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Bovine Theileriosis: Comprehensive Insights into Etiology, Epidemiology, Pathogenesis, Diagnostics, Therapeutics, and Immunoprophylaxis

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Key Points

- **India's rabies elimination challenge:** Incomplete post-exposure prophylaxis (PEP), gaps in vaccine and immunoglobulin availability, and inadequate dog vaccination coverage continue to hinder progress toward the global "Zero by 30" target.
- **Successful models demonstrate the value of One Health:** Goa's integrated rabies-control programme and Sikkim's sustained dog vaccination and sterilization initiatives highlight the importance of coordinated surveillance, community engagement and veterinary–public health collaboration.
- **Strategic interventions can accelerate elimination:** Sustained canine vaccination, oral rabies vaccines, affordable human vaccination, monoclonal antibodies, digital surveillance, targeted pre-exposure prophylaxis and public awareness are proposed pathways toward reducing rabies deaths.

Abstract

Bovine theileriosis, caused by tick-borne apicomplexan protozoans of the genus *Theileria*, represents one of the most economically devastating livestock diseases across tropical and subtropical regions globally. Among the species impacting cattle, *Theileria parva* (causing East Coast fever) and *Theileria annulata* (causing tropical theileriosis) are the most pathogenic, while species like *Theileria orientalis* (notably the Ikeda genotype) impose emerging threats to livestock production systems worldwide. This critical popular article provides a comprehensive overview of bovine theileriosis, covering etiology, vector-host transmission dynamic, species diversity, and multi-factorial disease susceptibility based on age, gender, breed, geography, and environmental drivers. Pathophysiological changes including dramatic alterations in hematological profiles (severe pan-leukopenia, normocytic normochromic to hypochromic anemia, thrombocytopenia) and serum biochemical markers (hyperbilirubinemia, elevated AST/ALT, hypoalbuminemia, elevated blood urea nitrogen and creatinine) are systematically reviewed. Furthermore, conventional diagnostics (blood/lymph smear microscopy) are evaluated alongside advanced serological (ELISA, IFAT) and molecular assays (nested PCR, real-time PCR, multiplex PCR). Therapeutic strategies using specific anti-theilerial molecules (buparvaquone, parvaquone, oxytetracycline) coupled with supportive care, and vaccination strategies including live attenuated tissue culture vaccines and the infection-and-treatment method (ITM), are critically analyzed. This article synthesizes contemporary research published in high-impact veterinary journals



(NAAS rating > 6.0) to serve as a practical, authoritative guide for field clinicians, disease control authorities, and researchers.

Keywords: Bovine theileriosis, *Theileria annulata*, *Theileria parva*, Hyalomma, Buparvaquone, Lymphoproliferation, Anemia, Diagnostic tests, Cell culture vaccine.

1. Introduction

Bovine theileriosis is a globally significant, tick-borne hemoparasitic disease caused by obligate intracellular protozoans belonging to the phylum Apicomplexa, order Piroplasmida, and family Theileriidae (Jabbar et al., 2015). It severely impacts cattle production systems across Africa, Southern Europe, the Middle East, Central Asia, South Asia, and parts of the Asia-Pacific region. The disease is characterized by fever, lymphadenopathy, severe respiratory distress, progressive anemia, emaciation, and high mortality rates, particularly in non-indigenous, high-yielding dairy cattle (Gharbi et al., 2020).

The global economic losses attributed to theileriosis run into billions of US dollars annually, stem directly from high mortality, drop in milk yield, loss of draft power, weight loss, reproductive failure, and the substantial costs associated with tick control, diagnostic testing, and therapeutic interventions (Sivakumar et al., 2014; Kiara et al., 2018). Moreover, the clinical management of theileriosis is complicated by tick vector distribution shifts driven by climate change, emerging resistance to acaricides and anti-protozoal drugs, and the presence of subclinical carrier animals that serve as reservoirs (Roy et al., 2019). Understanding the multi-faceted nature of bovine theileriosis is essential for developing integrated disease management frameworks.

