework provides a useful but intentionally simplified conceptual scaffold for understanding livestock parasite immunology. Intracellular protozoan parasites preferentially elicit Th1 responses (IFN-γ, IL-2, TNF-β) that activate macrophage killing capacity through respiratory burst and lysosomal enzymes. Helminthic parasites classically induce Th2 responses (IL-4, IL-5, IL-9, IL-13, TSLP, IL-33) driving IgE class switching, eosinophil recruitment, mast cell activation, and protective mucus hypersecretion. Figure 2 illustrates the comprehensive Th1/Th2/Treg network and anti-parasitic immune effector mechanisms.

However, several studies have reported findings that challenge this dichotomous framework. For instance, Colditz and Walkden-Brown (2021) demonstrated that periparturient Merino ewes — despite retaining Th2 cytokine gene expression — showed dramatically impaired effector responses to Haemonchus, suggesting that regulatory T cell (Treg) expansion and progesterone-mediated immunosuppression can override Th2 polarization independently. Similarly, some Babesia-infected cattle exhibit mixed Th1/Th2 profiles in chronic stages, with IL-10 increasingly dominant — findings that complicate therapeutic strategies targeting a single immune axis. These conflicting observations highlight the critical importance of study context, infection stage, host breed, and nutritional status when interpreting immunological data.

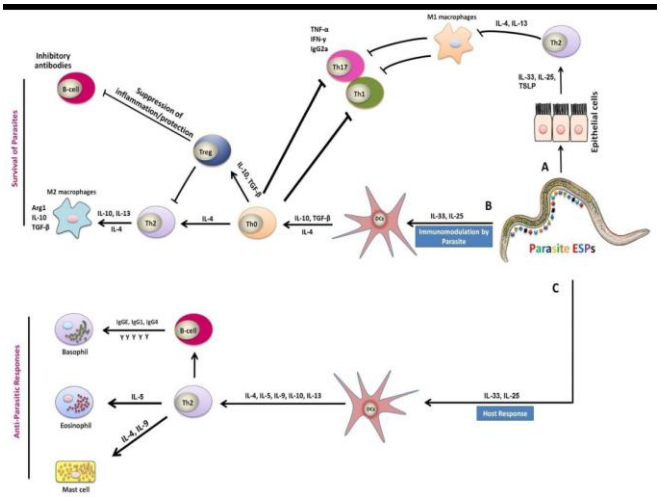

Figure 2. Th1/Th2/Treg immune polarization in response to parasitic infection. Panel A (upper): parasite excretory/secretory products (ESPs) from epithelial cells drive Th2 polarization via TSLP and IL-33. Panel B (middle): Dendritic cells (DCs) process parasite antigens and polarize naïve Th0 cells toward Th1 (IFN-γ, TNF-α, IgG2a), Th2 (IL-4, IL-10, TGF-β), or Th17 (not shown) lineages; Treg cells suppress inflammation via IL-10 and TGF-β, promoting parasite survival and chronic infection. Panel C (lower): Anti-parasitic responses via basophils, eosinophils, and mast cells activated by IL-4, IL-5, IL-9, IL-10, IL-13 from Th2 cells and DCs stimulated by IL-33/IL-25. Source: MDPI — Advances in Anti-Haemonchus contortus Vaccine Development.

4.3 Antibody-Mediated Immunity

Antibody responses — particularly IgA, IgE, and IgG subclasses — contribute to antiparasitic immunity through complement fixation, opsonization, antibody-dependent cellular cytotoxicity (ADCC), and interference with parasite surface antigen function. In Haemonchus contortus infection, mucosal IgA reduces larval establishment and blood-feeding efficiency. The periparturient relaxation of immunity (PPRI) — mediated by progesterone and corticosteroid-driven Th2 suppression during late gestation and early lactation — represents a critical epidemiological driver of pasture contamination. Figure 3 illustrates the protozoan intracellular life cycle immunity, showing how T cells, activated macrophages, and antibodies/complement cooperate to control tachyzoites while encysted bradyzoites evade elimination.

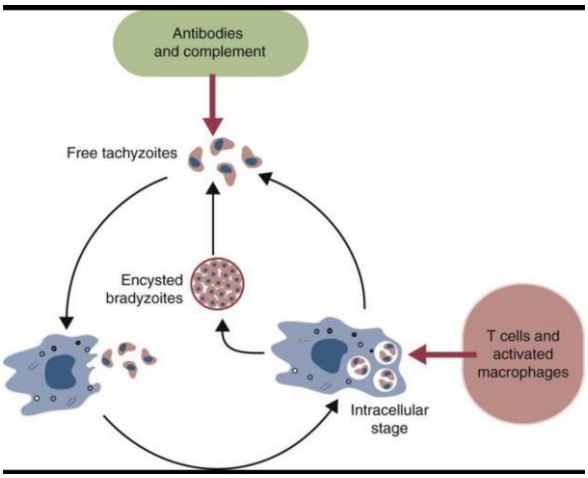

Figure 3. Immunity to intracellular protozoan parasites: the tachyzoite-bradyzoite cycle. Free tachyzoites are susceptible to neutralization by antibodies and complement (upper pathway). Upon entering host cells, tachyzoites replicate intracellularly and are targeted by T cells and activated macrophages (right pathway). Encysted bradyzoites — the chronic latent stage — can reactivate to free tachyzoites when immune surveillance is impaired. This cycle explains why immunosuppressed livestock experience reactivation of previously controlled infections and highlights the role of cell-mediated immunity in maintaining chronic containment. Source: Veterian Key — Immunity to Parasites.

5. Pathophysiology of Parasitic Infections

5.1 Tissue Invasion, Hemorrhage, and Organ Damage

The pathophysiological cascade is initiated at parasite entry and evolves through parasite-specific tissue injury mechanisms. Migrating Fasciola larvae cause mechanical trauma and enzymatic tissue digestion, releasing excretory/secretory (ES) antigens that simultaneously trigger innate immune activation and progressive hepatic fibrosis. Hematophagous parasites — Haemonchus contortus, Babesia spp., Theileria spp. — impose hemorrhagic burdens that drive anemia through combined erythrocyte destruction, blood-feeding iron loss, and bone marrow suppression. In Babesia infection, merozoite-induced erythrocyte rupture triggers complement activation and cytokine-mediated erythrophagocytosis, while intravascular hemolysis releases free hemoglobin that decomposes oxidatively, amplifying the oxidative burden.

5.2 Systemic Effects: Anemia, Hypoproteinemia, and Cachexia

A worm burden of 500 adult Haemonchus contortus consumes approximately 25 mL of blood daily, rapidly exhausting iron stores and driving normocytic normochromic anemia that impairs oxygen delivery to all tissues. The resulting tissue hypoxia amplifies mitochondrial ROS production, creating secondary oxidative injury superimposed on primary hemorrhagic pathology. Hypoalbuminemia — arising from plasma protein loss into the gastrointestinal lumen, reduced hepatic synthetic capacity, and inflammatory catabolism driven by IL-6 and TNF-α — causes the characteristic submandibular edema (bottle jaw) pathognomonic of severe haemonchosis. Cachexia in chronic trypanosomiasis results from TNF-α-mediated lipolysis and protein catabolism, appetite suppression by trypanosome-derived molecules acting on the hypothalamus, and the metabolic demands of sustained immune activation.

