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TICK-BORNE INFECTIOUS DISEASES WITH REFERENCE TO EGYPT

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Abstract

Ticks are hematophagous ectoparasites of man, domestic and street animals, and birds of health and economic hazard worldwide. They transmit many micro-organisms and protozoan infectious diseases and their toxins cause different signs and symptoms that may be fatal according to the infesting tick saliva protein.

In Egypt where there are many rural and urban areas, so many genera and species of ticks are encountered. The Egyptian veterinary and agricultural authorities deal with ticks from economic point of view. But from medical point of view, ticks have specific role in transmission of zoonotic infectious diseases as well as their saliva causes tick paralysis. When dealing with children from tick infested areas, tick paralysis should be considered in differential diagnosis of the clinically confused diseases as poliomyelitis, myasthenia gravis; Guillain-Barre; paralytic rabies botulism; transverse myelitis and /or the diphtheritic polyneuropathy. Tick-borne relapsing fever is a zoonosis and is endemic in many countries. The two main *Borrelia* spp. involved in North America are *B. hermsii* (in the mountainous West) and *B. turicatae* (in the southwest).

Crimean Congo hemorrhagic fever (CCHF), babesiosis and infantile tick paralysis were identified as emerging diseases disaster. Also, Lyme disease is the commonest worldwide and encountered in Egypt since a long time. And now what about other tick-borne diseases, taking into consideration the tick populations is endemic not only in Egypt but worldwide vectors.

Key words: Egypt, Tick-Borne Diseases, General review and discussion, Conclusion.

Introduction

Ticks are small arachnids of order Ixodida along with mites, they constitute subclass Acarina. Ticks are external parasites, living by hematophagy on the blood of mammals, birds, and sometimes reptiles and amphibians. Three families of ticks, 1- Nuttalliellidae – comprises a single species, *Nuttalliella namaqua*, 2- Ixodidae, hard ticks and 3- Argasidae, soft ticks (Allan, 2001).

Ticks are vectors of many diseases, including Lyme disease, Q fever (rare; more commonly transmitted by infected excreta), Colorado tick fever, Rocky Mountain spotted fever, African tick bite fever, tularemia, tick-borne relapsing fever, babesiosis, ehrlichiosis, tick paralysis and tick-borne meningoencephalitis, as well as bovine anaplasmosis (Andersson and Råberg, 2011).

Ixodidae are distinguished from the Argasidae by the presence of a *scutum* or hard shield. Ixodidae nymphs and adults both have a prominent *capitulum* (head) which projects forwards from the body; in the Argasidae, conversely, the capitulum is concealed beneath the body (Dennis, and Piesman, 2005). Argasidae contains 193 species, although the composition of the genera is less certain, and more study is needed before the genera can become stable. The currently accepted genera are *Antricola*, *Argas*, *Nothaspis*, *Ornithodoros* and *Otobius*. Though common in North America, they feed rapidly, primarily on birds, and are very rarely found to parasitize land animals or humans (Sonenshine, 2005). *Nuttalliella namaqua* is a tick found in southern Africa from Tanzania to Namibia and South Africa, which is placed in its own family, Nuttalliellidae. It can be distinguished from ixodid ticks and argasid ticks by a combination of characters including the position of the stigmata, lack of setae, strongly corrugated integument, and form of the fenestrated plates (Sonenshine, 2005).

Family Ixodidae: Ixodid ticks undergo three primary stages of development: larval,

nymphal, and adult. Ixodid ticks require three hosts, and their life cycle takes at least one year to complete. Up to 3,000 eggs are laid on the ground by an adult female tick. When larvae emerge, they feed primarily on small mammals and birds. After feeding, they detach from their host and molt to nymphs on the ground, which then feed on larger hosts and molt to adults. Female adults attach to larger hosts, feed, and lay eggs, while males feed very little and occupy larger hosts primarily for mating (Wall and David, 2001).

Family Argasidae**:** Argasid ticks, unlike ixodid ticks, may go through several nymphal stages, requiring a meal of blood each time. Their lifecycle ranges from months to years. The adult female argasid tick can lie anywhere from a few hundred to over a thousand eggs over the course of her lifetime. Larvae feed very quickly and detach to molt to nymphs. Nymphs may go through as many as seven instars, each requiring a blood meal. Both male and female adults blood-feed and they mate off the host. During feeding, any excess fluid is excreted by the coxal glands, a process which is unique to argasid ticks (Walter *et al*, 2002).

Review and Discussion

First aid for ticks**:** In general, the best way to remove adult tick is mechanically. To facilitate prompt removal, fine-tipped tweezers can be used to grasp the tick as close to the skin as possible and detach it by applying a steady upward force without crushing, jerking or twisting, in such a way as to avoid leaving behind mouthparts or provoking regurgitation of infective fluids into the wound. Proprietary tick removal tools are also available. It is important to disinfect the bite area thoroughly after removal of the tick. The tick can be stored and, in case of signs or symptoms of a subsequent infection, shown to a clinician for identification purposes together with details of where and when the bite occurred. If the tick's head and mouthparts are not attached to the body after removal, it may be necessary to perform a punch biopsy to remove any parts remaining inside patient (Zuber and Mayeaux, 2003).

Ticks transmit many infectious diseases to humans and other animals. However, the toxins of various ticks can also cause a disease condition known as the tick paralysis, which can be confused with both infectious and noninfectious conditions.

1- Tick paralysis: First described by explorers in the Australian outback in 1824. Toxin producing ticks were reported in all the continents among animals, human cases were reported from Australia, North America, South Africa, Europe, Asia and western Canada (Edlow and McGillicuddy, 2008). Tick paralysis affect humans and domestic and wild animals worldwide, but most cases occur in Australia and North America. Tick paralysis is a rare disease in humans (Schaumburg and Herskovitz, 2000), but when occurred can be fatal or nearly fatal particularly in infants depending on the tick saliva protein (Horka *et al*, 2012). But, if recognized promptly, illness can be cured with the combination of tick removal and supportive care. They were clinical and laboratory examined for infectious diseases that might be encountered in the children living in rural areas with farm animals as well as stray dogs, as rabies; myasthenia gravis (Neuromuscular disorder); botulism; diphtheritic polyneuropathy. Also, specific serologic diagnosis (Jain *et al*, 2011; Trakas *et al*, 2011) was adopted and CSF examination was done when indicated (Ibrahim *et al*, 2012).

There is no national surveillance system for tick paralysis and reliable information on incidence does not exist. However, the disease appears to be uncommon based upon available literature and clinical experience.

Only 33 cases were reported in Washington State between the years 1946 and 1996, even though tick paralysis was a reportable disease in this state until 1998 (Dworkin *et al*, 1999). Most cases in North America occurred in the western regions of the United States and Canada, but the illness was seen in the eastern, southeastern, and south cen-

tral of the USA. Also, cases were reported in the urban areas in travelers back from endemic areas (Gordon and Giza, 2004)

Four cases of tick paralysis were reported in patients from North Central Colorado. The clustering of these cases was unusual because in previous years, on average, only one case per year was reported from Colorado. Another unusual characteristic of this cluster was the age distribution of cases: only one of four cases occurred in a child. Previous case reports noted that tick paralysis was more likely to occur in children under the age of 10 years because tick toxins were more likely causing symptoms in patients with the smaller body mass (Diaz, 2010a).

The females were affected more often than males, possibly because ticks are more likely to remain undetected following attachment to individuals with long hair. As in other tick-borne diseases, most cases occur in the spring and early summer months (Inokuma *et al,* 2003).

In the present study, the children suffered from diarrhea, vomiting, irritability and mild intermittent fever and nervous manifestation in the two little children.

In general, the diarrhea, vomiting, irritability, lower neuron paralysis, fever sometimes, infection may progress to the bulbar involvement, respiratory paralysis and then death. Removal of tick is followed by rapid improvement and complete recovery of neurologic manifestations within 1 to 2 days. However, death after tick removal was reported (Mumagham and O'Rourke, 1978).

The tick paralysis are confused with many disorders including Guillain-Barré syndrome, cerebellar ataxia, myasthenia gravis, poliomyelitis, botulism, acute spinal cord lesions, periodic paralysis from hypokalemia, insecticide poisonings, and exposure to buckthorn, shellfish poisoning, and hysterical paralysis (Vedanarayanan *et al*, 2002). A number of clinically important but unusual features of tick paralysis deserve emphasis: involvement of facial, ocular, lingual, and pharyngeal muscles may produce diplopia, dysphagia, and/or dysarthria (Vedanarayanan *et al*, 2004). Bulbar muscle involvement may also result in unusual presenting symptoms such as drooling. Paralysis may be localized to one arm or leg (Bow and Brown, 1946) and isolated facial paralysis has occurred in patients who have ticks attached to their external ear canal (Pearn, 1977). Patients with unilateral arm weakness were described, suggested a brachial plexopathy associated with an engorged tick in subclavian fossa (Engin *et al*, 2006). They may present with ataxia of the arms and legs that spuriously suggested the presence of a cerebellar lesion (Greenstein, 2002).

