

Biology of Vectors and Agent of Skin Disease and River Blindness (Onchocerciasis) In the World

Hassan Vatandoost^{1,2*}

¹Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

²Department of Environmental Chemical Pollutants and Pesticides, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran

*Corresponding author

Hassan Vatandoost, Department of Medical Entomology and Vector Control, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran and Department of Environmental Chemical Pollutants and Pesticides, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran

Submitted: 25 Oct 2022; Accepted: 01 Nov 2022; Published: 07 Dec 2022.

Citation: Vatandoost, H. (2022). Biology of Vectors and Agent of Skin Disease and River Blindness (Onchocerciasis) In the World. *J Mari Scie Res Ocean*, 5(4), 253-264.

Abstract

Objectives: Blackflies are the aquatic insects. A total of 1800 species of this insect have been identified worldwide. The main important species is *Simulium damnosum*. They suck the blood of other animals and human. They spread several diseases, including river blindness (Onchocerciasis) in Africa and America. The agent of disease is *Onchocerca volvulus*. The aim of this review article is to explain the bio ecology, medically importance, different control measures for agent and vector of disease and status of resistant to drug and insecticides in the agent and vector.

Methods: In this research all, the relevant information regarding the topic of research is research through the internet and used in this paper. An intensive search of scientific literature was done in "PubMed", "Web of Knowledge", "Scopus", "Google Scholar", "SID", etc.

Results: The results indicated that this insect play an important role in disease worldwide. Ivermectine (Mectizan®) drug is an important for killing the agent of disease. Several larvicides recommended by WHO for vector control. Due to high use of drug and pesticide for control of disease, the resistant to drug and pesticide have been reported worldwide.

Conclusion: Monitoring and mapping of drug and insecticide resistance is a major factor for disease control worldwide.

Keywords: Blackflies, River Blindness, World, Control

Background

Blackflies belong to Order: Diptera, Su-order: Nematocera, Family: Simuliidae, Genus: Simulium, Species: *Simulium damnosum*, *S. neavei*, *S. callidum*, *S. metallicum*, *S. ochraceu*. They are called as: black fly, buffalo gnat, turkey gnat and white socks. Common names of black flies in other languages are: German: kriebelm, Norweigan: knott, Polish: meszkowate, French: simulie, Swedish: knott, Central America: bocone, South America: Chile, Jerjel. 1800 known species of black flies (of which 11 are extinct).

The majority of species belong to the immense genus Simulium. Most black flies sucking the blood of other animals and human. Although the males feed mainly on nectar. They are usually small, black or gray, with short legs and antennae. They are a common nuisance for humans. They spread several diseases, including river blindness in Africa (*Simulium damnosum* and *S. neavei*). In the Americas (*Simulium callidum*, *S. metallicum* and *S. ochraceu*) are exist. Eggs are laid in running water in batches ranging from 100-600 (Figure.1).

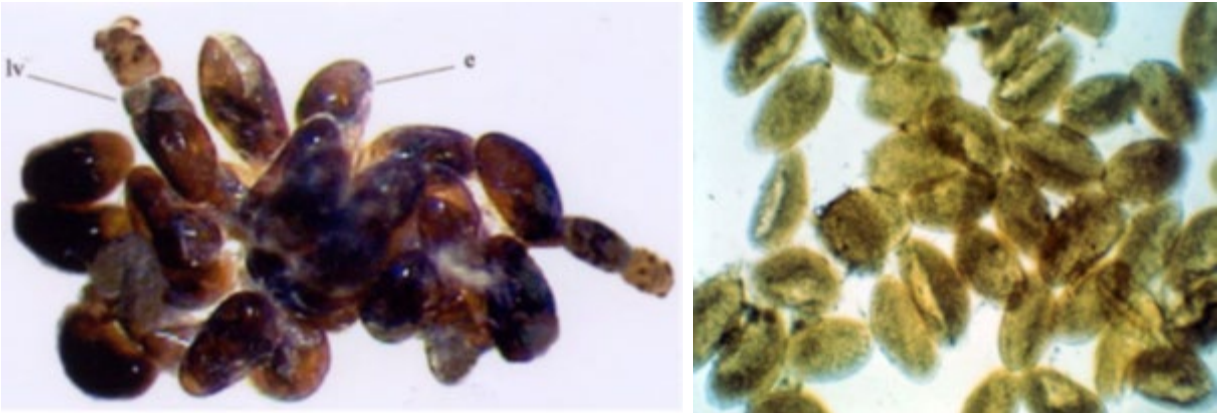


Figure 1: Eggs of blackfly

The larva have 6-9 instar. They are feeding on organic material. They have delicate cephalic fans comprised from a series of rays. The filter feeding mechanism is passive with debris being filtered directly from the passing current. Another morphological feature of the larva to facilitate feeding is a series of hooks at the rear of the abdomen. These are used to anchor the larva to a silk pad which the larva produce. The combination of the silk pad and abdominal hooks maintain the larvae position on the substrate in the fast flowing water. The cephalic fans are held into the current and periodically contracted to bring food particles to the cibarium by the mandibular brushes. On the body lying ventral to the head is a proleg which serves to produce two water currents traveling to

the left and right of the head and into the cephalic fans. Samples of gut content has shown that bacteria can contribute a considerable portion of the diet. Larvae attach themselves to rocks. Breeding success is highly sensitive to water pollution. The larvae use tiny hooks at the end of the abdomen to hold on to the substrate, using silk holdfasts and threads to move or hold their place. They have foldable fans surrounding their mouths. When feeding, the fans expand, catching passing debris (small organic particles, algae and bacteria). Black flies depend on lotic habitats to bring food to them. They will pupate under water and then emerge in a bubble of air as flying adults. During emergence, they are often preyed upon by trout (Figure.2) .