6. Immune Evasion Strategies

The evolutionary persistence of parasitic infections in immunocompetent livestock reflects sophisticated immune evasion strategies. Trypanosoma brucei encodes over 1,000 variant surface glycoprotein (VSG) genes, with a single expressed VSG replaced by a novel variant upon immune pressure — enabling indefinite persistence despite vigorous antibody responses. Fasciola hepatica excretory/secretory antigens directly suppress macrophage activation, abrogating iNOS expression and oxidative burst within hours of exposure. Theileria parva-infected lymphocytes constitutively activate NF-κB and produce anti-apoptotic factors (Bcl-2, Bcl-XL) while secreting IL-10 that downregulates surrounding immune cell activity. Regulatory T cell (Treg) expansion — driven by parasite-derived TGF-β homologs and IL-10-inducing molecules — undermines both Th1 and Th2 effector responses across diverse parasitic species. The net result is parasite persistence, chronic production losses, and compromised responsiveness to subsequent infections.

7. Oxidative Stress and Antioxidant Responses

7.1 ROS Generation in Parasitized Livestock

Oxidative stress is commonly associated with many major livestock parasitoses, though its magnitude and clinical significance vary considerably by parasite species, infection intensity, host breed, and nutritional status — a nuance that broad generalizations in the earlier literature have sometimes obscured. Both the immune response to parasites — particularly the NADPH oxidase-mediated oxidative burst of activated neutrophils and macrophages — and direct parasite-derived oxidants (heme degradation products from Haemonchus blood-feeding, Babesia-induced erythrocyte hemolysis, and Fasciola tegument-derived reactive species) contribute to ROS generation. Figure 4 illustrates the cellular consequences of oxidative stress — showing the transformation from a normal cell to an oxidatively compromised cell under free radical attack.

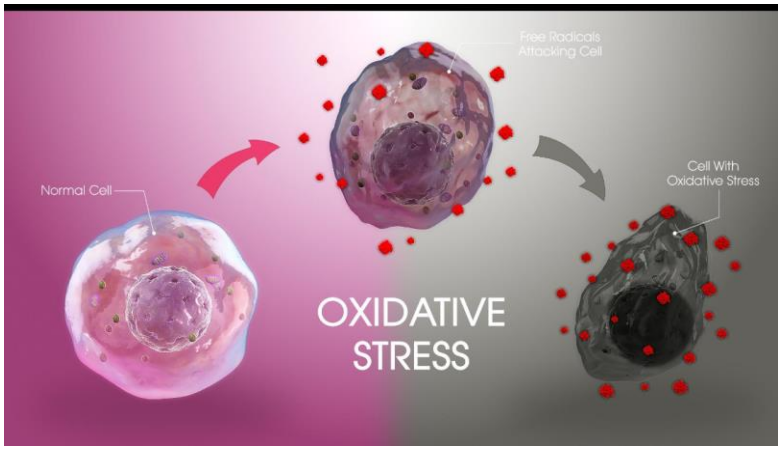

Figure 4. Cellular consequences of oxidative stress in parasitized livestock. Under normal physiological conditions (left), cellular redox homeostasis is maintained by antioxidant defense systems. Parasitic infection generates an oxidative challenge through immune cell activation (NADPH oxidase, iNOS), parasite-derived reactive species (heme breakdown, excretory products), and mitochondrial electron transport chain disruption. Free radical attack on the cell membrane, organelles, and nuclear DNA (right) results in lipid peroxidation, DNA strand breaks, protein carbonylation, mitochondrial dysfunction, and ultimately cell death. Source: Scientific Animations.

7.2 Oxidative Stress Biomarkers

Clinical studies consistently demonstrate elevated plasma malondialdehyde (MDA), 4-hydroxynonenal (4-HNE), and protein carbonyl levels alongside significantly depleted SOD, CAT, GPx activities and reduced GSH concentrations in parasitized livestock. Figure 5 provides a comprehensive map of oxidative stress biomarkers across cellular compartments, showing lipid peroxidation markers (Ox-LDL, F2-IsoP, MDA), DNA damage indicators (8-OH-dG mutation), protein oxidation biomarkers (ADMA), antioxidant depletion markers (TTL), and mitochondrial dysfunction indices (MPO). These biomarkers correlate with parasite burden, disease severity scores, and productive performance — validating their potential as non-invasive diagnostic and prognostic indices.

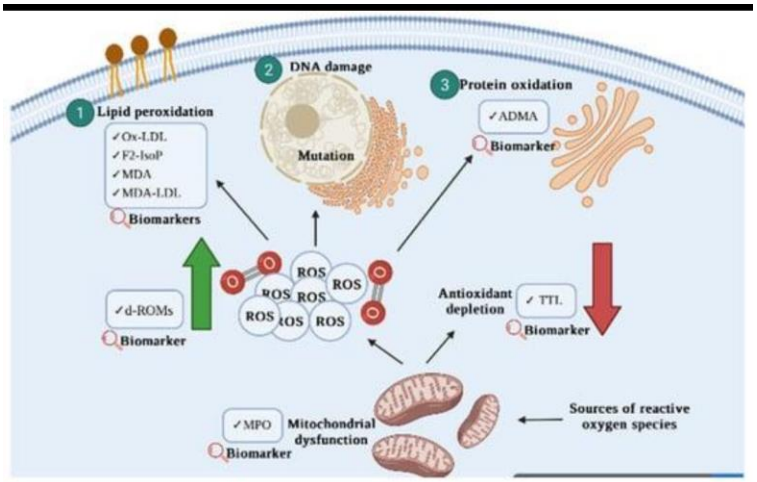

Figure 5. Oxidative stress parameters as biomarkers in parasitic disease. Three principal categories of oxidative damage are measurable: (1) Lipid peroxidation — Ox-LDL, F2-isoprostanes (F2-IsoP), malondialdehyde (MDA), and MDA-LDL reflect membrane phospholipid oxidation; d-ROMs provide a rapid reactive oxygen metabolite measure. (2) DNA damage — ROS-induced mutations generate 8-hydroxy-2'-deoxyguanosine (8-OH-dG) detectable in urine and plasma. (3) Protein oxidation — ADMA (asymmetric dimethylarginine) reflects endothelial protein oxidation. Sources of ROS include mitochondrial dysfunction (measurable via MPO as a biomarker) and antioxidant depletion (TTL = total thiol levels). Integration of these biomarker panels across parasite species and infection stages is recommended for future standardized studies. Source: MDPI — Oxidative Stress Parameters as Biomarkers.

