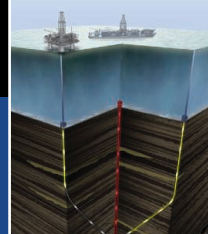




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CHRONIC FATIGUE SYNDROME

Conflicting Papers on Hold as XMRV Frenzy Reaches New Heights

It was just a snippet of news, reported by an obscure journal in the Netherlands. And yet it lit up the Internet. Twitter was all atwitter, scientists' mailboxes on both sides of the Atlantic began filling up, and dozens of bloggers started jubilating. "It's happened. I cannot tell you all how this changes the world as we have known it for 25+ years," one patient wrote on her blog. "Now to work on the vindication part!"

The reason for all the excitement? Scientists at the U.S. National Institutes of Health (NIH) and the Food and Drug Administration (FDA) were reported to have confirmed the link, first published in *Science* last year, between a human retrovirus and the elusive condition called chronic fatigue syndrome (CFS). Earlier this year, three other groups reported being unable to replicate such a connection. That federal scientists now confirmed it was a huge mood-lifter for patients, many of whom are desperate to find a biological cause, and a cure, for their debilitating ailment.

But the story wasn't as simple as that. *Science* has learned that a paper describing the new findings, already accepted by the *Proceedings of the National Academy of Sciences (PNAS)*, has been put on hold because it directly contradicts another as-yet-unpublished study by a third government agency, the U.S. Centers for Disease Control and Prevention (CDC). That paper, a retrovirus scientist says, has been submitted to *Retrovirology* and is also on hold; it fails to find a link between the xenotropic murine leukemia virus-related virus (XMRV) and CFS. The contradiction has caused "nervousness" both at *PNAS* and among senior officials within the Department of Health and Human Services, of which all three agencies are part, says one scientist with inside knowledge.

The remarkable impasse is the latest twist in a story that keeps arousing fierce passions. It started in 2009 when a group of researchers led by Judy Mikovits of the Whittemore Peterson Institute (WPI) for Neuro-Immune Disease in Reno, Nevada, reported in *Science*

finding traces of XMRV in peripheral blood mononuclear cells, a type of white blood cell, of 67% of CFS patients. By contrast, only 3.4% of healthy controls were found to harbor the virus. The team also showed that XMRV could infect human cells and concluded that the virus—which had previously been linked to prostate cancer—might play a role in causing CFS (*Science*, 23 October 2009, p. 585).

Many scientists were skeptical, however, and in May, *Science* published three Technical Comments that tried to poke holes in the study, along with a rebuttal by Mikovits and first author Francis Ruscetti of the National



Real-time results for XMRV

- stemcell4autism** News in a nutshell: XMRV and GM Animals... <http://blog.the-scientist.com/2010/06/28/news-in-a-nutshell-4/>
about 1 hour ago via web
- NoFun_Blog** XMRV : CAUSA O EFECTO DE LA INMUNODEPRESION DEL SINDROME DE FATIGA CRÓNICA? <http://tinyurl.com/236ki3l>
about 2 hours ago via web
- laikas** wht do do if patients react emotional abt a @researchblogging-post & just write letters in response w/out reading urs? <http://bit.ly/az7oVZ>
about 3 hours ago via TweetDeck
- FIBRO 360** The NIH tweeted their support for preliminary research linking CFS to the XMRV. This may help with funding for research. <http://bit.ly/9FZu6>
about 4 hours ago via web
- HEIRS_Health** NIH Supports Findings of XMRV in Chronic Fatigue Syndrome <http://fb.me/DnUQCuf>
about 5 hours ago via Facebook
- CFSyndrome** Further Evidence of an XMRV-Chronic Fatigue Syndrome Connection A report that a respected NIH expert supports... <http://bit.ly/b2qalz>
about 11 hours ago via twitterfeed
- overcome_ME_CFS** Further Evidence of an XMRV-Chronic Fatigue Syndrome Connection ... <http://bit.ly/cQcVlc>
about 15 hours ago via twitterfeed
- overcome_ME_CFS** BREAKING NEWS: FDA & NIH confirm WPI team's XMRV & CFS findings ... <http://bit.ly/d9ldTM>
about 18 hours ago via twitterfeed
- mailtosabrina** Further Evidence of an XMRV-Chronic Fatigue Syndrome Connect | Health: Further Evidence of an XMRV-Chronic Fatigue... <http://bit.ly/aGsell>
1 day ago via twitterfeed
- Diplead RT @fibroadrienne** NIH Supports Findings of XMRV in Chronic Fatigue Syndrome: <http://bit.ly/9Uys4h>
1 day ago via HootSuite