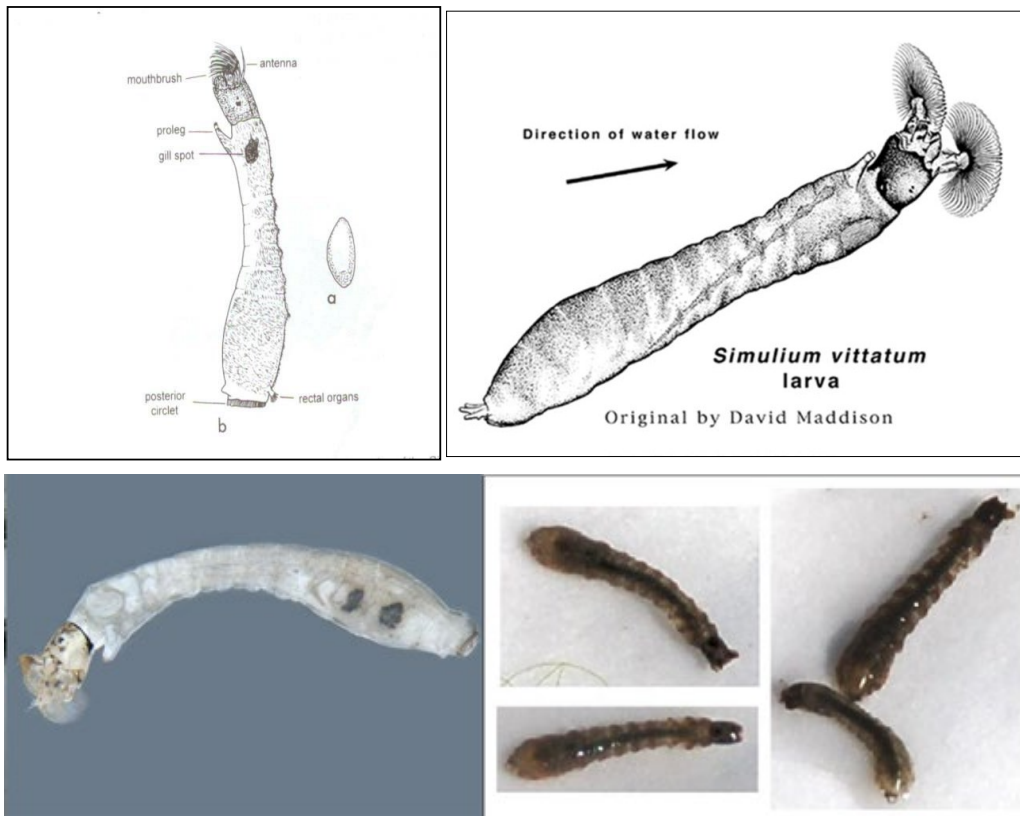




Figure 1: Larvae of blackfly

Pupae have the filaments on the anterior end (Figure.2)



Figure 2: Pupae of blackfly

The adult is recognized by its wings, antennae and abdominal base. The wings are short and broad, and have tubular veins only toward the leading edge. Eye facets on the upper half of the head are larger than those on the lower half in the male but are the same

in the female. The antennae are short and cylindrical, consisting of the scape, pedicel and 7–9 flagellar segments. The first abdominal segment is modified to form a prominent flange (Figure. 3).

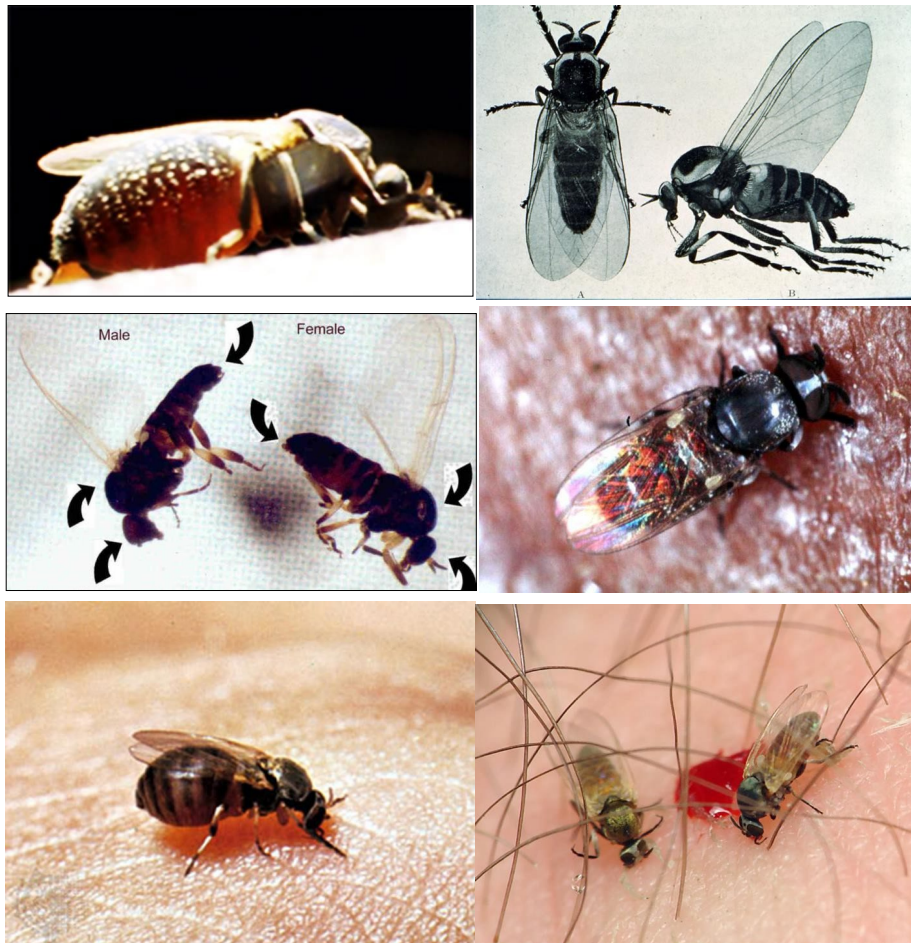


Figure 3: Adults of blackfly

Adults have special compound eyes (Figure.4)

