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VIEW OF MALARIA AS ONE OF THE CAUSES OF FEVER OF UNKNOWN ORIGIN

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Abstract. *This article discusses malaria as one of the possible causes of fever of unknown origin. On the territory of Ukraine, there are mosquitoes of the Anopheles genus, which carry the causative agent of malaria - malaria plasmodium, therefore malaria cases may occur in our country.*

Key words: *malaria, malarial plasmodium, transmissible diseases, fever of unknown origin*

Introduction.

Fever of unknown origin is a clinical syndrome of various etiology, the main symptom of which is fever that does not go away on its own and lasts for more than 3 weeks, the cause of which has not been established [2]. One of the causes of this clinical syndrome can be a disease caused by the malaria plasmodium. Malaria is the deadliest human communicable disease in the world.

Main text.

Malaria is an ancient human disease, and fatal intermittent fever and splenomegaly have been mentioned as early as 2700 BC in Egypt and China. Malaria arrived in Rome in 200 BC, spread throughout Europe during the twelfth century, and arrived in England by the fourteenth century. This suggests that European explorers, conquistadors, and colonists imported Plasmodium malariae and Plasmodium vivax to the Americas. The arrival of Plasmodium falciparum coincided with the importation of African slaves, and by the early 1800s it had spread worldwide [4].

Analyzing the statistical reports of the Public Health Center of Ukraine in 2016, 43 imported cases of malaria were registered, one of the victims died. In 2017, 29 imported cases of malaria were registered in Ukraine, 3 victims died. 2020 - 19 cases of malaria, and in 2021 - 38 cases. Thus, we observed a 200% increase in diagnosis of this disease. In 9 months of 2022, 10 cases of malaria were registered in Ukraine, in the same period of 2021 there were 26 cases. The intensive indicator in 2021 was 0.06, and in 2022, respectively - 0.02.

Malaria is caused by six species of parasites belonging to the genus Plasmodium: P. falciparum, P. knowlesi, P. vivax, P. malariae, P. ovale curtisi and P. ovale wallikeri. [3] In addition to infecting mosquitoes and humans, other primates, bats, birds, and lizards can also be infected. As a result of travel to endemic countries, increasing urbanization, people become more prone to the risk of diseases. Although the overall global trend in malaria has decreased and stabilized over the past few

decades, there is an expectation that global warming will increase the incidence of malaria worldwide [5].

In the mosquito-human life cycle, six species of malaria parasites that infect humans (Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale wallickeri, Plasmodium ovale curtisi, Plasmodium malariae, and Plasmodium knowlesi) go through 10 or more morphological states, repeating between one and 10,000 + cells [6] Evidence suggests that P. vivax may account for 80% of infections, as this species is also most widely distributed in the tropics, subtropics, and temperate climates [4].

Malaria pathogens are characterized by two cycles of development with a change of host: 1) sexual — sporogony, 2) asexual — schizogony. Sporogony takes place in the stomach of the female Anopheles mosquito: fertilization of the female germ cell — zygote — ookinete — oocyst. Oocyst → sporozoites that enter the hemolymph of the mosquito and then the salivary glands. [7] Sporozoites become infectious for 2 weeks, after this period the female mosquito is contagious for another 1-2 months. It is during this period that a person becomes infected.

The course of schizogony in different species of Plasmodium is different. In it, two phases are distinguished: exoerythrocytic or tissue and erythrocytic. After entering the human blood, sporozoites circulate for about 30 minutes, and then penetrate the liver and tissue macrophages, where they become erythrocytic schizonts. Gradually, the schizonts divide and turn into a large number of merozoites. Merozoites enter the blood, where the erythrocytic cycle of the pathogen's development begins. After 3–4 erythrocyte cycles, a part of merozoites in erythrocytes forms sexual forms - gametocytes. Mature gametocytes appear in the peripheral blood several hours later than asexual forms. Further development of germ cells is possible only in the stomach of the mosquito, where they are fertilized and where they enter with the patient's blood during a bite. If the gametocytes do not enter the mosquito's body, after maturation they die in a few hours, and only in the case of tropical malaria - after 6 weeks. [7] Understanding the pathogenesis of malaria is important in understanding the course of the disease and appropriate treatment.

