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Medical and Veterinary Entomology: The good and bad flies that affect human and animal life

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Abstract: Medical and veterinary entomology encompasses the study of the insects which are vectors, transmit disease, cause wounds, inject venom and create nuisances together with their application as useful providers of drugs, and model systems for genetic studies. Thus the study on insects and how they affect the human and animal lives have gained importance in recent times. Insect Genomics involving the studies of the whole genome sequences are being developed and gene expression and regulation studies are elucidating their roles in regulating the vector competence. This finds importance in deducing strategies for vector control thereby preventing disease spread that is fatal to man and animal life. In this review we have studied the medical entomology (i) from historical perspective (ii) diverse role of arthropods in causing diseases (iii) common pathogens transmitted by arthropod vectors (iv) major arthropod borne diseases (v) pharmaceutically important insects. The future scope of this review remains to study in depth insects under Diptera that are causative agents of diseases.
Keywords: Diptera, vectors, animals, zoonosis,epidemic, diseases

INTRODUCTION

Insects exhibit tremendous in number and diversity and play a significant role in human civilisation. The majority of the free-swimming marine insects, serve as food for other animals of which the planktons---minute Crustacea form the dominant animal life in the sea. Insects also play a similar dominant role on the land also. Their number together with their enormous adaptive potential in both land and water out-rank any other plant or animal association. Their free living phytophagous nature enable them to scavenge water bodies from dead and dying and play role in clean aquatic environment. Flying terrestrial insects predate, parasitize, pollinate, act as prey or pest, killers, scavengers and vectors of deadly diseases, thus affecting human welfare and development.

Together with their role in human welfare they may also act as nuisance thus endangering the man's very existence and pose a threat to his existence.

Most human diseases are either transmitted from man to man contact or through an invertebrate (like arthropod/insect) or a vertebrate transmitting the disease to other animals or human. Although there is an increased awareness among people about resurgence/emergence of zoonotic diseases in India and globally, the present work reviews the major vector-borne zoonotic diseases of public health significance.

Of six major vector-borne diseases in India, i.e., malaria, dengue, chikungunya, filariasis, Japanese encephalitis (JE), leishmaniasis, and cutaneous leishmaniasis (CL) are zoonotic.

Most of the protozoan diseases are transmitted by arthropods. Protozoa ubiquitous in nature, existing in both free-living and symbiotic forms occur as commensal inhabitants of the human alimentary canal. Organisms like *Entamoeba histolytica; flagellates* of the genus Trypanosomes and Leishmania, *Trichomonas vaginalis;* Cliliophora like *Balantidium coli;* Coccidian like *Isospora belli*, *Cryptosporidium parvum*, *Toxoplasma gondii*, *Plasmodium* spp are transmitted by the blood stream and reaches the human tissues and produce disease. *Trichomonas vaginalis* and *Giardia lamblia*, inhabit the gastrointestinal and urogenital tracts causing infections leading to mild to moderate morbidity but no mortality. In contrast, sporozoan organisms cause infection lethal to man: malaria and toxoplasmosis. Most of these parasitic incidents are caused by endocellular protozoa of different genera or species [1-7].

The different medical conditions are caused by arthropods including fly, mosquito, flea, ticks, bugs, mites and lice.

Myiasis includes the invasion of human and other animals tissue by the dipterous fly larva, which feed on the live host, necrotic or dead tissues of animals. Houseflies are known to transmit a number of bacterial, viral, and protozoal diseases to humans owing to their habits of visiting back forth faeces and other unhygienic matter and human food, thereby transmitting pathogens by their contaminated feet, body hairs and mouthparts of flies leading to infection causing a number of diseases. Fleas act as ectoparasites, sometimes causing allergic dermatitis and are intermediate hosts for bacteria like *Yersinia pestis* and *Rickettsia typhi*. In tropical America and Africa the flea Tunga penetrates about 1 mm in length turning into about 1 cm after burrowing into the skin, causing extreme irritation, requiring surgical removal. Lice, the ectoparasite includes three types: head lice (*Pediculus humanus capitis*), body lice (*Pediculus humanus corporis*) and pubic /crab lice (*Phitrius pubis*). Lice transmit diseases like relapsing fever and epidemic typhus, most reported from the highlands of Ethiopia. *Triatoma* commonly called as Kissing bug are disease vector of *Trypanasoma cruzi*, observed mostly in Latin America. Ticks cause mechanical injury to the skin, sometimes releasing toxins, affecting release of acetylcholine at the neuromuscular junctions, leading to progressive ascending paralysis causing 'tick paralyses" terminating in diseases like francella and Rickettsial illnesses. *Sarcoptes scabies* causes itchy eruptions in the skin causing scabies. House dust mites produce or concentrate potent allergens [8-17] causing allergy disorders.

In this review we have highlighted the (i) medical entomology from historical perspective (ii) diverse role of arthropods in causing diseases (iii) common pathogens transmitted by arthropod vectors (iv) major arthropod borne diseases (v) pharmaceutically important insects.

A. Medical entomology in the past-a historical journey:

Mercurialis (1530-1606), an Italian physician, is considered to have observed that flies spread disease. With initial observation that plague also called as Black Death, which ravaged the then Europe were spread by flies feeding on the internal secretions of the dead and dying and then depositing their faeces on the carcass. Souza (1587) suspected flies of spreading yaws (framboesia) and Bancroft (1769) propounded a similar theory from his observations in Guiana; and many years later Castellani (1907) demonstrated that flies play a part in the dissemination of this disease after isolating *Treponema pertentie* from the sores of the sick. Many years later Beauperthuy (1854) and Nott (1848), proposed the well-defined theories of insect propagation of disease related to the transmission of yellow fever by mosquitoes. In 1857 Pasteur, discovered pathogenic bacteria [18-22].

In 1866 Dr. Patrick Manson, took up work first at Formosa and later in1871 at Amoy, China, where he observed abundant filariasis in the blood of his Chinese patients, that showed "periodicity" of their appearance in the peripheral circulation, and in 1879 published the role of *Culex fatigans*, as an intermediate host in the developmental cycle of a parasite. Manson was a pioneer in the field of medical entomology. He also encouraged Ronald Ross, who later elucidated the correct etiology of malaria which marked the discovery in the field of medical entomology. Sir Ronald Ross was awarded the Nobel Prize in 1898 for his discovery of the malarial parasite in the gastrointestinal tract of the mosquito. This was instrumental in the setting up of Calcutta School of Tropical Medicine in Calcutta in 1921 by the British Government and possibly the introduction of Indian scientists to the field of medical entomology [18-22].

B. **The diverse role of Arthropods in causing diseases**.

The arthropods may cause direct impairment to humans or may indirectly impair human well-being (Table 1). Bites, stings, and allergic reactions are three major categories of injuries caused by arthropods. Arthropods also affect man by annoying and disturbing him. Biting arthropods bite to feed, probe (taste), or defend themselves. Most penetrations of human skin are made by mouthparts that are developed for ingesting blood, tissue, and tissue fluids of animals or plants. These bites usually result in the arthropod injecting salivary fluids or regurgitating its digestive tract products into the man or animal. Some biting arthropods can also produce skin injuries. Each individual's reaction to arthropod bites can be very different. Biting arthropods are grouped according into short-term or long-term based on their time of contact with the host. *Bloodsucking (hematophagous) arthropods* normally suck blood from warm-blooded animals (including man), is used both for life support and growth and/or egg development. Only the females of the mosquitoes, black flies, biting midges, horseflies, and deer flies are bloodsuckers, while both males and females of tsetse flies and stable flies are bloodsuckers. Other examples of blood sucking arthropods that are short-term are fleas, true bugs (conenose bugs and bedbugs), and soft ticks. Some stinging arthropods affect man by injecting venom (insect toxins) through stingers, fangs, modified front legs, or spines. Spiders and centipedes are arthropods in the category that uses mouthparts for envenomization. Allergic reactions are caused by both the bites and stings of arthropods. Additionally, arthropod parts both live and dead and their body fluids can cause allergic reactions. Allergic reactions are extremely variable in different people ranging from very mild to severe reactions [23-27].

Houseflies or red ants, silverfish, cockroaches and bedbugs may be of immense nuisance value as is in case of. Their capacity to spread malaria,

dengue, chikungunya, kala-azar, yellow fever, filaria and onchoceriasis made them immensely dreaded. Different insect species causes wounds, inject venom, and transmit diseases to domestic and human animals. Insect nuisance is caused due to high densities of a particular species like bush flies (*Musca vertustisima*) in rural Australia or ants and silverfish in the house and adjoining areas. Some insects like arachnids, arouse unwarranted responses of phobia. Microscopic mites can bite and cause skin rashes causing undiagnosed local or widespread infestation. Insect biting are associated with a sensation of pain. Honey bee delivers venom by a modified ovipositor, the sting [23-33].