2. Causative Agent and Transmission Dynamic

2.1 Species Diversity and Taxonomic Classification

The genus *Theileria* comprises several species capable of infecting cattle, which vary widely in their pathogenicity, geographic distribution, primary tick vectors, and target host cells. The two most economically important transformational pathogenic species are *Theileria parva* and *Theileria annulata*:

- ***Theileria parva*:** The causative agent of East Coast Fever (ECF), Corridor disease, and January disease. *T. parva* induces uncontrolled proliferation of infected T-cells and B-cells, functioning similarly to a metastatic lymphoid malignancy (Mans et al., 2015).
- ***Theileria annulata*:** The causative agent of Tropical or Mediterranean Theileriosis. *T. annulata* infects macrophages and dendritic cells, causing acute lymphoproliferative and leuko-destructive disease across North Africa, Southern Europe, Middle East, and the Indian subcontinent (Sivakumar et al., 2014).

- ***Theileria orientalis* complex:** Includes benign or non-transforming strains (*T. buffeli*, *T. orientalis*, *T. sergenti*). However, pathogenic genotypes within this complex, particularly the Chitose and Ikeda genotypes, induce severe oriental theileriosis characterized by severe hemolysis without schizont-driven leukocyte transformation (Gondard et al., 2020).
- ***Theileria mutans* and *Theileria velifera*:** Generally considered mild or non-pathogenic species common in sub-Saharan Africa, often existing as co-infections with *T. parva*.

2.2 Vector Transmission Dynamics

Transmission of *Theileria* species occurs exclusively through hard ticks (family Ixodidae) in a biological, transtadial manner (i.e., parasite persists from larva to nymph, or nymph to adult, but is NOT transmitted transovarially from female tick to egg) (Scolamacchia et al., 2010). When an infected tick feeds on a bovine host, infectious sporozoites present in the salivary glands are inoculated into the host's bloodstream along with tick saliva within 48 to 72 hours of attachment. The principal vector species include:

Theileria Species	Primary Vector Ticks	Transmission Mode	Geographic Range
<i>Theileria parva</i>	<i>Rhipicephalus appendiculatus</i> , <i>R. zambeziensis</i>	Transtadial (Larva->Nymph, Nymph->Adult)	Eastern, Central & Southern Africa
<i>Theileria annulata</i>	<i>Hyalomma anatolicum</i> , <i>H. dromedarii</i> , <i>H. detritum</i>	Transtadial (Larva->Nymph, Nymph->Adult)	North Africa, Southern Europe, Middle East, South Asia
<i>Theileria orientalis</i> (Ikeda/Chitose)	<i>Haemaphysalis longicornis</i> , <i>H. punctata</i>	Transtadial	Asia-Pacific, Australasia, North America, Europe
<i>Theileria mutans</i>	<i>Amblyomma variegatum</i>	Transtadial	Sub-Saharan Africa, Caribbean

Table 1: Vector species, transmission routes, and geographical ranges of major bovine *Theileria* species.

3. Predisposition and Epidemiological Drivers

3.1 Host Factors: Age, Gender, and Breed Predisposition

Host susceptibility to bovine theileriosis is governed by an interplay between genetic factors, age, immunological maturity, and physiological status (Gharbi et al., 2020). Crossbred (*Bos taurus* x *Bos indicus*) and purebred exotic European cattle (*Bos taurus*, such as Holstein-Friesian and Jersey) demonstrate extreme susceptibility to *T. annulata* and *T. parva*, often experiencing clinical mortality rates exceeding 40% to 80% if untreated. Conversely, indigenous Zebu cattle (*Bos indicus*) exhibit high innate resistance (endemic stability),

suffering milder clinical disease due to evolutionary co-adaptation with tick vectors and parasites (Glass et al., 2012).

Young calves (aged 1 to 6 months) are particularly vulnerable to acute tropical theileriosis and ECF, suffering high case fatality rates due to incomplete immunological competence. However, in endemic stability zones, calves born to immune dams receive maternal antibodies via colostrum, which confer partial protection against clinical severity while allowing natural exposure and active immunity development (Scolamacchia et al., 2010). Gender does not directly dictate innate genetic susceptibility; however, high-producing lactating cows and heavily pregnant cows face significantly higher stress-induced immunosuppression, predisposing them to clinical relapse or severe manifestation.