Clinical manifestations of malaria and their evolution can vary greatly. Both depend on the specific species of Plasmodium, the host's innate and acquired immunity, and the choice of appropriate and timely treatment. Malaria is usually divided into three types: asymptomatic, uncomplicated and severe [5].

Malaria symptoms usually appear 10-15 days after being bitten by an infected mosquito. The first manifestations, such as fever, headache, excessive sweating, weakness, can be expressed weakly, which complicates the initial detection of malaria. Indigestion, nausea, vomiting, diarrhea may also occur. Characteristic features of all types of malaria are a triad of symptoms - febrile attacks, hepatosplenomegaly, anemia [1]. When carrying out a differential diagnosis of a febrile condition in a patient who has returned after traveling to endemic areas, the possibility of malaria should be considered. Even if the trip, it would seem, was a long time ago. The risk group is also those persons who inform the doctor about taking prophylactic drugs against malaria. Children, pregnant women or people with weakened immunity deserve special attention. Clinical relapse of infections caused

by inactive P. vivax and P. ovale may recur several months after the initial infection, even if it has been cured [5].

The difficulty in diagnosing children, especially in the first three years of life, is that there are no typical malaria attacks. Possible acrocyanosis and cold extremities as an analogue of chills. Also, instead of typical attacks, hiccups are possible. Children are more prone to rapid progression of the disease with the development of exicosis. Hepatoleinal syndrome and anemia progress rapidly as well. Cramps, dyspeptic disorders, and abdominal pain may often be present.

Strong signs of suspected malaria are:

- stay in an endemic area for the past 2 years and the intermittent nature of the temperature curve lasting more than 5 days with an unknown disease;
- fever of unclear genesis that does not respond to antibacterial, antiviral, antifungal therapy;
- increased body temperature in patients with a history of malaria;
- progressive enlargement of the spleen and liver;
- anemia with fever of unknown origin;
- the patient has: chills, fever, sweating and the classic triad of malaria [1].

A physician practicing in countries generally considered non-endemic should have a high index of suspicion for malaria, including other hemorrhagic fevers (eg, dengue or, less commonly, Ebola), in patients with a history of fever who are traveling to or immigrating from an endemic area . Viral hemorrhagic fever can manifest itself in a similar way [5].

To identify Plasmodium species, blood microscopy is the main method used worldwide. Two decades ago, rapid diagnostic tests were introduced and improved over the years. They are very useful in remote areas where laboratory facilities are not available, but they only distinguish P. falciparum from other Plasmodium species (such as P. vivax); they also provided only limited sensitivity for low-level parasitemias [8]. Their performance can also be affected by parasite polymorphism [9]. In addition, ending malaria requires being able to accurately diagnose all types of malaria that infect humans, including P. malariae, P. ovale curtisi, P. ovale wallikeri, P. knowlesi, and other zoonotic variants. These results will also allow us to update their geographic distribution and obtain epidemiological data [3].

Malaria is currently under control with varying levels of eradication success in different countries. The development of new molecular tools and the use of next-generation sequencing (NGS) technologies and new bioinformatics approaches have improved our knowledge of malaria epidemiology, diagnosis, treatment, vaccine development and surveillance strategies [3].

Conclusions.

Malaria eradication is one of the directions of WHO's unceasing work. In recent years, enough information has been accumulated about the disease, parasites and mosquito vectors to realize that only a global approach can end this disease. Despite the fact that Ukraine is not an endemic center of malaria, we still have cases of infection. Due to the development of tourism and greater urbanization of wild areas, the probability of infection with anthroponoses, particularly malarial plasmodium, increases. In case of fever of unknown origin, one should not forget about the

possibility of infection with malaria plasmodium. A disease diagnosed in time and treated accordingly reduces the risk of contamination of the environment. The development of vaccines, the identification of genes associated with drug resistance should be considered in the future on a global scale.

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