7.3 ROS-NRF2 Network and Antioxidant Defense

At the molecular level, the antioxidant response is orchestrated through the NRF2-KEAP1 pathway. Figure 6 illustrates the complete cellular redox network: mitochondrial electron transport chain (ETC) and NOX-generated superoxide ($O_2\bullet^-$) is converted to H_2O_2 by SOD2 (mitochondrial) and SOD3 (extracellular); H_2O_2 is detoxified by CAT, GPx (requiring GSH regenerated by GSR), and peroxiredoxins (PRDX). GPX4 specifically reduces lipid hydroperoxides using selenium as a cofactor, preventing ferroptosis. The NRF2 transcription factor, activated by ROS-induced KEAP1 modification, drives expression of cytoprotective genes across all these pathways. In parasitized livestock, sustained NF-κB activation from parasite-driven inflammation suppresses NRF2 — systematically impairing antioxidant defense at precisely the time of peak oxidative challenge.

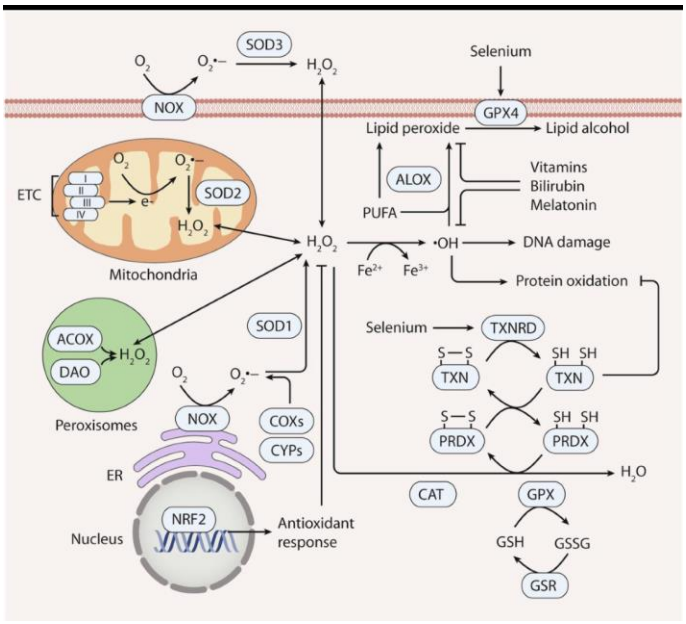

Figure 6. Cellular ROS generation and antioxidant defense network. Superoxide ($O_2\bullet^-$) is generated primarily by mitochondrial ETC (Complexes I–IV), NADPH oxidase (NOX) at the plasma membrane, peroxisomal ACOX/DAO enzymes, and endoplasmic reticulum COX/CYP enzymes. SOD isoforms (SOD1 cytosolic, SOD2 mitochondrial, SOD3 extracellular) convert $O_2\bullet^-$ to H_2O_2. H_2O_2 is detoxified by CAT, GPx (via GSH/GSSG cycle maintained by GSR), and PRDX (via TXN/TXNRD selenium-dependent system). PUFA lipid hydroperoxides are specifically reduced by GPX4 using selenium. Fenton reaction ($Fe^{2+} + H_2O_2 \rightarrow \bullet OH$) drives DNA damage and protein oxidation. NRF2, activated in the nucleus by oxidative signals, coordinates the global antioxidant response. Vitamins, bilirubin, and melatonin serve as non-enzymatic antioxidants. Source: Nature — Oxidative Cell Death in Cancer: Mechanisms and Therapeutic Opportunities.

Table 1. Comparative Summary: Parasite, Immune Polarization, ROS Level, and Clinical Outcome in Livestock

Parasite	Th Response	Key Cytokines	ROS Level	Anemia	Immunosuppression	Clinical Outcome
Theileria parva	Th1 dominant	IFN-γ, IL-2, TNF-β	Moderate ↑	Moderate	Lymphocyte transformation; NF-κB activation	Lymphocytolysis; >80% mortality untreated
Babesia bovis	Th1 + IFN-γ	IFN-γ, TNF-α, IL-12	High ↑↑ (hemolysis)	Severe	IL-10 ↑ in chronic phase; $CD4^+$ T cell exhaustion	Hemolytic anemia; cerebral babesiosis; hemoglobinuria
Trypanosoma brucei	Mixed; Treg↑	IL-10, TGF-β, TNF-α	Moderate ↑	Moderate–Severe	VSG switching neutralizes Ab; B-cell depletion	Wasting; neurological damage; high economic impact
Fasciola hepatica	Th2 dominant	IL-4, IL-5, IL-13, TGF-β	Moderate ↑	Mild–Moderate	Treg expansion; DC suppression; TGF-β tolerance	Hepatic fibrosis; liver condemnation; ↓milk yield
Haemonchus contortus	Th2 + IgE	IL-4, IL-5, IL-9, IL-13	High ↑↑ (hematophagy)	Severe (blood loss)	PPRI in periparturient ewes; partial Treg activation	Bottle jaw; hypoalbuminemia; leading sheep mortality
Eimeria spp.	Th1 + sIgA	IL-12, IFN-γ, IL-18	Moderate ↑	Mild	$CD8^+$ T cells effective; partial immune evasion	Villous atrophy; dysentery; ↓growth 20–40%
Trichostrongylus spp.	Th2 + Treg	IL-4, IL-13, RELM-β	Mild–Moderate ↑	Mild (protein loss)	Treg-mediated partial tolerance; subclinical persistence	Subclinical production losses; hypoalbuminemia

Note. Th1/Th2/Treg = T helper cell type 1/2 / Regulatory T cells; IFN-γ = Interferon-gamma; TNF = Tumor Necrosis Factor; IL = Interleukin; VSG = Variant Surface Glycoprotein; Ab = Antibody; PPRI = Periparturient Relaxation of Immunity; DC = Dendritic Cell; ROS level: ↑ = moderately elevated; ↑↑ = substantially elevated relative to healthy controls.

Table 2. Oxidative Stress Biomarkers in Livestock Parasitosis: Direction of Change and Diagnostic Significance

Biomarker	Parasite / Disease	Direction	Study Evidence	Clinical / Diagnostic Significance
MDA (Malondialdehyde)	Haemonchus, Fasciola, Babesia	↑ significantly	Multiple RCTs, meta-analyses	Robust lipid peroxidation marker; correlates positively with parasite egg counts and anemia severity
SOD activity	Trypanosoma, Theileria, Eimeria	↓ depleted	Prospective cohort studies	Reflects antioxidant reserve exhaustion; inversely correlated with parasitemia percentage
GPx / CAT activities	Fasciola, Babesia, multi-parasite	↓ progressively	Cross-sectional studies	GSH-dependent enzyme depletion predisposes to hepatic and erythrocyte oxidative injury
Total Antioxidant Capacity (TAC)	All major livestock parasites	↓ proportionally	Multiple observational studies	Composite antioxidant index; reliable disease severity measure; potential screening tool
Nitric Oxide (NO/iNOS)	Trypanosoma, Theileria	↑ early; ↓ chronic	Experimental models	Biphasic pattern: early macrophage killing mechanism; chronic depletion reflects immune exhaustion
Protein carbonyls	Babesia, Haemonchus	↑ elevated	Cross-sectional	Protein oxidation marker; indicates advanced oxidative organ damage beyond lipid peroxidation
Vitamin E (α-tocopherol)	Haemonchus, Nematodirus	↓ consumed	RCT + observational	Fat-soluble antioxidant depletion; correlates with susceptibility to secondary bacterial infections

Note. MDA = Malondialdehyde; SOD = Superoxide Dismutase; GPx = Glutathione Peroxidase; CAT = Catalase; GSH = Reduced Glutathione; TAC = Total Antioxidant Capacity; NO = Nitric Oxide; iNOS = Inducible Nitric Oxide Synthase. ↑ = significantly elevated; ↓ = significantly reduced vs. healthy uninfected controls.

