EDITORIAL

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Editorial

Zika. A pandemic in progress and an epidemiological challenge☆

Zika. Una pandemia en progreso y un reto epidemiológico

Rodrigo Pardo-Turriago (MD, MSc) *

Universidad Nacional de Colombia, School of Medicine, Hospital Universitario Nacional de Colombia, Colombia

The recent Zika pandemic has become the focus of attention for multilateral health organizations, researchers in centres and universities, specialized publications, mass media, and in particular for populations where it is now a reality, and those that are potentially at risk.

This does not come as a surprise, considering that an infection that used to be episodic and local has now reached dramatic levels of propagation that are difficult to control.

The Zika virus is an arbovirus of the Flaviviridae family to which other viruses like dengue, yellow fever, Japanese encephalitis and Nile fever belong. This virus was isolated for the first time in 1947 in a Rhesus monkey in the Zika forest in Uganda.

For decades, the virus infected monkeys in a narrow belt in equatorial Asia and Africa and only occasionally did it infect humans, causing a mild transient febrile disease.

Sixty years after it was first described, an epidemic was reported for the first time in the Federated States of Micronesia and, over the following years, there were other epidemics in four other nations in the Pacific. But it was during the epidemic in French Polynesia that the presence of the Zika virus was found to be a risk factor for the development of neurological complications, although when circulating simultaneously with the dengue virus.[1]

In May 2015, the World Health Organization (WHO) confirmed the presence of the Zika virus in America and in the early days of 2016 it became actively present in 33 countries, including also Cape Verde and Oceania, affecting close to 600 million people as stated in the WHO reports disseminated in the international edition of the New York Times published on February 6th of this year.

Researchers from the U.S. National Institute of Allergies and Infectious diseases called attention on the occurrence in America of four viral diseases transmitted by arthropods over the past twenty years: dengue, silently endemic for decades but responsible for an aggressive epidemic in the 1990s, the Western Nile fever which made its appearance in 1999, and more recently the chikungunya virus in 2013 and the Zika virus in 2015 in epidemic form.[2]

The question raised by this Institute is whether there is an intrinsic pattern in the successive migration of these viruses or if it is simply the result of new disease emergence patterns. African researchers know for a fact that the Zika epizootic transmitted by the Aedes mosquito tends to follow the unexplained mechanisms of the chikungunya epizootics and epidemics also transmitted by Aedes. Something similar is happening in the Western hemisphere, particularly in Latin America and the Caribbean.

Over many years of existence, Aedes has adapted to new ecosystems where humans are present together with their domestic animals, as is the case with horses in Venezuelan equine encephalitis and pigs in Japanese encephalitis.

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* *Corresponding author at*: Facultad de Medicina, Universidad Nacional de Colombia, Hospital Universitario Nacional de Colombia, Colombia.

E-mail address: rpardot@unal.edu.co

For centuries, Zika was considered a minor infection similar to dengue, but which did not produce bleeding or lead to death. However, during the epidemic of the French Polynesia, there were concomitant reports of 73 cases of Guillain–Barré syndrome and other neurological events in a population of approximately 270,000 inhabitants. More recently, during the epidemic in Brazil, there was more than a twenty-fold increase in the presence of microcephaly in babies born to mothers exposed to Zika during pregnancy. In both instances, these countries had also experienced dengue and chikungunya epidemics.

Although these facts and these figures are having a huge impact on governments, healthcare authorities and decision-makers, the causal relationship between Zika infection and teratogenic and neurological abnormalities is yet to be proven. The sudden increase in the number of neonates with microcephaly and cerebral damage like the one that occurs in cases of congenital infection, in a region attacked by an epidemic of a new circulating virus, strongly suggests a potential connection.

The scientific community has responded promptly and governments have been summoned to promote collaborative studies between affected countries and countries with the necessary resources to design and conduct epidemiological studies that can help elucidate the alleged association and estimate its effect.

The Brazilian government has developed a strategy for building a registry of microcephaly cases throughout the country, including variables of interest and confounding factors, and all pregnant women with a suspected Zika infection may be analysed under a case control study, which is mandatory in epidemic outbreaks, or a cohort study, in order to establish the actual effect estimator. The Pan-American Health Organization (PAHO) has recommended similar initiatives in other countries of the region. Data must consider, among others, historical underreporting, head circumference measurement errors, recall biases, and bad classification.

