Mini-Devils: Exploring the Zoonotic Potential of Ticks

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ABSTRACT

Ticks are prominent blood-sucking arthropods and are considered one of the biggest threats to the human and animal health globally because of their vector function for a wide range of bacterial, viral and protozoal zoonotic pathogens. After mosquitoes, ticks are regarded as the second most threatening vector for human health. The economic impact of diseases caused by ticks possesses notable significance and tends to rise every year. The spread of these pathogenic organisms is mostly unnoticed in the nature of the enzootic tick-vertebrate cycles. However, these may be responsible for causing remarkable morbidity and mortality in humans and animals when attacking in abundance. The anatomy and physiology of a tick helps it in exhibiting its behavior. The mouth-parts of ticks play a significant role in their penetration to their hosts. As ticks are blood-sucking parasites, so their survival, growth, development and reproduction depend on blood meals. There is secretion of certain substances when they feed on their hosts in order to anchor themselves to the host. These substances act as sedatives that cover up the pain from the bites and prevent coagulation of blood. This tenacious and efficient-feeding behavior makes them the potential vectors of zoonotic infections. Therefore, both the ticks infesting various hosts at the wildlife-domestic animal-human interface and the pathogenic organisms transmitted by these tick species occupy prime importance in one health perspective. The in depth knowledge of the host, tick disease and pathogen triangle involving various habitats and distribution of ticks, changes in the environmental conditions and global warming is of prime significance and must be considered while devising policies involving migration and trade of animals.

Keywords: Ticks, Zoonoses, Blood-sucking parasites, Mortality, Survival, Sedatives, Pathogen triangle.

CITATION

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INTRODUCTION

Zoonoses are the "diseases and infections that are naturally transmitted between vertebrate animals and man," according to the definition proposed by the World Health Organization (WHO) Expert Committee on Zoonoses in 1951. Rudolph Virchow coined the term zoonosis (zoonoses, plural) at the end of the nineteenth centuryfor the diseases caused in humans by animals. It is the fusion of two Greek words (*zoon*, animals and *noson*, disease). The word 'zoonosis ' is also viewed as more straightforward and shorterthan 'anthropozoonosis' (animals to humans) and 'zooanthroponosis' (humans to animals), which stemmed from the prevailing trend of transference between man and other vertebrates. The definition of zoonoses should comprise the term 'infestations' to envelop more properly parasitic infections (Chomel 2009). Fig. 1 illustrates the epidemiological classification of zoonoses.
Zoonoses occupy a crucial place in the global health program of the World Health Organization (WHO). A considerable number of animal species are involved in the transmission of zoonotic diseases in humans, either directly or indirectly. These zoonotic diseases are about four-fifths of overall infections that occur in humans and are responsible for causing remarkable mortality and morbidity in both sexes and all age groups (Pal 2005). Therefore, the treatment and control of zoonotic diseases is of prime importance.

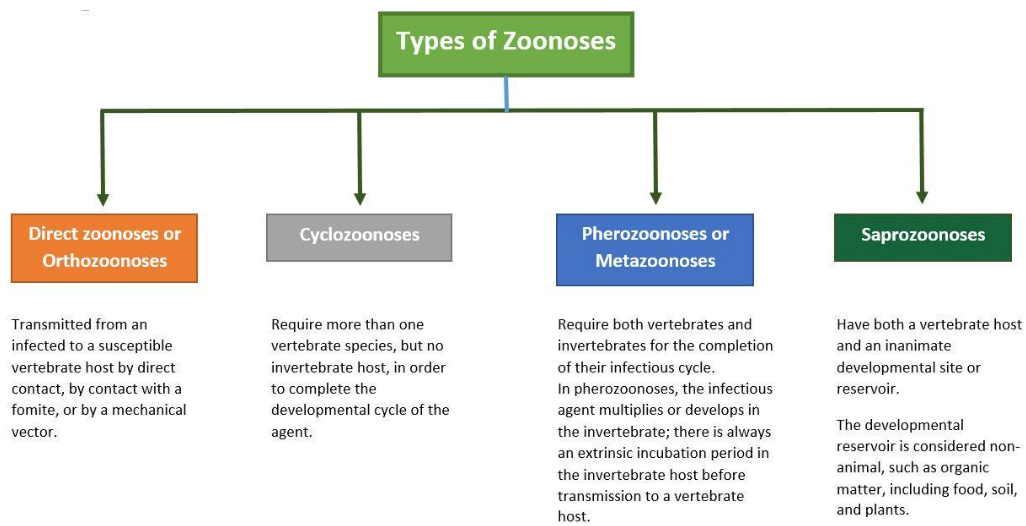

Fig. 1: Different types of zoonoses.