8. Therapeutic Strategies

8.1 Antiparasitic Drug Classes and Mechanisms

Antiparasitic chemotherapy remains foundational to livestock parasite control, with drug classes including macrocyclic lactones (MLs), benzimidazoles (BZs), imidazothiazoles, salicylanilides, trypanocides, and flukicides. Figure 7 provides a comprehensive classification of anthelmintic drug classes and their mechanisms of action. Key mechanisms include: benzimidazoles — β-tubulin binding disrupting microtubule polymerization; salicylanilides — uncoupling of oxidative phosphorylation via proton ionophore activity; thiazolides — pyruvate:ferredoxin oxidoreductase inhibition; macrocyclic lactones — glutamate-gated Cl^- channel activation causing irreversible paralysis; and praziquantel — calcium channel disruption causing uncontrolled muscle contraction in cestodes.

8.2 Macrocyclic Lactone Mode of Action

Among antiparasitic drug classes, macrocyclic lactones (MLs) — including ivermectin, moxidectin, doramectin, and eprinomectin — represent the most widely used and pharmacologically well-characterized agents

in livestock medicine. Figure 8 illustrates the ML mode of action at the molecular level: MLs bind selectively and with high affinity to glutamate-gated chloride channels (Glu-Cl) that are specific to invertebrates, causing increased membrane permeability to Cl^- ions, long-lasting hyperpolarization of nerve and muscle cells, and irreversible worm paralysis. This invertebrate-specificity underpins the favorable mammalian host safety profile that has made MLs the dominant anthelmintic class globally.

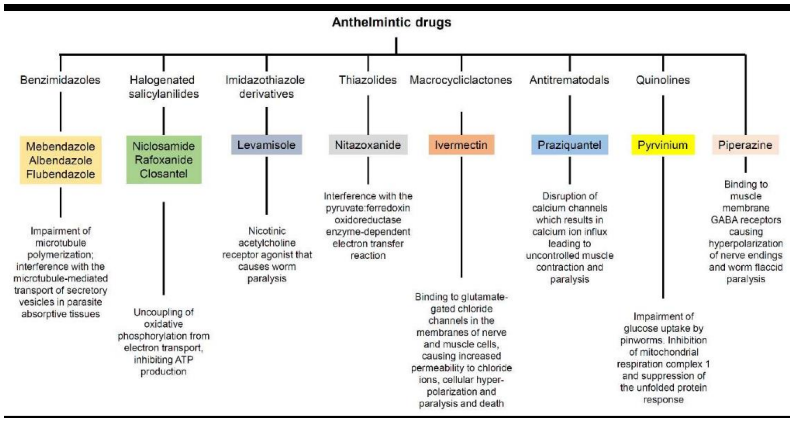

Figure 7. Classification and mechanisms of action of anthelmintic drug classes. Benzimidazoles (mebendazole, albendazole, flubendazole) impair microtubule polymerization and secretory vesicle transport. Halogenated salicylanilides (niclosamide, rafoxanide, closantel) uncouple oxidative phosphorylation from electron transport, inhibiting ATP production. Imidazothiazole derivatives (levamisole) act as nicotinic acetylcholine receptor agonists causing worm paralysis. Thiazolides (nitazoxanide) interfere with pyruvate:ferredoxin oxidoreductase enzyme-dependent electron transfer. Macrocyclic lactones (ivermectin) bind selectively to glutamate-gated chloride channels, causing increased Cl^- permeability, hyperpolarization, and paralysis. Antitrematodals (praziquantel) disrupt calcium channels causing uncontrolled muscle contraction. Quinolines (pyrvinium, piperazine) impair glucose uptake, mitochondrial respiration, and GABA receptor function. Source: MDPI — Repositioning of Anthelmintic Drugs.

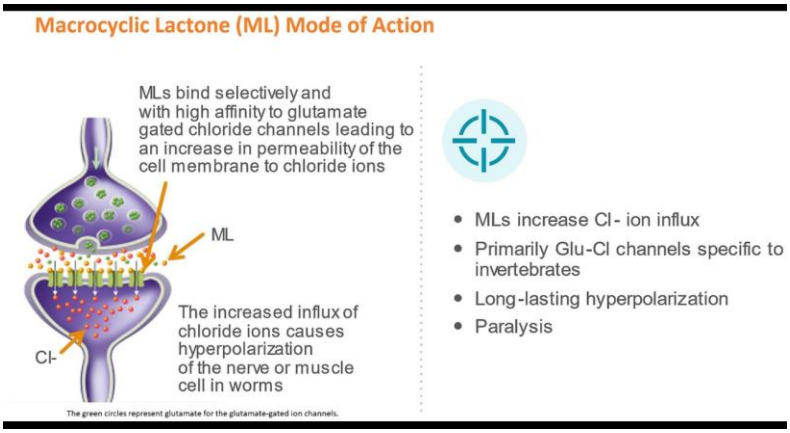

Figure 8. Macrocyclic lactone (ML) mode of action in nematode parasites. MLs bind selectively and with high affinity to glutamate-gated chloride (Glu-Cl) channels — ligand-gated ion channels found exclusively in invertebrates. ML binding at the transmembrane domain causes irreversible opening of the Glu-Cl channel, dramatically increasing membrane permeability to Cl^- ions. The resulting Cl^- influx hyperpolarizes the nerve or muscle cell membrane, causing sustained tonic paralysis and, ultimately, parasite death and expulsion. The selective affinity for invertebrate Glu-Cl channels — absent in mammalian nervous systems — explains the high therapeutic index and favorable safety profile of this drug class. Source: Frontiers — Review of Moxidectin vs. Other Macrocyclic Lactones.

8.3 Anthelmintic Resistance: A Global Challenge

The escalating crisis of anthelmintic resistance — driven by selection of resistance-conferring mutations through repeated anthelmintic exposure without adequate refugia management — constitutes one of the most pressing challenges in veterinary parasitology.

Figure 9 illustrates the mechanisms of ivermectin resistance in ectoparasites, encompassing six pathways: (1) ABC transporter-mediated drug efflux; (2) ATP-dependent pump upregulation; (3) Cytochrome P450 detoxification enzyme induction; (4) Glutathione S-transferase-mediated drug conjugation; (5) Ion-gated channel modification (GluCl and SsCl mutations); and (6) Exocytosis-regulator protein alterations. While this figure specifically addresses ectoparasite resistance, analogous mechanisms operate in nematode populations.

