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Kamlesh K Sahoo
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

DK Gupta
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Kabita Roy
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Amita Tiwari
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Arpana Raikwar
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Shashi Pradhan
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Sonali Namdeo
Department of Animal Nutrition, I.V.R.I., Izatnagar, Uttar Pradesh, India

Govind P Choudhary
Department of Veterinary Gynaecology and Obstetrics, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Ayushi Sawhney
Department of Veterinary Surgery and Radiology, S.K.U.A.S.T.-J, Jammu and Kashmir, India

Shruti Bhatt
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Mitali Singh
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Corresponding Author
Kamlesh K Sahoo
Department of Veterinary Medicine, Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh, India

Canine ehrlichiosis: A review

Kamlesh K Sahoo, DK Gupta, Kabita Roy, Amita Tiwari, Arpana Raikwar, Shashi Pradhan, Sonali Namdeo, Govind P Choudhary, Ayushi Sawhney, Shruti Bhatt and Mitali Singh

Abstract
Canine ehrlichiosis is a tick borne disease of canines caused by the intracellular, gram-negative bacteria and clinically characterized by pyrexia, anorexia, lymphadenopathy, splenomegaly, anaemia, peripheral edema, haemorrhagic tendencies, ocular and neurological signs. It affects dogs, other domestic, wild animal species and humans. *E. canis* and *E. ewingii* are commonly found in dogs and *E. chaffeensis* is commonly known as human monocytic ehrlichiosis. With global warming, expanding tick habitats and increasing international travel the spread of disease to former non-endemic areas is of great concern**.** Diagnosis is performed on the basis of history of tick infestation, clinical manifestations, parasitological examination, haematobiochemical examination, serological and molecular diagnosis. The drug of choice is doxycycline and other effective drugs like imidocarb dipropionate, *Crotalus horridus*, rifampicin etc. may be used along with symptomatic and supportive therapy. Prevention involves avoidance of tick exposure and use of tick preventive measures as there is no successful vaccine currently available.

Keywords: canine pancytopenia, haemorrhagic fever, canine tick typhus, canine ehrlichiosis

Introduction
Ehrlichiosis affects dogs and humans as well as other domestic and wild animal species. With global warming, expanding tick habitats and increasing international travel, the spread of disease to former non-endemic areas is of great concern. *Ehrlichia canis* has a worldwide distribution; high infection rates and disease in dogs are primarily observed in tropical and subtropical areas (Lanza– Perea *et al.*, 2009) [12]. Canine ehrlichiosis in also known as Tropical Canine Pancytopenia or Canine Rickettsiosis or Canine Haemorrhagic Fever or Tracker Dog Disease or Canine Tick Typhus or Nairobi Bleeding Disease or Idiopathic Hemorrhagic Syndrome. It is a tick borne disease of canines caused by the intracellular, gram-negative bacteria. *Ehlrichia* species that have been detected in the blood and tissues of clinically ill dogs are granulocytic or monocytic ehrlichiosis. *E. canis* and *E. ewingii* (canine granulocytic ehrlichiosis) are commonly found in dogs and *E. chaffeensis* is commonly known as human monocytic ehrlichiosis (Rani *et al*., 2010) [21].

History
The disease was initially described at Pasteur Institute in 1935 in Algeria by Donatein and Lestoquard. They noticed the experimental dogs infested with ticks, *Rhipicephalus sanguineus* developed severe illness characterized by anemia and blood smears from infected dogs stained with Giemsa technique, showed small rickettsia like organism in monocytes which was noted as *Rickettsia canis.*
Mudaliar (1944) [15] reported Ehrlichiosis in Chennai for the first time in India. Later on, Ragavachari and Reddy (1958) [20] reported the incidence of *E. canis* infection in Hyderabad**.** Wilkins *et al.* (1967) [33] described a highly fatal and haemorrhagic disease in Military dogs in Singapore and South-East Asia. Tropical canine pancytopenia during Vietnam war was recorded by Nyindo *et al.* (1971) [18]. According to Keefe *et al.* (1982) [8], the disease was higher in tropical and temperate zone, while lower in cold zone. Rickettsial disease of animals and humans was reported by Rikihisa (1991). Stiles (2000) [27] revealed that *Ehrlichia* species are found in tropical and subtropical regions.