3.2 Geographic and Environmental Predisposition

Geographic distribution is directly tied to the ecology, microclimate, and abundance of specific vector ticks. Environmental variables including ambient temperature (20°C to 35°C), high relative humidity (>65%), rainfall patterns, and vegetation cover are vital for vector tick survival, molting, and host-seeking activity (Roy et al., 2019). Seasonal spikes in clinical theileriosis cases strongly coincide with peak nymphal and adult tick population dynamics during humid summer and post-monsoon months.

Risk Parameter	High Predisposition / High Risk Group	Low Predisposition / Resistant Group
Breed Genetics	<i>Bos taurus</i> (Holstein, Jersey) & high crossbreds	Indigenous Zebu (<i>Bos indicus</i>) & Sanga breeds
Age Group	Young calves (1–6 months) & elderly debilitated stock	Adult indigenous cattle with acquired immunity
Physiological State	Peak lactation, late pregnancy, poor nutritional state	Dry adult cows, non-stressed oxen
Season / Climate	Hot-humid summer, post-monsoon season	Cold, dry winter months (low tick activity)
Management System	Zero-grazing with tick entry, open pastures with heavy tick load	Strict acaricide-treated farms, tick-free housing

Table 2: Multifactorial predisposing factors influencing bovine theileriosis susceptibility.

4. Effect on Animal Health and Livestock Production

The economic impact of bovine theileriosis is catastrophic across dairy and beef farming sectors. Pathophysiological damage causes severe systemic distress, leading to massive production losses through multiple channels (Kiara et al., 2018):

- **Milk Yield Collapse:** In acute cases involving high-yielding dairy cows, daily milk yield drops precipitously by 50% to 90% within 48 to 72 hours of fever onset. Full recovery of peak lactation yield in surviving cows is rarely achieved during the same lactation cycle.
- **Reproductive Impairment:** Infection causes high fever (40.5°C to 41.5°C), triggering acute luteolysis, embryonic mortality, and early abortion in pregnant cows. In bulls, prolonged hyperthermia causes transient to permanent testicular degeneration and reduced sperm motility.
- **Body Weight Loss and Emaciation:** Profound anorexia, muscle wasting, severe toxic anemia, and tissue destruction cause rapid loss of body condition score (BCS), resulting in long recovery periods and loss of draft capabilities in working oxen.
- **Mortality and Replacement Costs:** Without early, aggressive therapeutic intervention, mortality in susceptible crossbred cattle ranges between 50% and 90%, imposing severe economic stress on resource-poor smallholder farmers.

5. Clinical Signs and Symptoms

The incubation period of bovine theileriosis ranges from 8 to 21 days following tick bite. Clinical manifestations can be categorized into acute, subacute, and chronic/carrier forms (Gharbi et al., 2020; Microorganism pathogenesis studies):

- **Acute Form:** Characterized by high continuous fever (40.0°C–41.5°C), marked enlargement of superficial lymph nodes (prescapular and precrural lymph nodes), severe lethargy, complete anorexia, drop in milk production, lacrimation, and nasal discharge. As schizogony advances, affected animals develop severe pulmonary edema, leading to dyspnea, moist coughing, frothy nasal discharge, cyanosis, corneal opacity, petechial hemorrhages on conjunctiva and vulval mucosa, and terminal recumbency.
- **Subacute Form:** Observed frequently in indigenous Zebu cattle or partially immune crossbreds, showing moderate fever, mild lymph node enlargement, progressive weight loss, pale mucous membranes, and mild icterus.
- **Chronic / Carrier Form:** Animals surviving acute infection remain persistent carriers, displaying subtle unthriftiness, rough hair coat, mild intermittent anemia, and persistent low-grade parasitemia, acting as tick infection reservoirs.

6. Hematological and Serum Biochemical Pathomorphology

6.1 Hematological Alterations (Blood Picture)

The hematological picture during bovine theileriosis undergoes marked changes reflecting both leuko-proliferative/leuko-destructive phases and severe erythrocyte destruction (Ganguly et al., 2017). During the early stage, transient leukocytosis occurs due to schizont-

driven lymphoproliferation. However, as schizonts invade lymphoid organs, pan-leukopenia, severe neutropenia, and lymphopenia ensue due to lymphoid tissue exhaustion and necrosis. Intra-erythrocytic piroplasm invasion leads to dramatic falls in Packed Cell Volume (PCV), total Red Blood Cell (RBC) count, and Hemoglobin (Hb) concentration, resulting in normocytic normochromic to hypochromic macrocytic anemia. Anemia pathogenesis involves immune-mediated extravascular hemolysis, oxidative damage to cell membranes, and erythrophagocytosis in the spleen and liver. Thrombocytopenia is also a hallmark feature, predisposing to systemic hemorrhages.