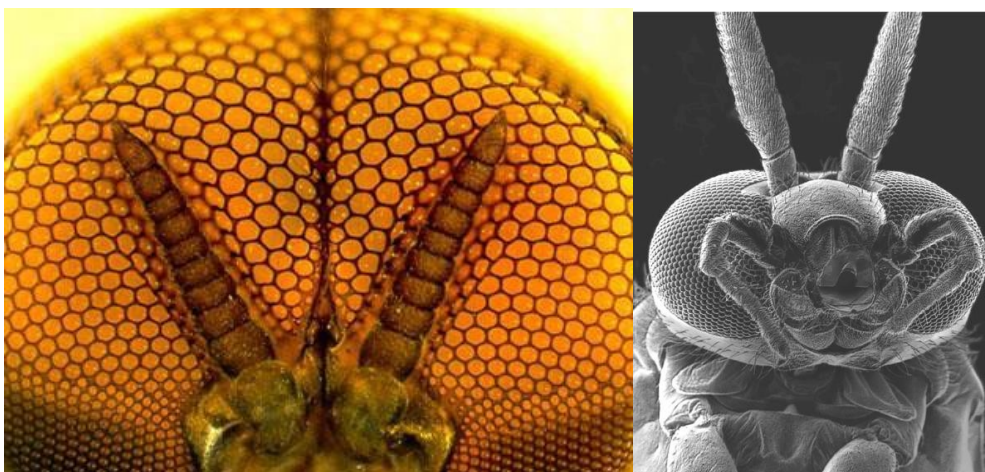


Figure 4: special compound eyes in adults

Some species in Africa can range as far as 40 miles from aquatic breeding sites in search of their blood meals, while other species have more limited range. Fig. 6 show the breeding places of blackflies.



Figure 6: Breeding places of blackflies

There are several species of blackflies in the world including: *Simulium aestivum* Davies, Peterson et Wood, 1962, *Simulium albicinctum* (Enderlein, 1933), *Simulium albilineatum* (Enderlein, 1936), *Simulium albopictum* Lane et Porto, 1940, *Simulium alirioi* Perez et Vulcano, 1973, *Simulium amazonicum* Goeldi, 1905, *Simulium anamariae* Vulcano, 1962, *Simulium anatinum* Wood, 1963, *Simulium angrense* Pinto, 1931, *Simulium antillarum* Jennings, 1915, *Simulium antonii* Wygodzinsky, 1953, *Simulium antunesi* Lane et Porto, 1940, *Simulium aranti* Stone et Snoddy, 1969, *Simulium arcticum* Malloch, 1914, *Simulium argentatum* Enderlein, 1936, *Simulium argus* Williston, 1893, *Simulium aureum* Fries, 1824, *Simulium auripellitum* Enderlein, 1933, *Simulium auriatriatum* Lutz, 1910, *Simulium baffinense* Twinn, 1936, *Simulium baiense* Pinto, 1931, *Simulium barbatipes* Enderlein, 1933, *Simulium beaupertuyi* Perez, Rassi, Ramirez, 1977, *Simulium bicoloratum* Malloch, 1913, *Simulium bicorne* Dorog., Rubtsov, et Vlasenko, 1935, *Simulium bivittatum* Malloch, 1914, *Simulium blancasi* Wygodzinsky, Coscaron, 1070, *Simulium bordai* Coscaron, Wygodzinsky, 1910, 1848, *Simulium botulibranchium* Lutz, 1910, *Simulium brachycladum* Lutz, Pinto, 1931, *Simulium bracteatum* Coquillett, 1898, *Simulium brevifurcatum* Lutz, 1910, *Simulium caledonense* Adler et Currie, 1986, *Simulium callidum* Dyar et Shannon, 1927, *Simulium canadense* Hearle, 1932, *Simulium canonicola* (Dyar et Shannon, 1927), *Simulium catarinense* Pinto, 1931, *Simulium cauchense* Floch, Abonnenc, 1946, *Simulium cerqueira* Almeida, 1974, *Simulium chalcocoma* Knab, 1914, *Simulium clarkei* Stone et Snoddy, 1969, *Simulium clarki* Fairchild, 1940,

Simulium clavibranchium Lutz, 1910, *Simulium congareenarum* (Dyar et Shannon, 1927), *Simulium conviti* Perez et Vulcano, 1973, *Simulium corbis* Twinn, 1936, *Simulium cormonsi* Wygodzinsky, 1971, *Simulium costaricense* Smart, 1944, *Simulium coto-paxi* Wygodzinsky et Coscaron, 1979, *Simulium craigi* Adler et Currie, 1986, *Simulium croxtoni* Nicholson et Mickel, 1950, *Simulium cuneatum* (Enderlein, 1936), *Simulium decollectum* Adler et Currie, 1986, *Simulium decorum* Walker *Simulium defoliarti* Stone

