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Data from across globe defines distinct Kawasaki disease season

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After more than four decades of research, strong evidence now shows that Kawasaki disease has a distinct seasonal occurrence shared by regions across the Northern hemisphere.

The first global analysis of the seasonality of Kawasaki disease, published September 18 by *PLOS ONE*, was carried out using data obtained between 1970 and 2012. It included 296,203 cases from 39 locations in 25 countries around the globe, with 27 of those locations in the extra-tropical Northern hemisphere, eight in the tropics, and four in the extra-tropical Southern hemisphere.

Kawasaki disease (KD) is a severe childhood disease that many parents, even some doctors, mistake for an inconsequential viral infection. In fact, if not diagnosed or treated in time, it can lead to irreversible heart damage. Decades of research have been unable to pinpoint the cause of the disease, although genetic studies show a heritable tendency to acquiring the disease.

Findings of an international team of scientists - organized by Jane C. Burns, MD, professor of pediatrics and director of the Kawasaki Disease Research Center at the University of California, San Diego School of Medicine and Rady Children's Hospital-San Diego – now support earlier evidence that KD cases are linked to large-scale wind currents that track from Asia to Japan and also traverse the North Pacific.

The study found that 40 percent more cases of Kawasaki disease in the

Northern hemisphere occurred from January through March than from August through September – coinciding with high and low intensities of tropospheric winds. Previous studies showed that when winds blew from the northwest across Japan in a southeasterly direction, the number of KD cases there increased. At the conclusion of the epidemics, the wind had reversed direction and commenced blowing across Japan from the Pacific Ocean in a northwesterly direction. This same pattern was repeated from year to year.

The passage of these large-scale wind patterns across the Pacific was similarly associated with an increase in KD cases in San Diego, California.

This study built and expanded upon earlier research investigating a possible influence from large-scale environmental factors, (published by this scientific team in a November 2011 study in Nature *Scientific Reports*) by a team of researchers that also included two contributors to this study: Daniel R. Cayan, Climate Atmospheric Science and Physical Oceanography (CASPO) at Scripps Institution of Oceanography in La Jolla, and Xavier Rodó of the Institut Català de Ciències del Clima and the Institució Catalana de Recerca (IC3) in Barcelona, Spain.

"Our data suggest a seasonal exposure to a KD agent that operates over large geographic regions and is concentrated during winter months in non-tropical regions of the Northern hemisphere," Burns said.

Datasets were much sparser in the tropics and the Southern hemisphere, but showed a maximum incidence in May through June, with approximately 30 percent of the cases occurring in that time period; however, the pattern was not considered statistically significant.

"During winter months, there are stronger seasonal winds across the Northern hemisphere, which could lead to increased transport of the

suspected KD agent," said Burns. "This may explain, in part, the consistency in the seasonal nature of Kawasaki disease that we observe in our pediatric patients."

While there is no diagnostic test, signs of KD include prolonged fever associated with rash, red eyes, mouth, lips and tongue, and swollen hands and feet with peeling skin. The disease causes damage to the coronary arteries in a quarter of untreated children and may lead to serious heart problems in early adulthood. The aneurysm rate for Kawasaki disease is 5 percent, and the death rate is 0.1 percent.

While seasonality of the disease has been noted in many regions – particularly in Japan, the country of highest incidence for KD – the search for factors that might contribute to epidemics and fluctuations in KD occurrence has been elusive. A study of KD cases in Japan since 1970 showed three dramatic nationwide epidemics, each lasting several months and peaking in April 1979 (6,700 cases), May 1982 (16,100 cases) and March 1986 (14,700 cases). These three peaks represent the largest KD epidemic events ever recorded in the world.

Previous epidemiological investigations suggest that the causative agent for KD is widely distributed in the environment, that there is no person-to-person transmission and that genetic susceptibility plays a part in at least some of the disease variation across different ethnic and racial groups. Japan continues to be the country of highest incidence, but seasonality of the disease has been documented in Hawaii and San Diego as well.

The scientists report that this recent comprehensive analysis to detect seasonal cycles of KD cases from around the world could be significant in efforts to isolate the cause of this devastating childhood disease.