B. (i). Insects and veterinary entomology:

Insects are vectors for diseases and are known to transmit, protists, bacteria, virus, and nematodes. These pathogens cause diseases like yellow fever, dengue, malaria, onchocerciasis, filariasis, plague, trypanosomiasis [33-35]. The significance of vector efficiency in disease transmission from reservoir to host is related to many species-related factors like vector reproductive capacity, physiology, morphology, and genetics; with other physical and related environmental factors that affect the vector's ability to transmit disease are temperature, moisture, rainfall, pH, weather, geographical and topographical location, photoperiod, and wind [33-35].

Insects could cause direct injury to animal life like head louse (*Pediculus humanus corporis*), mites that can burrow the skin causing scabies. Calliphoridae, Sarcophagidae and Muscidae can develop larvae, or maggots in flesh [23-33].

More harmful than direct injury by insects, is mediated by the action of vectors, transmitting pathogens from one animal or human host to the other. This could be by mechanical transfer, when the disease causing agent is passively transferred from one host to the other and do not increase in the vector *eg* myxomatosis is transferred from rabbit to rabbit in the blood on its proboscis [23-33].

The other type of transfer is biological which involves association of three components insect vector, pathogen and host. The disease causing agents replicates within insect which forms the main agent of biological transfer. Thus strategies employed in control of such a disease would require a thorough understanding of all three components: vector, pathogen and host (i) to stop the disease by interrupting contact between vector and host, attack on the pathogen, (ii) directly target the pathogen within the host.

Human pathogens can complete their parasitic life cycles within the insect vector and human host. Some diseases are of (i) single cycle *eg* malaria caused by *Anopheles* mosquitoes, malarial parasites and humans as these diseases require co-evolution of pathogen and vector and human (ii) many diseases are secondary cycle diseases that affect human through a non human vertebrate host like yellow fever in monkey. In such diseases, non human cycle is primary while when outbreaks occur, the disease spread in human population.

Disease causing pathogens transmitted by insects include arbovirus, bacteria, protists or nematodes. Transfer of parasites from vector to host is mediated by (i) a blood feeding insect by injection with anticoagulant salivary gland products that keeps the wound fresh while feeding (ii) deposition of infected faeces close to the wound. A detailed description is as follows.

B. (ii). Insect nuisance and phobia:

Insects are a major source of nuisance and phobia. An aversion for insects is usually due to one or more of the three things like: experience or knowledge (bees), repulsion (cockroaches) or fear based on inadequate information (crickets) causing entomophobia (or insectophobia). Licks, bites or sting of flies, midges, biting ants, bees, wasps, and bedbugs, hovering activity of cockroaches, harmless moths, contaminating ants, creepy actions of the c**rane flies** are annoying to one's senses. Spiders can trigger unwarranted phobic response like arachnophobia or delusory parasitosis, bedbugs feeding on human blood all act as insect nuisance. A phobic person can experience anxiety, panic attack expressing physical symptoms like trembling, sweating, chills, hot flushes, shortness of breath, difficulty breathing, nausea, rapid heartbeat, dizziness, dry mouth and disorientated feeling can occur during the anxiety or panic attack [23-33].

B (iii).Insect Venoms

Venomous insects belong to the orders Lepidoptera, Hemiptera, and Hymenoptera. The method of venom delivery may be very active, through mouthparts of Hemiptera (stylets), sting apparatus of Hymenoptera (bees and wasps), and the passive modified setae in some lepidopteran larvae (caterpillars) that pierce the outer surface of the receiving organism or are broken on contact. Some insects of the orders Coleoptera, Diptera, and Neuroptera, also possess oral venoms that is ejected, composed of mainly peptides and proteins with polysaccharides, alkaloids, terpenes, biogenic amines (such as histamine), organic acids (formic acid), and amino acids [1-2, 36] that cause hemorrhage, neurotoxicity, hemolysis, and algogenic activity. Both the bees and the wasps possess venom sacs accompanying the sting and leave behind both the sting and the venom in their prey, ants on the other hand liberally spray their venom into the wound cut by the jaws [1-2, 36].

C (iv). Insect blisters and itches

Blister beetles (Meloidae) possess toxic chemicals like cantharidins which cause blistering of the skin and

irritates the urinary and genital tracts. Cantharidin, which is collected mainly from *Mylabris* and the European species *Lytta vesicatoria,* commonly called Spanish fly. *Cantharidin* is used medically as a topical skin irritant to remove warts. Bites from midges, mosquitoes and gnats often cause small papules or lumps on the skin that are usually very itchy. In an individual sensitive to insect bites, he may develop bullae that are fluid-filled blisters or weals which are circular, fluid-filled areas surrounding the bite. A flea bite sensitive person may develop papular urticaria where a number of itchy red lumps form causing. bullae. Fleas from cats and dogs can often bite below the knee, commonly around the ankles, or forearms. A bite from a horsefly can be very painful or weal formed around the bite. Blandford fly bites often occur on the legs and are very painful producing a severe, localised reaction confined to the area of the bite, with swelling, blistering and joint pain. Tick bites symptoms are also similar in nature and can carry bacterial infection called *Borrelia burgdorferi,* causing Lyme disease which if left untreated causes serious ailments. Mites cause very itchy lumps and blisters on the skin. Spider bites causes small puncture marks on the skin and cause pain, redness and swelling. Swollen, red marks often form on the skin, which can be itchy and painful in wasps and hornet bite. Some staphylinid beetles produce contact poisons and paederin which cause severe blistering and ulcerations. Caterpillars of moths are observed to cause urtication or skin irritation when they come in contact with skin because of the toxins released from the subcutaneous skin glands which release the venom when the spines of the caterpillars are broken [37-39].

B (v). Insect allergies

Stinging insects include honeybees, yellow jackets, hornets, wasps and fire ants; biting insects include black flies, fleas, horseflies, mosquitoes and kissing bugs. Insects that cause respiratory allergies include cockroaches, midges, lake flies and caddis flies. Insect allergies often show aggravated expressions in young children, with history of other types of allergies (like hay fever), and occupations that expose people to insects or the regular exposure to dust-containing insect allergens. An allergy to biting and stinging insects can affect the area around the bite or sting and causes skin rash, hives, itching, swelling, redness, hotness, difficulty breathing, shortness of breath, coughing, wheezing, dizziness, fainting and life-threatening anaphylactic reactions. The most important of all the arthropod mediated allergies are from the fecal matter of the house dust mites, *Dermatophagoides farinae* and *D. pteronyssinus.* Tenebrionid larvae and chironomid larvae are well known for this [23, 36, 40].

C. Insects as vectors of diseases

Vector-borne diseases account for more than 17% of all infectious diseases, causing more than 1 million deaths annually. Malaria causes more than 600000 deaths every year globally, most of them children under 5 years of age. More than 2.5 billion people in over 100 countries are at risk of contracting dengue alone. Other diseases such as Chagas disease, leishmaniasis and schistosomiasis affect hundreds of millions of people worldwide [33, 35, 41].

Many of these vectors are bloodsucking insects, which ingest disease-producing microbes during their blood meal from an infected host (animal or human) and later inject it into a new host during their subsequent blood meal. Mosquitoes are the best known disease vector. Others include ticks, flies, sandflies, fleas, triatomine bugs and some freshwater aquatic snails (causes schistosomiasis) [33, 35, 41-46].

Mosquitoes borne diseases by *Aedes mosquito are* dengue fever, rift Valley fever, yellow fever and chikungunya; by *Anopheles it is m*alaria of different types; by *Culex mosquito it is* japanese encephalitis, lymphatic filariasis, west Nile fever. Sandflies causes leishmaniasis and sandfly fever (phelebotomus fever). Crimean-Congo haemorrhagic fever, lyme disease, relapsing fever (borreliosis), rickettsial diseases (spotted fever and Q fever), tick-borne encephalitis, and tularaemia are ticks borne disease. Chagas diseases (American trypanosomiasis) are mediated by triatomine bugs, sleeping sickness (African trypanosomiasis) by tsetse flies [2] and fleas causes plague (transmitted by fleas from rats to humans) and rickettsiosis [41-46].

In tropical and subtropical countries insects play a major role in transmission of pathogens like protists, viruses, bacteria and nematodes. Some of these pathogens are causative agents of diseases like malaria, dengue, chikunguniya, yellow fever, onchocerciasis, leishmaniasis, filariasis and trypanosomiasis. Again the causative agent for the disease may be the insect itself, as in the case of the head louse, *Pediculus humanus corporis* which causes pediculosis or the mite *Sarcoptes scabiei* causing scabies while in myiasis causing blow flies, house flies and flesh flies, the larvae can develop in living flesh both as primary agents and through a wound or damage caused by other insects like ticks and mites. As the flesh putrefies through bacterial decomposition and the animal dies, the wound would be further invaded by the blow fly *Chrysomya bezziana* and the screw worm larva *Cochliomyia hominivorax* till the animal is treated or it dies. The sheep nostril fly or *Oestrous ovis* which develops as a endoparasitic larva in the nasal and head sinuses of the sheep can deposit its larvae sometimes in the conjunctiva of humans causing ocular myiasis [41-46].Of all the arthropods the flies (Order: Diptera) are most potent and even sometimes fatal if not treated. The other groups are the Siphonaptera (fleas), Pthiraptera (lice), Hemiptera (bugs), and Acari (mites) [26-28,31, 33, 35,42-47].