Epidemiology
The disease is endemic in every continent except Australia (Sykes, 2014) [29]. India, due to varied agro-climatic zones is endemic to many vector borne parasitic diseases including canine ehrlichiosis.

Prevalence studies of CME from Northern India were mainly concentrated from Ludhiana in Punjab over the last few years in pet dogs and non-descript local dogs that were bought to the clinic. Singla *et al.* (2011) [25] reported a high sero-prevalence of 61% in pet dogs when tested by commercial serological kit. A multi- centric study by Rani *et al.* (2011) [22] reported 20.6% of molecular prevalence among the stray dogs from Delhi, Mumbai, Ladakh and Sikkim. Samaradni *et al.* (2003) from Nagpur reported 18.9% prevalence by microscopy. A single study conducted in Chennai by Lakshmanan *et al.* (2006) [11] reported 50% prevalence by PCR.

Dhankar *et al.* (2011) [2] reported dogs of 24-36 months of age revealed the highest prevalence of ehrlichiosis among the Ehrlichia affected dogs. Karthika *et al.* (2014) [7] noted maximum cases of canine ehrlichiosis in females as compared to males. The prevalence of ehrlichiosis is higher in pure breeds as compared to non- descript dogs and occurrence of disease is maximum in post monsoon and winter seasons. Lakshmannan *et al.* (2006) reported higher prevalence of ehrlichiosis in German Shepherd (36%) followed by Pomeranians / Spitz, Labrador and Doberman.

Etiology

It is caused by Ehrlichia, is an alpha proteobacteria (intracellular and gram- negative) belongs to the family Ehrlichiaceae. Canine vector borne diseases (CVBDs) constituted an important group of illnesses affecting dogs around the world.

Table 1: *Ehlrichia* species detected in clinically ill dogs

S. No.	Species	Cell Tropism	Primary Tick Vector
1.	*E. canis*	Monocytes	*Rhipicephalus sanguineus*
2.	*E. chaffeensis*	Monocytes	*Amblyomma americanum*
3.	*E. ewingii*	Neutrophils	*Amblyomma americanum*

Transmission

A sizeable population of working dogs in India principally comprise of Labrador retriever and German Shepherd breeds. Deployment of these working dogs in difficult terrains like grassland and forests possess a potential exposure to the infected wild canids; while carrying out duties in semi-urban or rural areas these animals get exposed to the stray dogs. Thus, these working dogs are also at the continuous risk of exposure to ticks and other tick borne diseases.

Ehrlichiae have a complex life cycle involving a tick vector and a mammalian host. Typically, tick nymphs or larvae are infected with *E. canis* after feeding on a persistently infected dog. Transtadial transmission occurs to subsequent stages of the tick vector. A new host is infected via salivary gland secretions during blood feeding. Transmission of the disease has also been reported via blood transfusion. A natural reservoir of infection is maintained in both wild and domestic canids, including but not limited to, dogs, wolves, coyotes and foxes. The failure of canids to completely clear *E. canis* is one important mechanism of this ongoing persistence and should be considered when selecting canine blood donors from endemic regions.

Pathogenesis

A dog acquires infection through the bite of an infected tick, delivering the causative organism, *E. canis* into the host. The organism adheres to the monocytic membrane and enters the cell through endocytosis. It divides by binary fission leading to the formation of morulae, which ruptures releasing the organism and spread to the adjacent cells via cytoplasmic projections, thereby spreading throughout the body of the host.

Acute phase: After an incubation period of 8-20 days, the organisms multiply within circulating mononuclear cells and infrequently seen in neutrophils and eosinophils due to tropism for haemopoitic cells and the phagocytic tissues of the liver, spleen and lymph nodes. During the 2-4 weeks of this acute phase, infected cells adhered to the vascular endothelium, inducing a vasculitis and subendothelial tissue infection. In this phase clinical symptoms are manifested such as anemia, leukopenia and thrombocytopenia.

Mechanism of thrombocytopenia:

1. Increased platelet consumption by endothelial blood vessels.
2. Increased platelet destruction by spleen.
3. Antiplatelet antibodies.

Subclinical phase: Dogs which do not receive adequate treatment in the acute phase either die or may enter in the subclinical phase. The organism sequestered in the spleen. Anti-ehrlichial antibody play important role for maintenance of the long term carrier stage (Weisigar *et al.*, 1975) [32].