Some environmental variables must be considered, because it is known that higher temperatures may expand the geographic range of the vector, reduce the extrinsic incubation period of the pathogen, and increase the frequency of mosquito bites. Likewise, research on these viruses and their ecologic and entomologic determinants are of paramount importance.

The Zica pandemic is an ideal setting for translational research, starting with biology through to genetics and immunology, in order to unveil the secrets of why the virus is capable of adapting to new environments. Concomitantly, work needs to be done in genetic control of Aedes by means of infection with modified lethal strains or the generation of mosquitoes that are resistant to arbovirus infection; laboratory work to develop immunological tests to detect the virus and its serotypes; entomologists doing their part at identifying the Aedes species that become vectors in various regions; clinicians following-up on patients or populations at risk in order to achieve early identification of known and unknown complications; and public health professionals implementing vector control measures based on basic sanitation, protection and prevention, and promoting the adoption of safe and effective policies.

Until the epidemiological data required for quantifying the actual risk become available, the region has declared a state of alert. WHO and PAHO have issued recommendations addressed to pregnant women living in epidemic areas regarding the use of insecticides and repellents, and the need to cover exposed parts of the skin in order to avoid contact with the mosquito. Recommendations have also been issued regarding sexual activity, considering the big question mark about this potential route of infection resulting from the report out of the state of Colorado about an infection potentially due to contact with a partner infected with the virus.

Viral infections transmitted by arthropods must trigger a reflection about the health conditions of migrant populations, sanitary controls required for international flights, community education programmes about these diseases and the way to avoid them or reduce their impact, education of the healthcare staff working in communities at risk, and public health actions required to improve overall health conditions of the population.

Are we really prepared to confront this threat successfully?

For decades, we have been the losers in the battle against the vector, which has adapted with great biological efficiency and developed resistance against several pyrethrins and other insecticides. Despite spraying efforts, the lack of continuity of the eradication campaigns becomes a permanent risk that facilitates continuous circulation of dengue virus strains and perhaps other similar ones.

The same may be said of education strategies. In 2013, a campaign to prevent the propagation of Aedes was broadcast intensively in the media, but the enthusiasm apparently waned with the end of the dengue epidemic peak. Reservoir control must be a permanent, on-going measure.

Until the discussion of the legal and ethical issues of allowing abortion in exposed pregnant women begins, contraception programmes must be made readily available to the population at risk. Similarly, are we in a position to provide adequate care to pregnant women in urban and suburban communities with poor sanitation? The time has come to revisit antenatal care programmes and ensure the use of additional testing whenever and as many times as they are required.

While we lose the battle against the mosquito, the promise of vaccine development is still far from becoming a reality, and we still do not have a serological roadmap for targeting the most prevalent viruses. Should the number of Guillain-Barré cases show a substantial increase, does the Ministry have sufficient medications in stock to prevent the complications that are sure to occur? The so-called "*Around Colombia for Zika Control*" strategy may well be showy, but it is far from being a measure that is here to stay.

Are the geopolitical issues in our borders a hurdle for joint campaigns in the populations of the Caribbean that are at high risk? Not more encouraging is the landscape in Venezuela or Panama, countries with which we share territories with a significant need of care coverage. No matter where we look, there is a need to centralize the information in an agency that

inspires credibility and trust. Such an agency should be the National Health Institute and it should be made responsible for communicating clear and unambiguous information about the size of the epidemic, the control mechanisms, and the policies for local implementation.

The academia in Colombia is working silently but making important valuable progress in this field, with efforts like those of the National University Natural Sciences Institute, the Programme for the Study and Control of Tropical Diseases (PECET), Antioquia University's project for the elimination of dengue in Colombia, and the project for the development of vaccines against dengue, under way at the Industrial University of Santander. In private universities, meetings for dissemination and analysis are held in order to make sure that the discussion will remain open and promote collective awareness of the importance of paying attention to these threats to public health.

If epidemiology in the 19th and 20th centuries was built around tuberculosis, syphilis, cholera and malaria among others, the main players in the early 21st century are migrant viruses. The principles of causality proposed by Koch and Bradford Hill still prevail in relation to these challenges, and epidemiology is up against a very hard job. It will surely rise to the occasion.

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