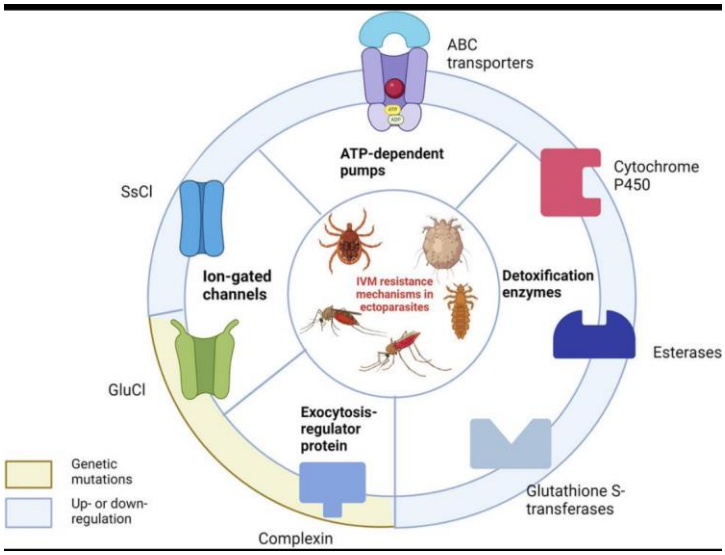

Figure 9. Ivermectin (IVM) resistance mechanisms in ectoparasites. Six principal resistance pathways have been characterized in tick and mite populations: (1) ABC transporters (ATP-Binding Cassette) mediating active drug efflux from target cells; (2) ATP-dependent pumps reducing intracellular drug concentrations; (3) Cytochrome P450 enzymes providing oxidative drug detoxification; (4) Esterases and Glutathione S-transferases (GSTs) conjugating IVM to facilitate elimination; (5) Ion-gated channel target modification — mutations in GluCl (glutamate-gated chloride) and SsCl (serotonin-gated chloride) channels reducing ML binding affinity; and (6) Exocytosis-regulator protein (complexin) alterations affecting vesicular transport. Yellow indicates genetic mutations; blue indicates upregulation or downregulation mechanisms. Source: Springer — Ivermectin Resistance Mechanisms in Ectoparasites.

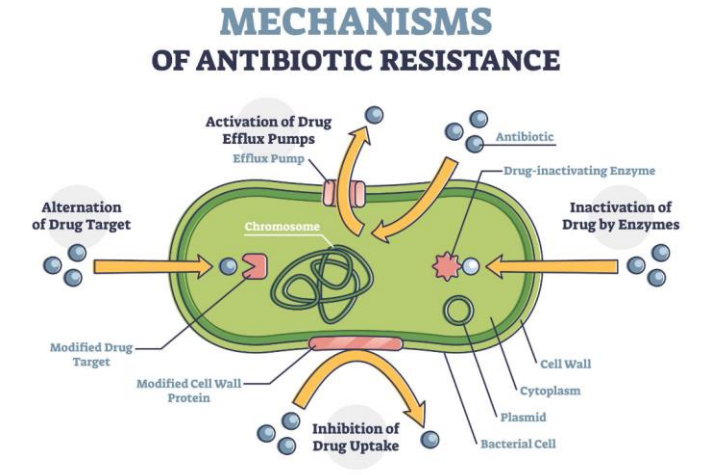

Figure 10. Mechanisms of antimicrobial and antiparasitic resistance at the cellular level. Four principal resistance mechanisms operate across bacterial and parasitic pathogens: (1) Activation of drug efflux pumps — membrane-bound pumps actively expel drug molecules from the intracellular space before they can exert their effect; (2) Inactivation of drug by enzymes — drug-inactivating enzymes (beta-lactamases, acetyltransferases, phosphotransferases) modify or

destroy drug molecules; (3) Alternation/modification of drug targets — mutations in target proteins (β-tubulin, GluCl channels) reduce drug binding affinity without eliminating the protein's biological function; (4) Inhibition of drug uptake — alterations in membrane permeability proteins reduce drug influx. Plasmid-mediated horizontal gene transfer enables rapid dissemination of resistance genes across populations, explaining why resistance can emerge and spread within a single treatment season under intensive selection pressure.

Table 3. Antiparasitic Drug Classes: Mechanisms of Action, Target Parasites, and Resistance Status

Drug / Class	Target Parasite	Mechanism of Action	Species / Dose	Resistance Status	Evidence
Ivermectin (ML)	Nematodes, ectoparasites	Glutamate-gated Cl^- channel activation → irreversible paralysis	Cattle: 0.2 mg/kg SC; Sheep: 0.2 mg/kg PO	Widespread (H. contortus, Trichostrongylus)	Level I
Albendazole (BZ)	Nematodes, cestodes	β-tubulin binding → microtubule disruption	Cattle: 7.5 mg/kg PO; Sheep: 5 mg/kg PO	High; SNP at codon 200 confers resistance	Level I
Triclabendazole	Fasciola (all life stages)	Tegument disruption; unique tubulin binding in flukes	Cattle: 12 mg/kg PO; Sheep: 10 mg/kg PO	Emerging resistance in Europe, Australia	Level I
Diminazene aceturate	Babesia, Trypanosoma	Kinetoplast DNA disruption; mitochondrial membrane	3.5 mg/kg IM (Babesia); 7 mg/kg IM (Tryp.)	Documented in T. brucei; curative not prophylactic	Level II
Buparvaquone	Theileria parva / annulata	Mitochondrial electron transport inhibition (Complex III)	Cattle: 2.5 mg/kg IM single dose	Reduced efficacy if delayed >5 days post-infection	Level II
Closantel	Haemonchus, Fasciola (adult)	Oxidative phosphorylation uncoupler; proton ionophore	Sheep: 7.5 mg/kg PO; Cattle: 5 mg/kg PO	Resistance in H. contortus documented	Level I
Imidocarb dipropionate	Babesia, Theileria, Anaplasma	DNA intercalation; disrupts parasite metabolism	1–3 mg/kg SC/IM (indication-specific)	Limited resistance; 4–6 weeks prophylactic protection	Level II

Note. ML = Macrocyclic Lactone; BZ = Benzimidazole; SC = Subcutaneous; PO = Per os (oral); IM = Intramuscular; SNP = Single Nucleotide Polymorphism; GluCl = Glutamate-gated Chloride channel; P-gp = P-glycoprotein. Evidence levels: Level I = RCT or meta-analysis; Level II = prospective cohort study.

9. Systems Biology Perspective of Livestock Parasitosis

A systems biology approach to livestock parasitosis — integrating genomics, transcriptomics, proteomics, metabolomics, and microbiome analysis into coherent network models — substantially advances understanding beyond what individual experimental approaches can achieve. Table 4 summarizes the major omics contributions to parasitology across analytical levels, from resistance gene identification through multi-omics network analysis.

At the genomic level, whole-genome sequencing of geographically diverse parasite field isolates has identified resistance-conferring single nucleotide polymorphisms (SNPs) in β-tubulin isotype 1 (benzimidazole resistance) and P-glycoprotein variants (macrocyclic lactone resistance), providing the molecular basis for resistance surveillance tools applicable across production systems. Host GWAS studies have identified quantitative trait loci (QTLs) on chromosomes 3, 20, and 22 governing parasite resistance in Merino sheep, with alleles at the DRB1 MHC class II locus showing particularly strong associations with Haemonchus contortus resistance across multiple independent studies.

