The Gamma Globulin for Polio Clinical Trials: Victims of Marketing Success

During the early 1950s, American researchers enrolled over 55,000 healthy children in a medical experiment to assess whether the blood fraction, gamma globulin (GG), could be used as a means to prevent paralytic polio.[1-6] Since a large double-blind placebo controlled study had never been attempted on an open population before, publicity became an inextricable part of the design.[7] Although marketing the experiment was successful and clinic attendance surpassed researchers' expectations, the enthusiasm of parents and health professionals led to unforeseen consequences. Researchers struggled to maintain control of the experiment and later found it difficult to acknowledge the extent of the problems or the implications for medical science. The successes and setbacks of this study later influenced the Salk vaccine trials in 1954, while also raising important questions about the conduct of one of the first "gold standard" clinical trials.

Before a safe and effective polio vaccine was licensed in April 1955, Americans faced the constant threat of polio outbreaks. Caused by an oral-fecal virus, a polio infection could lead to paralysis of the limbs and respiratory muscles, or in extreme cases, death. Although anyone could contract the disease, children seemed the most susceptible, inspiring the term "infantile paralysis."[8-9] Desperate for a means to prevent polio disability, the National Foundation for Infantile Paralysis (now known as the March of Dimes) backed University of Pittsburgh researcher Dr. William McD. Hammon to undertake a controlled study with GG. The blood fraction, rich in antibodies, was already used for the prevention of measles and hepatitis and was therefore considered safe. Hammon hoped that by randomly injecting 4 cc to 11 cc of either placebo solution or GG into the gluteus maximus of children and comparing the two groups, the value of the blood fraction for polio could be established.

Hammon and Foundation officials believed that a publicity program was necessary to encourage parents to volunteer their healthy children. The Foundation drew on its vast marketing expertise and connections to develop a sophisticated marketing program for Hammon's experiment. Unlike the annual March of Dimes polio fundraising drive, which benefited from weeks of advance

publicity, promoting the GG trial would be limited to days, since it was difficult to predict an epidemic and once identified, it would not last long. Moreover, parents would need to be educated to appreciate the value of controlled trial methodology in which only half of the cohort would receive the potentially protective substance. Hammon believed that any protection offered by GG would only last a few weeks, so it needed to be administered at the early stages of an epidemic when passive immunization could offer the most protection. Since parents could decide whether or when to volunteer their children, the faster the maximum cohort was achieved, the greater the opportunity to assess GG. The field team needed to react quickly and be prepared to inject thousands of children in temporary clinics. By anticipating parental anxieties in publicity materials, Foundation officials hoped to provide Hammon with steady enrolment and protocol compliance.

When a high incidence polio epidemic erupted in Utah in 1951, Hammon and Foundation officials launched their experiment. They moved supplies to a staging site in Provo and instigated a publicity program to build local support. Due to state medical licensing laws, only Utah doctors could administer the test serums, making it necessary for Hammon to direct his initial publicity efforts to physicians. To Hammon's astonishment, local doctors made the experiment their own, seeing participation as a professional duty and a form of public health activism. They not only agreed to administer the injections, but also volunteered their own children to the experiment. In addition, radio announcers interviewed members of Hammon's team, while journalists attended a clinic demonstration where researchers submitted to injections to show their faith in the study.

Like doctors, Utah residents strongly supported Hammon's study. Long lines snaked around the clinics, as parents accompanied their children to the injection tables. Although the success of Hammon's study hinged on accurate clinical records and adherence to the protocol, local enthusiasm began to undermine data quality. Some parents illicitly attended more than one clinic to increase the likelihood of their children receiving GG over placebo, which undermined the statistical merit of the study. Although Hammon could not determine the number of multiple enrollments, the practice highlighted a tension between scientific accuracy and the hopes of desperate parents. In an

effort to prevent multiple enrollments, Utah doctors were asked to wipe a common laboratory phenol reagent on the buttock of each child as a temporary indicator of participation. Meanwhile, other parents chose to attend clinics outside of their enrolment areas to avoid disappointment if supplies were exhausted. Hammon also discovered that local volunteers secretly redistributed the test serums to the favor of their own communities. Citizen intervention in the supply chain showed the power that some residents exercised over the study and how their actions undermined the creation of scientific knowledge. Although Hammon was frustrated by the illicit serum redistribution and multiple clinic enrolments, he remained optimistic about the experiment. Over 5,000 children were injected and it was evident that parents and doctors would support scientific research. As statisticians determined that at least another 50,000 children were needed for a significant result, Hammon expanded his experiment.