6.2 Serum Biochemical Changes

Serum biochemistry reveals profound hepatic, renal, and systemic metabolic dysfunctions (Osman et al., 2017). Liver parenchymal damage and intravascular/extravascular hemolysis produce marked hyperbilirubinemia (predominantly unconjugated bilirubin) and significant elevations in liver diagnostic enzymes: Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Gamma-Glutamyl Transferase (GGT), and Alkaline Phosphatase (ALP). Renal impairment is reflected by elevated Blood Urea Nitrogen (BUN) and serum creatinine. Hypoalbuminemia develops due to hepatic dysfunction and vascular leakage.

Laboratory Parameter	Normal Reference Range	Altered Value in Acute Theileriosis	Clinical Interpretation
Hemoglobin (Hb)	8.0 - 14.0 g/dL	3.5 - 6.5 g/dL (Severe drop)	Severe hemolytic anemia
Packed Cell Volume (PCV)	24 - 46 %	12 - 20 % (Severe drop)	Severe anemia / hypoxia
Total Erythrocyte (RBC)	5.0 - 10.0 x10 ⁶ /uL	2.0 - 4.2 x10 ⁶ /uL	Extravascular hemolysis
Total Leukocyte (WBC)	4,000 - 12,000 /uL	1,800 - 3,500 /uL (Leukopenia)	Lymphoid depletion & necrosis
Platelet Count	250,000 - 800,000 /uL	80,000 - 150,000 /uL	Thrombocytopenia, hemorrhages
Total Bilirubin	0.1 - 0.5 mg/dL	1.8 - 5.5 mg/dL (Elevated)	Hemolytic & hepatic icterus
AST (SGOT)	48 - 100 U/L	180 - 450 U/L (Elevated)	Hepatic tissue cellular damage
Blood Urea Nitrogen (BUN)	10 - 25 mg/dL	35 - 75 mg/dL (Elevated)	Renal hypoperfusion / necrosis
Serum Albumin	2.7 - 3.8 g/dL	1.5 - 2.2 g/dL (Decreased)	Hepatic insufficiency & leak

Table 3: Typical hematological and serum biochemical profiles in cattle affected by acute

bovine theileriosis.

7. Diagnosis and Diagnostic Modalities

Definitive diagnosis of bovine theileriosis requires combining clinical signs, regional tick epidemiology, pathomorphology, and reliable laboratory testing. Diagnostic techniques range from field-level microscopy to sophisticated molecular assays (Kundave et al., 2014; Roy et al., 2019):

Diagnostic Test	Target / Principle	Sensitivity & Specificity	Clinical Application & Limitations
Blood Smear Microscopy	Giemsa stain to identify intra-erythrocytic piroplasms (ring/comma shapes)	Moderate sensitivity in acute cases; Low sensitivity in carriers (<10%)	Gold standard field test; fast, cheap, but cannot differentiate species reliably
Lymph Node Biopsy Smear	Giemsa stain to identify Koch's blue bodies (schizonts) in lymphocytes	High sensitivity in early acute stages of <i>T. annulata</i> & <i>T. parva</i>	Confirmation of schizogony stage; invasive, unsuitable for carrier detection
Indirect Fluorescent Antibody Test (IFAT)	Detects circulating anti-Theileria antibodies in serum using antigen slides	Moderate-high sensitivity; Cross-reactivity between species possible	Epidemiological surveillance; cannot distinguish active vs past infection
Enzyme-Linked Immunosorbent Assay (ELISA)	Detects specific antibodies using recombinant antigens (e.g., TSpM, <i>T. annulata</i> TAMS1)	High sensitivity (>90%) and specificity; high throughput	Large-scale epidemiological studies and herd monitoring
Polymerase Chain Reaction (PCR / qPCR)	Amplifies parasite DNA (18S rRNA, tams-1, or p67 genes)	Gold standard: Extremely high sensitivity (>98%) & species specificity	Identifies low parasitemia carrier animals and specific species/genotypes

Table 4: Comparative evaluation of diagnostic assays for bovine theileriosis.