Chronic phase: Bone marrow depression or bone marrow hypoplasia results into pancytopenia and very low parasitemia at this stage. *Ehrlichia spp.* lives and reproduces in white blood cells but it has particularly devastating effect on the lymphatic system, so called AIDS of the canine world. It affects multiple system organs such as respiratory, circulatory, CNS, kidney, liver, spleen and endothelium of capillaries etc. Severe depression of immune system enhances the complications due to secondary bacterial infections (Kumari, 2007) [10].

Zoonotic potential

A few decades ago, ehrlichiosis was considered to only have veterinary relevance. The first human infection with *E. chaffeensis* was diagnosed in 1986 raising the awareness of *Ehrlichia* spp. as zoonotic pathogens (Maeda *et al*., 1987) [13]. Nowadays *E. canis*, *E. chaffeensis* and *E. ewingii* are all known to cause ehrlichiosis in humans (Straube, 2010) [28]. *E. canis* DNA has been detected in some human patients with clinical signs of human monocytic ehrlichiosis suggesting that *E. canis* might be a cause of monocytic ehrlichiosis in people. Affected people have headache, fever and thrombocytopenia, with or without leukopenia and respond to doxycycline treatment. Although direct dog-to-human transmission does not reported and blood from affected dogs should be handled with caution (Sykes, 2014) [29].

Clinical manifestations

Canine monocytic ehrlichiosis (CME) has three clinical forms: acute, subclinical and chronic.

Acute form: Acute phase lasts between 3 to 5 weeks with clinical findings of pyrexia, anorexia, depression, lymphadenopathy (Fig. 1) and splenomegaly. More variably ocular discharge, pale mucous membranes, haematochezia (Fig. 2), haemorrhagic tendencies (dermal petechiae, ecchymoses (Fig. 3) or epistaxis, haematoma) and neurological signs (seizures, incoordinated gait).

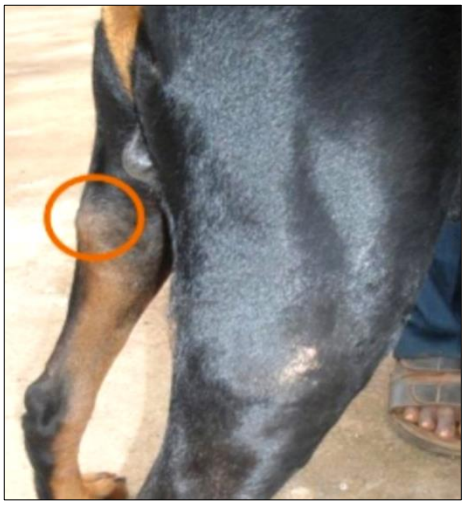

Fig 1: Lymphadenopathy

Fig 2: Haematochezia

Fig 3: Ecchymotic haemorrhages

Subclinical form: A long-term subclinical phase usually follows the subsidence of clinical signs and can last for several years. Dogs that are unable to eliminate the infectious agent develop subclinical persistent infections and become asymptomatic carriers. Persistent ehrlichimia with no overt clinical signs and normal haematological parameters.

Chronic form: Some infected dogs progress to a chronic phase, which can be mild or chronic. This is characterized by recurrent clinical and haematological signs including thrombocytopenia along with thrombocyte suffer from functional deficiency, anaemia is severe and non-regenerative and pancytopenia. Chronic form of ehrlichiosis is characterized by multiple organ dysfunction syndrome (often liver, kidneys and bone marrow) or multi-systemic life threatening complications. Specific clinical signs includes such as pyrexia, pallor, hind limb edema**,** lameness, limping movement, tetraparesis, lymphadenopathy, polymyositis, muscle wasting, chronic weight loss, haemorrhagic tendencies like epistaxis, melena, haematuria and non- specific signs like lethargy, anorexia, vomiting, dyspnea, polyurea, polydipsia, ascites, splenomegaly, ocular signs (hyphema, retinal detachment, ocular pain, blindness, corneal opacity), various types of neurological signs. Chronic infections are responsible for autoimmune diseases such as glomerulonephritis, uveitis, polyarthritis, articular pain and haemorrhagic retinitis. In severe cases, the response to antibiotic therapy is poor and dogs often die from massive haemorrhage, severe debilitation or secondary infections. *E. canis* causes immuno-suppression but currently little is known about the immunobiology of this infection.