et Peterson, 1958, *Simulium dinellii* Joan, 1912, *Simulium diversibranchium* Lutz, 1910, *Simulium diversifurcatum* Lutz, 1910, *Simulium dixiense* Stone et Snoddy, 1969, *Simulium downsi* Vargas, Palacio, Nayera, 1946, *Simulium duplex* Shewell et Fredeen, 1958, *Simulium dureti* Wygodzinsky, Coscaron, 1967, *Simulium ecuadoriense* Enderlein, 1934, *Simulium emarginatum* Davies, Peterson et Wood, 1962, *Simulium enciso* Vargas et Diaz Najera, 1949, *Simulium escomeli* Roubaud, 1909, *Simulium ethelae* Dalmat, 1950, *Simulium euryadminiculum* Davies, 1949, *Simulium excisum* Davies, Peterson et Wood, 1962, *Simulium exiguum* Roubaud, 1906, *Simulium fibrinflatum* Twinn, 1936, *Simulium flavifemur* Enderlein, 1921, *Simulium flavipictum* Knab, 1914, *Simulium flavopubescens* Lutz, 1910, *Simulium fulvibnotum* Cerqueira et Mello, 1968, *Simulium furculatum* (Shewell, 1952), *Simulium gabaldoni* Perez, 1971, *Simulium gaudeatum* Knab, 1914, *Simulium gaurani* Coscaron et Wygodzinsky, 1972, *Simulium giganteum* Rubtsov, 1940, *Simulium goeldi* Cerqueira et Mello, 1967 *Simulium gouldingi* Stone, 1952, *Simulium grerreroi* Perez, 1071, *Simulium griseum* Coquillett, 1898, *Simulium guianense* Wise, 1911, *Simulium guttatum* (Enderlein, 1936), *Simulium haematopotum* Malloch, 1914, *Simulium haematoptum* Malloch, *Simulium hay-si* Stone et Snoddy, 1969, *Simulium herreri* Wygodzinsky et Coscaron, 1967, *Simulium hirtipupa* Lutz, 1910, *Simulium hoffmanni* Vargas, 1943, *Simulium hunteri* Malloch, 1914, *Simulium ignacioi* Perez et Vulcano, 1973, *Simulium ignescens* Roubaud, 1906, *Simulium impar* Davies, Peterson et Wood, 1962, *Simulium inaequale* Paterson Ans Shannon, 1927, *Simulium incertum* Lutz, 1910, *Simulium incrustatum* Lutz, 1910, *Simulium inexorable* Schrottky, 1909, *Simulium innocens* (Shewell, 1952), *Simulium iracouboense* Floch et Abonnenc, 1946, *Simulium itaunense* D'andretta et Gonzalez, 1964, *Simulium jacumbae* Dyar et Shannon, 1927, *Simulium jaimeramirezi* Wygodzinsky, 1971, *Simulium jenningsi* Malloch, 1914, *Simulium johannseni* Hart, 1912, *Simulium jonesi* Stone et Snoddy, 1969, *Simulium jujuyense* Paterson et Shannon, *Simulium acarayense* Coscaron, Wygodzinsky, 1972, 1927, *Simulium jundiaense* D'andretta et Gonzalez, 1964, *Simulium kabanayense* Perez et Volcano,

1973, *Simulium lahillei* Paterson et Shannon, 1927, *Simulium lakei* Snoddy, 1976, *Simulium laneportoi* Vargas, 1941, *Simulium lassmanni* Vergas, Martinez, 1946, *Simulium laticox* Enderlein, 1933, *Simulium latidigitus* Enderlein, 1936, *Simulium latipes* Meigen, 1804, *Simulium lewisi* Perez, 1971, *Simulium limbatum* Knab, 1915, *Simulium longistylatum* Shewell, 1959, *Simulium luggeri* Nicholson et Mickel, 1950, *Simulium lurybayae* Smart, 1944, *Simulium lutzianum* Pinto, 1931, *Simulium machadoallisoni* Vulcano, 1981, *Simulium major* Lane et Porto, 1940, *Simulium maly-schevi* Dorog., Rubtsov, et Vlasenko, 1935, *Simulium manicatum* Enderlein, 1933, *Simulium maroniense* Floch et Abonnenc, 1946, *Simulium matteabanchia* Anduze, 1947, *Simulium mbarigui* Coscaron et Wygodzinsky, 1973, *Simulium mediovittatum* Knab, 1916, *Simulium meridionale* Riley, 1887, *Simulium meruoca* Mello, Almeida, Dellome, 1973, *Simulium metallicum* Bellardi, 1859, Hagen, 1880, *Simulium mexicanum* Bellardi, 1862, *Simulium minus* (Dyar et Shannon, 1927), *Simulium minusculum* Lutz, *Simulium morae* Perez, Rassi, Ramirez, 1977, *Simulium mutucuna* Mello et Silva, 1974, *Simulium nebulosum* Currie et Adler, 1986, *Simulium nigricoxum* Stone, 1950, *Simulium nogueirai* D'andretta et Gonzalez, 1964, *Simulium notatum* Adams, 1904, *Simulium notiale* Stone et Snoddy, 1969, *Simulium nunestovari* Perez, Rassi, et Ramirez, 1977, *Simulium nyssa* Stone et Snoddy, 1969, *Simulium obesum* Vulcano, 1959, *Simulium ochraceum* Walker, 1861, *Simulium opalinifrons* Enderlein, 1934, *Simulium orbitale* Lutz, 1910, *Simulium ortizi* Perez, 1971, *Simulium oviedo* Perez, 1971, *Simulium oyapockense* Floch et Abonnenc, 1946, *Simulium paraguayense* Schrottky, 1909, *Simulium paranense* Schrottky, 1909, *Simulium parnassum* Malloch, 1914, *Simulium paynei* Vargas, 1942, *Simulium penobscotensis* Snoddy et Bauer, 1978, *Simulium perflavum* Roubaud, 1906, *Simulium pertinax* Kollar, 1832, *Simulium petersoni* Stone et Defoliart, 1959, *Simulium pictipes*, *Simulium pilosum* (Knowlton et Rowe, 1934), *Simulium pinto* D'andretta et D'andretta, 1946, *Simulium piperi* Dyar et Shannon, 1927, *Simulium podostemi* Snoddy, 1971, *Simulium prodexargenteum* (Enderlein, 1936), *Simulium pruinatum* Lutz, 1910, *Simulium pseudoexiguum* Mello et Almeida, 1974, *Simulium pugetense* (Dyar et Shannon, 1927), *Simulium pulverulentum* Knab, 1914, *Simulium quadrifidum* Lutz, 1917, *Simulium quadristrigatum* Enderlein, 1933, *Simulium quadrivittatum* Loew, *Simulium quebecense* Twinn, 1936, *Simulium racenisi* Perez, 1971, *Simulium rangeli* Perez, 1977, *Simulium rivasi* Perez, 1971, *Simulium rivuli* Twinn, 1936, *Simulium rorotaense* Floch et Abonnenc, 1946, *Simulium rubiginosum* Enderlein, 1933, *Simulium rubrithorax* Lutz, 1909,