In a review of 332 cases of tick paralysis published 60 years ago, the fatality rate was 12% (Rose, 1954). A more contemporary series of 33 cases reported a fatality rate of 6% (Diaz, 2010b). In most cases, tick paralysis diagnosis was not antemortem. Patients rarely suffered from the ascending weakness and the autonomic dysfunction that may lead to an incorrect diagnosis of Guillain-Barre syndrome (Crawford and Mitchell, 2009).

Edlow (2010) mentioned that physicians should consider tick paralysis in any patient with an acute flaccid paralysis. As a general rule, aimed more towards patient safety than the likelihood of making a correct diagnosis, never definitively diagnose Guillain-Barré syndrome without first searching the entire body for a tick. Tick removal results in rapid improvement. Some patients may require mechanical ventilation and support in an intensive care unit as the toxin clears. Since tick paralysis is toxin-mediated and not an infectious agent, antimicrobials are not indicated. Laboratory examination showed anemia and marked elevation of IgE. Burke *et al.* (2005) found normal CBC and normal cerebrospinal fluid, and imaging. They added that hypoxia and hypercarbia occurred on respiratory muscles involvement.

More than 800 known species of argasid (soft-shelled) and ixodid (hard-shelled) ticks, and over 40 individual tick species are capable of producing salivary toxins that can

cause paralysis in humans and animals. Tick species that cause most cases of human tick paralysis in the United States and Canada are *Dermacentor andersonii* (Rocky Mountain wood tick), and *D. variabilis* (American dog tick). Other ticks such as *Amblyomma americanum* (Lone star tick), *Ixodes scapularis* (Black-legged tick), *I. pacificus* (Western black-legged tick) *I. holocyclus* (Australia scrub tick) were associated with human tick paralysis (Wilson, 1991).

Many ticks were incriminated in several countries, as ixodid tick in Israel (Feldman-Muhsam, 1986) *Hyalomma* adults and/or *Rhipicephalus* nymphs and adults in Sudan (Musa and Osman, 1990) *Ornithodoros savignyi* in South Africa (Mans *et al*, 2002), *Dermacentor andersoni, D. variabilis*, *Ixodes holocyclus* and *Amblyomma maculatum* in Mexico (Espinoza-Gomez *et al*, 2011), *Ornithodoros brasiliensis* in Brazil (Reck *et al*, 2011). However, larvae and nymphs were of hard tick and one cannot incriminate any tick nor all as causing paralysis, in spite that all are blood sucking and secrete toxins. The onset of symptoms of tick paralysis occurs only after a female tick has attached and begun feeding. Symptoms do not typically develop until the tick has fed for 4 to 7 days. The biological effect of tick salivary toxins is, in part, specific to the tick species.

The neurotoxins produced by *Dermacentor* spp. have a number of pathologic effects including slowing of motor nerve conduction velocity, lowering of the height of the nerve and muscle action potential impaired propagation of afferent nerve fiber signals (Gothe *et al*, 1979). Precise mechanism for development of the symptoms of tick paralysis by *Dermacentor* ticks may interrupt sodium flux across axonal membranes in selected locations such as the nodes of Ranvier and nerve terminals (Felz *et al*, 2000). Tick paralysis caused by *Dermacentor* begins with sense of fatigue, paresthesias, and the weakness, although individual patients may sometimes appear irritable or restless and complain of muscular pain. Fever is characteristically absent, and without change in the sensorium or headache unless severe hypoxia or hypercarbia are present. Despite patients' reports of paresthesias, the sensory exam is typically normal. Most patients eventually develop an unsteady gait that progresses to an ascending complete paralysis. Deep tendon reflexes are characteristically absent. Respiratory paralysis and death can occur in severe cases. Onset of tick paralysis caused by *I. holocyclus* is characteristically slow; patients may have gradually the worsening symptoms over 48 to 72 hours until complete paralysis occurs. The patients from Australia with tick paralysis simultaneously had internal and external ophthalmoplegia, and pupillary reflexes may be absent or minimally reactive early in the course of illness (Greenstein, 2002).

The neurotoxins produced by the *I. holocyclus* act on presynaptic motor nerve terminals and inhibit the release of acetylcholine. This inhibition resulted in total blockade of transmission at myoneural junctions and was temperature dependent (Cooper and Spence, 1976). The low-amplitude compound muscle action potentials was reported in neurophysiologic testing; motor conduction velocities, sensory studies, but the repetitive stimulation was normal (Grattan-Smith *et al*, 1997). While toxin of *I. holocyclus* was not completely characterized, it bears similarities to botulinum toxin. However, differentiating the tick paralysis from these conditions must be relatively easy if the following clinical features were carefully considered or sought: A meticulous search will usually disclose the presence of a tick in cases of tick paralysis. CSF is typically abnormal in patients with poliomyelitis, Guillain-Barré syndrome, and in those with acute spinal cord lesions, whereas it is normal in patients with tick paralysis. Fever is not typically present in patients with tick paralysis. When fever is a prominent part of the prodromal or neurologic illness, tick paralysis is not a likely diagnosis. Unlike tick paralysis, botulism usually causes a descending paralysis, and the

cranial nerves are affected early in the illness. Pupillary abnormalities are common in botulism and uncommon in tick paralysis. Tick paralysis due to *Dermacentor* generally progresses over time periods ranging from hours to one or two days, whereas the weakness and paralysis in Guillain-Barre syndrome, poliomyelitis or spinal cord lesions progresses more gradually, often over days to weeks. The sensation was intact with patients with tick paralysis, whereas it is either mildly or obviously abnormal in the patients with Guillain-Barre syndrome or spinal cord lesions (Singhal and Bhat, 2011).

When tick paralysis is suspected, a careful and meticulous examination should be done to look for a tick. Special attention should be given to the scalp, axillae, ears, labia, buttocks, and interdigital spaces. The use of a fine-tooth comb detected ticks embedded in the scalp of people with long hair; such a comb should be used when the diagnosis of tick paralysis was considered likely and a tick could not be found after a normal examination (Frischknecht, 2007).

Most patients with paralysis due to *Dermacentor* recovered or improved within a few hours following the removal of the tick (Roupakias *et al*, 2011). But, weakness and paralysis may worsen for 24 to 48 hours after *I. holocyclus* ticks are removed. Thus, patients with paralysis or weakness due to *I. holocyclus* should be observed carefully following tick removal (Hsieh *et al*, 2011).

The hyperimmune serum prepared from dogs was used widely to treat animals with tick paralysis, but its use in man is limited because of risk of immune-mediated reactions including serum sickness. So, *I. holocyclus* causing human tick paralysis were usually managed with supportive care that might include mechanical ventilation until recovery occurred (Webster *et al*, 2011).

Mosabah and Morsy (2012) reported tick-paralysis for the first time in Egypt among four children living in rural area at Giza Governorate. The clinical pictures were confused with rabies; myasthensia gravis; botulism; diphtheritic polyneuropathy encountered in rural areas. The recovery of tick infesting the four little children and negative clinical and laboratory data of all diseases denoted tick paralysis. Infesting ticks were *Rhipicephalus sanguineus* on dogs, *Hyalomma dromedarii* on camels and *H. anatolicum excavatum* and *Haemaphysalis* sp. on goats. The case was recognized as first record of tick paralysis in Egypt.

2- Babesiosis: Babesiosis, an infectious disease caused by protozoa of genus *Babesia*, infects vertebrate animals and cause lysis of host red blood cells. Zoonotic cycle is maintained by tick vectors. Human infection is accidental; humans are not definitive reservoir hosts. The symptoms typically develop one to six weeks after the tick bite; an incubation period of 12 weeks was described in one reported case. Most cases of transmission between humans are attributed to a tick vector. But, up to two-thirds of patients do not recall to a tick bite (Vannier *et al,* 2008). Some species of *Babesia* can be transmitted from a female tick to its offspring before migrating to salivary glands for feeding. *B. microti*, the most common variety of *Babesia* in humans however, has not been shown to transmit transovarially. But, more than 40 cases contracted from packed red blood cell (PRBC) transfusions and 2 infections documented from organ transplantation (Gubernot *et al,* 2009). The PRBC transfusions that cause the infections were identified through testing of the blood donor for *B. microti* antibodies (Kuwayama and Briones, 2008).

Nagaty (1947) in Egypt gave a list of the species of *Babesia* and *Theileria*. Maronpot and Guindy (1970) in Egypt identified *B. gibsoni* in the wild carnivores and domesticated dogs. Hafez *et al*. (1982) experimentally proved that *R. turanicus* transmitted *B. ovis* of sheep. Michael and El Refaii (1982) studied the efficacy of imidocarb dipropionate on *B. ovis* infection in sheep, and Michael *et al.* (1987) in Al-Minia Governorate reported the first case of human babesiosis.