Immunology of canine ehrlichiosis

Cell meditaed immunity (CMI) has a significant role in determining the course of the disease in dogs infected with *E. canis.* Specific and non specific immuno-suppression occurs due to *E. canis*. Canine leucocyte migration- inhibition factor has been successfully isolated and shown to be physically and functionally similar to human and Guinea pig migration inhibition factor. Severe chronic affected dogs do not develop CMI as compared to acute and mild chronic. The CMI responses decrease while humoral antibody titers increase with time (Nyindo *et al*., 1980) [19].

Diagnosis: Diagnosis can be made on the basis of history of tick infestation, clinical sign and symptoms, physical examination and laboratory examinations.

Laboratory examinations:

Parasitological examination / cytological examination: Three types

- Blood smear examination: Microscopic examination of Giemsa stained blood smears to identify the presence of morulae in mononuclear cells (*E. canis or E. chaffeensis*) and neutrophils (*E. ewingii or A. phagocytophilum*) (Fig. 4) can strengthen a diagnosis of ehrlichiosis but it is not sensitive and may only detect 4-10% of positive cases. *E. canis* can be detected for a short period of time in monocytes but they cannot be found during subclinical and chronic stages of infection.

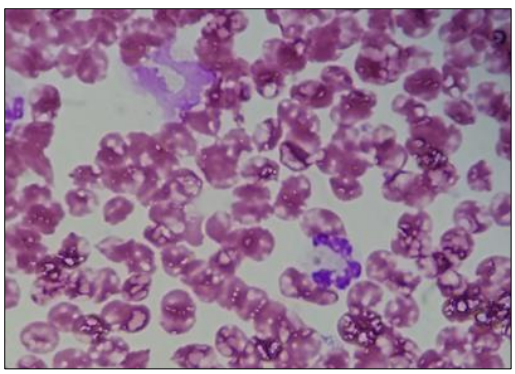

Fig 4: *E. ewingii* in neutrophil

- Impression smear examination: Impression smear made from lungs, spleen, liver and kidney revealed morulae on

Giemsa staining (Kumari, 2007) [10].

- Buffy coat examination: Examination of buffy coat smear seems to be more appropriate method of diagnosis under field conditions. In Giemsa stained buffy coat smear, morulae and inclusion bodies are important aid in diagnosis of canine ehrlichiosis (Elias, 1992) [4].

Haemato-biochemical examination

Haematology

Haematological examination revealed moderate to severe thrombocytopenia, non-regenerative normocytic normochromic anaemia, leukocytosis, neutropenia, lymphopenia and eosinophilia. Pancytopenia due to bone marrow hypoplasia is characteristic of the chronic ehrlichiosis. The most commonly observed haematological abnormalities are thrombocytopenia and anaemia. In endemic areas platelet counts on blood smear are used as a screening test for CME (Kottadammane *et al.,* 2017) [9].

Serum Biochemistry

Biochemical investigation revealed increased level of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) due to hepatocyte damage in acute phase. Elevation in the level of blood urea nitrogen, creatinine, globulin, bilirubin and reduction in albumin, albumin and globulin ratio. *E canis* can occasionally induce a protein losing nephropathy as a result of immune complex glomerulonephritis with consequent proteinuria and azotemia (Kottadammane *et al.,* 2017) [9].

Serology

In serology, the Indirect Fluorescent Antibody Test (IFAT) and Dot-ELISA kits are recommended to confirm a diagnosis of ehrlichiosis for the detection of *E canis*- IgG antibodies (Nakaghi *et al.,* 2008) [17]. Occurrence of positive serology and negative nPCR samples may be an indication of the carrier state or treatment of the animals, because dogs with anti-*E canis* antibodies may not carry the parasite.

Indirect fluorescent antibody test

It is a gold standard test. Antibodies can be detected between 7 and 28 days after initial infection. Dogs with acute ehrlichiosis may have false-negative test results if sufficient time has not elapsed for antibody production to occur. Serologic cross-reactivity to other *Ehrlichia* species occurs, which includes *E. ewingii* and especially *E. chaffeensis*. Cross-reactivity to *A. phagocytophilum* antigens can occur to a lesser extent (Sykes, 2014) [29].