In the past few years, one-third of the emergence of infectious diseases is due to zoonotic vector-borne infections, which have a harmful impact on human and animal health and welfare on a global scale (de la Fuente et al. 2015). Especially, the occurrence of Lyme disease in the USA is anticipated to hike up by about 20% in the coming years due to changes in climatic conditions (Dumic et al. 2018). After mosquitoes, ticks are regarded as the second most threatening vector for human health as these are involved in the transmission of a wide range of pathogenic organisms (Toledo et al. 2009). In order to alleviate the production losses of livestock and bad effects on animal welfare and mitigate disease exposure in humans, the transmission channels of tick-borne diseases must be comprehended (Tamzali 2013). This is important as the incidence of tick-borne zoonotic diseases is elevating in the 21st century due to climate change's effects on the tick lifecycle and the transboundary locomotion of animals infested with ticks (Parola et al. 2013).

The economic impact of diseases caused by ticks possesses noteworthy significance and escalates every year. In the USA, the reported expense per patient diagnosed with Lyme disease was USD $8172 in the year 2002(Zhang et al. 2006), which equals to $11 838 in the year 2019,according to CPI inflation calculator (Rochlin and Toledo 2020). On the basis of 42 743 cases reported to the Centers for Disease Control and Prevention (Xiao et al. 2021) in 2017, the estimated cost was over USD $500 million yearly. These expenses can be even greater in patients with post-treatment Lyme disease syndrome (Adrion et al. 2015). Economic additional expenditures are associated with tourism and hospitality in endemic regions (Donohoe et al. 2015). The economic importance of Lyme disease is not limited to the USA only. The costs of millions of euros are also found to be associated with Lyme disease in Europe (Mac et al. 2019). As the cumulative impact of all tick-borne zoonotic infections remains unquantified in most situations, it is highly significant to study and comprehend tick-associated zoonoses.

2. BIOLOGY OF TICKS AND THEIR BEHAVIOUR

Ticks are one of the most prominent blood-sucking arthropods. Their body is generally divided into two major parts, i.e. a flat capitulum or head called gnathosoma and an oval-shaped body called idiosoma (Anderson 2002). Like other arthropods, nymphs and adult ticks have eight legs while in the larval stage ticks have six legs. A distinct head is not present in the ticks. The mouth-parts of ticks are present on the capitulum (John and Anderson 2008). These are made up of hypostome and chelicerae. These mouth-parts play a significant role in the penetration ticks into their hosts. As ticks are blood-sucking parasites, so their survival, growth, development and reproduction depend on blood meals. Substances are secreted by the ticks when they feed on their hosts in order to anchor themselves to the host. These substances act as sedatives that cover up the pain from the bites and avoid blood coagulation. As ticks are tenacious and efficient feeders, they are potential vectors of zoonotic infections(John and Anderson 2008).

Ticks undergo three basic stages throughout their life, i.e. larva, nymph and adult (Anderson 2002). They spend each life stage on a different host. Fig. 2 briefly describes the general life cycle of ticks.

Ticks generally don’t fly, jump or drop from trees on the hosts. They seek out their hosts. This host-seeking behaviour of ticks is known as “questing”(Richardson et al. 2022). This behaviour refers to a sequence of actions or behaviour in which the ticks mount vegetation especially tall grasses, stop and extend their forelimbs and wait for a host to get attached to (Holderman 2013).

3. MAJOR TICK-BORNE PATHOGENS CAUSING ZOONOTIC INFECTIONS

Ticks are considered one of the biggest threats to the human and animal health globally because of their vector function for a wide range of bacterial, viral and protozoal zoonotic pathogens. The dissemination of these pathogenic organisms is mostly unnoticed in the nature of the enzootic tick-vertebrate cycles. However, these may be responsible for causing remarkable morbidity and mortality in humans and animals when attacking in abundance (Jahfari 2016). Fig. 3 demonstrates various viral, bacterial and protozoal tick-borne pathogens.