The transfer of pathogens from the vectors to the host (animals or human) may be by mechanical transfer or by biological transfer. Mechanical transfer is

a passive transmission like the transmission of myxomatosis from rabbit to rabbit through the blood in the proboscis of mosquitoes or transmission of enteric disease bacteria from the legs, mouth parts of the house fly or cockroaches. Biological transfer like transmission of malaria is on the other hand a more complicated process involving a specific association between the arthropod vector, the pathogen and the host and the transfer involves all the three components. The causative agent replicates within the vector insects which is the vital link between the transfer and the finally the outbreak of the disease [26-28, 31, 33, 35,42-47].

Biological carriers are of four types. In propagative carrier (Yellow fever virus in *Aedes* mosquito) the multiplication of the parasite takes place with no developmental change. Both multiplication and developmental changes goes on in cyclopropagative carrier (*Plasmodium* species in *Anopheles* mosquito). There is developmental change of the parasite but no multiplication in cyclo developmental carrier (Wucherera *bancrofiti* in Culex mosquito). When the parasite passes to progeny arthropods vectors through the ova then it is transovarian carrier (*Ricketsia typhi* in ticks) [42-48].

Usually a blood feeding insect, typically a dipteran fly will transmit a parasite from animal to animal, human to human, animal to human but rarely from human to animal. Again biological transfer may involve single cycle transmission and outbreak of secondary cycle transmission as in the case of plague in rats, yellow fever in monkeys or leishmaniasis in rodents. In case of secondary cycle diseases the non-human cycle is the primary cycle and the man may not be the all inclusive factor of maintenance of the disease. Breakouts often happen in case the human population wanders off into the natural territories of the vector and the animal hosts which act as reservoirs. *Phlebotomus* sand flies for example depend on arid zone rodents for transmitting *Leishmania*. Recurrence of leishmaniasis is occurring due to the suburban infiltration of the humans into the habitats of the rodent reservoir even after successful eradication [31, 44].

Common pathogens transmitted by arthropod vectors.

Arthropod borne diseases alone were responsible for the loss of 15,576,000 man-days among US Armed Forces during World War II. Today, harmful arthropods represent one of the greatest environmental hazards to soldiers in the field [49-50].

The common disease causing organisms may be viruses (arbovirus, i.e., arthropod borne virus), bacteria (including rickettsias), protists like plasmodium and filarial nematode worms (Table-1). Transfer of parasites from the vector to host or vice versa may occur through a blood meal form a vertebrate host. The transfer from host to uninfected vector is through parasite infected blood and the transmission to a host by an infected insect is through an injection along with an anticoagulant and salivary gland products. Deposition of infected faeces into the wound site may also transmit the disease[35,42-47,49-51].

D.Major arthropod borne diseases:

a. Malaria:

In 1880 Laveran, working in Algeria, discovered the parasite of malaria in the red blood cells of patients. Little progress was made till Manson evolved his mosquito theory and impressed it on Ronald Ross, a young British surgeon working in India. Ross in 1897 recorded his great discovery that "dappled-winged" *Anopheles* mosquitoes served as the definitive hosts of species of *Plasmodium*. His results were fully confirmed by Bastianelli, Bignami, and Grassi (1898, 1899), Manson (1898), and Sambon and Low (1900). This discovery by Ross is undoubtedly one of the great landmarks in medical history. There are four major malarial parasites, *Plasmodium vivax, P. falciparum, P. malariae and P.ovale* all of are spread by some 30 species of *Anopheles* mosquito. Though more than 100 years have passed after the discovery of the malarial parasite still 120 million new cases arise each year. Even after a century of the discovery of malaria transmission by mosquitoes in India by Sir, Ronald Ross in 1897, malaria contributes to be one of India's leading public health problems of the country. Historically, the highest incidence of malaria in India occurred in the 1950s, with an estimated 75 million cases and 0.8 million deaths per year (World Health Organization, Country Office for India). The launch of the National Malaria Control Program (NMCP) in 1953 resulted in a significant decline in the number of reported cases to <50,000 and no reported mortality, by 1961. In 1947, an estimate suggested 75 million cases i.e nearly 21.8% of the population and by 2014 the number is quite decreasing but still malaria incidence is still is common health concern in India. The annual parasite incidence (API) is a malariometric index to express malaria cases per thousand populations. As per the National Vector Borne Disease Control Programme (NVBDCP) incidence records, regions with >5 API were scattered in the states like Rajasthan, Gujarat, Karnataka, Goa, southern Madhya Pradesh, Chhattisgarh, Jharkhand and Orissa, and in the northeastern states, 2–5 API was in scattered regions, <2 was in most parts of India (WHO, India epidemiology report) [42,52-53].

The life cycle involves exoerythrocytic and erythrocytic cycle in human and sporogonic cycle in mosquito vector. The life cycle of malaria is completed in two hosts (alternation of hosts) with alternation of generations between sexual and asexual stage. The intermediate vertebrate host is man, where the asexual cycle takes place. The formation of male and female gametocytes by gametogony and the parasite multiplies

by schizogony. In mosquito, the invertebrate definitive host, the sexual cycle takes place, and the union of male and female gametes ends in the formation of sporozoites by sporogony [54-55].

P. falciparum occurs almost exclusively in tropical and subtropical regions. Weather(rainfall, temperature & humidity) remains the cause of seasonality in malaria transmission. In Ethiopia, even though all the four species of plasmodium infecting man have been recorded, *P. falciparum* followed by *vivax* and *malariae* are the most important causes of epidemic disease. *P. vivax* is most prevalent with the widest geographic distribution, including the tropics, subtropics, and temperate regions. However, it is the second most prevalent in Ethiopia following *P. falciparum. P. malariae* infection occurs primarily in the same sub-tropical and temperate regions as infections with the other plasmodia but is less prevalent. *P. ovale* is distributed primarily in tropical Africa. It is also found in Asia and South America. The primary vectors of malaria in India are *Anopheles stephensia, An. culicifacies, An. fluviatilis, An. minimus, An. dirus, An. baimaii, An. elegans* and *An. sundaicus* [42, 56].

Even in malaria transmission free countries like Australia, reports 1-5 deaths due to malaria today. Today research on insect genomics has shed new light on the vector pathway interaction. The genomes of *Anopheles gambiae* has already been decoded and found that natural malaria infection is regulated by one single genomic controlled region [57-58].

Although malaria is preventable and treatable mosquito-borne disease, recent reports by WHO have revealed that globally out of an estimated 3.4 billion people at risk on malaria, about 1.2 billion people are at high risk accounting for more than one in every 1000 individuals. In 2012, from an estimated 207 million cases of malaria reported, 473 000 – 789 000 adults and 483000 children under five years of age died [42-59].

Drug and insecticide resistance in malaria

The most widely recommended drug used for *P. vivax* malaria treatment is Chloroquine. Throughout the globe, the incidence of Chloroquine resistance of parasites has increased widely. Generally artemisinin-based combination therapy (ACT)s are highly recommended in the treatment of chloroquine-resistant *P. vivax* malaria infections. But quite recently, it has also being reported, the parasites are turning out to be resistant also to artemisinin, proving both chloroquine and artemisin to be major drawbacks in treatment and control of malaria. The resistant varieties of malarial parasites are turning out to be more widespread in nature. So new strategies are generated nowadays to introduce reformulations of old drugs and reinvent develop new therapies. The main reason for drug resistance and antigenic variation within *P. vivax* populations lies in their genetic diversity that allows the parasite to evade the host immune response and to evolve immunity to anti-malarial compounds. The knowledge of this parasite genomics to understand the detailed genetic variation of parasites is critical for the development of new drugs, vaccines and intervention strategies [60-61].

Because chloroquine – resistant strains of *P. falciparum* are present in many parts of the world, infection of *P. falciparum* may be treated with other agents including mefloquine, quinine, guanidine, pyrimethamine – sulfadoxine, and doxycycline. In reports of mixed infection involving *P. falciparum* and *P. vivax*, the treatment strategy is designed to eradicate not only *P. falciparum* from the erythrocytes but also the liver stages of *P. vivax* to avoid relapses provided that the person no longer lives in a malaria endemic area. The problem of drug resistance has also been studied using molecular markers [60-62].