E. canis IFAT detects antibodies reactive to whole-cell *E. canis* antigens. Antibodies to *E. chaffeensis* and *E. ewingii* may cross-react with *E. canis*, thus IFA should not be used to speciate an *Ehrlichia* infection. A two-fold increase in serial dilutions between acute and convalescent serum samples, collected approximately 4 weeks apart, can confirm an *Ehrlichia* infection. A decline in *E. canis* IFA titers is variable after treatment and not recommend for monitoring treatment efficacy. Some dogs will remain *E. canis* IFA positive for up to a year after apparent elimination of the *E. canis* infection.

10.3.2 Witness *Ehrlichia* test- A rapid immuno-migration (RIM) test for the serological detection of canine monocytic ehrlichiosis (witness Ehrlichia, Zoetis, France). The sensitivity of this test is 97%. The WE test represents a simple, fast and reliable test for the detection of anti-*E. canis* antibodies. Its implementation for diagnosis of clinical cases has been validated in the field and its use allows easy detection of asymptomatic dogs that may be carriers of *E. canis* (Davoust *et al*., 2014) [1].

Speed Ehrli ™: Can be used to detect recent contamination with *E. canis* but also animals that are chronic carriers of bacteria and prior to their introduction. Kit is ideally suited to a regular monitoring. It can be used to minimize the risks of contamination during blood transfusion. The method is based on membrane immunochromatography for detection of anti-*Ehrlichia canis* antibodies with whole blood with or without anticoagulant or serum or plasma. Sensitivity of the test is 87%.

Speed Duo Leish K/ Ehrli: Detection of circulating antibodies against both Leishmania infantum and *Ehrlichia canis*. Sensitivity is 87%.

Serodiagnosis detecting antibodies in the serum of the canines cannot differentiate between present or past infection. Animals may be negative for the pathogen but may show positive antibody response due to previous exposure.

ELISA

A variety of ELISA assays have been developed for detection of antibodies to *E. canis*.

SNAP 4Dx Plus test

A point-of-care, enzyme-linked immunosorbent assay (ELISA) detect antibodies to peptide antigens from *E. canis* and *E. ewingii* (Fig. 5). A positive result is not quantitative and represents exposure or potential infection. Dogs can remain positive for years after apparent elimination of the *Ehrlichia* infection. While a dog previously positive by SNAP 4DX Plus may not be currently infected, it is important to remember that there is no evidence supporting long-lasting, protective immunity, thus dogs can be re-infected or recrudescence can occur after the initial infection. SNAP 4DX Plus *Ehrlichia* positive dogs without clinical signs should be tested for Ehrlichia infection by PCR or a CBC examined for any evidence of current infection.

Limitation

Positive result indicates presence of antibodies but cannot differentiate between two species of *E. canis* and *E. ewingii*, *A. phagocytophilum* and *A. platys*.

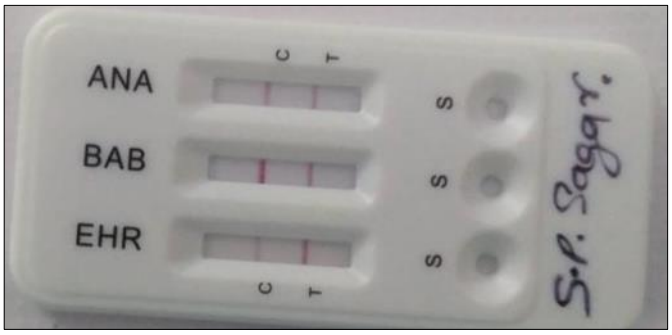

Fig 5: Rapid Test Kit

Dot: ELISA Immunocomb- For screening of antibodies to *E. canis* by this kit. eg. Immunocomb (Biogal Galed Laboratories, Israel) (Mittal *et al*., 2017) [14].