Simulium rubtzovi Smart, 1945, *Simulium rugglesi* Nicholson et Mickel, 1950, *Simulium samboni* Jennings, 1915, *Simulium sanguineum* Knab, 1915, *Simulium schmidtummi* Wygodzinsky, 1973, *Simulium scutistriatum* Lutz, 1909, *Simulium seriatum* Knab, 1914, *Simulium sicuani* Smart, 1944, *Simulium*

simplicicolor Lutz, 1910, *Simulium slossonae* Dyar et Shannon, 1927, *Simulium snowi* Stone et Snoddy, 1969, *Simulium solaris* Stone, 1948, *Simulium spadicidorsum* (Enderlein, 1934), *Simulium spinibranchium* Lutz, 1910, *Simulium spinifer* Knab, 1914, *Simulium strigatum* (Enderlein, 1933), *Simulium strigidorsum* (Enderlein, 1933), *Simulium striginotum* (Enderlein, 1933), *Simulium suarezi* Perez, Rassi et Ramirez, 1977, *Simulium subclavibranchium* Lutz, 1910, *Simulium subnigrum* Lutz, 1910, *Simulium subpallidum* Lutz, 1910, *Simulium tallaferrae* Perez, 1971, *Simulium tarsale* Williston, 1896, *Simulium tarsatum* Macquart, 1847, *Simulium taxodium* Snoddy et Beshear, 1968, *Simulium tescorum* Stone et Boreham, 1965, *Simulium townsendi* Malloch, 1912, *Simulium transiens* Rubtsov, 1940, *Simulium travassosi* D'andretta et D'andretta, 1947, *Simulium trivittatum* Malloch, 1914, *Simulium truncata* (Lundstrom, 1911), *Simulium tuberosum* (Lundstrom, 1911), *Simulium underhilli* *Simulium pifanoi* Perez, 1971, 1969, *Simulium urubambanum* Enderlein, 1933, *Simulium varians* Lutz, 1909, *Simulium venator* Dyar et Shannon, 1927, *Simulium venustum* Say, 1823, *Simulium verecundum* Stone et Jamnback, 1955, *Simulium vernum* (Macquart, 1826), *Simulium versicolor* Lutz et Tovar, 1928, *Simulium violacescens* Enderlein, 1933, *Simulium virgatum* Coquillett, 1902, *Simulium vittatum* (Zetterstedt, 1838), *Simulium wuayaraka* Ortiz, 1957, *Simulium wyomingense* (Stone et De Foliart, 1959), *Simulium yacuchuspi* Wygodzinsky et Coscaron, 1967.

Methods

In this research all the relevant information regarding the topic of research is research through the internet and used in this paper. An intensive search of scientific literature was done in "PubMed", "Web of Knowledge", "Scopus", "Google Scholar", "SID", etc.

Results and Discussion

Medical Importance of blackflies

The black fly is central to the transmission of the parasitic nematode *Onchocerca volvulus*, which causes Onchocerciasis, also known as river blindness. It serves as the larval host for the nematode and acts as the vector by which the disease is spread. Transmission of the parasite

occurs through the bite of a black fly when feeding on human blood. Fishermen, farmers and loggers are frequently bitten by the black flies that transmit onchocerciasis. Figure 7 shows the world distribution of Onchocerciasis (river blindness). The disease is endemic across equatorial Africa where an estimated 99% of those infected live, and in certain areas of Central and South America. Up to 86 million are at risk of acquiring infection, and an estimated 600,000 people are visually impaired by the disease, with half of them partially or totally blind. In hyper endemic areas, infection rates approach 100%, and over a lifetime, 50% of the population will be blinded by the disease.

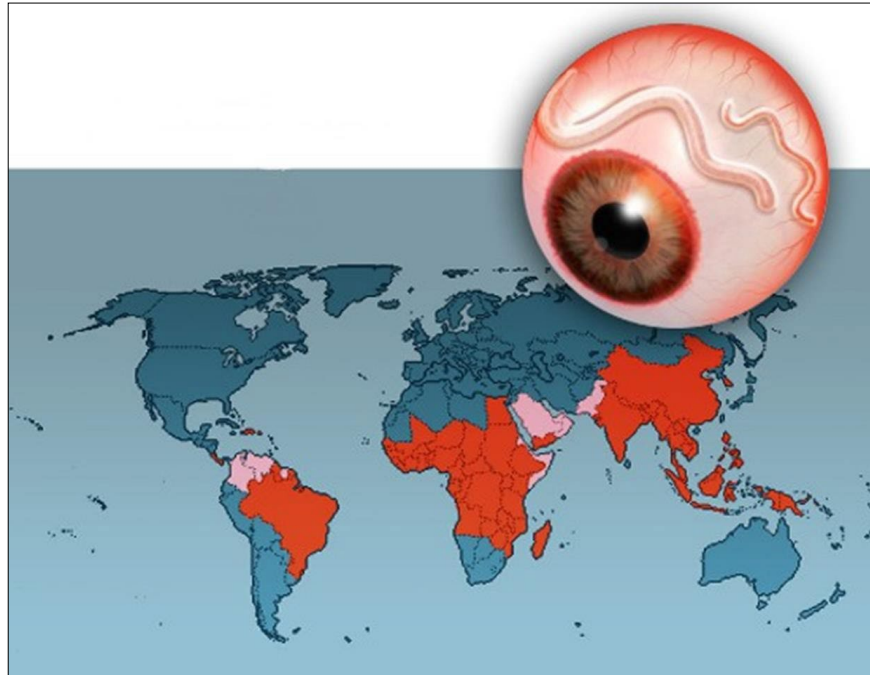


Figure 7: world distribution of Onchocerciasis (river blindness)