4. COMMONLY FOUND TICK-BORNE ZOONOTIC INFECTIONS

Different species of ticks carry different types of zoonotic infections. Table 1 indicates various types of zoonotic diseases, their causative agents, the tick vectors, the symptoms and the geographical distribution of that zoonotic infection.

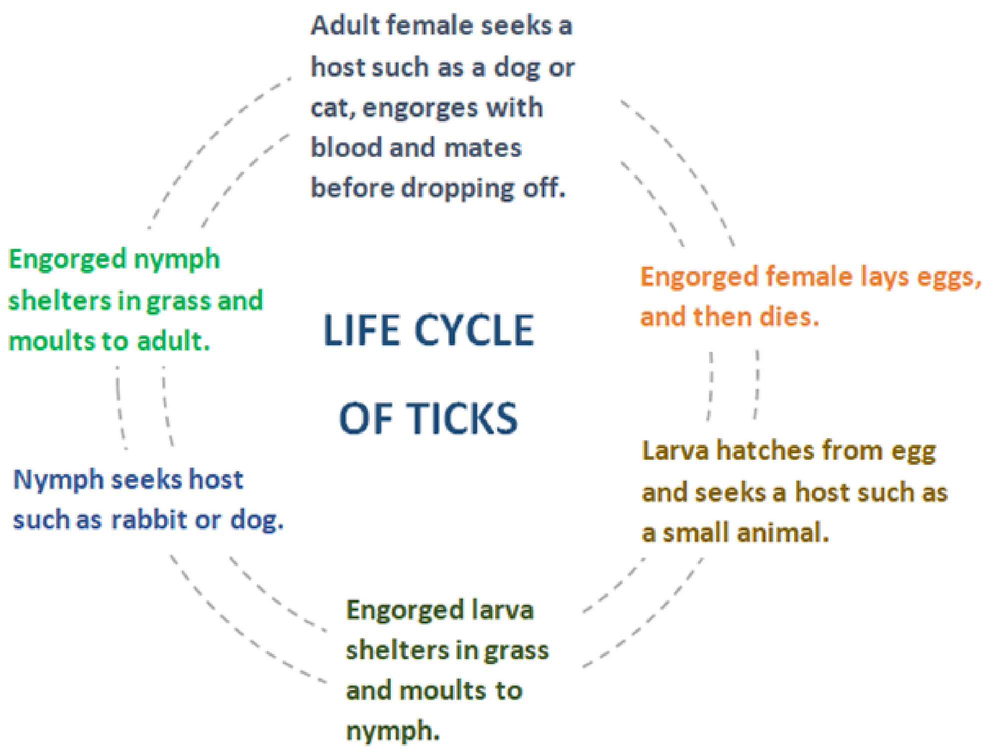

Fig. 2: General life cycle of ticks

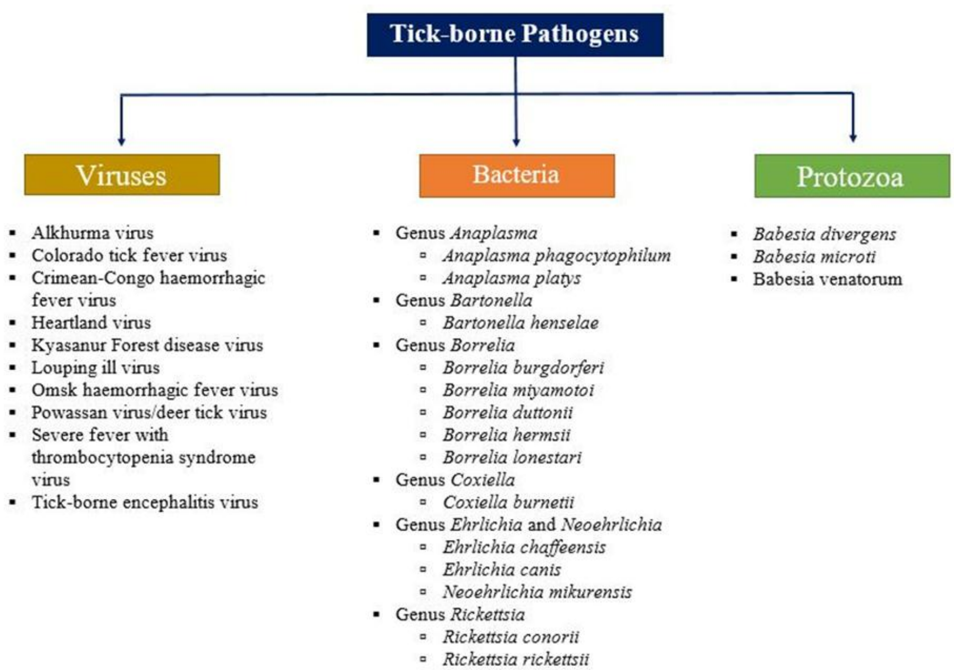

Fig. 3: Major tick-borne pathogens causing zoonotic infections

5. DIAGNOSTIC APPROACHES AND TREATMENT OF TICK-BORNE DISEASES

Earlier only microscopic examination of blood smears was considered to be the widely used method for diagnosis of tick-borne diseases. Although it is a quick and economical method, other methods are being used nowadays; these methods are faster and more sensitive.

5.1. NUCLEIC ACID AMPLIFICATION TECHNIQUES

Nucleic acid amplification techniques are generally more sensitive and faster than other methods like pathogen culture as pathogen culture is slow and difficult (Springer et al. 2021).

5.2. REAL-TIME QUANTITATIVE PCR

Real-time qPCR is quite beneficial in observing the course of infection as the DNA load of the given pathogen tells the level of infection in patient (Che et al. 2019). That is why real-time qPCR is considered to be hypersensitive and faster than conventional PCR (Springer et al. 2021).

5.3. REAL-TIME DIGITAL PCR

Real-time dPCR detects and analyzes the rarely found target sequences by segregating the sample into several parallel PCR reactions which makes it a hypersensitive test (Das et al. 2020).