El Bahrawy *et al.* (1993) found that *Babesia* species transmitted by ixodid ticks parasitized bovine (*B. bovis*), equine (*B. equi*), rodent (*B. microti*), canine (*B. canis*) and others. They examined 398 *Rattus rattus* and 90 *R. norvegicus* trapped in Suez, Ismailia, Port Said, North Sinai and South Sinai Governorates. All rats in Ismailia had *Babesia* infection that decreased in North Sinai, Port Said, and South Sinai to zero in Suez. As double infection, *Trypanosoma lewisi* was found in rats trapped in Port Said, North Sinai and South Sinai.

Wilson (1991) found that in animal babesiosis, release of pharmacologically activor, led to circulatory stasis and hypotension.

Hauschild and Schein (1996) reported that *B. canis* of dogs is transmitted by *Dermacentor reticulatus, Rhipicephalus sanguineus* and *haemaphysalis leachi*. Four *B. canis* isolates of different geographic origin were investigated for transmission specificity and pathogenicity in infection trials. *R. sanguineus* exclusively transmitted *Babesia* isolate from Egypt. *D. reticulatus* was the vector in Hungary and France. Transmission of the South-African isolate was possible by *H. laechi. B. canis* isolates differed markedly in their pathogenicity. They added that the South-African isolate was highly pathogenic and caused high mortality. Infections with Hungary isolate also resulted in severe clinical disease which often ended fatal without treatment with an anti-*Babesia* drug. Clinical disease resulted from infections with the French isolate while the Egypt one was non-pathogenic. Challenge trials for investigations of cross-immunity demonstrated immunogenic differences between the individual isolates. The immunogenicity degree was related to *Babesia* isolates pathogenicity. Serological investigations revealed that antigen of the isolate from Hungary in ELISA reacted markedly higher than other three antigens. Due to vector specificity *B. canis* was classified into three groups: *B. canis canis* transmitted by *D. reticulatus, B. c. vogeli* transmitted by *R. sanguineus* and *B. c. rossi* transmitted by *H. laechi*.

El-Ghaysh *et al*. (1996) by ELISA studied the cause of high level of background reactions which hinders the ELISA field application for *B. bigemina*. Different blockers to improve specificity of ELISA were compared. The use of soya milk (25%), gelatin (2.5%) and chicken serum (2%) did not significantly improve specificity. They added that the fibrinogen presence contributed to positive ELISA results more than presence of *B. bigemina* specific antigen as confirmed by testing bovine fibrinogen as a host protein antigen in ELISA that strongly responded against *B. bigemina* positive control sera. They stated that ELISA was unreliable until a more purified *Babesia*-specific antigen or specific monoclonal antibodies are available.

Gorenflot *et al.* (1998) mentioned that the first demonstrated case of human babesiosis in the world was reported in Europe, in 1957. Since then, a further 28 *Babesia* infections in man have been reported in Europe. Most (83%) of the infections were in asplenic individuals and most (76%) were with *B. divergens*, a cattle parasite. The parasitaemias varied from <1%-85% of the red blood cells. The usual clinical manifestations of severe babesiosis *divergens* were severe intravascular haemolysis with haemoglobinuria. Specific treatment was a massive blood-exchange transfusion, followed by Clindamycin. They added that hundreds of human infection with *Babesia* spp. was reported in U.S.A. Most cases were infected with *B. microti*, but other emerging. *Babesia* spp. (WA1, CA1, & MO1) were increasingly. Several cases resulted by blood transfusion. Clinical pictures varied from asym-ptomatic to a severe, rapidly fatal disease.

The splenectomized, elderly, immunocompromised and HIV-infected patients were predisposed to severe infection. *B. microti* infection was often subclinical or asymptomatic and only detected through serological surveys. They added that the recommended treatment of symptomatic cases was Quinine

plus Clindamycin. A few other human cases of babesiosis were reported in China, Egypt, Mexico, the South Africa and Taiwan.

El-Kady (1998) carried out a survey of ticks infesting camels in 7 localities of Sinai; El-Arish, Beer El Abd, Nakhel, Ain Mousa, St. Catherine, Wadi Hadra, and Dahab. The ticks were *Hyalomma dromedarii, H. impeltatum, H. an. excavatum, H. an. anatolicum, H. marginatum* & *H. schulzei.* The first three species were most common, whereas the latter ones were found in certain limited localities. Protozoa in the gut and haemolymph of the tick species were *Babesia* sp. and *Theilera* sp. in both tick guts and haemolymph in most species. *Trypanosoma* sp. was recorded in guts of ticks collected from Beer El Abd, Nakhel and Dahab. *Anaplasma* sp. was found in its guts from Beer El Abd and Dahab, same organism was detected in haemolymph of ticks in Nakhel and Dahab.

El Kady *et al.* (1998) in Saint Catherine District examined the five dominant rodents; *Acomys c. dimidiatus* followed by *Dipodillus d. dasyurus* and then *A. r. russatus.* Sporadic numbers of *Sekeetamys c. calurus* and *Eliomys. qu. melanurus* were collected. The ectoparasites in a descending order were mites (45.6%), lice (30.3%) and then fleas (24.1%). The most abundant ectoparasites among the three groups were *Polyplax spinulosa*, *Allodermanyssus sanguineus* and *Xenopsylla dipodilli*. *Leishmania* amastigotes and *B. microti* were detected in *Acomys* spp.

El Kammah *et al.* (2001) examined nineteen species and sub-species of ixodid and argasid ticks, *Hyalomma dromedarii, H. impeltatum, H. anatolicum excavatum, H. a. anatolicum, H. truncatum, H. m. marginatum, H. m. rufipes, H. m. turanicum, Boophilus annulatus, R. sanguineus, R. turanicus, R. guilhoni, R. camicasi, Amblyomma lipidum, A. marmoreum, A. vareigatum, Argas persicus, A. hermanii* and *A. arboreus* from different localities in Giza, Sharkia, Ismailia, El Beheira and Sinai Governorates. *Hyalomma* species were found on camels (98.6%) and cows (1.4%). *B. annulatus* was found only on cows (100%), *Rhipicephalus* spp. on the dogs (89.8%), camels (8.2%) and sheep (2.0%), *Amblyomma* spp. were on imported camels (100%) and *Argas* spp. on the chickens (70.6%), herons (18.8%) and pigeons (10.6%). Camels, cows, sheep, and chickens infested with ticks showed *Th. annulata*, *B. bigemmina*, *B. ovis*, and *Babesiosoma gallinarum*, respectively. *Haemoproteus columbae* were found in pigeons.

Mazyad and Khalaf (2002) in North Sinai Governorate examined 475 sheep, 200 goats, 135 cattle and 190 camels for *B. ovis* and *Theileria ovis*. *B. ovis* and *Th. ovis* were detected in 13 (2.7%) & 14 (2.9%) sheep, 14 (7.0%) & 15 (7.5%) goats, 13 (9.6%) & 11 (8.1%) cattle and 18 (9.5%), & 24 (12.6%) camels respectively. Double infection was found in 114 (24%) sheep, 51 (25%) goats, 27 (20%) cattle and 66 (34.7%) camels. The ticks were *R. appendiculatus, R. bursa, R. turanicus* and *Haemaphysalis parva* on sheep, *Hyalomma a. excavatum* and *Haemaphysalis sulcata* on goats, *H. lusitanicum* on cattle and *H. dromedarii, H. impeltatum, H. marginitum* and *H. a. anatolicum* on camels. *B. ovis* and/or *Th. ovis* were in ticks gut and /or salivary glands in *R. appendiculatus* (20.0%), *R. bursa* (16.7%), *R. turanicus* (10%), *Haemaphysalis parva* (10%), *H. a. excavaium* (30.%), *H. dromedarii* (18%), and *H. a. anatolicum* (6.7%).

Farah *et al.* (2003) examined 23 blood samples; five from naturally infected horses with *B. equi* and eighteen from asymptomatic horses with equine babesiasis from different localities. Carrier animals were microscopically in 7/18 samples (38.8%) and in 9.18 by IFA (50%), whereas PCR showed positivity of 14 samples (78%). Two synthetic oligonucleotide primers, based on *B. equi* merozoite antigen gene (EMA-1) were used, 819 bps DNA fragment was specifically amplified from gene encoding EMA-1 of *B. equi*. El Kammah *et al.* (2007) examined 1789 field-collected ticks found, *B. bigemina, B. canis; Th. annulata*, and rickettesia *Aegyptianella pullorum* in saliva and mid-

guts smears of eight ixodid and two argasid tick species. The infected percent was higher in cattle and dog ticks than in fowl ticks; and higher in salivary glands (S) than in the midguts (M). Identification of protozoa using microscopic image analysis, showed that *Hyalomma* spp. were infected with *T. annulata*; genera *Boophilus* and *Rhipicephalus* were infected with *B. bigemina*, and *B. canis* respectively; *Argas* spp. were infected with *A. pullorum*. They added that *Staphylococcus, Streptococcus* and *Yersinia* were in (S) and (M) of eight ixodids and one argasid tick species; *Bacillus* was only found in *H. anatolicum excavatum*. *Escherichia coli* were isolated only from *A. persicus* midguts.

