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Letter to the Editor

Dengue: Should WHO Guidelines Be Expanded?

Patrice Bouree[1*]

[1]Tropical Diseases Department, Institut A. Fournier, Paris, France

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To Editor,

The best prophylaxis for infectious diseases is usually vaccination. However, in the case of dengue, the vaccine exists but its effectiveness is highly debated. The WHO provides limited recommendations. What is the current situation?

Dengue is the most widespread arboviral disease in the world, with approximately 400 million people infected each year, spread across 100 countries, affecting nearly half of humanity (1). In Asia, 10% of febrile patients are affected by dengue. In Europe, imported cases are significant, but indigenous cases are increasing. The vectors are mosquitoes from the *Aedes* family: *A. aegypti* and *A. albopictus*, whose geographical range is expanding each year, facilitated by human density, population mobility, and climate change. These mosquitoes transmit numerous viruses, including the 4 dengue viruses DENV1, DENV2, DENV3, and DENV4, with no cross-immunity between these viruses. Many patients remain asymptomatic (2). In other cases, symptoms begin a few days after the infesting bite, with fever, myalgias, headaches, a diffuse rash, and sometimes digestive disorders. The progression is usually favorable within a week. However, in 0.01% of cases, severe forms can occur, leading to death, with 500 000 hospitalizations and 20 000 deaths each year, particularly among children (3).

The critical phase can occur as soon as the fever subsides, with plasma leakage progressing towards shock. The biological assessment then shows hemoconcentration, hypoproteinemia, hypoalbuminemia, thrombocytopenia, and hepatic cytolysis. In the presence of any of these anomalies, there is a fivefold increased risk of progression to severe dengue (4). The first episode of dengue is usually moderate and mild, but a second episode is often more severe with a hemorrhagic risk. Complications are possible and varied, including cardiac, digestive, renal, pulmonary, hematological, neurological, or even ocular (5). This disease occurring in tropical environments, it is also necessary to mention other local febrile pathologies such as malaria, chikungunya, leptospirosis, rickettsiosis... The diagnosis is based on the epidemiological context and clinical symptoms and confirmed by the laboratory (leukopenia, thrombocytopenia, hepatic cytolysis, serology, presence of NS1 antigen).

The treatment is only symptomatic, avoiding anti-inflammatories and corticosteroids while favoring paracetamol. Prophylaxis is based on fighting mosquitoes and vaccination. But research in this field, which began more than 80 years ago, has proven to be more complicated than expected. A Brazilian vaccine, in a single dose, has shown an 80% efficacy. A TV005 vaccine studied by the National Institute of Allergy and Infectious Diseases is well tolerated. But the immunogenicity of these vaccines does not seem satisfactory for the 4 viruses. Moreover, the WHO has selected two live, attenuated, recombinant, and quadrivalent vaccines: Dengvaxia (Sanofi) and Qdenga. (Takeda). The Dengvaxia vaccine, prepared from a yellow fever vaccine strain, received marketing authorization in 2015. But it showed a risk of severe form in individuals who had never contracted dengue before. As a result, it was only recommended for individuals aged 9 to 45 who had already been infected with dengue and lived in endemic areas (6).

The indication being very limited at that time, the production of this vaccine was halted in 2024. There remains the Qdenga vaccine, developed from an attenuated DENV2 virus strain, which requires two doses to achieve an efficacy of 61% to 84% in subjects with a history of dengue. The immunogenicity obtained is lower in dengue-seronegative patients. Since May 2024, the WHO recommends this vaccine for children aged 6 to 16 in endemic areas who have evidence of a previous infection, confirmed by clinical symptoms or biological tests (RT-PCR or NS1 antigen). As it is the only vaccine currently available, infectious disease societies recommend expanding the WHO guidelines to include people living in endemic areas, children from the age of 4 living in endemic areas, as well as at-risk adults (age > 65 years, obesity, diabetes mellitus, pulmonary or liver diseases, blood disorders, anticoagulant treatments), and travelers going to these regions. Certainly, the existing vaccine is not the ideal vaccine, but given the spread of dengue and its

*Corresponding Author: Patrice Bouree, Email : patrice.bouree@gmail.com

potential severity, we must assess the benefit-risk equation and promote this vaccination by significantly expanding the official limits set by the WHO (7,8).

Conclusion

All WHO health guidelines and protocols on tropical infectious diseases transmitted by insects should be expanded.

Competing Interests

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