Sulfadoxine pyrimethamine (SP) resistance data is quite limited and the efficacy of this drug is within acceptable limits except in limited areas like Arunachal Pradesh, Assam, West Bengal and Indo-Myanmar border [42, 63-64]. Dihydrofolate reductase (DHFR), Dihydropteroate synthase (DHPS) mutations of parasites carrying double or single mutants also showed increased minimum inhibitory concentration (MIC) value for sulfadoxine and pyrimethamine both. Different Indian hospitals are reporting drug-resistant or complicated cases of malaria infections. Prevalence of malaria incidence in pregnant woman, complications of cerebral malaria, renal or kidney failure, severe anemia is the recorded cases of *P. falciparum* infections. Age specific distribution of malaria showed a higher prevalence in men of all ages as compared to females [42, 63-64].

DDT, hexachlorocyclohexane (HCH), and malathion are used in malaria control throughout India, especially in rural areas. However, the development of insecticide resistance in the predominant malaria vectors like *An. culicifacies* and *An. stephensi* threatens to halt these once effective methods of control and prevention [65-66].

b. Trypanosomiasis:

In 1895 Bruce discovered *Trypanosoma brucei*, the causative agent of nagana or tsetse fly disease of cattle in Zululand, Africa and demonstrated that the tsetse fly, *Glossina mozsitas* could transmit the disease. In 1901 Forde, in West Africa, observed a parasite in the blood of a European patient suffering from Gambian fever; later Dutton (1902) recognized it as a trypanosome and described it as *Trypanosoma gambiense* Dutton; Castellan (1903) and Bruce and Nabarro (1903) proved this trypanosome was the causative agent of sleeping sickness and that *Glossina palpalis* was the transmitting fly. In South America Chagas (1909) demonstrated that a trypanosome, *T.*

cruzi, was transmitted by a bug, *Triatoma megista* Burm responsible for the South American Chagas disease. Some 150 mammal species are susceptible to *T. cruzi*, ranging from marsupials such as the opossum (*Didelphis marsupialis*) to primates. High rates of prevalence is reported in cats, dogs, rodents, and both domestic and wild lagomorphs, taken together which constitute an important reservoir for human infection. Birds and cold-blooded vertebrates are refractory to *T. cruzi* infection, but domestic birds are important food sources for the vector. The vectors are reduviid bugs of the family Triatomidae. It has been confirmed that about a hundred species are susceptible to the infection, but the most important vectors are *Triatoma infestans* in southern Peru; *Panstrongylus megistus* in northern Argentina, southern Brazil, and Paraguay; and *Rhodnius prolixus* in northern South America, parts of Central America, and Mexico. African trypanosomiases multiply in the blood, lymph, cerebrospinal fluid, and intercellular spaces, but they do not penetrate cells. This parasite is the etiological agent of South American trypanosomias is also termed as Chagas' disease. Recent studies reveal, sleeping sickness threatens millions of people in 36 countries in sub-Saharan Africa. History records the major epidemics in Africa over the last century, the earliest in 1896, 1906, 1920 and 1970 [43, 67-70].

Depending on the type of parasite, human African trypanosomiases are mostly revealed in two forms. In the life cycle of these species, there are amastigote, promastigote, epimastigote, and trypomastigote stages. In the human African trypanosomes, however, the amastigote and promastigote stages of life cycle development are absent. The subspecies *T. b. gambiense*, *T. b. rhodesiense* and *T. b. brucei*, are morphologically indistinguishable. Though they are morphologically indistinguishable, they are mostly distinguished on the basis of their sensitivity to the drug tryparsamide, their infectivity and pathogenicity for rats, their pathogenicity for man and differential electrophoretic behavior of their isozymes. *T. b. gambiense and T. b. rhodesiense* are the subspecies that affect man. *T. b. brucei* does not affect man, but it is pathogenic for domestic animals in Africa [43, 67-71].

Although both species causes sleeping sickness, the progress of the disease is different. *T.gambiense* induced disease runs a low-grade chronic course over a few years. One of the earliest signs of disease is an occasional ulcer at the site of the fly bite. As reproduction of organisms continues, the lymph nodes are invaded, and fever, myalgia, arthralgia, and enlarged lymph node results. Swelling of the posterior cervical lymph nodes is characteristic of Gambian sleeping sickness and is called winter bottom's sign [43, 67-72].

Chagas' disease may be asymptomatic acute or chronic disease. One of the earliest signs of the disease develops at the site of the bug bite of an erythematous and indurated area called a chagoma, often followed by a rash and edema around the eyes and face; in young children frequently an acute process with CNS involvement may occur. Acute infection is also characterized by fever, chills, malaise, myalgia, and fatigue. The chronic Chagas' disease is characterized by hepatosplenomegaly, myocarditis, and enlargement of the esophagus and colon as a result of the destruction of nerve cells (E.g. Auerbach's plexus) and other tissues that control the growth of these organs. Involvement of the CNS may produce granulomas in the brain with cyst formation and a meningoencephalitis. Death from chronic Chagas' disease results from tissue destruction in the many areas invaded by the organisms, and sudden deaths result from complete heart block and brain damage. The drug of choice is nifurtimox. Alternative agents include allopurinol and benzimidazole [43, 67-73].

Recent reports from WHO reveal that *Trypanosoma brucei gambiense* is predominant in 24 countries in west and central Africa, accounting for chronic infection of more than 98% of reported cases of sleeping sickness. Infection may be asymptomatic for months or even years. Eventually with the progress of infection, in the CNS, the symptoms emerge. *Trypanosoma brucei rhodesiense* on the other hand is reported from 13 countries in eastern and southern Africa accounting for acute infection of under 2% of reported cases [43, 67-74]. In this type of infection the first signs and symptoms are observed within a few months or weeks after infection, progressing rapidly invading the CNS. Other form of trypanosomiasis predominant in 21 Latin American countries is known as American trypanosomiasis or Chagas disease caused by a different species [43, 67-74].

c. Animal trypanosomiasis

T.b. rhodesiense causes animal trypanosomiasis, the host being wild and domestic animals. In cattle the disease is known as *Nagana*, originating from a Zulu word meaning "to be depressed". The animals infected with *T.b. gambiense* can also act as a reservoir. The trypanosome disease in cattle and livestock is highly detrimental to the economic development of the affected rural areas. The life cycle of trypanosome in human and Triatomine bug is schematically presented in Fig. 1. [43, 67-75].*Trypanosoma evansi* causes Surra disease of cattle widespread in India spread by horse flies, tabanids and the blood sucking housefly *Stomoxys.* [43,67-76].

T. rhodesiense, causes a more acute, rapidly progressive disease that is usually fatal, growing in greater numbers in the blood. Lymphadenopathy is uncommon, and an early infection and CNS invasion occurs, resulting in lethargy, anorexia, and mental

disturbance. The chronic stages described for *T. gambiense* are not often seen due to rapid CNS disease, the organism produces kidney damage & myocarditis, leading to death [43,67-77].

The most common mode of infection is through the bite of an infected tsetse fly to any organisms. Other modes of transmission of infection include the passage of trypanosome across the placenta and infect the fetus *and so* it is mother-to-child infection. Mechanical transmission is mediated through other blood sucking insects and accidental transmission due to pricks from contaminated needles [43, 67-77].

The major diagnosis includes the screening for potential infection by using serological tests, testing for clinical signs like swollen cervical glands and detection of the parasite in the blood. After the detection of the parasite, the state of disease progression was also determined by examining cerebrospinal fluid (CSF) obtained by lumbar puncture indicating the course of treatment [43, 67-78].

The initial treatment of the disease includes usage of the drugs like Pentamidine, Suramin with low toxicity and easy administration. The second stage treatment of the disease includes choice of a toxic drug having the ability to cross the blood-brain barrier to reach the parasite. Melasoprol and Eflornithine are effective in treatment of both the initial and second stages of the disease. Eflornithine is less toxic and effective only against *T. b. gambiense*. In syngergistic mode of treatment combination of both drugs eflornithine and nifurtimox, is found to be more effective [43, 67-78].

d. Leishmaniasis:

The sand flies (*Phlebotomus & Lutzomyia*) (Diptera) are vectors of a small group of flagellates *Leishmania*, which causes internal visceral disfiguring and external ulcerative diseases in humans and dogs. The life cycle is depicted in Fig. 3. About 2 million people are diagnosed each year with 12 million infected at a given time [31, 44,79-84]. Visceral leishmaniasis (kala-azar or black fever or Dumdum fever) caused by *L. donovani* is widespread in India at one time, inevitably kills when untreated and is now feared to have a HIV co-infection too. *L. donovani infantum* has similar geographical distribution, reservoir host and vector like *L. donovani*. *L. donovani chagasi* is found in South and Central America, and the West Indies. Reservoir hosts are dogs, foxes, and cats, and the vector is the Lutzomiya sand fly. The life cycle of *Leishmania* is depicted in (Fig. 4D). The disease was endemic in West Bengal, India but has been reported at its most deadly in East Africa today [31,44,79-84].