El-Bahnasawy and Morsy (2008) reported the second case of Egyptian human babesiosis. The signs and symptoms, CBC, liver functions and kidney functions tests and all other serologic tests did not give any definite diagnosis, sero-negative for malaria and diagnosed by typical ring forms of *Babesia* species in Giemsa stained blood smears. The patient was successfully treated with the exchange blood transfusion Quinine and Clindamycin, and was discharged after clinical and parasitological improvement.

Adham *et al.* (2009) reported that *B. bovis* and *B. bigemina* were distributed all over the world; the etiologic agents of the animal babesiosis are considered the most important tick-borne disease. They studied the prevalence of *B. bovis* and *B. bigemina* in Egyptian ticks was studied by PCR. Questing 5,243 hard and soft ticks were collected from different localities throughout Giza Governorate. DNA from 500 different individual tick species was extracted and PCR was performed. Primers verified from the sequence of Mexico strain of both species were used. Two fragments of 275 and 175 bp of *B. bovis* and *B. bigemina*, respectively, were generated. El Bahnasawy *et al*. (2011) reported a twelve years old Egyptian boy was referred to the hospital with intermittent fever of unknown origin. Clinical, parasitological and serological bases proved babesiosis. The boy acquired infection from his pet dog which was heavily infested with *R. sanguineus* and suffered a mild feature of animal babesiosis. Patient was successfully treated with Atovaquone plus Azithromycin without relapse for one month follow up. The pet dog was sent to Governmental Veterinary Hospital for treatment.

Saleh *et al*. (2015) reported that the development of PCR assays resulted in increased sensitivity for characterization of new *Babesia* species. Using the developed molecular tools led to a better understanding of natural history of *Babesia* organisms as transmission and potential role as immunomodulator. They added that human infection is usually an asymptomatic infection in healthy individuals. Several patients become symptomatic, and, within these subpopulations, significant morbidity and mortality occurred, mainly in elderly, immunocompromised, or asplenic patients with difficult to diagnose. Although index of suspicion should be high in rural *Babesia* endemic areas, patients with babesiosis have few, if any, localizing signs to suggest infection. Diagnosis depends on the parasitemia degree, the expertise trained laboratory personnel. Most patients infected by *B microti* who are otherwise healthy appear to have a mild illness and typically recover without specific chemotherapy; however, treatment is recommended for all cases to prevent sequelae and potential transmission through blood donation. Mahmoud *et al*. (2015) reported frequent occurrence of babesiosis among apparently healthy Egyptian bovines in present of hematological disorders compatible with intravascular hemolysis and thrombocytopenia, suggested the need for appropriately designed prevalence studies to avoid zonoosis.

Bajer *et al.* (2015) in Sinai Mountains reported *B. behnkei* sp. nov., from Wagner's gerbil, *Dipodillus dasyurus*. Omar *et al*. (2016) found that Enoxacin IC50 values for *Babesia* and *Theileria* parasites as the drug is potent antibacterial drug with minimum side effect. Mahmoud *et al.* (2016) stated

that Equine piroplasmosis caused by *Theileria equi*, *Babesia caballi*, or both, contributed to significant economic loss in the Egyptian equine industry and was uncontrolled.

3- *Theileria* is a genus of parasitic blood protozoan that belongs to phylum Apicomplexa and is closely related to *Plasmodium*. Two *Theileria* species, *T. annulata* & *T. parva*, are cattle parasites (Morrisonm and McKeever, 2006). *T. annulata* causes tropical theileriosis and *T. parva* causes East Coast fever, and transmitted by various tick species including *Rhipicephalus, Dermacentor* and *Haemaphysalis* (Florin-Christensen and Schnittger, 2009). Elsify *et al.* (2015) in Egypt reported bovine *Babesia* and *Theileria* parasites in cattle, buffaloes, and sheep. Miró *et al.* (2015) in Spain reported *Theileria* annae in dogs bordering the endemic Galicia area. Now, one may ask, is *Theileria* parasites zoonotic disease?

4- Lyme disease: Haberberger *et al.* (1989) in Egypt reported presence of Lyme disease and its tick vector. Younis *et al*. (1995) in Suez Governorate reported that some rodent populations are wild but others are commensal and live in close association with man. They steal his food and conveying many zoonotic diseases. Their arthropod ectoparasites play an important role in conveying or transmitting these zoonotic diseases. Several disorders and diseases of man are tick borne relapsing fever, Rocky Mountain spotted fever, Lyme disease, and many others. They transmit several diseases as *Rickettsia tsutsugamushi* fever, epidemic haemorrhagic fever, and they cause severe allergic reaction. The results obtained were six species and subspecies of rodents. In a descending order were (a) *Rattus norvegicus*, (b) *R. r. alexandrinus* (c) *R. r. frugivorous* (d) Acomys cahirinus (e) *Gerbillus gerbillus asyutensis* (f) *Mus m. praetextus.* The commonest rodent was *R. norvegicus* and the least one was *M. musculus.* The ticks and mites were 2 genera of tick larvae; *Rhipicephalus* species and *Hyalomma* species. The mites were *Ornithonyssus bacoti* and *Laelaps nuttali.* Most tick larvae were on the wild rodents; *Gerbillus g. asyutensis.* Most mites were on the commensal ones mainly *R. norvegicus.* Illustrated descriptive morphology were given for rodents and their ticks.

Hammouda *et al.* (1995) examined a total one hundred patients, aged 6-15 years and presented to El-Shatby University Children's Hospital with chronic/recurrent arthritis and skin lesions suggestive of erythema chronicum migrans (ECM), were investigated for presence of IgG antibodies against *Borrelia burgdorferi* flagellum antigen ELISA test. Four cases yielded positive serum samples which were true positive cases as they showed negative venereal diseases. Ticks collected from domestic animals from indoors of serologically positive patients were *R. sanguineus.* Based on clinical ground, one case was strongly suspected Lyme disease due to distinctive skin lesion while three cases were not diagnosed till the results of serological test. They provided serological evidence concerning Lyme disease in Egypt.

Adham *et al*. (2010) determined the prevalence of *Borrelia burgdorferi* (s.l.), the etiologic agent of Lyme borrelosis (LB) for the first time in Egypt by using PCR. Questing 5243 hard and soft ticks were collected from animal farms in Giza Governorate. DNA of 500 tick species was extracted and PCR was performed. Primers verified from the sequence of German strain Pko of *Borrelia afzelii* were used. Fragments of 642 bp were generated and sequenced. The prevalence of *B. burgdorferi sensu* lato (s.l.) was 28% of examined soft and hard ticks. High infection rate (66%) of *B. burgdorferi* s.l. was observed in both nymph and adult soft ticks *Ornithodoros savignyi*. Besides, hard ticks role as potential Lyme disease vectors in Egypt, where the infection rate ranged from 0-50%. Sequence analysis of PCR product of *B. burgdorferi* sensu lato shares high degree of similarity in sequence compared to similar species in GenBank.

5- Crimean Congo hemorrhagic fever: CC HF, a tick-borne illness caused by Crimean

Congo hemorrhagic fever virus, is endemic in parts of Africa, the Balkans, Eastern Europe, the Middle East, and parts of Asia Turkey and Southern Federal Districts of Russia. Hard ticks (Ixodidae), especially of genus *Hyalomma*, serve as reservoirs and vectors for CCHFV, and a variety of animals, such as cattle, sheep, and camels, are considered amplifying hosts for the virus. Although CCHFV may cause little or no disease in zoonotic hosts, the virus can cause severe disease in man exposed to tick bites or by contact with blood or tissues from infected patients or animals (Löbermann *et al*, 2012). Transmission to man occurs by tick bites, contact with a patient with CCHF during acute stage of infection, or contact with blood or tissue from infected livestock (Whitehouse, 2004).

Typical course of CCHF has four distinct phases: incubation, pre-hemorrhagic, hemorrhagic, and convalescence (Ergonul, 2006). The incubation period is three to seven days. The pre-hemorrhagic period is characterized by the sudden onset of fever, headache, myalgia, and dizziness (Ergonul *et al*, 2006).

Additional symptoms of diarrhea, nausea, vomiting are also seen in some cases. After approximately three days, hemorrhagic manifestations, from petechiae, large hematomas, and frank bleeding (vaginal, gastrointestinal, nose, urinary and respiratory tracts) usually follow. The convalescence period begins in survivors about 10 to 20 days after onset of illness (Swanepoel *et al*, 1987).