5.4. LOOP-MEDIATED ISOTHERMAL AMPLIFICATION (Langford et al.2015)

LAMP is a cost-efficient DNA amplification method (Marins et al. 2013; Wang et al. 2017; Singh et al. 2019). LAMP assays require a constant temperature and do not need a thermo-cycler to work (Becherer et al. 2020).

5.5. MASS SPECTROMETRY

On the basis of comparison between protein signatures and existing databases, mass spectrometry–based techniques are generally used to detect cultured pathogens in laboratories (Neumann-Cip et al. 2020). This method is found beneficial in the diagnosis of *Babesia microti* infections (Magni et al. 2020). It may help in the detection of *Babesia canis* infections in canines (Adaszek et al. 2014).

5.6. ENZYME-LINKED IMMUNOSORBENT ASSAY (de Souza et al. 2021)

ELISA tests are likely to be performed but these tests are less specific. So, techniques like immune-blotting (Sanchez et al. 2016) or sero-neutralisation tests (Reusken et al. 2019) are usually recommended to confirm the ELISA tests.

5.7. IMMUNOFLUORESCENCE ANTIBODY TEST (Rifat et al. 2023)

IFATsare generally used to identify and analyze antibodies against *Babesia* (Sanchez et al. 2016; Solano-Gallego et al. 2016) and *Ehrlichia* (Dumler et al. 2007). This approach is time-consuming and could be subjective to some extent (Springer et al. 2021).

5.8. RAPID IMMUNOCHROMATOGRAPHIC TESTS

These tests are easy to use and available commercially but they only give binary outcomes (either positive or negative results) and do not allow analysis of antibody titers. Such tests are shown to be less sensitive (Smit et al. 2015; Liu et al. 2018; Springer et al. 2021).

