

Exposure to superbacteria among visitors to the tropics more extensive than previously thought

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Exploring exposure to superbacteria, researchers at the University of Helsinki and Helsinki University Hospital got unexpected results from



an international collaborative study conducted in real time among 20 travelers to Southeast Asia. All the participants were found to contract superbacteria within a week after arriving in the destination. A detailed sequence analysis showed that the traveler group acquired a variety of superbacteria comprising over 80 different strains altogether.

Before the corona pandemic, tens of millions international travelers annually headed to the tropics, getting exposed to local intestinal bacteria. A total of 20-70% of those returning from the tropics carry—for the most unknowingly—ESBL-producing bacteria resistant to multiple antibiotics. The likelihood of acquiring such superbacteria depends on destination and health behavior abroad. The risk is greatest in South and Southeast Asia, and a substantial increase is associated with contracting travelers' diarrhea and taking antibiotics while abroad.

An investigation led by professor of Infectious diseases Anu Kantele at Helsinki University together with MD Esther Kuenzli from Swiss Tropical and Public Health Institute involved a real-time scrutiny of superbacteria acquisition among a group of 20 Europeans over a three-week visit to Laos. The participants' daily stool samples were initially screened on site in Vientiane, Laos, and later, in Europe, the superbacteria strains isolated were analyzed in detail by whole-genome sequencing.

The study was recently published in *The Lancet Microbe*. It belongs to a series of Kantele's studies exploring the spread of antimicrobial resistance by international travel.

"Our study revealed that travelers to the tropics are much more predisposed to acquiring superbacteria than previously thought. In conventional studies, stool samples are only collected before and after travel, not while abroad as we did now. travelers to the tropics are known to be exposed to superbacteria, but the extent of the risk revealed by our



real-time sampling was unexpected," Kantele says.

Travelers contracted superbacteria within the first week abroad

In Laos, daily stool samples from the participants were analyzed locally in the Lao-Oxford-Mahosot Hospital-Wellcome Trust -Research laboratory. Had samples only been collected before and after travel, the proportion of superbacteria carriers had been approximately 70%. Daily real-time scrutiny already while abroad revealed, however, that all travelers had contracted a superbacter within a week after arrival.

The findings varied day by day. While some participants carried superbacteria for several days, others had a couple of days' breaks after which superbacteria were found again. Part of the travelers acquired several strains.

"It became evident that acquisition of superbacteria is a dynamic process: bacteria come and go, some strains persisting for a lengthy period of time," Kantele says.

Whole-genome sequencing revealed the great variety among strains of superbacteria

After returning home, to explore the isolated superbacteria strains in more detail, the researchers established a collaboration with Jukka Corander, professor of Statistics at the Universities of Helsinki and Oslo, and Alan McNally, professor of Microbial genetics at the University of Birmingham, England. Whole-genome sequencing and analyses proved colonization to be a dynamic process involving constant switches between the various strains. Indeed, all the travelers had been exposed to a much wider range of superbacteria than generally thought. Applying



the traditional approach, about 20 new strains would have been detected after travel, but daily sampling abroad and whole-genome sequencing enabled the researchers to unravel that the participants acquired 83 different strains altogether.

Only in four cases did two travelers share the same strains, indicating that the bacteria were not in general transmitted from one to another.

None of the participants developed a clinical infection caused by the superbacteria. Had they not been delivered their screening results on a daily basis, the study participants would have remained totally unaware of them carrying superbugs.

"It was wonderful to see how our intestinal bacteria stand up to the incomers: the great majority of all alien strains disappeared already before the end of the journey," Kantele rejoices.

Professor Jukka Corander points out that the study provides a completely new perspective to the bacterial colonization diversity in geographic regions where superbugs are endemic.

"We have earlier obtained robust modeling results concerning the stability of E. coli colonization in populations with low levels of antibiotic resistance, however, the new study conducted in Laos implies that we need to start building the model anew, so that we gain thorough understanding about the role of superbugs also in those circumstances where they colonize the majority of the people," Corander says.

Antibiotic resistance increases at an alarming rate in the tropics

The worldwide growth of antibiotic resistance is particularly alarming in



tropical regions with inadequate hygiene and uncontrolled use of antibiotics. Multidrug-resistant bacteria are carried both by animals and local inhabitants. Returning from such environments, many visitors carry superbacteria to their home countries.

Increasing resistance is also being witnessed by research: the proportion of travelers carrying these bacteria is growing. Usually acquisition of ESBL or other superbacteria does not cause any symptoms. After travelers return home, the <u>strains</u> usually disappear over time. Carriers can, however, pass these bacteria on to others. Among a small proportion, the superbacteria cause a symptomatic infection, most typically a urinary tract infection.

Treatment of infections caused by superbacteria is more challenging than of those caused by sensitive bacteria. In some cases, the infection may even turn out life-threatening.

Antibiotic use during travel further adds to the risk of carriage: favoring the resistant bacteria, antibiotic treatment makes space for newcomers.

Kantele stresses the grave threat increasing resistance poses to healthcare worldwide.

"Antibiotics are not only needed to treat infections, but they also enable high-risk operations such as major surgery and organ transplants, where they are given to prevent infections," she says.

More information: Anu Kantele et al. Dynamics of intestinal multidrug-resistant bacteria colonisation contracted by visitors to a high-endemic setting: a prospective, daily, real-time sampling study, *The Lancet Microbe* (2021). DOI: 10.1016/S2666-5247(20)30224-X



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