They include: (i) Visceral leishmaniasis (VL also known as kala-azar) with manifestations of symptoms of weight loss, anaemia, irregular bouts of fever, spleen and liver enlargement, and if left untreated turns out to be fatal. Kalazar is highly endemic in the East Africa and in the Indian subcontinent. In VL, the spleen, liver, and bone marrow are the most worst affected organs. In VL, hypersplenism, reduced bone marrow activity, lymphadenopathy, hyperglobulinemia, and cellular distraction in the spleen causes leucopenia, anaemia, and thrombocytopenia with concurrent secondary infections. Leishmaniasis is a curable and treatable disease. VL is mostly diagnosed by detecting a combination of clinical signs with serological or parasitological tests. (ii) Cutaneous leishmaniasis (CL) is the one of the most common form of leishmaniasis (Oriental sore) by *L. tropica.* CL causes serious disability and ulcers on the exposed parts of the body, leaving behind life-long scars. It is mostly predominant in the Africa, Middle East and Central Asia and Mediterranean basin. The urban CL is thought to be an anthroponosis while the rural CL is zoonosis with human infections occurring only sporadically. Phlebotomus sand fly is the vector for the old world CL. In the patients of the Ethiopian CL, similar kind of lesions were also seen, but in patients they may also give rise to diffuse cutaneous leishmaniasis (DCL).DCL patients had least cell mediated immunity against the parasite. Thus the patients had disfiguring nodules over the surface of their body. In CL, the diagnosis is confirmed by clinical manifestation with parasitological tests. HIV and Leishmania co-infection lead to full swing clinical disease, with high mortality and relapses rates. The better choice in treatment of such coinfection is the antiretroviral treatment which reduces the development of the disease [44,85-89]. (iii) Mucocutaneous leishmaniasis is caused by *Leishmania braziliensis.* Mucocutaneous leishmaniasis leads to partial or total destruction of mucous membranes of the mouth, nose and throat and is mostly predominant in the Central and South America and Yucatan peninsula. The vector of Mucocutaneous leishmaniasis is the Lutzomyia sand fly [31, 44, 80-84].

The chief drug of choice for leishmaniasis is sodium stibogluconate, a pentavalent antimonial compound and allopurinol or pentamidine or amphotercin B are the alternative therapeutic approaches [31, 44, 84]. The prevention and control of leishmaniasis require a combination of different strategies targeted against a complex biological system involving the four pillars- the parasite, human host, sandfly vector and animal reservoir [44, 67-84].

e. Post kala-azar dermal leishmaniasis (PKDL)

The sequel of visceral leishmaniasis is PKDL. Patients of PKDL has popular, macular or nodular rash usually found on face, upper arms, trunks and other parts of the body. Depending on the severity, the rash usually first starts around the mouth from where it gradually spreads to other parts of the body. It is mainly seen that 50% of VL treated patients in Sudan and 5—10% of VL cases in India has PKDL. Thus, it is largely

restricted to countries or areas where *Leishmania donovani* is the prevalent causative parasite [44,85-89]. In Sudan, the interval at which PKDL follows VL is 0—6 months and in India it is 2—3 years. In inter-epidemic periods of VL, PKDL acts as a reservoir for parasites and thus probably has an important role in transmission of VL. High concentrations of interleukin 10 in the peripheral blood of VL patients predict the development of PKDL. Interferon γ is not produced by peripheral blood mononuclear cells (PBMC) during VL. PBMC start producing interferon γ, after treatment of VL. Interferon-γ-producing cells causes skin inflammation as a reaction to the persisting parasites in the skin and as such the appearance of PKDL lesions occurs. Though the diagnosis of PKDL is mainly clinical, but parasites can be seen by microscopic smears with limited sensitivity. In more than 80% of cases, parasites may be detected by PCR and monoclonal antibodies techniques [44,85-89]. The leishmanin skin test and serological tests are of limited value. In Sudan mostly cases will self cure but treatment is required in severe and chronic cases. Treatment is also needed in Indian PKDL. In Sudan, sodium stibogluconate is given to patients at 20 mg/kg for 2 months and for 4 months in India. Liposomal amphotericine B also seems to be effective. Newer compounds of major potential interest like miltefosine can also be administered orally or topically. Although modern research has brought many new insights in the pathogenesis and management of PKDL, but several issues in particular in relation to control measures remain unsolved and deserve serious attention [44,85-89].

PKDL mainly occurs on the Indian subcontinent and in East Africa, where up to 5–10% and 50% of patients with VL, respectively, develop the condition. Mostly PKDL usually appears 6 months to 1 or more years after kala-azar has apparently been cured but it can occur earlier also. The PKDL patients act as reservoirs of parasites so people with PKDL are considered to be a potential source of kala-azar infection [44,85-89].

The key treatment strategies include-

(i) the prevalence of the disease is highly reduced by early diagnosis and effective case management. It also prevents disabilities and death. Currently the anti-leishmanial medicines particularly for VL are highly effective and safe and access to these medicines is also improving.

(ii) To reduce or interrupt transmission of disease, especially in domestic conditions, vector control helps in controlling transmission of diseases by sandflies. Vector control methods include the spray of insecticides, use of insecticide–treated nets, environmental management and also personal protection.

(iii) Early detection and treatment of patients in time helps to reduce the transmission, monitor the spread and burden of the disease. Thus effective disease surveillance is important.

(iv) At any local situation, control of reservoir hosts is complex and should be tailored properly.

(v) locally tailored communication strategies, mobilization and education of the community with effective behavioral change interventions are required to develop social mobilization and strengthening partnerships. Partnership and collaboration with various other stakeholders and different vector-borne disease control programmes is critical at levels [43-44, 85-89].

f. Filariasis:

Filariasis is endemic to tropical and subtropical regions of the Asia, Africa Central and South America. In 1863 Demarquay discovered a larval nematode in cases of chyluria; they were later seen by Wikherer in other cases, and Lewis (1872) discovered that the blood of man is the normal habitat of this filarial worm (*Filaria sanguinis hominis* of Lewis). The thread like filarial worms like *Wuchereria bancrofti*, *Brugia malayi and Brugia timori* are transmitted by the blood feeding *Culex quinuifasciatus* and sometimes the black flies[45, 90-93]. The lymphatic systems of the infected are paralysed, causing edema culminating in extreme swelling of the lower limbs and genitals commonly known as elephantiasis. The microfilaria parasites cannot mature without the mosquito phase and the movement into the peripheral circulation make them more available to the feeding mosquitoes. The life cycle is schematically represented in (Fig. 2). [45, 90-93].

Recent WHO reports suggest that in 73 countries over 1.4 billion people are at risk of this disease [45]. The combination or single dose of two medicines namely albendazole (400 mg) and ivermectin (150-200 µg/kg) are the recommended drug which clear microfilariae from the bloodstream. Other treatment strategies employed in disease control is the vector control of mosquito with indoor residual spraying or insecticide-treated nets that suppress the transmission of the disease[45].

g. Onchocerciasis:

Non-filarial elephantiasis by *Onchocerca volvulus* of the lower limbs is common in Ethiopia. Silicon, aluminum and iron particles in the red clay soil are absorbed through skin abrasions in bare footed persons. The mineral particles cause obstruction of the lymphatic [46, 94-95].

This disease scars the eyes causing blindness in several thousand humans every year. It is commonly called as river-blindness in West Africa and South America. The pathogen is a filarial worm *Onchocera volvulus* which is transmitted by *Simulium damnosum*, the black fly. *Simulium damnosum* invades the eyes and sometimes it causes blindness[46, 94-95].

In the humans, the adult worms produce microfilariae that migrate to the skin, eyes and other organs. When a female black fly bites an infected person during a blood meal, it also ingests microfilariae which develop further in the blackfly and are then transmitted to the next human host during subsequent bites[46, 94-95].

The disease, onchocerciasis or river blindness includes pathogenesis like skin fibrous nodules (onchocercomata) enclosing female worms. The nodules are common in neck, iliac crest and the coccyx. Skin hypo- or hyper- pigmentation, or dermatitis is present. In advanced cases, the skin becomes thickened and wrinkled, showing lizard or leopard skin appearance. Elephantiasis of the external genitalia and corneal opacity and optic atrophy may finally cause blindness[46, 94-95].

Onchocerciasis occurs mainly in tropical areas. Large-scale treatment of populations in affected areas with ivermectin, transmission of the disease had been interrupted in 10 foci by 2011. Currently there are no vaccine or medication to prevent infection with *O. volvulus [46,94-96].*

h. Dengue:

Dengue or breakbone fever, a disease of unknown etiology, was shown by Graham (1902) to be mosquito-borne and his results were confirmed by Ashburn and Craig (1907). The true vectors have since been shown to be *Aedes aegypti* and *Aedes albopictus*. In the recent past (2012) there was a dengue outbreak in Kolkata which had assumed epidemic proportions. The recent changes in climatic conditions are being held responsible for the excessive predominance of the vectors beyond controllable proportions nowadays [97-105].

