

# Rice could make cholera treatment more effective



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Scientists at EPFL have shown that, though undeniably effective, the current rehydration therapy for cholera could increase the toxicity of the cholera bacterium. Backed with new data, the scientists propose a change in the treatment, replacing glucose with starch from rice powder.

Cholera is caused when the bacterium *Vibrio cholerae* infects the small intestine, resulting in severe diarrhea and vomiting, which can result in dehydration and death. The main treatment involves oral rehydration therapy, where the patient drinks water mixed with salts and glucose. But although proven to be enormously effective, there are concerns that the glucose content might actually worsen the disease. EPFL scientists have now shown that this is indeed the case, as glucose increases the toxicity of the cholera bacterium, whereas replacing glucose with starch can reduce its toxicity by almost 75%. Their work is published in *PLOS Neglected Tropical Diseases*.

## **Cholera treatment: Effective, but could be improved**

The usual treatment for cholera comes in the form of “oral rehydration therapy” packs. Essentially, it involves feeding the patient water mixed with electrolyte salts and glucose. The idea is to replace the patient’s lost fluids and essential salts, while the glucose acts as a source of carbon that helps the intestine to absorb the salts more efficiently. The patient continues the therapy until the infection has ran its course.

Up to half of cholera patients would die without treatment, but oral rehydration therapy has been shown to lower the deaths to around 1%. However, there are concerns that using glucose in the rehydration mixture can actually exacerbate the disease. The problem is that the infecting bacterium also consumes glucose, and that increases the expression of its genes that make it toxic. On the other hand, some field studies have shown that using more complex carbon sources, like starch from rice powder, might be more effective. Despite this, there has never been a decisive study linking oral rehydration recipes with their effect on how the disease spreads.

The cholera bacterium, *Vibrio cholerae*, infects humans by releasing a protein called the “cholera toxin”. Consequently, regulating the genes that produce the cholera toxin can either increase or decrease the bacterium’s capacity to spread disease.

### **Alternatives to glucose**

Melanie Blokesch and Andrea Rinaldo at EPFL have now correlated data from a recent cholera outbreak in Haiti with the effectiveness of oral rehydration therapy. Blokesch’s lab grew the cholera bacterium with different sugars (e.g. glucose, sucrose) and starch from potatoes and rice to see how each would affect the cholera toxin genes.

The scientists found that both the activity of the genes, as well as the production of the cholera toxin itself were increased when the bacterium was fed with glucose, but they were considerably decreased when it was fed with starch from rice. Although the explanation for this is complicated, one of the reasons is that the type of sugar available (e.g. glucose, starch etc.) to the bacterium affects the mechanisms that regulate the activity of its toxin-producing genes. Ultimately, this effect influences the bacterium’s ability to infect humans.

The team of Andrea Rinaldo focused on matching this data to the actual cholera epidemics in Haiti. Using data from the outbreak of cholera that started in 2010 in the region, they developed a mathematical model of the disease's epidemiology. They then modified the model to include oral rehydration therapy based on rice starch instead of glucose. The results showed that using this alternative approach could have a 30% reduction of cholera cases (375'000 instead of 520'000 cases) on the island within the first 14 months of an epidemic.

The results feed into the current discussion of cholera treatment, and strongly suggest a review of current approaches. "Of course, we're not saying 'stop doing oral rehydration therapy with glucose right away' because it works so well," says Melanie Blokesch. "But still, the data suggests that the regimen can be significantly improved, and that the community needs to start discussing this possibility again – especially in areas endemic to cholera."

*This work represents a collaboration between EPFL's Laboratory of Molecular Microbiology (Melanie Blokesch) and Laboratory of Ecohydrology (Andrea Rinaldo), with the Milan Polytechnic and the University of Padova.*

## Reference

Kühn J, Finger F, Bertuzzo E, Borgeaud S, Gatto M, Rinaldo A, Blokesch M. **Glucose- but not rice-based oral rehydration therapy enhances the production of virulence determinants in the human pathogen *Vibrio cholerae*.** *PLOS Neglected Tropical Diseases* DOI: 10.1371/journal.pntd.0003347

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