8. Therapeutic Management and Treatment Protocols

Successful clinical management of bovine theileriosis depends heavily on early diagnosis and immediate administration of specific anti-theilerial therapeutics combined with rigorous supportive care (Mhadhbi et al., 2015; Muraguri et al., 2006).

8.1 Specific Anti-Theilerial Chemotherapeutics

- **Buparvaquone (Butalex):** The therapeutic gold standard. Administered at a dose of 2.5 mg/kg body weight via intramuscular (IM) injection in the neck muscle. A single dose is often curative in early stages, but a second dose 48 to 72 hours later is strongly recommended in advanced clinical cases with high parasitemia.
- **Parvaquone (Clexon):** Administered at 10 mg/kg IM, requiring two injections spaced 48 hours apart. Effective against macroschizonts and piroplasms.
- **Oxytetracycline (Long-Acting):** Administered at 20 mg/kg IM. Oxytetracycline is not effective against fully established late-stage schizonts, but acts as a highly effective schizonticide during the early incubation period. It is extensively used in combination with live vaccines in the Infection and Treatment Method (ITM).

8.2 Adjunctive and Supportive Therapy

Supportive care is essential to prevent mortality from pulmonary edema, severe anemia, and metabolic collapse during therapy:

- **Diuretics & Corticosteroids:** Furosemide (1–2 mg/kg IV/IM) combined with short-acting dexamethasone (0.05–0.1 mg/kg) to alleviate acute pulmonary edema and respiratory distress.
- **Hematinics and Vitamins:** Parenteral iron preparations, Vitamin B-complex, and Vitamin B12 to stimulate erythropoiesis and RBC recovery.
- **Fluid & Electrolyte Therapy:** Balanced electrolyte solutions (Isotonic Saline or Ringers Lactate) to combat dehydration and kidney hypoperfusion. Care must be taken not to overload circulation in severe pulmonary edema.
- **Blood Transfusion:** In severe cases where PCV falls below 12%, whole blood transfusion (10–15 mL/kg) from a healthy donor bovine is life-saving.

9. Vaccination Strategies and Immunoprophylaxis

Immunization is the most sustainable long-term strategy for controlling bovine theileriosis. Two primary vaccination methodologies are established globally (Pipano et al., 2002; Di Giulio et al., 2009):

Vaccine Type	Target Species	Composition / Strain	Efficacy & Duration	Limitations & Cold Chain
Attenuated Cell Culture Vaccine (e.g., Rakshavac-T)	Theileria annulata	In vitro schizont-infected schizont cell culture (e.g.,	High efficacy (>95%); confers long-lasting cell-mediated	Requires liquid nitrogen/ultra-cold chain (-196°C); potential strain

		Hisar or Hyderabad strain) attenuated by long passage	immunity (>3 years)	variation in distant geographies
Infection and Treatment Method (ITM) (Muguga Cocktail)	Theileria parva	Live virulent T. parva sporozoites inoculated simultaneously with long- acting Oxytetracycline	High protection against homologous field challenge (>90%)	Risk of inducing clinical disease if antibiotic dose is incorrect; creates carrier status

Table 5: Characteristics and clinical efficacy of major commercial anti-theilerial vaccines.

10. Conclusion and Future Directions

Bovine theileriosis remains a dominant constraint to livestock productivity, animal welfare, and rural economic stability across tropical and subtropical regions. Combating this disease effectively requires an integrated control paradigm combining strategic vector tick control (using rotated synthetic pyrethroids or organophosphates), routine sero-molecular surveillance to identify carrier animals, early intervention with buparvaquone during acute outbreaks, and widespread deployment of cell culture vaccines. Future research priorities must focus on developing next-generation subunit recombinant vaccines, uncovering molecular mechanisms behind buparvaquone resistance, and establishing point-of-care pen-side molecular diagnostics to safeguard global bovine herds against climate-driven tick expansion.

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