Table 1: Various types of zoonotic diseases, their causative agents, the tick vectors, the clinical manifestations and regional prevalence of that zoonotic infection

Type of Disease	Causative agent(s)	Tick-vector(s)	Clinical manifestations	Regional Prevalence	References
Anaplasmosis	*Anaplasma marginate* *Anaplasma phagocytophilum*	*Ixodes ricinus* *Ixodes trianguliceps, Ixodes scapularis, Ixodes pacificus*	Fever, anorexia, dyspnea, anemia, reduced milk production in cattle	Australia, South Africa and South America	(De La Fuente et al. 2005; Bown et al. 2008; Foley et al. 2008; Aubry et al. 2011; Keesing et al. 2012; Aktas et al. 2017; Hove et al. 2018; Akram et al. 2021)
Babesiosis	*Babesia bigemina* *Babesia equi* *Babesia microti*	*Ornithodo roserraticus, Ixodes scapularis, Ixodes dammini*	Fever, headache, myalgia, chills, fatigue and sweats	Central and South America, Africa, Australia, and Europe	(Homer et al. 2000; Boozer and Macintire 2003; Bock et al. 2004; Beugnet and Moreau 2015; Vannier 2020)
Colorado Tick Fever	Coltivirus	*Dermacentor andersoni*	Headache, fever, rash, myalgia, lymph-adenopathy, photophobia, GI disturbances	Mountain regions of Canada and the US	(Naides 2012; Petney et al. 2012; David Beckham 2015)
Ehrlichiosis	*Ehrlichia canis* *Ehrlichia chaffeensis* *Ehrlichia equi* *Ehrlichia phagocytophila*	*Amblyomma americanum, Ixodes ricinus, Ixodes scapularis, Rhipicephalus sanguineus*	Anaemia, arthritis, fever, anorexia, fatigue, diarrhoea, vomiting, dyspnea, and weight loss	South-Central America, Europe, Asian countries including Korea, China, and Siberian Russia	(Yabsley et al. 2002; Skotarczak and Medicine 2003; Demma et al. 2005a; Dumler et al. 2007; Vieira et al. 2011; Paulino et al. 2018; Springer and Johnson 2018)
Lyme disease or Lyme borreliosis	*Borrelia burgdorferi* *Borrelia afzelii* *Borrelia garinii*	*Ixodes scapularis*	Myalgia, malaise, fever, lymph adenopathy, headache, and joints pain	Europe, North America and some regions of Asia	(Steere 2001; Wormser 2006; Mead 2015)
Powassan Virus Disease	Powassan Virus (*Flavivirus*)	*Ixodes scapularis, Ixodes cookei*	Nausea, vomiting, dizziness, fatigue, fever, rashes, blurry vision, hemi-plegia, paralysis	Russia and North America	(Ebel 2010; Raval et al. 2012; Piantadosi et al. 2016; Santos et al. 2016; Fatmi et al. 2017; Hermance et al. 2017; Kemenesi and Bányai 2018)
Q Fever	*Coxiella burnetii*	*Amblyomma triguttatum triguttatum* *Dermacentor andersonii*	High-grade fever, malaise, myalgia, headache, flu-like symptoms, Pericarditis	All over the world except New Zealand	(McDiarmid et al. 2000; Parker et al. 2006; Sally et al. 2007; Angelakis and Raoult 2010; Duron et al. 2015b; Pierre-Edouard Fournier 2020; Körner et al. 2021)

Rocky Mountain Spotted Fever	*Rickettsia rickettsii*	*Rhipicephalus sanguineus Dermacentor spp.*	Fever, rash, myalgia, GI disturbance, headache	South and North America	(Masters et al. 2003; Demma et al. 2005b; Dantas-Torres 2007; Luke and Chen 2008; Alvarez-Hernandez et al. 2022)
Tick-borne Encephalitis	*Tick-borne encephalitis virus* [TBEV] (*Flavivirus*)	*Ixodes spp*	Fever, fatigue, flu-like symptoms, body aches, anorexia, slightly increased body temperature, and nausea	Northern regions of China, South Korea, Japan, Eastern and Central Europe and Russia	(Gritsun et al. 2003; Lindquist and Vapalahti 2008; Bogovic and Strle 2015; Valarcher et al. 2015)
Tularemia	*Francisella tularensis*	*Ambloyomma americanum Dermacentor andersoni Dermacentor variabilis*	Fever, malaise, myalgia, chills, headache, and sometimes regional lymph adenopathy	Korea, Japan, China, mainland Europe, and North America	(Parola and Raoult 2001; Feldman 2003; Sjöstedt 2007; Tärnvik and Chu 2007)

5.9. ENZYME-LINKED IMMUNOSPOT ASSAY (ELISPOT)

ELISPOT is considered to be a highly sensitive and specific technique to evaluate T cells cytokine response on antigen stimulation (Kalyuzhny 2005).

