Enders Game

The Playbook: Substitution, Assumption, Persuasion

MIKE STONE
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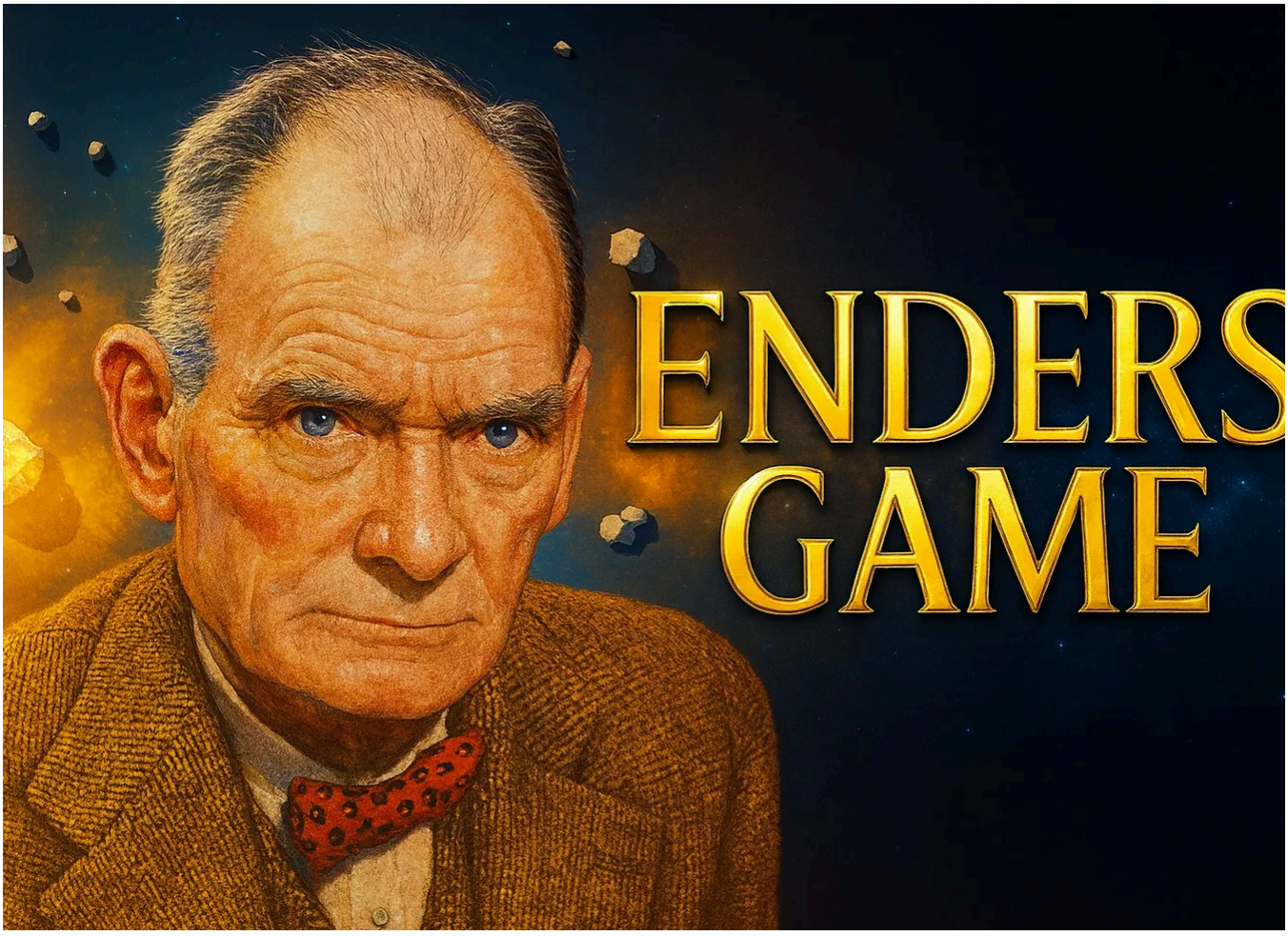


As the conventional history of virology tells it, virologist John Franklin Enders "isolated" and "proved" the measles "virus" in 1954 in his paper *Propagation in Ti Cultures of Cytopathogenic Agents from Patients with Measles*. He did this by develop culturing method that used throat washings from suspected measles patients—collected by gargling fat-free milk and *assumed* to contain a "virus."—which were added to human and monkey kidney cells along with bovine amniotic fluid, beef embryo extract, horse serum, antibiotics, soybean trypsin inhibitor, and phenol r

After several days of incubation, Enders observed morphological signs of cellula degeneration—what he had earlier termed cytopathic effects (CPE) in 1949—whi attributed to the presence of a replicating "virus." However, he had seen this sam effect in "uninfected" cultures, and it was observed in only five of seven clinicall diagnosed measles cases. This contradictory evidence did not deter Enders from proceeding. Based on these cell changes and indirect "immune-serum" reactions measles "virus" was declared "isolated," and the culture method Enders develope became a foundational pillar of modern virology.