Nearly 40% of the world's population and over 2.5 billion people are now at risk from dengue [97]. There may be 50–100 million dengue infections worldwide every year as currently estimated by WHO. At present, there is no specific treatment for dengue fever and there is no vaccine protection against dengue. The only method, at present, to control or prevent the transmission of dengue virus is to combat the mosquitos' vector [97-105].

i. Rickettsias and plague:

Rickettsias are bacteria associated with arthropods. The genus Rickettsia includes virulent pathogens of humans causing typhus with patients suffering from headache, high fever, rashes and delirium. The vectors of typhus are the body louse *Pediculus humanus* and *Pthirius pubis* and some fleas. Lice are also vectors of relapsing fever, spirochaete disease and endemic typhus. Their mode of infection in human is schematically represented in fig 3. Other rickettsial diseases include murine typhus(flea vectors), scrub typhus(mite vectors) and tick borne typhus. Plague on the other hand is a rodent –flea- rodent disease. Caused by the bacteria *Yersinia pestis*, transmitted by the plague bearing fleas , *Xenopsylla cheopsis* in India. The major vector fleas occur on house dwelling rats and the bandicoot in India are the reservoirs for plague. When humans become infected the resultant pandemic was the Black Death in the 14th century which ravaged the entire world [106-107].

j. Arboviruses:

Viruses which multiply in an invertebrate vector and a vertebrate host are arbovirus or arthropod borne virus. These viruses include the Bunyaviridae, Reoviridae, and Rhabdoviridae, Flaviviridae and Togaviridae. *Alphavirus* and *Flavivirus* are ixodid ticks and mosquitoes(*Aedes aegyptii*, *Aedes albopictus*) transmitted virus causing yellow fever, dengue, Japanese encephalitis, the West Nile fever and the Chikunguniya fever. Of the Reovirid group the bluetongue virus transmitted by the ceratopogonid, *Culicoides*is, the most debilitating causing severe mortality in cattle causing bluetongue disease in Australia, Europe, South Africa and India. Arboviral transmission cycle is represented in Fig-4. The epidemiology of arbovruses reveal that several of their groups are capable of transovarial transmission *ie. from* the adult mosquito to the egg , to the larva and to the progeny mosquito as in the case of Japanese Encephalitis in *Culex tritaenorhynchus* mosquitoes thus increasing the infection pattern manifold [19,35,51].

k. Chikungunya

Chikungunya is a viral tropical disease transmitted also by *Aedes* mosquitoes. It is relatively uncommon and poorly documented. The disease has been found in Africa, Asia, and on islands in the Caribbean, Indian and Pacific Oceans [19, 35].

Typical symptoms are an acute illness with fever, skin rash and incapacitating joint pains that can last for weeks. The latter distinguishes chikungunya virus from dengue, which otherwise shares the same vectors, symptoms and geographical distribution. As with dengue, the only method to reduce transmission of chikungunya virus is to control vector mosquitoes and protect against mosquitoes bites. The joint pain is often very debilitating, but usually lasts for a few days or may be prolonged to weeks [35].

There is no cure or commercial vaccine for the disease. Other symptoms include muscle pain, headache, nausea, fatigue and rash. Most patients recover fully but, in some cases, joint pain may persist for several months or even years. There is no cure for the disease. Treatment is focused on relieving the symptoms [35].

The proximity of mosquito breeding sites to human habitation is a significant risk factor for chikungunya. Since 2004, chikungunya fever has reached epidemic proportions, with considerable morbidity and suffering. In recent decades mosquito vectors of chikungunya have spread to Europe and the Americas. In 2007, disease transmission was reported for the first time in a localized outbreak in north-eastern Italy [35].

Chikungunya is a mosquito-borne viral disease first described during an outbreak in southern Tanzania in 1952. It is an RNA virus that belongs to the alphavirus genus of the family Togaviridae. The name 'chikungunya' derives from a word in the Kimakonde language, meaning "to become contorted" and describes the stooped appearance of sufferers with joint pain (arthralgia) [35,108-110].

Most patients recover fully, but in some cases joint pain may persist for several months, or even years. Occasional cases of eye, neurological and heart complications have been reported, as well as gastrointestinal complaints. Serious complications are not common, but in older people, the disease can contribute to the cause of death. Often symptoms in infected individuals are mild and the infection may go unrecognized, or be misdiagnosed in areas where dengue occurs[35,108-110].

The virus is transmitted from human to human by the bites of infected female mosquitoes. Most commonly, the mosquitoes involved are *Aedes aegypti* and *Aedes albopictus*, two species which can also transmit other mosquito-borne viruses, including dengue. These mosquitoes can be found biting throughout daylight hours, though there may be peaks of activity in the early morning and late afternoon. Both species are found biting outdoors, but *A. aegypti* will also readily feed indoors. After the bite of an infected mosquito, onset of illness occurs usually between four and eight days but can range from two to 12 days[35,108-110].

Several methods can be used for diagnosis like serological tests, such as enzyme-linked immunosorbent assays (ELISA), may confirm the presence of IgM and IgG anti-chikungunya antibodies. IgM antibody levels are highest three to five weeks after the onset of illness and persist for about two months. Samples collected during the first week after the onset of symptoms should be tested by both serological and virological methods (RT-PCR) [35,108-110].

The virus may be isolated from the blood during the first few days of infection. Various reverse transcriptase–polymerase chain reaction (RT–PCR) methods are available but are of variable sensitivity. Some are suited to clinical diagnosis. RT–PCR products from clinical samples may also be used for genotyping of the virus, allowing comparisons with virus samples from various geographical sources [35,108-110].

There is no specific antiviral drug treatment for Chikungunya. Treatment is directed primarily at relieving the symptoms, including the joint pain using anti-pyretics, optimal analgesics and fluids. There is no commercial chikungunya vaccine[35,108-110].

The proximity of mosquito vector breeding sites to human habitation is a significant risk factor for chikungunya as well as for other diseases that these species transmit. Prevention and control relies heavily on reducing the number of natural and artificial water-filled container habitats that support breeding of the mosquitoes. This requires mobilization of affected communities. During outbreaks, insecticides may be sprayed to kill flying mosquitoes, applied to surfaces in and around containers where the mosquitoes land, and used to treat water in containers to kill the immature larvae [35,108-110].

For protection during outbreaks of chikungunya, clothing which minimizes skin exposure to the day-biting vectors is advised. Repellents can be applied to exposed skin or to clothing in strict accordance with product label instructions. Repellents should contain DEET (N, N-diethyl-3-methylbenzamide), IR3535 (3-[N-acetyl-N-butyl]-aminopropionic acid ethyl ester) or icaridin (1-piperidinecarboxylic acid, 2-(2-hydroxyethyl)-1-methylpropylester). Mosquito coils or other insecticide vaporizers may also reduce indoor biting[35,108-110].Basic precautions should be taken by people traveling to risk areas and these include use of repellents, wearing long sleeves and pants and ensuring rooms are fitted with screens to prevent mosquitoes from entering.

Disease outbreaks of chikunguniya

Chikungunya has been reported to occur in Africa, Asia and the Indian subcontinent. Human infections in Africa have been at relatively low levels for a number of years, but in 1999-2000 there was a large outbreak in the Democratic Republic of the Congo, and in 2007 there was an outbreak in Gabon[35,108-110].

Starting in February 2005, a major outbreak of chikungunya occurred in islands of the Indian Ocean. A large number of imported cases in Europe were associated with this outbreak, mostly in 2006 when the Indian Ocean epidemic was at its peak. A large outbreak of chikungunya in India occurred in 2006 (35) and 2007. Several other countries in South-East Asia were also affected. Since 2005, India, Indonesia, Thailand, Maldives and Myanmar have reported over 1.9 million cases. Worldwide transmission of chikungunya virus infection was reported for the first time in Europe, in a localized outbreak in north-eastern

Italy in 2007. There were 197 cases recorded during this outbreak and it confirmed that mosquito-borne outbreaks by *A. Albopictus* are plausible in Europe [35,108-110].

E. Pharmaceutically important insects:

The insect venoms like that of the bees and wasps are frequently used for testing allergy reactions and development of medicines against the allergies. The blow fly maggots are often used in maggot debridement therapy for clearing up dead tissues from the wound and speeding up the healing process. Cantharidin extracted from blister beetles are used as an aphrodisiacs and also as medicines for warts and skin problems [36].