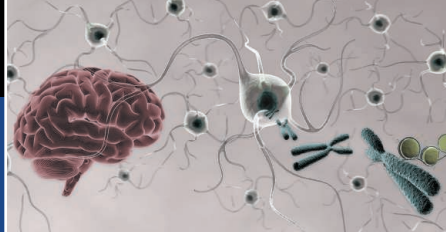
Going viral. News that federal scientists confirmed the virus link reported by Judy Mikovits (*inset*) sparked thousands of tweets.

Cancer Institute. By that time, two groups in the United Kingdom and one in the Netherlands had also published papers failing to find a link; in fact, they found little or no evidence of XMRV infection at all, either in patients or in healthy people. Three other groups, two from the United States and one from Europe, have also reported negative findings at meetings, says Kim McCleary, president of the Chronic Fatigue and Immune Dysfunction Syndrome Association of America, a patient advocacy group.

The FDA-NIH paper would offer fresh hope that Mikovits is on to something after all, but so far, details about the work are scant. *Ortho*, a Dutch magazine about nutrition and food supplements, last week issued a press release saying that Harvey Alter, a renowned virologist at NIH's Clinical Center, mentioned the study when he gave a talk at a blood safety meeting in the Croatian capital Zagreb in late May. In his Power-Point presentation, Alter wrote that the data in the 2009 study in *Science* "are extremely strong and likely true, despite the controversy." Another bullet point said: "We (FDA & NIH) have independently confirmed the Lombardi group findings." (WPI's Vincent Lombardi was the paper's first author.) But the presentation offered no detail beyond that tantalizing summary, and an NIH spokesperson says Alter is not available for comment.

Meanwhile, a group working with retrovirologist William Switzer at CDC, which has done an independent study, has held its cards close to its chest. But *Science* talked to several scientists who say they have seen the data, and they are negative. Although it's not unprecedented for government scientists to be on opposite ends of a scientific debate, two contradictory press releases on a flash-point issue like CFS would look odd, scientists say. With publication deferred, "they want to find out what's going on first," says one researcher who says he has been briefed about the controversy.

For patients, the stakes are huge. A viral cause would offer a path to better understanding, prevention, and treatment. A paper published in *PLoS ONE* in April showed that three registered antiretroviral drugs can inhibit XMRV in the test tube, and although many scientists warn that it's pre-



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mature even to consider them as treatment options, some patients have started testing out different combinations anyway. (One of them is Jamie Deckoff-Jones, a physician from Santa Fe, New Mexico, who is blogging about her experiences and those of her daughter, also a patient.)

Patients have become a loud voice in the scientific debate as well—and it's taking its toll on scientists who don't support the XMRV hypothesis. "It's ghastly," says retrovirologist Myra McClure of Imperial College London, the lead author on one of the three published studies that came up

empty-handed. "I've had people writing me, and I quote, that I don't know my arse from my elbow, and that I should be fired." Four months after her first paper on CFS came out, McClure says it was also her last one. "Nothing on God's Earth could persuade me to do more research on CFS," she says. "I feel bad for the scientists, because it's true, we are a very angry community," says Wilhelmina Jenkins, a physicist living in Atlanta who has had CFS since 1983.

