

Spread of Spanish Flu Was Never Experimentally Confirmed

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Young adults were the most vulnerable group to the 1918–1919 Spanish flu, the history’s deadliest pandemic that claimed about 50 million lives. Epidemiological observations suggest that the Spanish flu influenza virus spread by human contact. But human experiments seem to suggest otherwise.

Puzzling Human Studies

The landmark study of Milton J. Rosenau, MD, “Experiments to Determine Mode of Spread of Influenza,” was published in the *Journal of the American Medical Association* in 1919.

- They isolated microbial mixtures from the throat and noses of carefully selected influenza cases from an outbreak location. The researchers then administered these to 10 young U.S. navy volunteers without prior exposure to influenza. None fell sick.

- They drew blood from influenza patients and transferred it to the navy volunteers. None fell sick.
- They collected influenza patients' mucous membranes with swabs and filtered them to exclude larger microbes like bacteria. They then injected the filtrate into the navy volunteers. None fell sick.
- They brought the navy volunteers to meet influenza patients. They shook hands and conversed. The patients also exhaled (as hard as possible) onto the volunteers' face for five times. Then the patients cough directly onto the volunteers. None fell sick.
- In case these ten navy volunteers were somehow immune, though unlikely as they had no prior influenza exposure, the study recruited another set of 50 volunteers. They repeat the experiment with influenza patients from another outbreak location, but could not prove human-to-human transmission. And, intriguingly, one physician involved in the study contracted influenza.
- "I think we must be very careful not to draw any positive conclusions from the negative results of this kind. Many factors must be considered. Our volunteers may not have been susceptible. They may have been immune," Dr Rosenau addressed. "We entered the outbreak with a notion that we knew the cause of the disease, and were quite sure we knew how it was transmitted from person to person," he concluded. "Perhaps, if we have learned anything, it is that we are not quite sure what we know about the disease."

- Other eight human experiments, documented in “Experiments Upon Volunteers to Determine the Cause and Mode of Spread of Influenza, Boston, November and December, 1918,” also failed to confirm how the Spanish flu spread. “Our failure, however, to reproduce the disease with these discharges suggests that there may be unknown factors involved, either in the discharge of the virus from the body, or in its entrance into the victim, or both,” the document ended.
- “Perhaps, if we have learned anything, it is that we are not quite sure what we know about the disease.”
- Reviewing these studies, John M. Eyler, PhD in the historical science at the University of Minnesota, said in a 2010 paper: “It seemed that what was acknowledged to be one of the most contagious of communicable diseases could not be transferred under experimental conditions.”

Possible Explanations Are Unconvincing

- Some argue that participants in those studies were already immune. This is rather unlikely, however, as the volunteers recruited had no prior exposure to influenza. As a 2008 review wrote: “While possible, none of the volunteers reported symptoms in 1918, even a fever.” If the volunteers were indeed immune, an initial infection must happen first to generate adaptive immunity that ‘remembers’ the Spanish flu virus. But, again, the volunteers were never symptomatic.

- Another reason could be that the influenza patients had passed the infectious phase. This possibility, too, is dubious as Dr Rosenau ensured that influenza patients examined were in their first three days of illness, the period where virus shedding peaks.
- Could the participants never contract the Spanish flu virus? Even though no technology could confirm virus diagnosis at that time, “we doubt U.S. Public Health Service physicians had much trouble making an accurate clinical diagnosis of influenza in 1919,” the 2008 review added. Maybe the sick could not transmit the Spanish flu virus to the healthy? Equally improbable as countless healthy people fell sick with the flu at that time.

We'll Probably Never Know the Answer

- The Spanish flu virus eventually disappeared, only to be resurrected in 2005 for animal experimentations to understand its mechanism of virulence. And, indeed, the Spanish flu is a unique influenza virus. “No other human influenza viruses tested were as exceptionally virulent,” the CDC stated. “In that way, the 1918 virus was special — a uniquely deadly product of nature, evolution and the intermingling of people and animals.”
- As human infection experiments are no longer ethical and require extensive enrollment procedure, scientists may never solve why experimental human-to-human transmission of the Spanish flu could not be achieved. At least the human studies showed that human

contact alone does not explain the Spanish flu pandemic. Underlying factors are likely at play. Evidence has suggested that a tuberculosis co-infection might be a prerequisite to a severe flu infection during the 1918 pandemic. Or perhaps animals were the main culprit in driving the 1918 flu transmission.

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