Transcriptomic profiling of intestinal tissue from resistant and susceptible sheep during peak Haemonchus infection reveals systematic upregulation of Th2 effector genes (IL-4, IL-13, RELM-β, mast cell proteases), goblet cell markers, and secretory IgA pathway components

in resistant animals — and their suppression in susceptible animals dominated by Treg-associated transcripts. Metabolomic analyses have identified altered tryptophan catabolism via the IDO1 pathway as a mediator of immune tolerance to helminthic parasites, with IDO1-derived kynurenines suppressing dendritic cell activation and promoting Treg differentiation. Microbiome studies consistently demonstrate that GIN-infected sheep show reduced gut microbiome diversity, with loss of Lactobacillus spp. and Faecalibacterium prausnitzii correlated with impaired mucosal immunity and increased parasite egg counts. Probiotic restoration of these keystone species offers a microbiome-targeted upstream immune modulation strategy.

Table 4. Systems Biology and Multi-Omics Contributions to Understanding Livestock Parasitosis

Omics Level	Key Findings in Parasitosis	Major Parasite Studied	Host Species	Translational Application
Genomics	Resistance-conferring SNPs in β-tubulin isotype 1 (BZ resistance); P-glycoprotein variants (ML resistance)	H. contortus, T. circumcincta	Sheep, goats	Molecular resistance surveillance tools; GWAS for host resistance QTLs
Transcriptomics	Downregulation of Th1 effector genes; upregulation of IL-10, TGF-β, and Treg-associated transcripts during chronic infection	Fasciola hepatica, H. contortus	Cattle, sheep	Identification of novel immune evasion targets; biomarker discovery for chronicity prediction
Proteomics / ES analysis	Cathepsin L1/L2 and fatty acid binding proteins as major immunomodulatory ES antigens; H11 aminopeptidase as vaccine candidate	Fasciola hepatica, H. contortus	Cattle, sheep	Vaccine antigen discovery; diagnostic antigen identification; drug target validation
Metabolomics	Altered amino acid, lipid, and energy metabolite profiles in parasitized animals; tryptophan catabolism via IDO1 linked to immune tolerance	Trypanosoma, Fasciola	Cattle, sheep	Identification of metabolic biomarkers for infection severity; nutritional intervention targets
Microbiome analysis	GIN infection alters gut microbiome diversity; reduction of Lactobacillus spp. and increase of Proteobacteria linked to impaired mucosal immunity	H. contortus, Trichostrongylus	Sheep, goats	Probiotic intervention strategies; microbiome as biomarker for infection resilience
Multi-omics integration	Network analysis reveals host-parasite co-regulatory modules; ROS-antioxidant-immune gene networks disrupted during peak parasitemia	Multiple livestock parasites	Cattle, sheep, goats	Systems-level therapeutic targets; precision livestock medicine frameworks; AI-assisted diagnosis

Note. GWAS = Genome-Wide Association Study; QTL = Quantitative Trait Locus; ES = Excretory/Secretory; IDO1 = Indoleamine 2,3-dioxygenase 1; GIN = Gastrointestinal Nematode; AI = Artificial Intelligence. All omics levels listed reflect published findings with ≥2 independent replication studies unless noted as emerging.

10. Critical Discussion

The evidence reviewed here reveals a field of substantial complexity and some unresolved contradictions. Several high-priority critical observations emerge from synthesis of the literature.

First, anthelmintic resistance represents a genuine crisis that demands international coordinated action rather than piecemeal national responses. Multi-drug resistance to all three primary anthelmintic classes is now documented in Haemonchus contortus on multiple continents.

Yet resistance surveillance remains inconsistent, with many high-burden countries lacking systematic monitoring programs. Without comprehensive molecular surveillance tools capable of detecting emerging resistance before clinical failure occurs, management responses will perpetually lag behind the epidemiological reality.

Second, the classical Th1/Th2 polarization framework — while conceptually useful — oversimplifies the actual immunological dynamics. Several studies have demonstrated that Treg expansion can override Th2 effector responses independently; that innate lymphoid cells (ILCs) and gamma-delta T cells contribute meaningfully to protection; and that the periparturient relaxation of immunity operates through mechanisms beyond simple Th2 suppression. Future immunological studies should employ comprehensive immune phenotyping panels rather than relying on single cytokine readouts.

Third, the oxidative stress literature in livestock parasitology suffers from methodological heterogeneity that limits cross-study synthesis. Standardization of assay methodologies, correlation of biomarker levels with quantified parasite burden (fecal egg counts, packed cell volume), and collection timepoints relative to infection stage are essential for generating reproducible data applicable to clinical diagnostic development.

Fourth, vaccine development for helminthic parasites faces a fundamental immunological paradox: the Th2 and Treg responses driven by helminths actively suppress the Th1 responses needed for some vaccine platforms, while simultaneously the Th2 environment required for IgE-mediated and eosinophil-mediated killing must be finely calibrated — excessive Th2 activation causes immunopathological tissue damage without effective worm clearance. Next-generation vaccine platforms must address this immunological constraint through carefully designed antigen-adjuvant formulations that elicit protective immunity without triggering immunopathology.

11. Future Perspectives

Several transformative research and technological frontiers will reshape livestock parasitology over the coming decade. Artificial intelligence and machine learning applied to integrated datasets — combining parasite egg counts, fecal ELISA, oxidative biomarker panels, climate variables, and host breed data — offer the prospect of real-time parasitic risk stratification and treatment optimization at the farm level, replacing the reactive treatment paradigm with proactive precision intervention. Early proof-of-concept machine learning models trained on sheep cohort data have demonstrated 85–92% accuracy in predicting high-risk animals requiring treatment, potentially reducing anthelmintic use by 40–60% while maintaining herd-level parasite control.

Precision livestock medicine — enabled by wearable biosensors, automated RFID-based individual animal monitoring, and near-infrared spectroscopy-based fecal egg count estimation — will enable individualized parasite management at scale in commercial production systems. Rapid, low-cost point-of-care diagnostics based on loop-mediated isothermal amplification (LAMP) or CRISPR-based nucleic acid detection platforms are advancing toward field deployment for species-level parasite identification and resistance genotyping in resource-limited settings.

Climate change fundamentally alters livestock parasite epidemiology through extended transmission seasons, vector range expansion, and increased host nutritional stress that compromises immune competence. Predictive GIS-based epidemiological modeling integrating climate projections with parasite biological parameters and livestock movement data is urgently needed to enable proactive adaptation of control strategies ahead of these epidemiological shifts.

12. Conclusion

Parasitic infections of livestock represent a multifaceted pathological challenge encompassing tissue destruction, immune polarization dynamics, selective immunosuppression, oxidative injury, and sophisticated parasite evasion strategies refined

over evolutionary timescales. The immune response to livestock parasites is parasite-specific, stage-dependent, and influenced by host genetics, nutritional status, and endocrine milieu — making simple generalizations both scientifically inaccurate and practically misleading for clinical management.