The potential involvement of XMRV in CFS is having other ramifications as well. Last week, the AABB, an international asso-

ciation of blood banks, recommended to its members that they discourage CFS patients from donating blood (<http://bit.ly/chronic-fatigue>). A special task force on XMRV conceded that the evidence was preliminary but decided it's "prudent" to err on the side of caution, says task force member Louis Katz, the medical director at the Mississippi Valley Regional Blood Center in Davenport, Iowa. "If [XMRV] turns out to be important," says Katz, "I don't want to be criticized for doing nothing when I could have done something."

—MARTIN ENSERINK

BHOPAL

India Launches New Probe of Cyanide Disaster

NEW DELHI—More than a quarter-century after the world's worst chemical disaster, the Indian government last week ordered remediation of the contaminated site in Bhopal and the creation of a research institute to study the toxic legacy.

The tragedy began on the night of 3 December 1984, when more than 40 tons of methyl isocyanate gas escaped from Union Carbide Corp.'s pesticide plant in Bhopal. Investigators learned that three safety systems, including a flare tower that could have burned off the leaking gas, were all switched off at the time of the accident. The gas killed 5295 people within days, and, according to local authorities, nearly 10,000 more people have subsequently died of complications from cyanide lesions.

The government has now instructed the Indian Council of Medical Research (ICMR) to set up a center in Bhopal to study respiratory diseases, cancers, genetic disorders, and birth defects. The decision is controversial because years of research have uncovered only acute effects of the gas. The new center is a case of "political expediency," charges Sushil Kumar Jain, a lung specialist here at Moolchand Hospital and lead author of many Bhopal studies.

The move comes in the wake of public outrage over verdicts handed down last month to seven Union Carbide executives, each of whom was sentenced to a maximum of 2 years in prison for negligence. The light sentences in the long-running case are a

"travesty of justice," claims Sunita Narain, director of the Centre for Science and Environment, a nonprofit here. Stung by widespread criticism, the government is looking to retry the accused on the far more serious charge of "culpable homicide."

Bhopal is already familiar turf for ICMR. In an exhaustive report on the accident in 2004, ICMR found that the gas inflicted acute injuries to eyes and lungs but did not trigger cancers or other "progressive" diseases. ICMR also found no evidence of genetic or congenital abnormalities. There is "no interest among researchers to study this tragedy anymore," contends ICMR Director General Vishwa Mohan Katoch. In 2008, he notes, a call for proposals for more Bhopal medical studies drew a mere three responses. Still, Katoch says, ICMR must comply with the order to set up a new center within 90 days.

Also raising hackles is a decision to transfer control of Bhopal Memorial Hospital and Research Centre, established after the accident, to the Department of Biotechnology (DBT) and the Department of Atomic Energy. "This is the limit of absurdity," says molecular biologist Pushpa M. Bhargava, chair of the Sambhavna Trust in Bhopal, a nonprofit body helping victims. "What experience does the Department of Biotechnology have in patient



Paying homage. D. K. Satpathy of Gandhi Medical College and colleagues conducted over 2500 postmortems in 3 days in 1984.

care?" According to DBT Secretary Maharaj Kishan Bhan, the hospital will become a base for environmental biomedical research. The government has also allocated \$77 million to dismantle the plant and for "complete" restoration of the grounds by the end of 2012.

Earlier this year, the National Environmental Engineering Research Institute (NEERI) in Nagpur found no contamination of groundwater in five wells dug at least 25 meters deep at the site. What saved Bhopal from a bigger catastrophe, says NEERI Acting Director Tapan K. Chakrabarti, is a 17-meter-thick layer of clay that has blocked pollutants from leaching into the water table—a silver lining, perhaps, to Bhopal's gloomy story.

—PALLAVA BAGLA

CREDIT: PALLAVA BAGLA