Onchocerciasis is caused by *O. volvulus* (Figure.8,9) , a parasitic worm that lives for up to 14 years in the human body. Each adult female worm, thin but more than 1/2 meter in length, produces millions of microfilariae (microscopic larvae) that migrate throughout the body and give rise to a variety of symptoms: serious visual impairment, including blindness; rashes, lesions, intense itching and depigmentation of the skin; lymphadenitis, which results in hanging groins and elephantiasis of the genitals; and general debilitation. Onchocerciasis manifestations begin to occur in persons one to three years after the injection of infective larvae. Within the human body, the adult female worm (macrofilaria) produces thousands of baby or larval worms (microfilariae) which migrate in the skin and the eye (Figure.10). In the human host, adult worms can live for 15 years in the human body. The male and female worms enter in nodules in the subcutaneous tissue of the skin. After mating, the female worm releases around 1000 microfilariae larvae a day into the surrounding tissue. Microfilariae live for 1–2 years, moving around the body in the subcutaneous tissue. When they die, they cause an inflammatory response that leads to skin rashes, lesions, intense itching and skin depigmentation. Microfilariae also migrate to the eye, where they cause inflammation and other complications that can lead to blindness.

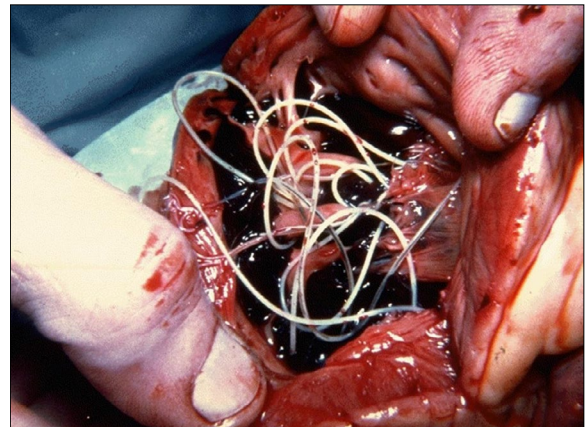


Figure 8: *Onchocerca volvulus* , the agent of river blindness.



Figure 9: *Onchocerca volvulus*: nodules (removed from under the skin of infected people) contain the adult worms.



Figure 10: symptoms of river blindness

Patient infected with *Onchocerca volvulus*. The parasite which causes onchocerciasis (river blindness). This elderly man shows nodules, skin changes and blindness, all manifestations of the disease (Fig.11) (1-3).



Figure 11: Manifestations of the disease

Drug Treatment: The development of ivermectin in the 1980s provided a safe, effective drug for killing microfilariae in infected people. Diethylcarbamazine (DEC) only kills microfilaria. Ivermectine (Mectizan®) (150 microgram/kg single dose) only kills microfilaria. Suramin only kills macrofilaria.

Vector Control: The insecticide is introduced into rivers and streams in several places. The number of application points should be determined from a preliminary survey and will vary by area and river according to the insecticide formulation used, the breeding habits of the local vector and the characteristics of the watercourse, such as flow rate. In the area covered by the Onchocerciasis Control Programme, temephos was initially the preferred larvicide because of its effectiveness, the distance down river from

the application point at which it remains effective and its relative safety for non-target fauna. The appearance of resistance in West Africa in 1980, however, required adoption of a strategy in which insecticides with other modes of action were used alternately, to stop further development and spread of resistance and to forestall the appearance of new cases of resistance. This strategy of rotation of insecticides proved effective during the 15 years in which it was implemented. *B. thuringiensis* H-14 is used at relatively high doses and has a short distance of effectiveness. Nevertheless, it was the main larvicide used during the last 10–15 years of the Onchocerciasis various larvicides can be applied including *Bacillus thuringiensis*, Carbosulf, Phoxim, Pyraclofos, Temephos, Permethrin and Etofenprox. Generally, *B. thuringiensis* H-14 is the preferred larvicide. In areas where there is no

resistance, this product can be supplemented by temephos, especially when river discharges are relatively high and cannot be measured precisely for the proper dosage of the insecticide. There are several reports of drug and insecticide resistance in the agent and vectors of disease worldwide [1-21].

Conclusion

Results showed ivermectin as drug resistance in agent (*Onchocerca volvulus*) and a wide variety of susceptibility/resistance status of *Simulium damnosum* to insecticides in the world. Due to the importance of these species in the transmission of diseases, resistance management strategies should be further considered to prevent insecticide resistance and replacement of novel approaches for vector control [22-53].

Conflict of interest

The author declare that there is no conflict of interest.

Acknowledgments

This research is financially supported by Ministry of Health and Medical Education, Iran, under code number of NIMAD 995633.