Table-1

Type	Pathogen	Affected host species	Disease	Vector Sp
Protozoa	*Trypanosoma gambiense*	Horses, dogs, cattle, pigs, sheep and goat	Cattle Nagana	Tsetse fly (*Glossina* spp.)
	Trypanosome rhodesiense, *T. gambiense*	Horse, sheep, cat, swine, camel, dog, ram	Trypanosomiasis	*Glossina spp., Tabanus spp., Hematopota spp., Chrysops spp., Hematobia spp., Stomoxys calcitrans*
	Trypanosoma cruzi	Dogs, cats, opossum	Chagas Disease	*Triatomid bugs*
	Theileria equi	Horse, cattle, sheep, cow, buffalo, birds, cat, dog, poultry	Theileriosis	*Rhipicephalus spp. Dermatocentor spp. Hyalomma spp*
	Babesia spp	Horse, sheep, cow, swine, camel, dog, ram, pig, cat	Babesiosis	*Rhipicephalus spp., ixodes spp., Hamaphysalis spp., Dermatocentor spp.*
	Plasmodium spp	primates	Malaria	*Anopheles*
	Leishmania spp.	Dogs, rodents	Leishmaniasis	Phlebotomus flies
Bacteria	*Bacillus anthracis*	Goat, cattle, sheep, horses, deer	Anthrax	Horse flies (*Tabanus* spp)
	Yersinia pestis	Rodents	Pague	fleas
	Rickettsia	ungulates	Q Fever	ticks
	Francisella tutarensis	Rabbits, rodents, birds, horse, sheep, swine	Tularaemia	*Chrysops discalis, Aedes cinereus, Dermacentor andersoni, Haemophysalis leporispalustris*
	Anaplasma phagocytophila, ehrichia equi, E. canis, E. bovis, E. equi., E. ovina	Horse, dog, cattle, sheep	Eq Equine granulocytic ehrlichiosis (EGE)	*Ixodes spp.*
	Rickettesia typhi	rats	Murine typhus	ticks
	Rickettsia conori	Dogs, rodents	Boutonneuse fever	ticks
	Rickettsia australis	rodents	Queensland tick typhus	ticks
	Rickettsia siberica	rodents	Siberian tick typhus	ticks
	Orientia tsutsugamushi	rodents	Scrub typhus	mites
	Borrelia burgdorferi	rodents	Lyme disease	ticks
	Borrelia spp.	rodents	Relapsing fever	Ticks and lice
Virus	Togaviridae	primates	Chikungunia	mosquito
	Togaviridae	Marsupials, horses	Ross river fever	Aedes camptorhynchus, A. polynesiensis
	Togaviridae	birds	Mayaro	mosquito
	Togaviridae	unknown	Onyong-nyong fever	mosquito
	Togaviridae	birds	Sindbis fever	mosquito
	Togaviridae	Horse, pig	Japanese encephalitis	*Culex tritaeniorhynchus*
	Togaviridae	Horses, birds	Eastern equine	*Culicoides melanura,*

			encephalomyelitis	*Aedes silicitans, A. vexans*
	Togaviridae	Horse, Birds, rabbits	Western equine encephalomyelitis	*Culex tarsalis, Culicoides melanura*
	Togaviridae	Horse, rodents	Venezuelan equine encephalomyelitis	*Culex aikenii*
	Togaviridae	Horse	Kunjin virus	*Culex annulirostris*
	Togaviridae	Horse, dog, poultry	Murray Valley encephalitis virus	*Culex annulirostris*
	Togaviridae	unknown	Barmah forest	mosquito
	Reoviridae	horse	African horse sickness virus (AHS)	*Culicodes imicola, Aedes silicitans, A. vexans*
	Retroviridae	horse	Equine infectious anemis (EIA)	*Tabanus sudeticus, Stomoxys calcitrans*
	Flaviviridae	primates	Dengue fever (serotypes 1-4)	mosquito
	Flaviviridae	primates	Yellow fever	mosquito
	Flaviviridae	Primates, rodents, camels	Kyasanur forest disease	ticks
	Flaviviridae	rodents	Omsk haemorrhagic disease	ticks
	Flaviviridae	birds	Japanese encephalitis	mosquito
	Flaviviridae	birds	Murray valley encephalitis	mosquito
	Flaviviridae	birds	Ricio	mosquito
	Flaviviridae	birds	St. Louis encephalitis	mosquito
	Flaviviridae	birds	West Nile encephalitis	mosquito
	Flaviviridae	rodents	Tick borne encephalitis	ticks
	Bunyaviridae	unknown	Sandfly fever	sandflies
	Bunyaviridae	unknown	Rift valley fever	mosquito
	Bunyaviridae	rodents	La Crosse encephalitis	mosquito
	Bunyaviridae	Rodents	California encephalitis	mosquito
	Bunyaviridae	Rodents, sheep	Crimean-Congo haemorrhagic fever	ticks
	Bunyaviridae	unknown	Oropouche fever	Midges, mosquitoes
	Vesicular stomatitis virus	Cattle, horses, pig	Vesicular stomatitis	Phlebotomus flies, mosquitoes
	Bluetongue virus	Cattle sheep, goat	Bluetongue	Culicoides flies
Helminths	*Brugia malayi*	primates	Brugian filarisis	mosquito
	Onchocerea spp	Horse, cattle	Onchoceraciasis	*Simulium spp., Culicoides spp.*
	Parafilarisis multipapillose	Horse, cattle	Parafilariasis	*Haematobia atripalpis*
	Thelazia lacrymalis	Horse, cattle, dog	Thelaziasis	*Musca autumnalis, M osiris*
	Habronemia muscae	Horse, donkey, mule, zebra	Habronemiasis	*Musca domestica, Stomoxys calcitrans*

