

MICROBIOLOGY

Going Viral: Exploring the Role Of Viruses in Our Bodies

'Virome' surveys reveal our vast number and variety of viruses

VANCOUVER, CANADA—In the past decade, scientists have come to appreciate the vast bacterial world inside the human body. They have learned that it plays a role in regulating the energy we take in from food, primes the immune system, and performs a variety of other functions that help maintain our health. Now, researchers are gaining similar respect for the viruses we carry around.

For a start, the variety and sheer number of viruses that inhabit us put our bacterial companions to shame. Many of the viruses prey on the bacteria in our bodies, altering their numbers and diversity and shuffling genes—including genes for antibiotic resistance—from one bacterium to another. “Ultimately, those viruses are incredibly important in driving what’s going on” in the human microbiota, says Curtis Suttle, a virologist at the University of British Columbia (UBC), Vancouver, in Canada. “To understand the bacteria associated with humans, you can’t do that without looking at the viruses as well,” he says. Studies presented here at the International Human Microbiome Congress earlier this month have begun to do just that. One provocative, albeit preliminary, finding has already emerged: Infants with unexplained fevers harbor many more viruses than healthy infants.

For years, virologists have documented specific viral infections, including HIV and SARS, by detecting identifiable viral DNA within blood or other tissues. But to do a comprehensive survey of the viruses in the body—the so-called virome—“is a true frontier,” says B. Brett Finlay, a microbiologist at UBC Vancouver. Last July, Jeffrey Gordon, a microbiologist at Washington University (WU) School of Medicine in St. Louis, and his colleagues described one such effort in a group of seemingly healthy people. They isolated and characterized the viromes of adult identical twins and their mothers, sampling stools for viral genetic material three times over the course of a year. The overall conclusion: Healthy people “are full of viruses,” says WU’s George Weinstock.

By one measure, the number of distinct viruses in the stool samples ranged from 52 to 2773. The viromes varied significantly from one individual to the next; they were even

more diverse than the bacterial communities within the same individuals. But each person’s viral community remained stable over the course of the year.

WU microbiologist Kristine Wylie and her colleagues have begun to look at how the virome may influence health, in particular what role it might play in unexplained fevers in infants. For children under 3, fevers are the most common cause of emergency room visits, but almost 90% of the time there’s no clear cause for the high temperatures.

Wylie, Weinstock, WU’s Gregory Storch, and their colleagues sequenced the DNA obtained from nasal swabs or blood plasma of 151 individuals, about half of whom had unexplained fevers. The team estimated there were 10,000 viral sequences in the plasma samples of the children with fever and only about 1000 in healthy children. Some of the viruses found were common human pathogens, such as herpes and cold viruses.

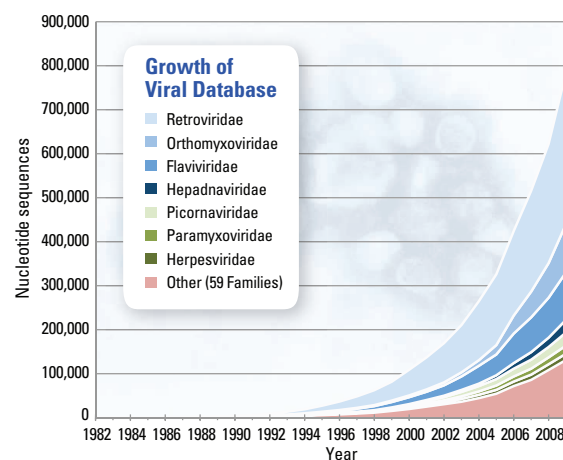
But there also seem to be unusual viruses, including an astrovirus, in the mix, Wylie reported. “There were new isolates that you might not have thought would be associated with febrile illness,” says Frederic Bushman, a virologist at the University of Pennsylvania.

Much more work is needed to establish that any of these viruses explain the fevers, but proving that could mean fewer antibiotics for infants, Wylie points out. To be on the safe side, physicians tend to prescribe antibiotics for unexplained fevers, but such drugs are ineffective against viruses.

While Wylie has focused on the viruses that infect human cells, Bushman has homed in on the bacteriophages, viruses that attack bacteria. For every bacterium in our body, there’s probably 100 phages, with an estimated 10 billion of these viruses packed into each gram of human stool. As part of a study of the interplay of diet, human gut microbes, and Crohn’s disease, an inflammation of the digestive system, Bushman and his colleagues have looked at the viromes of six healthy

adults. These volunteers were sequestered for 10 days and fed either a high-fat or a low-fat diet, and the researchers analyzed their stool samples for bacteria and viruses.

Overall, the median number of different kinds of phages was 44 per sample, Bushman reported at the meeting. But within 24 hours of a person starting the new eating regimen, the community of phages and bacteria began changing. Because the phages live in the bacteria, one would expect the number and kinds of bacteria and phages to change in parallel, but that was not always the case, Bushman noted. There was also a lot of variation between individuals, with the number of viral types differing by as much as 40-fold in the samples. But in those



Expanding universe. The tally of known viruses is exploding, and this graph doesn’t even include the incredible number that prey on bacteria.

people eating the same foods, the repertoire of viruses tended to converge.

These studies drive home that the human virome needs to be studied more closely, Suttle says. But there are many challenges. For one, most of the viral sequences that have turned up so far don’t have matches in any known databases, so the viruses can’t be characterized. And all the virome survey techniques have their drawbacks. Bushman filtered out all the human and bacteria cells and cleared out all nonviral DNA before sequencing any remaining DNA in his samples. “What [that approach] probably does is throw out most of the virus that was there,” Suttle says. Wylie and her colleagues, on the other hand, sequenced all of the DNA in the stool samples and used computer programs to sort sequences into human, bacterial, and viral bins. But with that strategy, “you usually wind up with a big bin of unknown [sequences],” Suttle adds. Bottom line, says WU’s Herbert “Skip” Virgin, “Bacteria are easier to count.”

—ELIZABETH PENNISI