Molecular diagnosis

PCR: Whole-blood PCR assays for *E. canis* DNA is more sensitive for early diagnosis of CME than IFAT or ELISA in dogs with acute disease. PCR detect *Ehrlichia* DNA as early as 4 to 7 days post-infection prior to seroconversion. Target gene for amplification of *Ehrlichia canis* is 16S rRNA. PCR assays for may be performed on blood, lymph node aspirates, splenic aspirates or bone marrow. Convalescent IFA or ELISA testing is much more sensitive than PCR assays for diagnosis of chronic CME. The sensitivity of PCR assays for diagnosis of CME when performed on bone marrow in dogs with chronic ehrlichiosis can range from 25% to 68%, depending on the laboratory. PCR assays may be useful to confirm infection in the first week of illness, when serologic assays are often negative. Depending on the assay used, when positive, PCR can also be used to confirm the *Ehrlichia* species involved (Gal *et al.*, 2008) [5].

Differential diagnosis

In general, ehrlichiosis should be suspected in dogs with pancytopenia, thrombocytopenia and aplastic anemia in areas endemic for the tick vector, *R. sanguineus*. But depending on the geographic region, similar clinical signs can occur with other relevant CVBD pathogens so veterinarians must perform a differential diagnosis to rule out following diseases-

- **Babesiosis:** Piroplasm present in erythrocyte on blood smear examination and no enlargement of lymphnode.
- **Anaplasmosis:** *Anaplasma* spp. are intra-erythrocytic, these look like dots and some of them are rods or even taled forms on parasitological examination of blood smear.
- **Hepatozoonosis:** *Hepatozoon canis* gamonts found in neutrophils on smear examination and neutrophilia. Radiography of long bones shows periosteal proliferation and histopathology of biopsied muscles shows "Myositis onion peel appearance".
- **Canine distemper:** The skin of foot pads and nose become hard due to hyperkeratosis and bronchopneumonia is a common finding, pustule formation on ventral abdomen.

Treatment

Demonstration at any phase of infection of *E. canis*-specific DNA from the blood or other tissues (e.g. BM or splenic aspirates) or a 4- fold increase in antibody titers should be considered as an active infection and justifies antimicrobial treatment regardless of the dog's clinical status because progression or non-progression to disease cannot be predicted. Treatment would also be recommended for clinically healthy, seropositive, PCR-negative dogs with compatible clinico-pathologic abnormalities (e.g. anemia, thrombocytopenia, hyper-globulinemia) that lack evidence of other inciting causes for these findings (Mylonakis *et al.*, 2019) [16]. Antimicrobial therapy included tetracycline (oxytetracycline, minocycline, doxycycline), rifampicin, imidocarb dipropionate and homeopathic medicine *Crotalus horridus* are effective.

Oxytetracycline used against canine ehrlichiosis with dose rate of 20 to 22 mg/ kg body weight by intravenous route BID for 2 weeks. Doxycycline is the drug of choice for canine ehrlichiosis. Dose rate used either 5 mg/ kg twice in a day or 10 mg/ kg body weight once in a day for 3 to 4 week, orally (Shropshire *et al*., 2018) [26].

Imidocarb dipropionate is an antiprotozoal drug has been successfully used in treating resistant *E. canis* infection with a dose rate 6.6 mg/ kg body weight two subsequently dose 14 days apart either deep intramuscular or subcutaneous route. It is also effective against Babesiosis and Anaplasmosis. It is costly but very effective. It is persist in the tissues for up to one month following one dose. When imidocarb was given as a single IM injection, 83.9% of dogs recovered (Eddlestone *et al.*, 2006) [3].

Rifampicin used as a potential alternative drug to doxycycline for treatment of canine monocytic ehrlichiosis. Dose rate 10 mg/kg, orally, SID for 3 weeks. After treatment haematological abnormalities resolved and *E. canis* DNA could no longer be PCR amplified from blood (Theodorou *et al.*, 2013) [30].

Minocycline used as alternative to doxycycline in veterinary practices @ 10 mg/ kg body weight orally, BID for 4 weeks. Minocycline has greater lipophilic properties and high tissue concentration could be beneficial in *E. canis* treatment as compared to doxycycline. This may be especially true if *E. canis* has invaded the central nervous system. Minocycline is widely available and may be remarkably much less expensive (Jenkins *et al.*, 2018) [6].

Homeopathic drug *Crotalus horridus* 200C at 4 pills orally for 20 days has almost equal intensity with doxycycline to manage the ehrlichiosis infection (Tungnunga *et al*., 2016) [31].

Blood transfusion is necessary in severely anaemic dogs to save their life. Along with above treatment symptomatic medication and fluid therapy is required.