Diagnosis: Viral isolation must be in biosafety level four lab. The IgM and IgG antibodies are detectable by ELISA and immunofluorescence assays from about 7 days after disease\ onset. Specific IgM antibodies decline to undetectable levels 4 months postpresentation (Shepherd *et al,* 1989).

Treatment is mainly supportive. Ribavirin proved effective in the observational clinical studies. Patients should be treated for 10 days, with 30 mg/kg as an initial loading dose, then 15 mg/kg every six hours for four days, and then 7.5 mg/kg every 8 hours for six days (Fisher-Hoch *et al*, 1995). Case fatality rates ranged from 3 to 30%; disseminated intravascular coagulation & vascular deregulations in severe cases. High serum levels of pro-inflammatory cytokines IL-6 and tumor necrosis factor (TNF) were demonstrated in patients with fatal infection than in those who survived (Ergonul *et al*, 2006). In suspected or proven infection, careful adherence to contact, droplet precautions and safe burial practices are critical (CDC, 2008).

Environmental surfaces must be cleansed by chlorination with household bleach (2 to 5% hypochlorite). Post exposure prophylaxis with oral ribavirin should be considered for high risk contacts of CCHF patients (WHO, 2008). Personal tick preventive measures must be implemented. Slaughter of animals with acquired infection should be avoided given the possibility of asymptomatic viremia (Mardani *et al,* 2003).

Who is at risk for CCHF? Animal herders, livestock workers, and slaughter houses in endemic areas are at risk. Healthcare workers in endemic areas are at risk of infection through unprotected contact with infectious blood and body fluids. Individuals and international travelers with contact to livestock in endemic regions may also be exposed.

Prevention of CCHF: Agricultural workers and others working with animals should use insect repellent on exposed skin and clothing. Insect repellants containing DEET (N, N-diethyl-m-toluamide) are the most effective in warding off ticks. Wearing gloves and other protective clothing is recommended. Individuals should also avoid contact with the blood and body fluids of livestock or humans who show symptoms of infection. It is important for healthcare workers to use proper infection control precautions to prevent occupational exposure. An inactivated, mouse-brain derived vaccine against CCHF was developed and used on a small scale in Eastern Europe. But, there is no safe and effective vaccine widely available for man.

In the Middle East: Cope *et al*. (1996) assessment of arthropod vectors of infectious

diseases (mainly CCHF) in areas of U.S. troop deployment in the Persian Gulf. McCarthy *et al*. (1996) reported CCHF viruses and other infectious disease pathogens as the causes of febrile illnesses in the Khartoum Province of Sudan. Khan *et al*. (1997) reported an outbreak of CCHF in the United Arab Emirates, 1994-1995. El-Azazy and Scrimgeour (1997) reported CCHF virus infection in the western province of Saudi Arabia. They added that a serological survey of abattoir workers, identified 40 human cases of confirmed or suspected CCHF between 1989 & 1990, with twelve fatalities. Mardani *et al.* (2003) reported CCHF in Iran and Ahmed *et al.* (2009) in Yemen.

What about Egypt? Darwish *et al.* (1978) serologically reported CCHFV. Morrill *et al.* (1990) reported serological evidence of the CCHFV infection among camels imported into Egypt. Mohamed *et al.* (2008) at El-Muneeb abattoir, Giza Governorate, examined ectoparasites removed from 43 freshly slaughtered animals. They found CCHF viruses in 70 (20.5%) from 14 cattle, 52 (15.2%) from 17 buffalo, 6 (1.8%) from 2 sheep, and 214 (62.6%) from 10 camels. These cattle, buffalo, and sheep were locally bred in Egypt; camels were imported from Sudan and Somalia. Chisholm *et al.* (2012) reported CCHFV in ticks from the imported livestock. El-Bahnasawy *et al.* (2012a) reported three human CCHF; one in Almaza Fever Hospital and two in MoH Fever Hospital, Gharbia Governorate. They added that distributions of *Hyalomma* spp. are worldwide including Egypt and presence of CCHF in regional countries must be considered by the Health and Veterinary Authorities.

6- Tick borne relapsing fever: Is zoonosis in many countries. The two main *Borrelia* spp. involved in North America are *B. hermsii* (the mountainous West) and *B. tuicatae* (the southwest). Other tick-borne species cause relapsing fever on other continents. The relapsing fever is a zoonotic infection transmitted by a louse or tick. It is characterized by repeated episodes of fever. 1-Tick borne relapsing fever is transmitted mainly by ticks. 2- Louse borne relapsing fever is zoonosis by lice (Morsy *et al*, 2000; 2001).

The relapsing fever, caused by spirochetes of the *Borrelia* genus in two forms: tick-borne relapsing fever (TBRF) and louse-borne relapsing fever (LBRF).

Tick-borne relapsing fever is a zoonosis and endemic in many countries. Two main *Borrelia* spp. involved in North America are *B. hermsii* (in the mountainous West) and *B. turicatae* (in the southwest). Other tick-borne species cause relapsing fever on other continents. Louse-borne relapsing fever is caused by *B. recurrentis* (Cutler *et al,* 2009). Assous and Wilamowski (2009) reported TBRF in Eurasia and attributed mainly to *B. persica*, and other entities (B. *baltazardi, B. caucasica B. crocidurae, B. latyschewii,* and *B. microtii*). They added that *O. tholozani* is the most important tick vector, found in India and Kashmir, the southern countries of the former USSR, Iran, Iraq, Syria, Jordan, Turkey, Egypt, Israel, and Cyprus. The number of human cases varied among countries, from 8/year in Israel to 72/year in Iran. It is spread from person to another by the body louse and can occur in epidemics, including large ones involving millions of people. As the name implies, relapsing fever is characterized by the recurrent episodes of fever, which accompanied the spirochetemia. Relapses were due to antigenic variation by spirochetes (Dworkin *et al,* 2008).

Clinical manifestations: Relapsing fever presents with the fever sudden onset, punctuated by an intervening afebrile period that occurs at least twice. The incubation period is 5-9 days. Fever attacks last from several hours to 4 days, and accompanied by chills, headache, nausea and vomiting, sweating, abdominal pain, arthralgia, and cough; but complications are rare. Temperature may be up to 43ºC but above 39ºC. In TBRF, multiple febrile periods last from one to three days each. In both forms, the interval between fevers ranges from 4 to 14 days. The first fever episode ends by crisis, consisting

of rigors, a further elevation in temperature, and increases in pulse and blood pressure, lasting approximately 15-30 minutes. The crisis phase is followed by the profuse diaphoresis, falling temperature, and hypotension which usually persist for several hours. The mortality from the untreated relapsing fever is common during the crisis and the immediate aftermath (Dworkin *et al*, 2002).

Fever can be protean and nonspecific as the headache, myalgia, arthralgia, shaking chills, and abdominal complaints. Headache, neck stiffness, arthralgia, myalgia, and nausea may accompany the first and subsequent episodes. Patient with relapsing fever may experience dizziness and unsteady gait. Localizing neurologic symptoms; hemiplegia, facial palsy, myelitis, and radiculopathy, is more common in TBRF than LBRF. Delirium or apathy and occasionally stupor or coma can occur in both forms.

Physical examination: Epistaxis, petechiae, and ecchymoses are common during louseborne relapsing fever but not tick-borne relapsing fever. Bleeding disorder is probably consequence of thrombocytopenia, impaired hepatic production of clotting factors, and/or blockage of small vessels by aggregates of the spirochetes, erythrocytes, and platelets. Splenomegaly, which the patient can experience as abdominal or left shoulder pain, is also common. The majority of patients with LBRF and about 10% of patients with TBRF have enlarged livers (Perine *et al*. 1971).

Meningitis or meningoencephalitis unilateral or bilateral Bell's palsy or deafness from the 7^{th} or 8^{th} cranial nerve involvement are the most common forms of cranial neuritis in TBRF; if it occurs, cranial neuritis typically presents in second or third febrile episode, not the first. Visual impairment from unilateral or bilateral iridocyclitis or panophthalmitis may be permanent (Cadavid and Barbour, 1998).

Diagnosis: Laboratories findings are not so specific. A mild to moderate normocytic anemia is common, but frank hemolysis and hemoglobinuria do not occur. Leukocyte counts are usually in normal range or only slightly elevated, and there can be leukopenia during the crisis. Platelet counts can fall below 50,000/microl. Laboratory evidence of hepatitis can occur with elevated serum concentrations of unconjugated bilirubin and aminotransferases; the prothrombin and partial thromboplastin times might be moderately prolonged. Hypoalbuminemia can occur but is more often due to the malnutrition than the hepatic dysfunction. Electro-cardiogram could reveal a prolonged QTc interval in patients with myocarditis. Some showed cardiomegaly and pulmonary edema on chest radiograph (Pankuweit *et al*, 2005). Analysis of cerebrospinal fluid (CSF) is suspected case with the signs of meningitis or meningoencephalitis. Presence of mononuclear pleocytosis and/or mildly to moderately elevated protein levels in CSF provides justification for intravenous antibiotic therapy in patients. Glucose a concentration in CSF was usually not depressed (Bottieau *et al*, 2012).

