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Juntendo University Corporate Communications

Juntendo University research: Malaria in Africa: Developing resistance

(Tokyo, 23 April 2018) Annual deaths from malaria are decreasing, but the disease is still a global health problem, with 216 million new cases estimated in 2016 alone, with 90% occurring in Africa. Toshihiro Mita from the Juntendo University School of Medicine in Tokyo, Japan, and colleagues report in *Emerging Infectious Diseases* an extensive study on the emergence of drug-resistant malarial parasites in northern Uganda.



Annual deaths from malaria are decreasing, but the disease is still a global health problem, with 216 million new cases estimated in 2016 alone. The emergence of drug resistance is one of the main threats in the global fight against malaria. Importantly, since 90% of malaria cases exist in Africa, the development of resistance to artemisinin—the major drug used to treat malaria—in this region would have profound consequences for global strategies to combat malaria.

Now, Toshihiro Mita from the Juntendo University School of Medicine in Tokyo, Japan, and colleagues report in *Emerging Infectious Diseases* an extensive study on the emergence of drug-resistant malarial parasites in northern Uganda.

The main reason why malaria incidence and deaths are decreasing is the deployment of combination therapies based on a drug called artemisinin. However, parasites can develop resistance to artemisinin, as was reported starting in 2007–2008, and resistance is known to be spreading in Southeast Asia. So far there was no evidence for the emergence of artemisinin-resistant parasites in Africa. However, in Africa many people have some form of immunity to malaria, thus they may respond to treatment even when infected by drug-resistant parasites.

Determining drug effectiveness based on conventional ex-vivo drug susceptibility assays is challenging, because reduced susceptibility to artemisinin is limited to the early ring stage of their development. A more recently developed survival assay, which evaluates ring-stage-specific reduction of artemisinin susceptibility is thus useful to study the emergence of drug resistance.

To assess artemisinin sensitivity in the period 2014–2016 in Gulu, a region with high malaria transmission in northern Uganda, the researchers performed 4 cross-sectional surveys and evaluated the emergence of artemisinin resistance by using 3 methods: conventional ex vivo drug susceptibility assay, the ring-stage-specific ex vivo survival assay and genotyping of the gene responsible for artemisinin resistance in Southeast Asia.

249 patients were enrolled in the study. Around 2% of the isolated parasites showed a high survival rate after being exposed to an artemisinin-derived drug, which is closely associated with delayed parasite clearance after drug treatment and is considered to be a proxy for the artemisinin-resistant parasite type. Only 1 of the parasites showed the genetic mutation associated with artemisinin resistance. The resistant parasites seem to have developed in Africa rather than migrated from Southeast Asia. Thus the study highlights the potential emergence of artemisinin-resistant parasites in Africa.

“Emergence and spread of artemisinin resistance impose substantial obstacles for effective malaria control and the approach toward elimination,” comment the authors in the paper. “It is thus imperative to perform further intensive surveillance for artemisinin resistance in various malaria-endemic regions in Africa and to elucidate genetic changes that confer resistance to artemisinin in parasites in Africa”.

Background

Artemisinin

The drug was discovered in 1972 by the Chinese scientist Tu Youyou, who received half of the 2015 Nobel Prize for this discovery. Artemisinin is isolated from an herb employed in Chinese traditional medicine, sweet wormwood, but can also be obtained from genetically engineered yeast. The use of this drug on its own is discouraged, as it's easier for the parasites to develop resistance. Therapies that combine artemisinin or its derivatives with other antimalarial drugs are thus preferred.

Life cycle of malarial parasites

When a mosquito carrying the parasite bites a person, first sporozoites (spore-like cells) enter the bloodstream and go to the liver. There they infect liver cells, where they divide and multiply into cells called merozoites. At this point they rupture the liver cells and return to the bloodstream. The merozoites infect red blood cells, where they develop into ring forms that in turn produce further merozoites.

Cross-sectional study

A cross-sectional study is a type of observational study that analyzes data from a population at a specific point in time.



Reference

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About Juntendo University

Mission Statement

The mission of Juntendo University is to strive for advances in society through education, research, and healthcare, guided by the motto “Jin – I exist as you exist” and the principle of “Fudan Zenshin - Continuously Moving Forward”. The spirit of “Jin”, which is the ideal of all those who gather at Juntendo University, entails being kind and considerate of others. The principle of “Fudan Zenshin” conveys the belief of the founders that education and research activities will only flourish in an environment of free competition. Our academic environment enables us to educate outstanding students to become healthcare professionals patients can believe in, scientists capable of innovative discoveries and inventions, and global citizens ready to serve society.

About Juntendo

Juntendo was originally founded in 1838 as a Dutch School of Medicine at a time when Western medical education was not yet embedded as a normal part of Japanese society. With the creation of Juntendo, the founders hoped to create a place where people could come together with the shared goal of helping society through the powers of medical education and practices. Their aspirations led to the establishment of Juntendo Hospital, the first private hospital in Japan. Through the years the institution’s experience and perspective as an institution of higher education and a place of clinical practice has enabled Juntendo University to play an integral role in the shaping of Japanese medical education and practices. Along the way the focus of the institution has also expanded, now consisting of four undergraduate programs and three graduate programs, the university specializes in the fields of health and sports science and nursing health care and sciences, as well as medicine. Today, Juntendo University continues to pursue innovative approaches to international level education and research with the goal of applying the results to society.