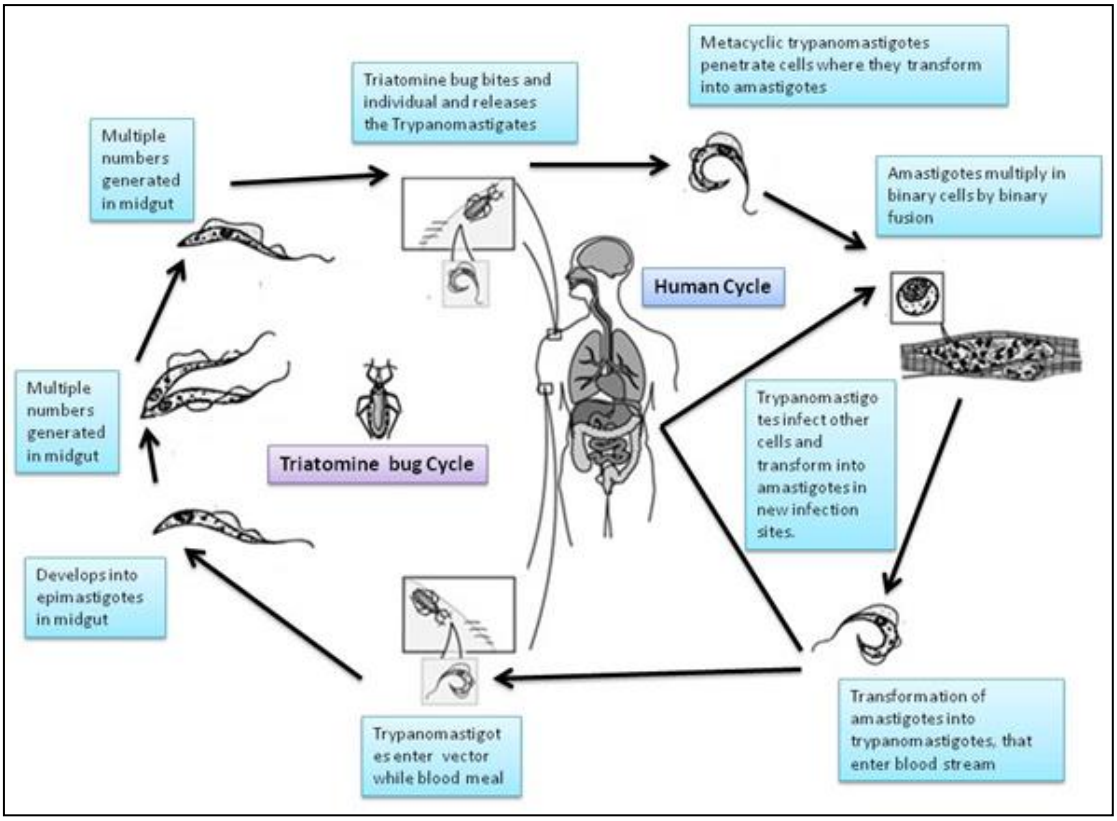

Fig-1: Life cycle in Triatome bug

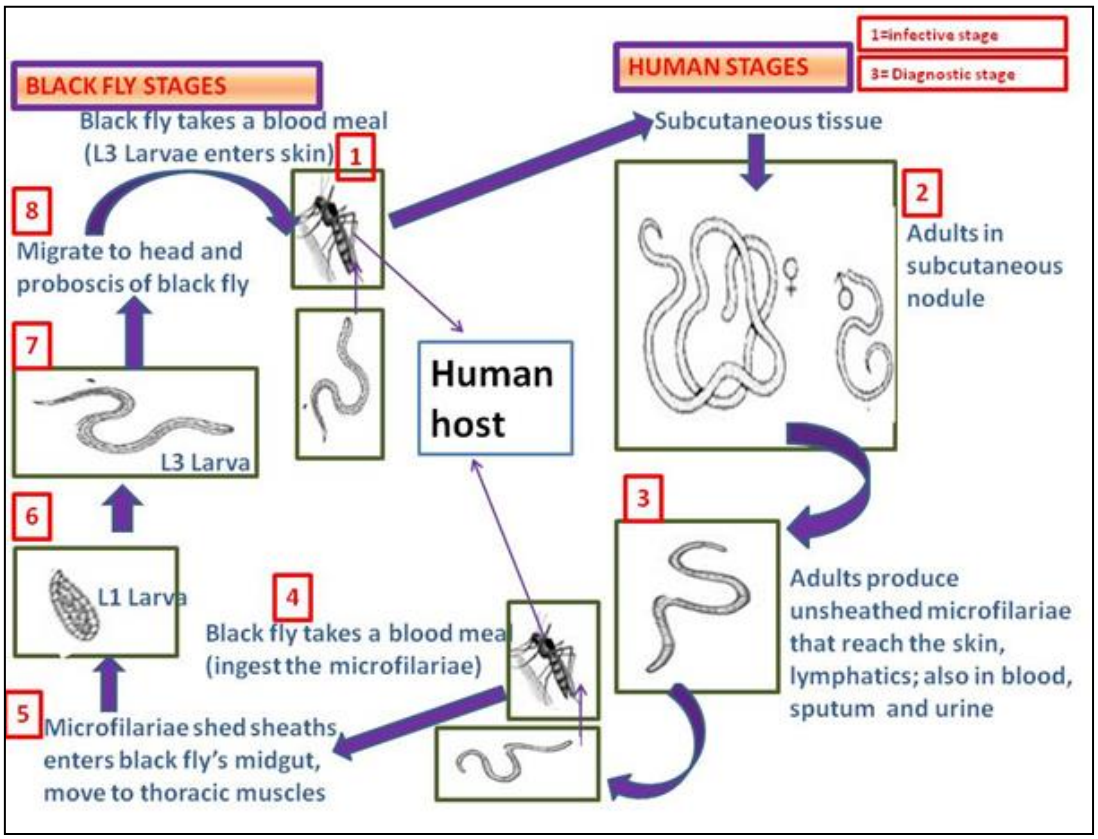

Fig-2: Life Cycle of Filaria.

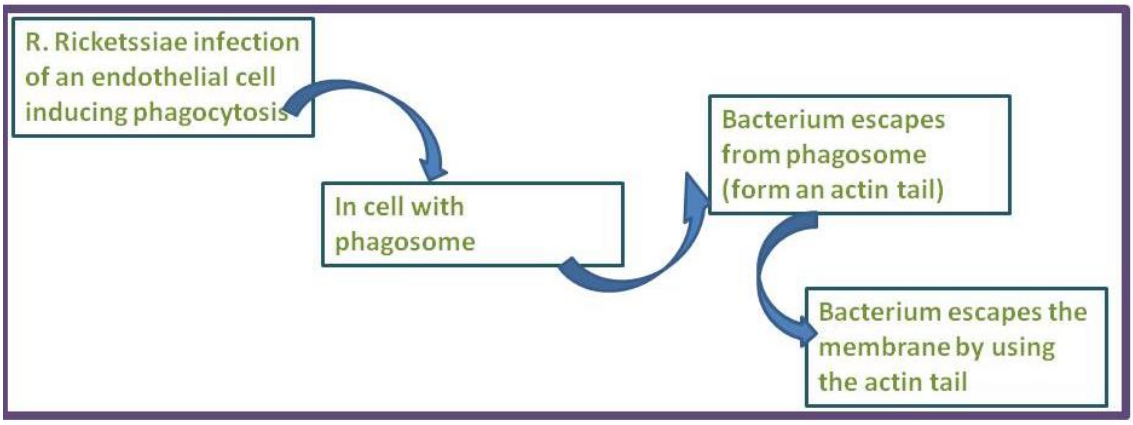

Fig-3: Life Cycle of *Ricketssia*.

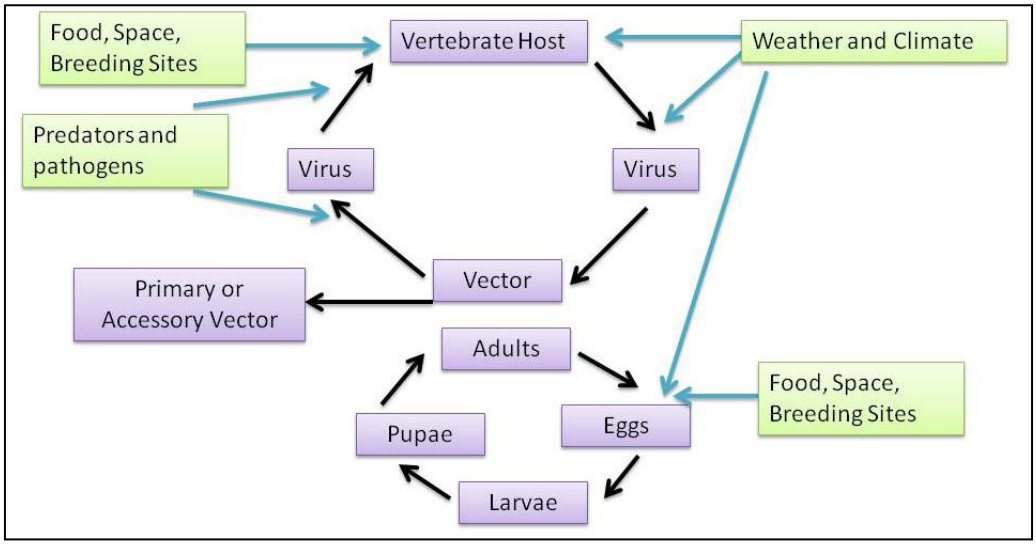

Fig-4: Arbovirus Transmission Cycle

DISCUSSION

The field of Medical Entomology has advanced in leaps and bounds. Application of knowledge from biotechnology, molecular biology, genomics have added to the today's research in the field of medical detection and control, of vector borne diseases (VBD). As diseases transmitted by arthropod vectors adversely affect both human and animal health and therefore vector Control Research is the key pathway to eradication of arthropod borne diseases. The once profusely used sterile male technique where native population of fly vector pupae were irradiated and the resultant sterile males were released in the population to mate with the females but could lay no eggs, are now thought to be archaic. The vector pathogen studies are now assuming different dimensions. The alternative strategy for VBD involving the vaccination with Subolesin/akirin (SUB/AKR) antigen is gaining importance. VBD is the vector control for mosquitoes, ticks and sandflies to reduce the female survival and fertility [111]. Multi-component DNA-prime/DNA-boost vaccine (TcVac1) have been reported to enable partial resistance to T. cruzi infection and Chagas disease against experimental T. cruzi infection in a dogs [112]. Vaccination strategies to control cutaneous Leishmaniasis have also been reported. Vaccination involves infection with live-attenuated Leishmania, immunisation with DNA vaccines or purified proteins and immunization against the saliva of vector [113].

The evolutionary response of the parasite evoked as key to co-evolutionary interactions between parasite and host [41]. A lot of research is gaining prevalence in the field of host-parasite co-evolution. A detailed understanding of vector borne parasitic diseases, migration patterns of different parasites, their demographic history, cophylogeny mapping and integrated understanding of haplotype network are the topic of modern researches [114-116].

Insect Genomics are expanding and whole genome sequences are being developed and gene expression and regulation studies are throwing new light on manipulation of genes to regulate the vector competence. Several vectors like the *Anopheles*

gambiae, *Aedes aegypti*, *Culex pipiens* have been sequenced for their whole genome. The i5k programme for sequencing the genomes of 5000 insect species of agricultural, medical and veterinary as well as forensic importance has taken off and India is also a part of this world wide sequencing programme. The dangers of non-fatal diseases assuming fatality and deadly proportions because of dual infections of mildly pathogenic but curable diseases with virulent incurable diseases (malaria with concomitant HIV infections) have already started to wreak havoc in the fields of vector borne diseases. An integrated system of vector control, reservoir destruction, pathogen mortality, prevention of parallel infections and disease cure should bring in a paradigm shift in control of both pathogen and the vectors and eradication of the disease [117].

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