

Never shy from infectious-disease mysteries

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I was attracted to tropical medicine when an astute professor in this field at the Federal University of Rio de Janeiro (UFRJ) carefully investigated the fever of a good friend of mine and saved her from death by diagnosing her *Plasmodium falciparum* infection. Because 99% of malaria cases in Brazil are acquired in the Amazon, outside of that region in Brazil, malaria is almost never considered as a cause of fever. It was only because this physician was so clever that she suspected malaria in a febrile patient with no history of travel from an urban area of Rio de Janeiro.

The local transmission of malaria in the state of Rio de Janeiro was considered eliminated in 1968. However, sporadic local cases have been described in different regions of the Atlantic Forest in the state, and data regarding the transmission mechanisms are scarce. Our group, through molecular investigation of parasite DNA, has demonstrated that it is not *Plasmodium vivax* but *Plasmodium simium* that naturally infects monkeys and humans in these areas. The recent rise of ecotourism and the so-called 'back to nature' movement increases the opportunities for vector sharing between monkeys and humans in this region, in an unequivocal demonstration of zoonotic transmission.

During my residency in infectious diseases at the Hospital dos Servidores do Estado in Rio de Janeiro, I learned that, in essence, every patient provides a research puzzle. In this period, I witnessed the first malaria epidemic among the Yanomami, one of the most vulnerable peoples on the planet, who eschew having their photo taken because they believe that cameras capture their souls.

Back in Rio, because of the growing anxiety among young people about AIDS, with its seemingly endless opportunistic infections, I sought to train in the diagnosis of parasitic and mycological opportunistic diseases of AIDS, in the Laboratory of Parasitology and Mycology at the Saint Louis Hospital in Paris. Motivated by research in biology initiated in France, I worked on the diagnosis of microsporidia in patients with AIDS to obtain my doctorate in sciences at Institute Oswaldo Cruz Foundation (Fiocruz),



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the largest public-health research institution linked to the Ministry of Health in Brazil.

I was divided between following a scientific career path and practicing my job as a physician in public-health assistance. During that time—throughout epidemic periods of leptospirosis, dengue and influenza, outbreaks of meningococcal disease and hemorrhagic fevers, and the many other infectious disease problems arising in the state—patients were referred to the Hospital São Sebastião. It was in that hospital that I developed a profound fascination for the clinical study of human infectious diseases. I realized that even the most routine investigation of sputum and urine can be useful in research: every specimen is new and unique. The fever of scientific research had already started in me.

In 2007, I joined Fiocruz, as an associate clinical researcher of the National Institute of Infectious Diseases Evandro Chagas, where I have worked ever since. There, I established the Acute Febrile Illness (AFI) clinic to conduct surveillance of emerging

and re-emerging infectious diseases. The clinic is operated in collaboration with national reference laboratories from Fiocruz for molecular diagnostics and records cases according to a flowchart of syndromic investigations. The application of this protocol permitted us to identify the beginning of an epidemic of a new disease marked by a skin rash, for which Zika virus (ZIKV) was identified as the etiologic agent in 2015. We have also demonstrated the viral neuro-invasiveness and the spectrum of neurological diseases associated with ZIKV and Chikungunya virus in Rio de Janeiro, Brazil. We have a large outpatient clinical service, and to date we have seen hundreds of cases of ZIKV and Chikungunya virus infection in our cohorts.

Because of our timely participation in addressing this epidemic through our AFI clinic, our studies have been centered on the most vulnerable population: pregnant women infected with ZIKV. Our cohort study of pregnant women provided definitive epidemiological evidence of causality between ZIKV infection during pregnancy and congenital Zika syndrome. Despite mild symptoms in pregnancy, ZIKV infection was associated with severe outcomes, including fetal death, placental insufficiency, fetal growth restriction and central-nervous-system injury. For the past 5 years, I've been conducting a prospective study in a cohort of pregnant women to evaluate the risks of adverse pregnancy outcomes after arboviral infections and neurodevelopment of exposed babies.

Finally, I should say that I found the courage and the strength to follow this path in my career in the eyes of my patients, in my research partners, in the unrestricted support of my family and in my daughter—my only masterpiece. □

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