Prevention and control

Prevention of Ehrlichiosis infection involves avoidance of tick exposure and use of tick preventative measures as there is no successful vaccine currently available against ehrlichiosis. Early tick removal also has the potential to reduce transmission. Potential blood donor dogs could be screened for infection with *Ehrlichia* specific ELISA and PCR assays. All newly introduced dogs into a kennel should be sero-tested and treated for ticks. Preventive efficacy is 95 – 100% in treated dogs living under natural conditions in endemic areas.

Tick control

Physical methods: Physical methods include burning of pasture, tick repellent grasses eg.- lavender, lemongrass, members of mint family (mints, catnip and sage), garlic, beautyberry, rosemary, marigold, wormweed etc.

A variety of devices are available to assist tick removal, which are placed around the area where the mouthparts enter the skin to avoid crushing or squeezing the tick and leaving the mouthparts behind. Fine-tipped tweezers can be used to grasp the tick as close to the skin as possible, followed by steady retraction to remove the tick.

Chemical methods: Chemical methods are of two types i.e. topical and systemic acaricides.

- Topical acaricides- Acaricides which are used locally over the animal's body is termed as topical acaricides. They are used by various methods and accordingly preparations are available in the market such eg.
- Systemic acaricides- Systemic acaricides offer another means of providing long- lasting and effective tick control. The toxicant is introduced into the host's blood to kill ticks as they feed on the treated animals. The most common routes used are subcutaneous and oral. eg.-

Ivermectin, Doramectin, Moxidectin, Fluralaner, Salolaner, Afoxolanar.

Clients should be instructed to remove ticks properly and avoid handling ticks with bare hands or crushing them, to prevent exposure to infected hemolymph. Appropriate precautions should be taken to prevent needle-stick injuries. Low dose of doxycycline (6.6 mg/kg q24h PO) has also been used to prevent infection in dogs residing in kennels in which *E. canis* infection is a problem.

Table 2: Anti-tick preparation available in market

S. No.	Preparation	Composition	Brand Name
1.	Dusting powder	1. Propoxur 1% 2.Herbal	Notix, Bolfo, Tick free, Tick Guard etc. Erina E.P.
2.	Shampoo	1. Propoxur 0.1% 2. Cypermethrin 1% 3. Herbal	Notix, Bolfo etc. Tikkill, Tick free, Reltix etc. Erina E.P., F- Shield
3.	Soap	1. Permethrin 2% 2. Permethrin 2% + Miconazole2% 3. Coumaphos 1%	Softas, Extick, Flick Out etc. Softas max etc. Asuntol etc.
4.	Spray	1. Fipronil 0.25% 2. Fipronil 0.25% + (S) Methoprene 0.22%	Freedom, Fiproforte, Vifi, QuicFip, Fiprotic, Fixotic, Nay Flee. Fixotic Advance
4.	Spot on	1.Imidacloprid (10%) + Permethrin (50%) 2. Selamectin (12%) 3.Fipronil 9.8% + (S) Methoprene 8.8%	Ban-flea, Advocate, Advantix Revolution(6mg/kg), Radicate QuicFip Plus, Fiprofort Plus, Fixotic, Tick Free,
5.	Plastic collar	1. Propoxur + Flumethrin 2. Amitraz + Amidine 3. Imidacloprid + Flumethrin	Kiltix, Bay-O-pet etc. Preventic etc. Seresto etc.
6.	Dipping solution	Amitraz 12.5%	Ridd, Amitraz, TakTic

Conclusion

Canine monocytic ehrlichiosis is distributed worldwide and still remains a disease of importance in pet dogs, stray dogs and working dogs. The disease manifests in many forms and it is fatal in severe cases. It is not possible to rely on a single serological result for diagnosis of *E. canis*, battery of tests are to be performed for confirmatory diagnosis. Empirical treatment is carried out leading to indiscriminate use of doxycycline and raising concern on possibility of positive selection of drug resistant strains of *E. canis*. It is suggested that doxycycline should be used with caution only when there is active infection in the affected dogs. As ehrlichiosis is a zoonotic disease so, owners or handlers of dogs, veterinarians and laboratory workers should be aware about this disease and care must be taken during handling of affected dogs and its samples.

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