References

1. Ya'cob, Z., Takaoka, H., Pramual, P., Low, V. L., & Sofian-Azirun, M. (2016). Distribution pattern of black fly (Diptera: Simuliidae) assemblages along an altitudinal gradient in Peninsular Malaysia. *Parasites & vectors*, 9(1), 1-16.
2. Service, M. W. (2008). *Medical Entomology for Students*. Cambridge University Press. 2008, 81-92.
3. World Health Organization (WHO) (2002). *Success in Africa; the Onchocerciasis Control Programme in West Africa, 1974-2002*. WHO, Geneva.
4. World Health Organization. (2016). *Guidelines for stopping mass drug administration and verifying elimination of human onchocerciasis: criteria and procedures (No. WHO/HTM/NTD/PCT/2016.1)*. World Health Organization.
5. World Health Organization (WHO) (2017). *Progress report on the elimination of human onchocerciasis, 2016-2017*. WHO Wkly. Epidemiol. Rec. 92:681-94.
6. Cheke, R. A. (2017). Factors affecting onchocerciasis transmission: lessons for infection control. *Expert review of anti-infective therapy*, 15(4), 377-386.
7. Davies, J. B., Crosskey, R. W., & World Health Organization. (1991). *Simulium-vectors of onchocerciasis (No. WHO/VBC/91.992*. Unpublished). World Health Organization.
8. Wilson, M. D., Post, R. J., & Gomulski, L. M. (1993). Multivariate morphotaxonomy in the identification of adult females of the *Simulium damnosum* Theobald complex (Diptera: Simuliidae) in the Onchocerciasis Control Programme area of West Africa. *Annals of Tropical Medicine & Parasitology*, 87(1), 65-82.
9. Remme, J. H. F. (1995). *The African programme for onchocerciasis control: preparing to launch*.
10. World Health Organization (WHO) (2017). *Integrating neglected tropical diseases into global health and development". Fourth WHO report on neglected tropical diseases*.
11. Davies, J. B. (1994). Sixty years of onchocerciasis vector control: a chronological summary with comments on eradication, reinvasion, and insecticide resistance. *Annual review of entomology*, 39(1), 23-45.
12. Boatin, B. (2008). The onchocerciasis control programme in West Africa (OCP). *Annals of Tropical Medicine & Parasitology*, 102(sup1), 13-17.
13. Norman, R. A., Chan, M. S., Srividya, A., Pani, S. P., Ramaiah, K. D., Vanamail, P., ... & Bundy, D. A. (2000). EPIFIL: the development of an age-structured model for describing the transmission dynamics and control of lymphatic filariasis. *Epidemiology & Infection*, 124(3), 529-541.
14. Duerr, H. P., Raddatz, G., & Eichner, M. (2011). Control of onchocerciasis in Africa: threshold shifts, breakpoints and rules for elimination. *International journal for parasitology*, 41(5), 581-589.
15. Colebunders, R., Stolk, W. A., Siewe Fodjo, J. N., Mackenzie, C. D., & Hopkins, A. (2019). Elimination of onchocerciasis in Africa by 2025: an ambitious target requires ambitious interventions. *Infectious diseases of poverty*, 8(1), 1-3.
16. Fobi, G., Yameogo, L., Noma, M., Aholou, Y., Koroma, J. B., Zouré, H. M., ... & ROUNGOU, J. B. (2015). Managing the fight against onchocerciasis in Africa: APOC experience. *PLoS neglected tropical diseases*, 9(5), e0003542.
17. Gustavsen, K., Hopkins, A., & Sauerbrey, M. (2011). Onchocerciasis in the Americas: from arrival to (near) elimination. *Parasites & Vectors*, 4(1), 1-6.
18. Basanez, M. G., Collins, R. C., Porter, C. H., Little, M. P., Brandling-Bennett, D. (2002). "Transmission intensity and the patterns of *Onchocerca volvulus* infection in human communities. *Am. J. Trop. Med. Hyg.*, 67, 669-679.
19. Sauerbrey, M., Rakers, L. J., & Richards, F. O. (2018). Progress toward elimination of onchocerciasis in the Americas. *International health*, 10(suppl_1), i71-i78.
20. World Health Organization (WHO) (2019). "Onchocerciasis elimination mapping of endemic countries is key to defeating river blindness", Geneva: World Health Organization
21. Turner, H. C., Walker, M., Lustigman, S., Taylor, D. W., & Basáñez, M. G. (2015). Human onchocerciasis: modelling the potential long-term consequences of a vaccination programme. *PLoS neglected tropical diseases*, 9(7), e0003938.
22. Légaré, D., & Ouellette, M. (2017). Drug resistance assays for parasitic diseases. In *Antimicrobial drug resistance* (pp. 1409-1463). Springer, Cham.
23. Hotterbeekx, A., Ssonko, V. N., Oyet, W., Lakwo, T., & Idro, R. (2019). Neurological manifestations in *Onchocerca volvulus* infection: A review. *Brain Research Bulletin*, 145, 39-44.
24. Jacob, B., Loum, D., Munu, D., Lakwo, T., Byamukama, E., Habomugisha, P., ... & Unnasch, T. R. (2021). Optimization of slash and clear community-directed control of *Simulium damnosum* sensu stricto in Northern Uganda. *The American Journal of Tropical Medicine and Hygiene*, 104(4), 1394.