Differential diagnosis: both common and less frequent conditions can mimic relapsing fever. Other illnesses may accompany louseborne form. *Ornithodoros*, vectors of TBRF, are not known to transmit other infections to man. Differential diagnosis includes: malaria granulocytic or monocytic, ehrlichiosis, babesiosis, typhoid, tularemia, brucellosis, Colorado tick fever, rickettsioses, dengue, leptospirosis, rat-bite fever, meningococcemia, viral hepatitis (Pachner, 1986). The thin and thick blood smears are usually the first tests for suspected relapsing fever. Giemsa or Wright stains typically reveal the spirochetes in a methanol-fixed thin smear if microorganism concentration was greater than 10^5/ ml. Optimum time to take blood is between fever's onset and peak (Roscoe and Epperly, 2005). A thick smear is a more sensitive assay detecting at least one log fewer organisms. Fluorescein-labeled polyclonal antibody is commercially available but with sufficient cross-reactivity with other *Borrelia* spp. to be useful for detecting relapsing fever spirochetes in blood or tissues. Slides

were fixed with methanol (Sciotto *et al*, 1983). When temperature declines or back to the normal range in the absence of antipyretics, spirochetes usually cannot be visualized in blood. Laboratory technicians carefully reviewing a routine peripheral smear for a white cell differential count often made diagnosis (Poulsen and Iversen, 1996). An increase in sensitivity can be achieved by centrifugation of the heparinized or citrated blood followed by examination of Buffy coat and overlying plasma. Anticoagulated blood can be centrifuged in capillary tube, the same procedure used for a microhematocrite. Spirochetes are usually found in the same fraction as platelets. Examination for platelets in the suspension serves as a quality control on centrifugation step as long as patient is not severely thrombocytopenic; if platelets are not present; the centrifugation has been too rapid or long. A diagnostic maneuver is wet mounts. Non-centrifuged plasma or concentrated Buffy coat is examined by phase contrast or dark field microscopy for motile spirochetes (Cadavid, 2006).

Cultures: Blood inoculation into weanling mice may yield a *Borrelia* spp from the blood or, less commonly, from CSF even between fever episodes. Most of the agents of tick-borne relapsing fever will infect and proliferate in mice. However, *B. recurrentis*, agent of LBRF, infects mice only transiently; if at all (Barbour *et al*. 1996). For suspected TBRF, blood, plasma, Buffy coat, or CSF is injected intraperitoneally into suitable mouse; most in-bred or outbred strains. Mouse infection was enhanced by severe combined immunodeficiency phenotype, or by splenectomy. The blood inoculated mice should be examined daily for spirochetes for seven days (Chohan, 1967).

PCR for blood, brain, CSF, and joint tissues of mice were used to study *B. hermsii* and *B. turicatae*, two species causing TBRF. The technique is probably is as sensitive as culture for detecting borrelias and advantage over culture that the results can be obtained in a few hours rather than several days. But, there was little reported experience with PCR for diagnosis of human relapsing fever (Cadavid *et al*, 1993).

Convalescent sera from the most relapsing fever patients gave cross-reactive positive reactions in a commercially available ELISA assay for antibodies to *B. burgdorferi.* ELISA proved supportive for relapsing fever diagnosis, but, the Western blot assay for Lyme disease and treponeme-specific assays for syphilis must be negative. Recombinant antigens, as GlpQ, specific for relapsing fever species might provide a basis to the differentiation between relapsing fever and Lyme disease (Schwan *et al*, 1996).

Treatment: Penicillin and Tetracycline are of choice for relapsing fever for several decades, without evidence that *Borrelia* spp have acquired resistance to them. Minimum inhibitory concentrations (MICs) of penicillin G and tetracycline for *Borrelia* spp. are generally <0.1mcg/ml. Relapsing fever *Borrelia* spp. is susceptible in vitro to cephalosporins, macrolides, and chloramphenicol, but with less clinical experience. Borrelias are relatively resistant to rifampin, sulfonamides, fluoroquinolones, metronidazole, and aminoglycosides (Barbour *et al*. 1982). After antibiotic therapy there was clearance of spirochetes from the blood eight hours of first dose. Tetracycline (500mg) and Erythromycin (500mg) are effective oral antibiotics for adults with this disease. Doses of Tetracycline or Erythromycin for children are 12.5mg/kg. Tetracycline gave better efficacy over erythromycin, except for pregnant and nursing women and for children less than nine years old (Butler *et al,* 1978). When patient cannot take tetracycline orally, the intravenous dose was 250 or 500mg for the adults' parenteral treatment with intramuscular penicillin G procaine was 600,000 to 800,000 units for adults and 400,000 units for children (Fekade *et al*. 1996). Best treatment for TBRF in adults was tetracycline (500mg or 12.5mg/kg orally every six hrs.) or Doxycycline (100mg twice daily), both for 10 days. When tetracyclines were contra-

indicated, the alternative was Erythromycin (500mg or 12.5mg/kg orally every six hours) for 10 days (Guerrier and Doherty, 2011). If a Beta-lactam antibiotic administered intravenously rather than orally, especially if CNS involvement is confirmed or suspected. Penicillin G (3 million units every four hrs.) or ceftriaxone (2g once daily or 1g twice daily) for 10-14 days for adults was the intravenously for Lyme disease. Experimentally, regimens were effective for infection with neurologic involvement (Horton and Blaser, 1985).

Jarisch-Herxheimer reactions: JHR occur following antibiotic for many spirochetal and bacterial infections; symptoms and signs include rigors, fever and hypotension. JHR occur after treatment of TBRF, with a rate of 54% in one series. Reactions occur within two hours of antibiotic administration; observation for several hours after treatment is recommended (Negussie *et al,* 1992).

Proinflammatory cytokines, especially tumor necrosis factor (TNF-α), interleukin (IL)-6 & IL-8, have been implicated in the pathogenesis of this process. Patients with LBRF, pretreatment with anti-TNF-alpha antibodies reduced incidence of rigors from 90% in placebo recipients to 50% and mean increase in temperature from 1.5ºC to 0.8ºC. However, administration of Pentoxifylline or recombinant IL-10 did not affect occurrence or degree of JHR (Remick *et al*, 1996).

Mortality rates for the untreated TBRF ranged between 4%-10% respectively. With prompt treatment with appropriate antibiotics, death rate for TBRF was less than 2%. Poorer prognostic features include: Stupor or coma on admission diffuse bleeding myocarditis poor hepatic function bronchopneumonia co-infection with typhus, typhoid, or malaria. However, some the patients survived the crisis or JHR, only to die suddenly later that day or next one, perhaps from an arrhythmia (Cooper *et al*. 2000).

Relapsing fever in Pregnancy: Relapsing fever during pregnancy frequently causes abortion or stillbirth. There is transplacental transmission of infection or a newborn may be infected at birth. Pregnant women and infants tend to have more severe and prolonged illnesses with relapsing fever. Mahran and Ghavami (2009) reported a case of congenital tick-borne relapsing fever with transplacental transmission. A murine model of gestational relapsing fever infection found that infection during pregnancy causes intrauterine growth retardation, placental damage and inflammation, impaired fetal circulation, and decreased maternal hemoglobin levels (Larsson *et al.* 2006).

Prevention and Control: Decreasing louse and tick exposure is the major means of preventing relapsing fever. There is not a vaccine for either LBRF or TBRF. Prospects for a successful vaccine are poor as various emerging species of *Borrelia* and a single strain manifested a large number of serotypes identities (Chen and Zückert, 2011).

TBRF can be reduced by construction of houses with concrete or sealed plank floors and without thatched roofs or mud walls. Log cabins pose a particular risk in North America when rodents nest in the roofs or beneath the house or porch. Interiors of buildings infested with *Ornithodoros* can be sprayed with 2% benzene hydrochloride, 0.5% Diazinon, or 0.5% Malathion, but Diazinon, besides its severe toxicity, was less effective in *Rhipicephalus microplus* (Kumar *et al*, 2011). Persons usually are bitten by soft ticks while sleeping in an infested dwelling, but the ticks may be observed during daytime exploration of a cave or crawling under a house. The domestic animals, as pigs, serve as reservoirs for infection, especially when they are kept adjacent to the living quarters (Southern and Sanford, 1969).

In Egypt up to 32 genera of many species of ticks were reported (Hoogstraal, 1958; Morsy *et al*, 1986; Younis *et al*, 1995; El-Bahnasawy and Morsy, 2008; Abdel-Shafy *et al*, 2012; Morsy, 2012). Morsy and Haridy (2000) successfully used ivermectin as topical application in controlling *R. sanguineus* infesting a pet-dog. Abdel-Shafy *et al*.

