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Feed a virus, starve a bacterial infection?

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A new study puts some old folk wisdom to "feed a cold and starve a fever" to the test. In mouse models of disease, Yale researchers looked at the effects of providing nutrients during infection and found opposing effects depending on whether the infections were bacterial or viral. Mice with bacterial infections that were fed died, while those with viral infections who were fed lived. The paper appears September 8 in *Cell*.

"We were surprised at how profound the effects of feeding were, both positive and negative," says senior author Ruslan Medzhitov, David W. Wallace Professor of Immunobiology and a Howard Hughes Medical Institute investigator at Yale School of Medicine. "Anorexia—not eating—is a common behavior during sickness that is seen in people and all kinds of animals. Our findings show that it has a strong protective effect with certain infections, but not with others."

In the first series of experiments, the investigators infected mice with the bacterium Listeria monocytogenes, which commonly causes food poisoning. The mice stopped eating, and they eventually recovered. But when the mice were force fed, they died. The researchers then broke the food down by component and found fatal reactions when the mice were given glucose, but not when they were fed proteins or fats. Giving mice the chemical 2-DG, which prevents glucose metabolism, was enough to rescue even mice who were fed glucose and allowed them to survive the infection.

When the researchers did similar studies in mice with viral infections, they found the opposite effect. Mice infected with the flu virus

A/WSN/33 survived when they were force fed glucose, but died when they were denied food or given 2-DG.

Further research showed that different areas of the brain were affected depending on which type of infection the mice died from, indicating that the animals' metabolic needs differ depending on which part of the immune system had been activated.

"Almost everything we know about infection is based on immune response studies and looking at how the immune system eliminates pathogens," Medzhitov says. "But that's not the only way we defend ourselves. There are also cases where we change and adapt so that microbes don't cause harm. Our study manipulated the ability of these mice to tolerate and survive infection without doing anything that had an effect on the pathogens themselves."

Medzhitov's Lab is now looking at the effects of another common sickness behavior—changes in sleep patterns—on how the immune system fights infection. His team is also doing follow-up studies on the pathways involved in food preference, which may explain the cravings that people have for certain foods when they're sick.

But he says their findings may have more immediate implications as well, for the design of clinical trials evaluating the benefits of providing nutrients to patients with sepsis. "Sepsis is a critical problem in hospital ICUs that defies most modern medical approaches," he says. "A number of studies have looked at nutrition in patients with sepsis, and the results have been mixed. But these studies didn't segregate patients based on whether their sepsis was bacterial or viral. The implication is that patients should be stratified by the cause of their sepsis, and trials should be designed based on that."

More information: *Cell*, Wang et al: "Opposing Effects of Fasting

Metabolism on Tissue Tolerance in Bacterial and Viral Inflammation." www.cell.com/cell/fulltext/S0092-8674(16)30972-2 DOI: 10.1016/j.cell.2016.07.026

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