

Researchers discover how noroviruses cause repeated outbreaks of 'stomach flu'

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Norovirus, a common cause of gastroenteritis ("stomach flu"), could potentially be controlled by a vaccine. But because the virus evolves to avoid the immune system, the vaccine might have to be modified from year to year, according to new research published in *PLoS Medicine* by Ralph Baric of the University of North Carolina, Chapel Hill, and colleagues.

Noroviruses, which are highly contagious, cause nausea, vomiting, and diarrhea. While most people recover within a few days, the very young and old may experience severe disease. Although maintaining hydration is essential, there is no specific treatment for infection.

As with influenza, epidemics of norovirus infection occur periodically (often in closed communities such as cruise ships), and most people have several norovirus infections during their lifetime. This winter the UK has seen almost twice as many norovirus cases compared to the same period last year.

Noroviruses infect cells after attaching to molecules called histo-blood group antigens (HBGA) present on the cell surface. HBGAs comprise a family of complex sugar molecules that exist in great variety among human beings. The researchers found that this variety provides the key to understanding how norovirus outbreaks continue to occur, even in populations that have previously been exposed to noroviruses and therefore harbor antibodies against them.

By analyzing noroviruses isolated from several outbreaks, the researchers found that the viruses evolved to avoid attack by antibodies the hosts developed against them. Over time, some viruses selected in this way attain a shape that enables them to bind to one of the other forms of HBGA, and thereafter are not only resistant to previously existing antibodies, but are also able to infect cells carrying that particular form of HBGA. These viruses can then cause a new outbreak, and the cycle repeats itself.

This continuing evolution of new replacement strains suggests that vaccines could be designed to protect against norovirus infection, but that, as with influenza vaccines, ongoing epidemiologic surveillance and reformulations of norovirus vaccines will be needed.

In a related perspective article, Ben Lopman and colleagues at the UK Health Protection Agency, who were not involved in the study, discuss the evolution of noroviruses and the implications of this research for the control of future outbreaks.

Citation: Lindesmith LC, Donaldson EF, LoBue AD, Cannon JL, Zheng DP, et al. (2008) Mechanisms of GII.4 norovirus persistence in human populations. PLoS Med 5(2): e31. (medicine.plosjournals.org/permalink/journal.pmed.0050031)

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