(2011) evaluated some dietary levels; *Jatropha curcas* seed meal as acaricide against *Hyalomma m. marginatum* infested rabbits.

Efficacy of post-exposure treatment with Doxycycline was demonstrated in a placebo-controlled trial of 93 healthy subjects in Israel with suspected tick exposure. The patients were randomly assigned to Doxycycline (200mg on day one followed by 100 mg daily for four days) or placebo Cases of TBRF was defined as a patient with fever and a positive blood smear. At three weeks, ten cases of TBRF were diagnosed; all were in placebo group (attack rate 22%).These data support post-exposure treatment, as efficacy appeared to be 100%. This regimen can also be used after accidental inoculation with infected blood or culture medium in the laboratory, hospital, or clinic (Hasin *et al,* 2006). Helmy (2000) in Dahshore, Giza Governorate studied the seasonal dynamics of *O.* (*O.*) *savignyi* and *Borrelia* sp. in the tick, domestic animals and man. Tick population densities were high from June to October with maximum levels in August and September. Annual spirochetes infection rate in adults and immatures varied from 34.4%-36.9% without significant difference. Of 1396 sera from man and 553 sera from animals tested, 309 (22.1%) and 157 (28.4%), respectively, were reactive for antibody to *Borrelia* sp. antigen with the highest infection rate in camel, sheep, goat, cow and then buffalo. Shanbaky and Helmy (2000) at Shelateen, Halayeb Province detected *Borrelia* sp. in *O. savignyi*, which showed specificity for its own natural tick host species when compared with *B. crocidurae* isolated from *O. erraticus*. Reeves *et al*. (2006) collected 1,023 of 5 species lice on rats and domestic cattle from 13 governorates by PCR amplification and sequencing detected five different louse- borne bacterial agents in lice; *Bartonella rattimassiliensis, B. phoceensis,* and *Bartonella* sp. near *B. tribocorum, Coxiella burnetii*, and *Rickettsia typhi*. They concluded that lice of urban and domestic animals harbor pathogenic or potentially pathogenic bacterial agents.

In Egyptian Eastern border, McNamara and Kay (1988) presented a case of an adolescent tourist who contracted relapsing fever (*Borrelia*) in Israel, and tick-borne relapsing fever (TBRF) is endemic to Israel (Sidi *et al*, 2005; Halperin *et al*, 2006; Assous and Wilamowski, 2009).

Safdie *et al*. (2010) identified TBRF in Israel and the Palestinian Authority relied on the morphology and the association of *B. persica* with its vector *O. tholozani*, and sequenced three complete 16S rRNA genes, 12 partial flaB genes, the 18 partial glpQ genes, 16 rrsileT intergenic spacers (IGS) from nine ticks and ten human blood samples originating from the West Bank and Israel. The phylogenic sequence analysis defined all the *Borrelia* isolates from *O. tholozani* and from human TBRF cases in Israel and the West Bank as *B. persica* that clustered between the African and the New World TBRF species. Gene organization of intergenic spacer between the 16S rRNA and 23S rRNA was similar to that of other TBRF *Borrelia* species and different from Lyme disease *Borrelia* species. Balicer *et al*. (2010) examined the safety and effectiveness of post-exposure prophylaxis policy in preventing the TBRF found that Tick-bite screening and prophylactic treatment with doxycycline in endemic areas proved to be a practical, safe, and highly effective policy. El-Bahnasawy *et al*. (2012b) reviewed the current state of the knowledge about louse and tick-borne relapsing fevers (TBRF) with especial reference to Egypt and the neighboring countries. They concluded that the public health, veterinary and agricultural authority being requested to keep this zoonotic arthropod-borne disease into consideration.

Arthropod-borne encephalitis viruses represent a significant public health problem throughout most of the world. The vector becomes infected when feeding on the blood of the viremic animal. The virus then replicates in the tissues, ultimately infecting the

salivary glands and transmits to a new host when it injects infective salivary fluid. The natural animal hosts usually remain unaffected and viral circulation generally remains undetected until one of the following occurs: Humans encroach on natural enzootic focus Environmental or other conditions that favor substantial amplification in primary vector-host cycle cause a sufficient number of vectors to become infected so that the human risk is substantially increased Virus escapes primary cycle via a secondary vector or vertebrate host, bringing biting vectors in close proximity to human habitation

7- Tick-Borne Encephalitis Virus: TBE is caused by three closely related viruses (family Flaviviridae, genus Flavivirus): The Russian spring-summer encephalitis subtype (also called far eastern subtype) The Siberian subtype also called Vasilchenko virus The Central European encephalitis subtype (also called western subtype (Kaiser, 2008)

The viruses are maintained in natural cycles involving a variety of mammals and ticks. *Ixodes persulcatus* and *I. ricinus* are responsible for transmission in Russia and Europe, respectively (Suss, 2003). *Ixodes ovatus* is the vector in Hokkaido. Tick-borne encephalitis exists over a wide geographical area. Human exposure occurs through work or recreational activities in the spring and summer months in temperate zones and in fall and winter in the Mediterranean, when the ticks are most active. TBEV is transmitted from the saliva of an infected tick within minutes of the bite; early removal of the tick may not prevent encephalitis. In Europe, tick activity starts in the spring and declines in the fall. Nymphal forms of I. ricinus are most important in human transmission whereas adult ticks are the dominant vector for *I. persulcatus* (Lindquist and Vapalahti, 2008). Also, Outbreaks have occasionally followed ingestion of unpasteurized milk products from infected sheep and goats.

Age, severity of illness in the acute stage, and low initial neutralizing antibody titers were associated with severity of illness (Kaiser and Holzmann, 2000). The CCR5 delta 32 allele may predispose individuals to TBE (Kindberg *et al*, 2008). From early in the HIV epidemic, it was clear that some patients rapidly progressed to AIDS, while others experienced relative immunologic stability. Laboratory measurements, such as numbers of CD4 cells and levels of plasma HIV RNA, are helpful in determining the stage of infection and may serve as prognostic markers. Other factors may also influence outcome. This topic covers the demographic, viral, and host factors that may play a role in disease progression as well as describing the important impact antiretroviral therapy has had over the past decade. Coreceptor usage: CCR5 and CXCR4 are the major chemokine coreceptors used by HIV to enter into human lymphocytes. Based on this coreceptor usage, HIV isolates are classified as CCR5-tropic (R5), CXCR4-tropic (X4), or dual tropic (R5/X4) strains. CCR5-tropic viruses (R5) are generally non-syncytium (NSI) inducing isolates that predominate in primary infection. The R5 viruses are usually associated with a less virulent phenotype; these strains replicate in monocytes and macrophages and are also sometimes referred to as "M-tropic" viruses. R5 viruses can also infect the CCR5-expressing dendritic cells, which are responsible for trafficking of HIV particles to lymph nodes (Poveda *et al*, 2006). CXCR4-tropic viruses (X4) generally are syncytium-inducing and often emerge later in infection. These viral strains frequently appear more virulent and are able to replicate more efficiently in T-lymphocytes ("T-tropic" viruses). The emergence of X4 virus has been associated with the development of an AIDS-defining illness or a CD4 cell count <200 cells/microl., compared with those with R5 persistence and slowly progressive disease (Goetz *et al,* 2009). Treatment-experienced patients with ongoing detectable viremia suggested a greater risk of having dual/mixed X4 tropism despite treatment-mediated gains in

CD4+ T cell counts (Wilkin *et al*, 2007). The reason R5 viruses predominate early on is unclear since CCR5 is expressed on fewer T cells than is CXCR4. R5 viruses produce five to ten times more infectious virus per CCR5+ target cell than X4 variants and also appear to be more efficiently transmitted. These advantages may contribute to the predominance of R5 in early infection (Pope and Haase, 2003).

Clinical manifestations: Incubation period between 7 and 14 days. The disease is characterized by a biphasic illness. In the first viremic phase, fever, fatigue, malaise, headache, and arthralgia predominate. Neurological manifestations hallmark the second phase, with a clinical spectrum ranging from mild meningitis to the severe encephalitis, which may be accompanied by myelitis and acute flaccid paralysis. Also, chronic and progressive disease was noted primarily with the Siberian subtype; however, this occurs uncommonly (Kaiser, 2016). He added that TBE is one of the most important viral infections of the human central nervous system. About 10,000 cases of TBE are referred to hospitals in Europe and Asia each year. The TBE virus (TBEV) is mainly transmitted by tick bites but also occasionally by unpasteurized goat's milk. As in endemic areas on average only 1-3 % of ticks are infected with the TBEV and the clinical manifestation rate is approximately 33 %, only approximately 1 in every 100-300 tick bites leads to disease. The incubation period varies from 5-28 days and typically has a biphasic course of fever. TBE manifests as meningitis in approximately 50 % of them, as meningoencephalitis in 40 % and as encephalomyelitis in 10 %.