5.10. LYMPHOCYTE TRANSFORMATION TESTS (LTTs)

LTTs detect the T cell's proliferative responses upon specific-antigen stimulation. These tests can be used for identification of human Lyme borreliosis but are not generally suggested as they are not highly specific (Dessau et al. 2014).

6. ONE HEALTH PERSPECTIVE

A number of tick species effectively transmit zoonotic pathogenic organisms, but some of these exhibit exceptional behavior due to their function as vectors for many zoonotic pathogens. Therefore, both the ticks infesting various hosts at the wildlife-domestic animal-human interface and the pathogenic organisms transmitted by these tick species occupy prime importance in one health perspective. *Ixodes scapularis*, *Ixodes ricinus* and *Ixodes persulcatus* are among the relatively significant tick vectors. These belong to the Ixodes ricinus complex which is a group that comprises 14 Ixodes species having global distribution (Xu et al. 2003). Ticks, belonging to Ixodes ricinus complex, are confirmed vectors of various bacteria (e.g. Rickettsiales and *Borrelia* spp.), three flaviviruses (Powassan virus, TBEV, and Louping ill) and protozoa (*Babesia* spp.) that are zoonotic. Moreover,*Amblyomma americanum*, *Dermacentor andersoni,* and *Dermacentor variabilis* are specifically crucial in North America considering the one health perspective (DE 2018) because of their vector function for a diverse range of zoonotic viral (e.g., Heartland and Powassan virus) and bacterial (e.g., *Ehrlichia* spp. and *Rickettsia* spp.) pathogenic organisms. Although hard ticks are involved in the transmission of most tick-borne diseases, soft ticks may also act as vectors (Akram et al.2022;Dantas-Torres et al. 2012). Several *Ornithodoros* spp. may also play a role in the transmission of relapsing fever borreliae (Talagrand-Reboul et al. 2018), and this tick genus can also be involved in the transmission of Alkhurma fever virus (Sawatsky et al. 2014) and *Coxiella burnetii*(Duron et al. 2015a).

7. TICK AND TICK-BORNE ZOONOSES CONTROL

According to the recommendations of the CDC, the best defense against tick-borne infections is personal protection (Beard et al. 2014), alongside landscaping alterations and the application of acaricides (Clark and Hu 2008; Hook et al. 2015). However, there is little observation regarding the effectiveness of any of these methods in lowering the tick exposure or incidence of disease (Connally et al. 2009; Hinckley et al. 2016). It is essential to reduce the tick population and tick prevalence in highly endemic areas in order to achieve adequate personal protection. Target deer or mice as hosts for either immature or adult life stages of ticks is the only area-wide available control choice to lower the number of tick population (Eisen et al. 2012). As the use of pesticides may induce adverse effects on animal as well as human lives, there is a need to devise alternative methods and approaches in order to control ticks and tick-borne zoonoses. Oils and organic compounds derived from plants can be used to control the population of ticks. These plant-derived products hinder blood feeding in the ticks.

8. CONCLUSION

Ticks affect animal and human health badly. This is because ticks are the vectors for various zoonotic pathogens. This makes tick-borne zoonotic infections perfect examples of the concept of One Health. Tick-borne zoonoses are an important issue worldwide. Significantly, countries with warm and humid climates provide favorable conditions for infections in animals and humans. So, control programs and the development of effective disease management strategies are needed. Moreover, animal movement due to trade or migration should be kept in mind for possessing probable infection as a risk of zoonoses. Strict quarantine measures need to be imposed in order to avoid the probability of reintroductions of ticks and tick-borne infections. In order to suppress the increased population of ticks, a better understanding of stimuli leading to distribution, accumulation, stability, and density-dependent mortality is required. The knowledge of the host, tick disease, and pathogen triangle concerning various habitats and distribution of ticks, changes in the environmental conditions, and global warming must be considered while devising policies involving migration and trade of animals. The administration of anti-tick agents and recombinant vaccines to prevent related infections can be done in order to disrupt this triangle, especially in the case of animals. The promotion of disease-resistant animal breeds instead of susceptible ones may be another tick control strategy. Overall, in-depth studies revolving around the control of tick-borne zoonoses should be considered a top priority plan.

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