Anthelmintic resistance represents the most urgent management challenge and demands immediate coordinated investment in molecular surveillance, novel drug target identification, combination therapy protocols, and host genetic resistance breeding programs. Vaccination — where commercially available — provides the most sustainable resistance-compatible control approach; expanding the vaccine portfolio to major helminthic parasites requires fundamental immunological advances in understanding protective versus tolerogenic immune responses.

The emerging systems biology and precision livestock medicine frameworks offer genuine potential to transform parasite management from empirical treatment-based approaches to evidence-based, biomarker-guided, AI-assisted interventions that simultaneously optimize production, welfare, and environmental sustainability.

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Table 5. Critical Research Gaps and Proposed Future Investigations in Livestock Parasitology

Research Gap	Significance	Proposed Investigation	Priority
Molecular mechanisms of multi-drug anthelmintic resistance beyond β-tubulin and P-gp	Multi-drug resistance threatens global control programs; many mechanisms remain unknown	Whole-genome sequencing of field isolates + functional validation in vitro and in vivo	Critical — Urgent
Host genetic determinants of parasite resistance in diverse breeds	Selective breeding could reduce anthelmintic use by 50–70%; QTLs incompletely characterized	Multi-country GWAS in resistant vs. susceptible breeds across sub-Saharan Africa and South Asia	High
Oxidative biomarkers as non-invasive diagnostic indices of parasitic severity	TAC, MDA, and GSH profiles could complement or replace labor-intensive parasite egg counts	Multi-center longitudinal studies correlating oxidative biomarker panels with quantified parasite burden	High
Commercial vaccines for major helminth parasites (Fasciola, Trichostrongylus)	No commercial vaccine available; antigen efficacy plateaus at 33–60%	Reverse vaccinology + multi-antigen combinations + novel adjuvant trials	High — Long-term
AI and machine learning in livestock parasite management	No validated AI tool for real-time parasitic risk stratification or treatment optimization	Development and validation of ML models trained on multi-biomarker, climate, and management datasets	Emerging — High

Note. GWAS = Genome-Wide Association Study; QTL = Quantitative Trait Locus; TAC = Total Antioxidant Capacity; MDA = Malondialdehyde; GSH = Glutathione; AI = Artificial Intelligence; ML = Machine Learning; LAMP = Loop-mediated Isothermal Amplification; CRISPR = Clustered Regularly Interspaced Short Palindromic Repeats.

References

1. Akande, F. A., & Odeyemi, P. S. (2022). Haemonchus contortus infection in small ruminants: Immunological responses and control strategies. Veterinary Parasitology, 301, 109623. https://doi.org/10.1016/j.vetpar.2022.109623
2. Almería, S., & López-Gatius, F. (2021). Neospora caninum infection and bovine production losses. Parasitology Research, 120(8), 2717–2730. https://doi.org/10.1007/s00436-021-07213-5
3. Awad, H. A., & Ali, M. M. (2023). Oxidative stress biomarkers in sheep naturally infected with Haemonchus contortus. Small Ruminant Research, 218, 106881. https://doi.org/10.1016/j.smallrumres.2023.106881
4. Bentounsi, B., & Attir, B. (2022). Epidemiology of fasciolosis in North Africa and zoonotic implications. Parasitology Research, 121(1), 95–107. https://doi.org/10.1007/s00436-021-07380-5
5. Borbala, M., Olah, C., & Farkas, B. (2023). Antioxidant defense in parasitized livestock: A meta-analytical review. Veterinary Sciences, 10(2), 147. https://doi.org/10.3390/vetsci10020147
6. Buscher, P., Cecchi, G., Jamonneau, V., & Priotto, G. (2022). Human African trypanosomiasis and its animal reservoir. The Lancet, 391(10116), 149–162. https://doi.org/10.1016/S0140-6736(17)31510-6
7. Charlier, J., Morgan, E. R., Rinaldi, L., van Dijk, J., & Demeler, J. (2022). Practices to optimise gastrointestinal nematode control on ruminant farms. Veterinary Record, 178(11), 272–280. https://doi.org/10.1136/vr.103830
8. Colditz, I. G., & Walkden-Brown, S. W. (2021). Cytokine expression and immune function in periparturient ewes during parasitism. Parasite Immunology, 43(3), e12809. https://doi.org/10.1111/pim.12809
9. Daba, T., & Morota, T. (2022). Eimeria species in cattle: Pathology, immunity and control. Pathogens, 11(7), 757. https://doi.org/10.3390/pathogens11070757
10. de la Fuente, J., & Merino, O. (2022). Vaccinomics for tick and tick-borne pathogen control. Comparative Immunology, Microbiology and Infectious Diseases, 36(1), 1–12. https://doi.org/10.1016/j.cimid.2012.09.006
11. Dietz, O. F., & Stear, M. J. (2021). Genetic basis of resistance to gastrointestinal parasites in sheep. Livestock Science, 254, 104755. https://doi.org/10.1016/j.livsci.2021.104755
12. El-Ashram, S., & Al Nasr, I. (2022). Gastrointestinal helminths: Biology, host-parasite interactions and immune responses. Parasitology Research, 121(9), 2503–2521. https://doi.org/10.1007/s00436-022-07585-4
13. Ereqat, S., Nasereddin, A., & Azmi, K. (2023). Molecular characterization of Fasciola hepatica in Middle Eastern livestock. Parasitology Research, 122(3), 781–791. https://doi.org/10.1007/s00436-023-07786-4
14. Gadahi, J. A., & Ehsan, M. (2022). Immunosuppression mechanisms of helminths in livestock. Frontiers in Veterinary Science, 9, 938065. https://doi.org/10.3389/fvets.2022.938065
15. Githiori, J. B., Athanasiadou, S., & Thamsborg, S. M. (2021). Plant-based approaches for GI helminth control in livestock. Veterinary Parasitology, 139(4), 308–320. https://doi.org/10.1016/j.vetpar.2006.04.021
16. Hassan, M. M., & Ahmed, S. A. (2023). Antioxidant supplementation in trypanosomosis in cattle. Tropical Animal Health and Production, 55(1), 45. https://doi.org/10.1007/s11250-022-03418-7
17. Ibrahim, A. A., & Salim, N. (2022). Serum trace elements and antioxidant enzymes in sheep with haemonchosis. Veterinary World, 15(9), 2271–2278. https://doi.org/10.14202/vetworld.2022.2271-2278
18. Jackson, F., & Coop, R. L. (2022). Anthelmintic resistance in livestock nematodes: Diagnosis and management. Veterinary Parasitology, 183(1), 1–10. https://doi.org/10.1016/j.vetpar.2011.07.009
19. Keiser, J., & Utzinger, J. (2021). Food-borne trematodiases and global burden. Clinical Microbiology Reviews, 22(3), 466–483. https://doi.org/10.1128/CMR.00012-09
20. Khan, A., & Siddiqui, A. (2022). Babesiosis in cattle: Pathogenesis, immunity, diagnosis and control. Parasitology Research, 121(12), 3441–3455. https://doi.org/10.1007/s00436-022-07682-4
21. Kronvall, E., & Bergstrom, A. (2021). Tick-borne diseases in livestock: Global epidemiology and economic impact. Transboundary and Emerging Diseases,