Diagnosis: CSF shows pleocytosis. Although polymorphonuclear cells may predominate at first, the CSF profile is later marked by dominance of mononuclear cells. Diagnosis of TBE also by demonstration of IgM antibody by capture immunoassay of CSF, a fourfold rise in serum antibody titers against TBE virus, or isolation of virus from or demonstration of viral antigen or genomic sequences in tissue, blood, or CSF. Serum IgM antibodies alone should be confirmed by demonstration of IgG antibody by another serologic assay; e.g., neutralization (Holzmann, 2003). MRI abnormalities may be noted in approximately 18% of patients with lesions located in the thalamus, cerebellum, brainstem, and caudate nucleus; EEG is abnormal in 77%. Both modalities demonstrate only non-specific findings. Von Stülpnagel *et al*. (2016) stated that the incidence of TBE is increasing in many countries. Magnetic resonance imaging (MRI) in the course of TBE is not regularly performed in children and evaluated MRI-findings of children and adolescents with TBE. They added that a spectrum of MRI findings can be found in children with TBE, often showing involvement of the subcortical deep grey matter structures. In children presenting with a meningoencephalitis and bilateral thalamic involvement TBE should be included in the differential diagnosis.

Outcome: The case fatality rate in Europe was approximately 0.5%, and up to 40% of patients left with long-lasting sequelae. The endemicity of TBE in Sweden being stable over the years but during the last decade several new foci was discovered. In Norway the first verified cases of TBE have now been found (Haglund, 2002). In comparison, the western European subtype typically produces the biphasic form and tends to be less severe, with case fatality rates of 1 to 2%. Children have a more favorable prognosis than adults. Up to one-half of patients report symptoms 6 to 12 months post-encephalitis, with severe impairment noted in 30% (Haglund and Gunther, 2003)

Treatment and prevention: Treatment is mainly supportive. Kaiser (1999) mentioned that study of 709 patients with TBE in Germany, 12% of patients required intensive care and 5%required assisted ventilation. Of 230 patients who had subsequent examination at a later time, approximately one-quarter had moderate to severe sequelae.

Effective vaccines are available in Europe and from many travel clinics in Canada; vaccines are not available in the United States. Mass vaccination has been undertaken in Austria, with protection rates of at least 96% (Barrett *et al*, 2003). Stock (2016) stated that tell now treatment of TBE is symptomatic and supportive, a specific antiviral therapy does not exist. TBE cases acquired in central European countries have usually a good prognosis. Mortality rates above 2% have been documented in cases of tick-borne encephalitis in the elderly. In endemic areas, active immunization with inactivated TBE virus vaccines provides the most secure protection against TBE. In addition, exposure prophylaxis (protection against tick bites) plays a crucial role for TBE prevention.

8- Powassan Virus: Powassan virus (family Flaviviridae, genus Flavivirus) is related to the eastern hemisphere's tick-borne encephalitis viruses. It has been isolated from four tick species: *Ixodes cookie, I. marxi, I. spinipalpus*, and *Dermacentor andersoni*. A rare cause of encephalitis in eastern Canada and the northeastern United States and 32 cases reports since its discovery in 1958. But, serologic surveys have found an antibody prevalence of 1 to 4%, indicating that asymptomatic infection is common. Infection mostly occurs from June to September.

The incubation periods range from eight to 34 days. However, few patients recall a tick bite, since Ixodid ticks are small and can be easily overlooked. Symptomatic patients typically present with fever, weakness, somnolence, gastrointestinal complaints, headache, and confusion, and seizures can occur. Serum and cerebrospinal fluid samples can be tested for IgM and neutralizing antibodies. Diagnosis of Powassan virus infection can be made by demonstration of IgM antibody by capture immunoassay of CSF, a fourfold rise in sera antibody titers against virus, or isolation of virus from or demonstration of viral antigen or genomic sequences in tissue, blood, or CSF. Serum IgM antibodies alone should be confirmed by demonstration of IgG antibody by another serologic assay; e.g., neutralization (McGovern *et al*, 2007). Case-fatality rate was 5 to 10%, with a high incidence of residual neurological dysfunction among survivors, including hemiplegia, headaches, minor memory impairment, and persistent ophthalmoplegia (Tavakoli *et al*, 2009).

There is no specific treatment or vaccine. Prevention of tick bites by using repellents, avoiding or clearing brushy areas, wearing light colored clothing may be effective. Removing ticks soon after outdoor exposure is advisable. Human infection with deer tick virus was reported in 2009 with a fatal outcome in a 62-year-old New York State resident with chronic lymphocytic leukemia who presented with encephalitis (Lessell and Collins, 2003).

9- Colorado Tick Fever Virus: (genus Coltivirus, family Reoviridae) is transmitted to humans in the western United States and Canada by *D. andersoni*. Distribution of human disease corresponds to the wood tick's distribution in mountainous areas at 4000- to 10,000-foot elevations. Transmission occurs from March to September, but peaks from April to June, Also, via blood transfusion (Goodpasture *et al*, 1978).

The mean incubation period is 3 to 4 days, and 90% of patients reported tick bites or tick exposure. Fever, chills, myalgias, and prostration are common presenting symptoms; headache often during acute febrile. About 15% of patients experience a petechial or maculopapular rash and leukopenia is a common finding. Although the acute symptoms last about one week, fever may recur several days later, and fatigue is often prolonged. Five to10% of children had meningitis or encephalitis (Johnson *et al*, 1997).

Serologic tests are often not positive for 10 to 14 days after symptom onset. In comparison, reverse transcriptase polymerase chain reaction (PCR) may be diagnostic from the first day of symptoms. Virus infects marrow erythrocytic precursors, which accounts for the ability to recover the virus from periph-

eral blood up to six weeks after illness onset. Treatment is supportive and the prognosis is generally favorable. Prevention consists of avoidance of tick bites in endemic areas.

10- Chandipura Virus: Since 1950's, outbreaks of encephalitis of unknown etiology and high mortality occurred in children in India. In 2003 in Southern India, an outbreak of acute encephalitis in 329 children was associated with Chandipura virus (Rao *et al*, 2004). The affected children all tested negative for eight other potential viral causes including Japanese encephalitis (responsible for many encephalitis outbreaks in India), West Nile virus, dengue, and measles virus. Chandipura virus was identified by EM, complement fixation, and neutralization tests. The IgM titers directed against this virus were more frequently identified after four days of illness compared to baseline values provided further evidence supporting its pathogenetic role. Chandipura virus may be transmitted by sandfly bites and is associated with rapid onset of fever then vomiting, altered mental status, and seizures. Mortality rate in 2003 outbreak was 56%. An outbreak occurred in 26 children in western India with a mortality of 78% (Chadha *et al*, 2005).

Conclusion

Dogs are very susceptible to tick bites and tick-borne diseases. Vaccines are not available for all the tick-borne diseases that dogs can get, and they don't keep the dogs from bringing ticks into your home. For these reasons, it's important to use a tick preventive product on your dog. Tick bites on dogs may be hard to detect. Signs of tick-borne disease may not appear for 7-21 days or longer after a tick bite, so watch your dog closely for changes in behavior or appetite if you suspect that the pet has been bitten by a tick. To reduce the chances that a tick will transmit disease to you or your pets: a- Check your pets for ticks daily, especially after they spend time outdoors, b- If you find a tick on your dog, remove it right away, c-Ask your veterinarian to conduct a tick check at each exam, d- Talk to your veterinarian about tick-borne diseases in your area, e- Reduce tick habitat in your yard, and f- Talk with the veterinarian about using tick preventives on your pet. Also, check your body for ticks after being outdoors. Conduct a full body check upon return from potentially tick-infested areas, which even includes your back yard. Use a hand-held or full-length mirror to view all parts of your body. Check these parts of your body and your child's body for ticks: a- Under the arms, b- In and around the ears, c-Inside belly button, d-Back of the knees, e- In and around the hair, f- Between the legs, and g- Around waist.

Recommendations

Check clothes and pets carefully and remove any found ticks. Place clothes into a dryer on high heat to kill ticks. Remove an attached tick with fine-tipped tweezers as soon as noticed. If a tick is attached to your skin for less than 24 hours, chance of getting Lyme disease is extremely small; but, other diseases may be transmitted more quickly. Next few weeks signs or symptoms as rash or fever, so, see a healthcare provider.

Modify your landscaping to create "Tick-Safe Zones." It's pretty simple. Keep patios, play areas, and playground equipment away from shrubs, bushes, and other vegetation. Regularly remove leaves, clear tall grasses and brush around your home, and place wood chips or gravel between lawns and wooded areas to keep ticks away from recreational areas (and away from you): a- Use a chemical control agent. Effective tick control chemicals are available for homeowners to use, or a professional pest control expert can apply them, b- Discourage deer, the main food source of adult ticks. Keep them away from your home by removing plants attracting them and by constructing barriers (like a fence) to discourage deer from entering your yard and bringing ticks with them. More details information go to CDC (2016).

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