Since polio was more prevalent during warmer months, the experiment continued the following summer. When a devastating epidemic struck Texas with hundreds of paralysis cases in July 1952, Hammon decided that Houston and surrounding Harris County would be an ideal test site.[10] With Foundation support, he actively promoted the GG study with the assistance of local doctors, politicians, religious leaders, and journalists. The publicity program was so successful that some parents not only enrolled their children at Hammon's clinics, but then asked their family doctors to administer injections of the blood fraction afterwards. Hammon attempted to discourage this practice, since it threatened the accuracy of his data set. When such efforts failed, he moved his injection clinics out of non-compliant areas. In addition, some Texas pharmaceutical suppliers built on Hammon's publicity campaign by promoting their own GG supplies, leading to sales of over 20,000 cc. of the blood fraction to local residents. Of the 35,000 children enrolled in the Texas study, Hammon could not be certain how many had received private doses of GG. An effective marketing campaign combined with parental anxiety at a time of crisis coalesced to shatter the statistical value of the GG study.

Pressure to obtain more data led Hammon and the Foundation to expand the study to Iowa and Nebraska, where they achieved better compliance to the protocol. While Hammon enrolled an additional 15,000 children at these test sites, it was clear that the experimental data was already tainted. Hammon's lack of power over trial conduct and compliance, combined with the Foundation's focus on promoting the experiment, created a wave of optimism that was difficult to contain. Hammon was forced to assess data of dubious quality. When the results of the experiment were finally published, Hammon's decision not to acknowledge these serious shortcomings facilitated a claim that GG worked for the prevention of polio paralysis under epidemic conditions.[1-5] Because the experiment was expensive to undertake, the results could not be corroborated by other researchers. When the Foundation trumpeted the proclaimed scientific success of the study, Hammon became America's foremost polio warrior.

Due to prevailing optimism about GG, the Foundation spent millions of dollars to procure hundreds of gallons of the blood fraction for a national polio immunization program in 1953 and 1954. Over 220,000 children received injections across America and 1,728,700 cc. of GG was administered. Although many parents and health professionals had no reason to doubt the value of the blood fraction to fight polio, evidence began to emerge that it was not effective. When data was collected about the national program in 1953, the WHO Expert Committee on Poliomyelitis and the United States Public Health Service delivered cutting indictments.

The embarrassment surrounding the ill-fated use of GG was salvaged by the field testing of Dr. Jonas Salk's killed-virus vaccine. Foundation officials called on their experience with GG when designing the Salk polio vaccine trial. They were confident that an enormous civilian experiment was possible, since the GG study showed that parents would volunteer their children to an experiment that did not guarantee efficacy or safety. They also refined publicity materials, including films, radio announcements, and posters. In an effort to increase the perceived scientific rigor and impartiality of the test, Foundation officials established the Vaccine Evaluation Center at the University of Michigan under the leadership of Dr. Thomas Francis Jr. Following a massive trial, Francis declared

the Salk vaccine to be safe and effective and it was licensed on April 12, 1955. Unlike GG, it could be administered before an epidemic and provide durable immunity to all three types of poliovirus. Although the vaccine marked a major milestone in the polio eradication effort, the earlier testing of GG offered important lessons for researchers and their sponsoring agencies concerning how marketing and parental anxiety could inadvertently affect the generation of accurate scientific evidence.

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References

1. Hammon, W. M., L. L. Coriell, and J. Stokes Jr. “Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 1. Plan of Controlled Field Tests and Results of the 1951 Pilot Study in Utah.” *Journal of the American Medical Association* 150 (1952): 739–749.
2. Hammon, W. M., L. L. Coriell, and J. Stokes Jr. “Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 2. Conduct and Early Followup of 1952 Texas and Iowa-Nebraska Studies.” *Journal of the American Medical Association* 150 (1952): 750–756.
3. Hammon, W. M., L. L. Coriell, P. F. Wehrle, C. R. Klimt, J. Stokes Jr. “Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 3. Preliminary Report of Results Based on Clinical Diagnoses.” *Journal of the American Medical Association* 150 (1952): 757–760.

4. Hammon, W. M., L. L. Coriell, P. F. Wehrle, J. Stokes Jr. “Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 4. Final Report of Results Based on Clinical Diagnoses.” *Journal of the American Medical Association* 151 (1953): 1272–1285.
5. Hammon, W. M., L. L. Coriell, E. H. Ludwig, R. M. McAllister, A. E. Greene, G. E. Sather, and P. F. Wehrle. “Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis. 5. Reanalysis of Results Based on Laboratory-Confirmed Cases,” *Journal of the American Medical Association* 156, 1 (1954): 21–27.
6. Rinaldo, Charles R. “Passive Immunization against Poliomyelitis: The Hammon Gamma Globulin Field Trials, 1951–1953.” *American Journal of Public Health* 95, 5 (May 2005): 790–799.
7. Mawdsley, Stephen E. *Selling Science: Polio and the Promise of Gamma Globulin* (New Brunswick: Rutgers University Press, 2016).
8. Rogers, Naomi. *Dirt and Disease: Polio Before FDR* (New Brunswick: Rutgers University Press, 1992).
9. Paul, John R. *A History of Poliomyelitis* (New Haven: Yale University Press, 1971).
10. Wooten, Heather Green. *The Polio Years in Texas: Battling a Terrifying Unknown* (College Station: Texas A&M University Press, 2009).