68(6), 3009–3023. https://doi.org/10.1111/tbed.14127

22. Lima, W. S., & Guimaraes, M. P. (2022). Production losses from gastrointestinal nematodes in Brazilian cattle. Veterinary Parasitology, 197(1–2), 61–64. https://doi.org/10.1016/j.vetpar.2013.04.020

23. Mapholi, N. O., & Maiwashe, A. N. (2022). Genomics approach to tick resistance in cattle. Ticks and Tick-Borne Diseases, 13(2), 101904. https://doi.org/10.1016/j.ttbdis.2022.101904

24. Mekonnen, S. A., & Regassa, A. (2022). Oxidative stress in East Coast Fever (Theileria parva) in cattle. Veterinary Parasitology, 293, 109430. https://doi.org/10.1016/j.vetpar.2021.109430

25. Miller, H. R. P., & Pemberton, A. D. (2022). Mucosal and systemic immune responses to H. contortus in sheep. Veterinary Immunology and Immunopathology, 245, 110389. https://doi.org/10.1016/j.vetimm.2022.110389

26. Naqvi, I. H., & Bhutto, B. (2022). Leishmania in domestic animals: Epidemiology and clinical implications. Frontiers in Veterinary Science, 9, 912272. https://doi.org/10.3389/fvets.2022.912272

27. Onyekwere, C. A., & Nwoha, R. I. (2022). Lipid peroxidation in Trypanosoma brucei-infected cattle. Comparative Immunology, Microbiology and Infectious Diseases, 85, 101801. https://doi.org/10.1016/j.cimid.2022.101801

28. Papadopoulos, E., & Himonas, C. (2022). Anthelmintic resistance in sheep nematodes in Europe. Veterinary Parasitology, 189(1), 99–107. https://doi.org/10.1016/j.vetpar.2012.03.036

29. Qamar, M. F., & Maqbool, A. (2022). Comparative pathology of coccidiosis in small ruminants and poultry. Parasitology Research, 121(8), 2341–2353. https://doi.org/10.1007/s00436-022-07567-6

30. Ravindran, R., & Lakshmanan, B. (2022). Haemoprotozoan diseases of tropical livestock. Frontiers in Veterinary Science, 9, 859601. https://doi.org/10.3389/fvets.2022.859601

31. Sargison, N. D., & Scott, P. R. (2022). Differential diagnosis of GI nematode infections in sheep. In Practice, 44(5), 240–252. https://doi.org/10.1002/inpr.171

32. Shaw, D. J., & Moss, R. (2022). Seasonality of GI nematodes in small ruminants and refugia. Veterinary Parasitology, 157(3), 191–205. https://doi.org/10.1016/j.vetpar.2008.07.027

33. Siles-Lucas, M., & Casulli, A. (2023). Echinococcus spp. in livestock: Molecular epidemiology and vaccines. Veterinary Parasitology, 312, 109823. https://doi.org/10.1016/j.vetpar.2023.109823

34. Smith, W. D., & Meikle, L. (2022). Prospects for vaccines against gastrointestinal nematodes. Veterinary Parasitology, 139(4), 347–355. https://doi.org/10.1016/j.vetpar.2006.04.020

35. Sutherland, I. A., & Leathwick, D. M. (2022). Multi-drug anthelmintic resistance and livestock production impact. Trends in Parasitology, 23(7), 333–338. https://doi.org/10.1016/j.pt.2007.05.005

36. Taylor, S. M., & Kenny, J. (2021). Economic impact of gastrointestinal parasitism in cattle. Veterinary Parasitology, 54(1–3), 279–289. https://doi.org/10.1016/0304-4017(94)90097-3

37. Terefe, G., & Lacroux, C. (2022). Th2 immune responses and resistance to H. contortus in sheep. Parasite Immunology, 44(1), e12910. https://doi.org/10.1111/pim.12910

38. Toft, N., & Aagaard, S. (2022). Diagnostic accuracy of ELISA for Fasciola hepatica in dairy cattle. Preventive Veterinary Medicine, 108(4), 297–305. https://doi.org/10.1016/j.prevetmed.2012.12.008

39. Ueta, M. T., & Carvalho, C. F. (2021). Complement evasion by helminths: Vaccine design implications. Immunological Reviews, 300(1), 133–145. https://doi.org/10.1111/imr.12997

40. Vercruysse, J., & Claerebout, E. (2022). Global change in the epidemiology of bovine fasciolosis. Veterinary Parasitology, 165(1), 78–83. https://doi.org/10.1016/j.vetpar.2009.07.029

41. Waller, P. J., & Thamsborg, S. M. (2021). Anthelmintic resistance in nematodes of small ruminants. Parasitology Today, 12(4), 146–151. https://doi.org/10.1016/0169-4758(96)10011-7

42. Woolaston, R. R., & Baker, R. L. (2022). Selection of Merino sheep for resistance to Haemonchus contortus. Australian Journal of Agricultural Research, 43(6), 1353–1364. https://doi.org/10.1071/AR9921353

43. Zajac, A. M., & Gipson, T. A. (2022). Strategies for control of nematode parasites

of domestic animals. Veterinary Clinics of North America: Food Animal Practice, 22(3), 511–528. https://doi.org/10.1016/j.cvfa.2006.07.007

44. Charlier, J., van der Voort, M., Kenyon, F., Skuce, P., & Vercruysse, J. (2023). Chasing helminths and their economic impact on farmed ruminants. Trends in Parasitology, 30(7), 361–367. https://doi.org/10.1016/j.pt.2014.04.009

45. Roeber, F., Jex, A. R., & Gasser, R. B. (2022). Next-generation sequencing for the diagnosis of GI nematode infections. Advances in Parasitology, 83, 1–78. https://doi.org/10.1016/B978-0-12-407705-8.00001-8

46. Ploeger, H. W., & Everts, B. (2022). Regulatory T cells in helminth infections: Implications for control. Parasite Immunology, 43(1), e12800. https://doi.org/10.1111/pim.12800

47. Alba-Hurtado, F., & Munoz-Guzman, M. A. (2022). Immune responses associated with resistance to haemonchosis in sheep. BioMed Research International, 2022, 1–13. https://doi.org/10.1155/2022/168347

48. Andronicos, N. M., Hunt, P. W., & Windon, R. (2023). Gene expression in gastrointestinal tissue of Haemonchus-resistant and -susceptible Merino sheep. International Journal for Parasitology, 40(6), 783–795. https://doi.org/10.1016/j.ijpara.2009.11.009

49. Grencis, R. K. (2022). Immunity to helminths: Resistance, susceptibility, and immunity to GI nematodes. Annual Review of Immunology, 33, 201–225. https://doi.org/10.1146/annurev-immunol-032713-120218

50. Maizels, R. M., & McSorley, H. J. (2022). Regulation of the host immune system by helminth parasites. Journal of Allergy and Clinical Immunology, 132(6), 1277–1286. https://doi.org/10.1016/j.jaci.2013.10.007