25. Paugy, D., Fermon, Y., Abban, K. E., Diop, M. E., & Traoré, K. (1999). Onchocerciasis Control Programme in West Africa: a 20-year monitoring of fish assemblages. *Aquatic Living Resources*, 12(6), 363-378.
26. Kurtak, D. C. (1990). Maintenance of effective control of *Simulium damnosum* in the face of insecticide resistance. *Acta Leidensia*, 59(1-2), 95-112.
27. Yaméogo, L., Crosa, G., Samman, J., Nabé, K., Kondé, F., Tholley, D., & Calamari, D. (2001). Long-term assessment of insecticides treatments in West Africa: aquatic entomofauna. *Chemosphere*, 44(8), 1759-1773.
28. Bourguinat, C., Ardelli, B. F., Pion, S. D., Kamgno, J., Gardon, J., Duke, B. O., ... & Prichard, R. K. (2008). P-glycoprotein-like protein, a possible genetic marker for ivermectin resistance selection in *Onchocerca volvulus*. *Molecular and biochemical parasitology*, 158(2), 101-111.
29. Kumar, A., Muthamilselvan, S., & Palaniappan, A. (2020). Computational studies of drug repurposing targeting P-glycoprotein-mediated multidrug resistance phenotypes in priority infectious agents. In *Biomarkers and Bioanalysis Overview*. IntechOpen.
30. Montagna, C. M., Anguiano, O. L., Gauna, L. E., & Pechen DE D-Angelo, A. M. (2003). Mechanisms of resistance to DDT and pyrethroids in Patagonian populations of *Simulium* blackflies. *Medical and Veterinary Entomology*, 17(1), 95-101.
31. Lévêque, C., Hougard, J. M., Resh, V., Statzner, B., & Yameogo, L. (2003). Freshwater ecology and biodiversity in the tropics: what did we learn from 30 years of onchocerciasis control and the associated biomonitoring of West African rivers?. In *Aquatic Biodiversity* (pp. 23-49). Springer, Dordrecht.
32. Curtis, C. F., & Hill, N. (1993). Are there effective resistance management strategies for vectors of human disease?. *Biological Journal of the Linnean Society*, 48(1), 3-18.
33. Hougard, J. M., Poudiougou, P., Guillet, P., Back, C., Akpoboua, L. K. B., & Quillévéré, D. (1993). Criteria for the selection of larvicides by the Onchocerciasis Control Programme in West Africa. *Annals of Tropical Medicine & Parasitology*, 87(5), 435-442.
34. Hemingway, J., Callaghan, A., & Kurtak, D. C. (1991). Biochemical characterization of chlorphoxim resistance in adults and larvae of the *Simulium damnosum* complex (Diptera: Simuliidae). *Bulletin of Entomological Research*, 81(4), 401-406.
35. Lacey, L. A., Escaffre, H., Philippon, B., Seketeli, A., & Guillet, P. (1982). Large river treatment with *Bacillus thuringiensis* (H-14) for the control of *Simulium damnosum* sl in the Onchocerciasis Control Programme. *Tropenmedizin und Parasitologie*, 33(2), 97-101.
36. KURTAK, D., MEYER, R., OCRAN, M., OUÉDRAOGO, M., RENAUD, P., Sawadogo, R. O., & TELE, B. (1987). Management of insecticide resistance in control of the *Simulium damnosum* complex by the Onchocerciasis Control Programme, West Africa: potential use of negative correlation between organophosphate resistance and pyrethroid susceptibility. *Medical and veterinary entomology*, 1(2), 137-146.
37. Kurtak, D., Jamnback, H. U. G. O., Meyer, R. O. L. F., Ocraan, M., & Renaud, P. (1987). Evaluation of larvicides for the control of *Simulium damnosum* (Diptera: Simuliidae) in West Africa. *Journal of the American Mosquito Control Association*, 3(2), 201-210.
38. Yameogo, L., Tapsoba, J. M., Bihoum, M., & Quillevere, D. (1993). Short-term toxicity of pyraclofos used as a blackfly larvicide on non-target aquatic fauna in a tropical environment. *Chemosphere*, 27(12), 2425-2439.
39. Garms, R., & Cheke, R. A. (1985). Infections with *Onchocerca volvulus* in different members of the *Simulium damnosum* complex in Togo and Benin. *Zeit Ange Zool*, 72, 479-495.
40. Regis, L., da Silva, S. B., & Melo-Santos, M. A. V. (2000). The use of bacterial larvicides in mosquito and black fly control programmes in Brazil. *Memórias do Instituto Oswaldo Cruz*, 95, 207-210.
41. Hendy, A. (2018). Blackfly ecology and** *Onchocerca volvulus*** transmission in three formerly hyperendemic foci in Uganda, Tanzania and Cameroon (Doctoral dissertation, University of Antwerp).
42. Palmer, R. W. (1995). Biological and chemical control of blackflies (Diptera: Simuliidae) in the orange river, Onderstepoort Veterinary Institute. South Africa, PP.119.
43. Adiamah, J. H., Raybould, J. N., Kurtak, D., Israel, A., Mae-gga, B. T. A., & Opoku, A. K. (1986). The susceptibility of *Simulium damnosum* sl larvae from the Volta River in southern Ghana to temephos after nearly eight years of intermittent treatment. *International Journal of Tropical Insect Science*, 7(1), 27-30.
44. Osei-Atweneboana MY, Wilson MD, Post RJ, Boakye DA. (2000)."Temephos-resistant larvae of *Simulium sanctipauli* associated with a distinctive new chromosome inversion in untreated rivers of south-western Ghana ".*Med .Vet. Entomol.*, 15(1), 113-116.
45. Osei-Atweneboana MY. (1996). "Studies on in vitro colonization, karyomorphology, and temephos susceptibility of *Simulium damnosum* Theobald complex". UGSpace. <http://197.255.68.203/handle/123456789/6224>.
46. Palmer, R. W., & Rivers-Moore, N. A. (2008). Evaluation of larvicides in developing management guidelines for long-term control of pest blackflies (Diptera: Simuliidae) along the Orange River, South Africa. *Onderstepoort Journal of Veterinary Research*, 75(4), 299-314.
47. Hemingway, J., Callaghan, A., & Kurtak, D. C. (1989). Temephos resistance in *Simulium damnosum* Theobald (Diptera: Simuliidae): a comparative study between larvae and adults of the forest and savanna strains of this species complex. *Bulletin of Entomological Research*, 79(4), 659-670.
48. Montagna, C. M., Gauna, L. E., D'Angelo, A. P. D., & Anguiano, O. L. (2012). Evolution of insecticide resistance in non-target black flies (Diptera: Simuliidae) from Argentina. *Memórias do Instituto Oswaldo Cruz*, 107, 458-465.

-
49. Boakye, D. A. (1999). Insecticide resistance in the *Simulium damnosum* sl vectors of human onchocerciasis: distributional, cytotaxonomic and genetical studies. In *Insecticide resistance in the Simulium damnosum SL vectors of human onchocerciasis: distributional, cytotaxonomic and genetical studies*.
50. Hougard, J. M., Escaffre, H. E. N. R. I., Darriet, F. R. E. D. É. R. I. C., Lochouart, L., Rivière, F., & Back, C. (1992). An episode of resistance to permethrin in larvae of *Simulium squamosum* (Diptera: Simuliidae) from Cameroon, after 3 years of control. *Journal of the American Mosquito Control Association*, 8, 184-186.
51. Barry, M. A., Murray, K. O., Hotez, P. J., & Jones, K. M. (2016). Impact of vectorborne parasitic neglected tropical diseases on child health. *Archives of Disease in Childhood*, 101(7), 640-647. doi: 10.1136/archdischild-2015-308266.
52. Sam-Wobo, S. O., Adeleke, M. A., Mafiana, C. F., & Surakat, O. H. (2011). Comparative repellent activities of some plant extracts against *Simulium damnosum* complex. *Vector-Borne and Zoonotic Diseases*, 11(8), 1201-1204.

Copyright: ©2022: Hassan Vatandoost. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.