What is often omitted from the historical narrative is that Enders did ***not*** claim t had conclusively proven that his "agent" was the measles "virus" in his 1954 pap Although he stated that he had "considerable indirect evidence" supporting an etiological role, he explicitly acknowledged that two critical experiments still ha performed before causation could be established—a standard formalized as Koch Postulates. These were: (1) experimental production of measles in monkeys and i humans using his tissue culture material, and (2) re-isolation of the same agent fr those newly sickened hosts.

Enders wrote:

> "Although we have thus already **obtained considerable indirect evidence** supporting the etiologic role of this group of agents in measles, 2 experiments essential in the establishment of this relationship remain to be carried out. **Th will consist in the production of measles in the monkey and in man with tis culture materials** after a number of passages in vitro sufficient to eliminate ar virus introduced in the original inoculum. **The recovery of the virus from the experimental disease in these hosts should then be accomplished.**
>
> Conclusion. The findings just summarized **support the presumption that this group of agents is composed of representatives of the viral species responsib measles.**"

Despite the caution expressed in his paper, contemporary media quickly transfor Enders' tentative findings into claims of definitive discovery. In a November 19,

article titled ***Enders States Measles Virus Now Isolated***, *The Harvard Crimson* reporte Enders had "very suggestive" evidence that he had "isolated and grown the long-sought measles virus." Enders was quoted as saying, "All evidence points to the conclusion that we have successfully isolated the virus for the first time." He cite "antibody" reactions as strong support for the view that the "suspected virus is it measles." Yet even as these claims circulated publicly, he acknowledged that "fin proof" was still lacking, admitting: "But we have not yet completed the final proc inoculating a susceptible monkey and actually producing the disease." The articl further noted that this "conclusive proof" would be delayed until Enders returne from Stockholm, where he was to receive his Nobel Prize.

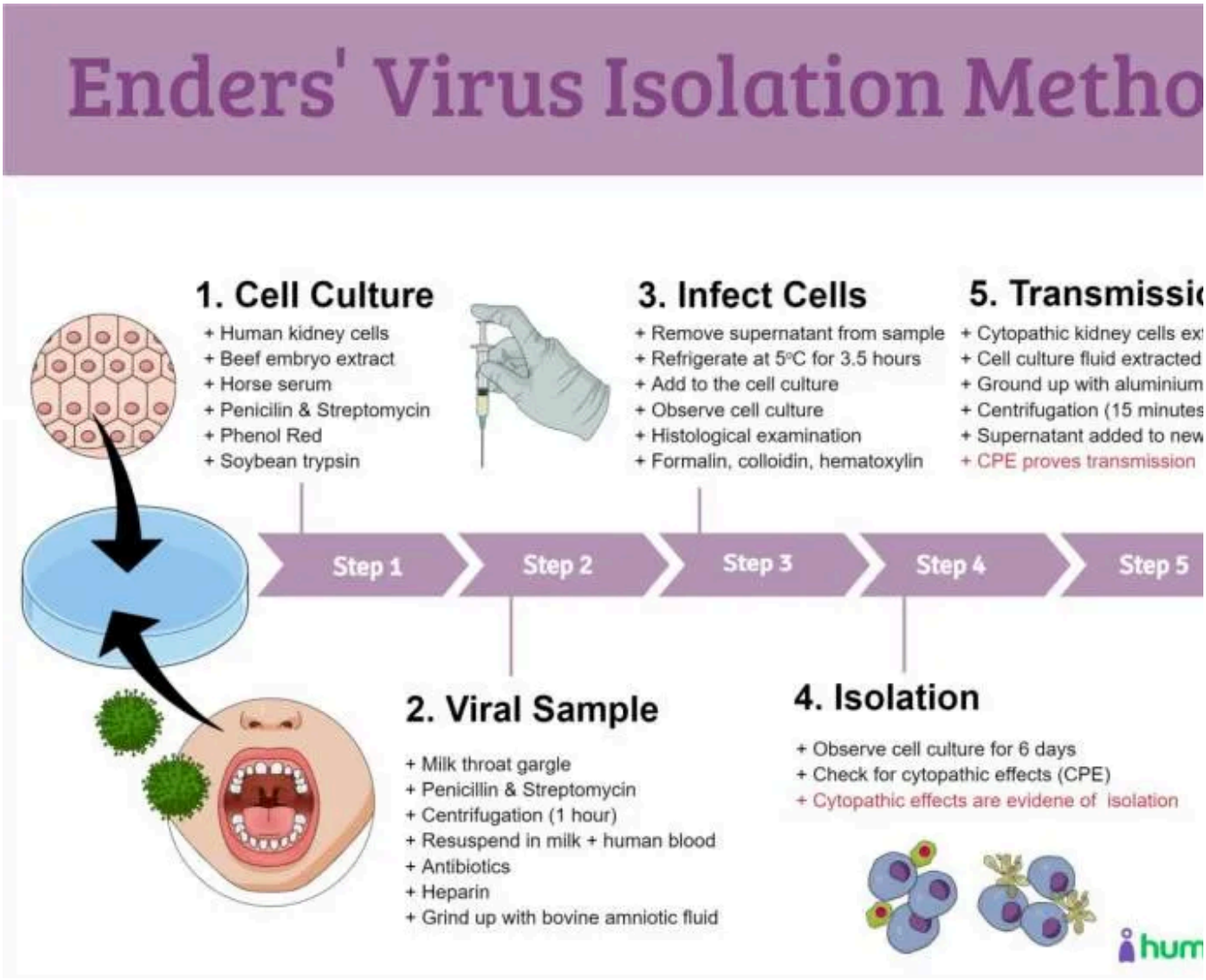
The following day, ***The Key West Citizen*** echoed the story, with Enders emphasizi that while certain tests suggested the agent might be the causative organism of measles, its role remained unproven until disease could be recreated in an experimental animal:

> "He announced Wednesday "**very suggestive**" **evidence of the long-sought isc of the elusive measles virus**—and of **possible means for its laboratory growth** method described **uses a "tissue culture" method** like that which paved the w the Salk vaccine for polio.
>
> Enders told an audience of scientists at the National Institutes of Health that and assistants had found in washings and blood of measles patients "an agent which has passed certain tests **indicating it may be the actual causative orga of measles.**
>
> **It remains to be proved, he said, that it actually is the measles virus**—and **su proof must await production of measles in an experimental animal with the newfound agent.**"

Enders further noted that *if* the proof could be established, *then* it might be possi develop a skin test or a vaccine. In other words, he explicitly did ***not*** view the 195 findings as definitive.

On December 10, 1954, while reporting on Enders' Nobel Prize award, *The Harva Crimson* reiterated that Enders believed he had isolated the measles "virus," whil again conceding that final proof required recreating the disease in animals—something that still had not been done. The article emphasized that Enders had *inoculated monkeys* with the cultured material and that confirmation remained pe though he expressed confidence that disease would result:

> "Nor have Enders and Weller yet reached the limits on research with tissue cu methods. **Ender now believes he has isolated the measles virus**--by using the basic process.
>
> "**It's not a very serious disease** although though it does produce deaths and ha secondary effects in parts of the world like Yugoslavia," Enders notes. He is n least apologetic about **taking up a new project of less significance** than that o isolating the polio virus. "After all," he notes, "**measles are an abominable nuisance.**"
>
> **Final proof of measles virus growth must await Enders' return from Sweden however.** For the 57-year-old research scientist **has not yet innoculated monk with the test-tube grown measles virus.**
>
> **Enders has no doubt** that animals, if exposed, or innoculated **will come down measles.**"



This is especially important given the methodological limitations of the study its By Enders' own admission, both in his 1954 paper and in public statements, criti links in the logical chain of causation were absent. In formal terms, these criteria summarized as Koch's Postulates—require that the suspected microorganism be consistently found in all cases of disease, isolated independently of host material pure culture, shown to reproduce the disease when introduced into a healthy hos then recovered from that experimentally induced illness. Enders' own evidence n it clear that even the first two steps (consistency in cases and isolation in pure cu were not fully satisfied, and the final steps (disease reproduction and re-isolation remained unperformed at the time his findings were publicly declared a discover

Disregarding the fact that the first two logical criteria were overlooked and unm central question practically asks itself: Did Enders ever succeed in producing the disease in animals or humans using his cultured "measles agent," as he himself s

would be required for final proof? Did he ever provide the evidence he publicly acknowledged was necessary?

Let’s find out.

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