Animal Research

Jeffrey L. Fox closes his article on changes in animal care policy (News and Comment, 27 Apr., p. 364) with the comment that scientists should not use dramatic testimony from patients who have benefited from animal research because it "runs the risk of widening rather than narrowing the gap between the animal welfare and research communities." I disagree. The nuclear power industry is in trouble in part because they chose to disregard those who opposed the infant technology. Now those in opposition have such power that it is nearly impossible to contradict them.

Similarly, the research community must take the strongest possible action now while the animal rightists are still relatively vulnerable. I have watched them in action and attended rallies. They are not often open to reason. If we as scientists are to continue to be able to work on research with animal systems, we must use all of the tools at our disposal. In this case, it means using those extremely powerful emotional testimonials, showing up at animal rights rallies with literature supporting animal use in research, and generally trying to reach the public with the importance and necessity of animal research. I encourage local scientific groups to get together and fight this destructive movement to ban animal research before it is too late.

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Yellow Fever Research

Colin Norman, in his article "The unsung hero of yellow fever" (News and Comment, 30 Mar., p. 1370), does an excellent job of defining the controversy over who really solved the riddle of yellow fever. But, as coauthors of *Guinea Pig Doctors*, we feel obligated to comment on several critical points.

One of those points involves the nature of the key discovery itself. The decisive piece of information was not the 12-day incubation period, as stated in the article. The key was the fact that yellow fever was only contagious during the early stages of the disease, when it was difficult to distinguish from typhoid, malaria, and influenza. Earlier experiments with mosquitoes failed because researchers, not wanting to clutter their data with misdiagnosed patients, always used late-state cases. By that time the patients definitely had yellow fever but, unknown to the scientists, could no longer pass it on.

Ask yourself, as we asked ourselves, which of the players was in a position to make this discovery? Was it Walter Reed and James Carroll, who were convinced almost until the very end that yellow fever was caused by bacteria? Or was it Jesse Lazear, who had spent years studying mosquito-borne disease?

The Reed scholars are saying, in essence, that Jesse Lazear, the mosquito expert, was not capable of understanding his own notes on mosquitoes but that the bacteriologists, finding the notebook after Lazear's death, understood instantly what it all meant. Our readings tell us that, while Lazear may have been self-effacing to a fault—while he may have been too sincere, too honest, and too naïve for the world he found himself in—the one thing he was not was stupid.

In any event, William Bean suggests that Reed should get the credit for brilliant confirming experiments, and that after all there was plenty of credit to go around. By that argument we could quit making so much of mere discovery and start awarding Nobel Prizes to the folks who do the follow-up.

Finally, we are bemused by the author's slightly condescending attitude toward the popular style in which we presented our work in *Guinea Pig Doctors*. What we are objecting to is a question of tone and example that was probably quite unintentional. Nevertheless, it opens up the issue of popularization, its purposes, and its place in the literature of science.

Norman complains that our book is not scholarly enough, and he implies that our research relied heavily on a single paper published in the alumni magazine of the Columbia University College of Physicians and Surgeons, Lazear's alma mater. It is true that such a paper exists, that we found it, and that it bolsters our conclusions. But it is hardly the cornerstone of our case against Reed.

A far stronger piece of evidence, for example, comes from the writings of Albert E. Truby (*1*), the Army doctor who cataloged Lazear's personal effects after his death. Truby found what he termed "the precious notebook" and gave it to Reed.

Reed, said Truby, became very excited about the discovery. "Hurrying back to his quarters, he immediately began to investigate the papers obtained from Lazear's quarters. In the notebook he found the data he wanted."

Granted, we do not tell the reader all this in footnotes. Granted, the lack of footnotes means that Norman must call us and ask us questions. But it emphatically does *not* mean that we skimped on our homework.

The hard reality is that, in a world of great ignorance about science, scholarly tomes are notorious for going unread. Our purpose in writing *Guinea Pig Doctors* was to share some of the human drama of science with the lay public—to excite them with our vision of research as a deeply human process.

Whatever the readers' conclusions regarding the case of Reed and Lazear, it is important to remember that truth is not necessarily a function of footnotes and that "popular" writing is capable of great substance.

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1. A. E. Truby, *Memoir of Walter Reed* (Hoeber, New York, 1943).

Norman's article intimates a dispute as to whether Reed or Lazear discovered the spread of yellow fever by the mosquito: the fact is, neither one did!

Reed planned and carried out a brilliant, controlled human experiment that definitively proved that the mosquito was the vector of yellow fever, but he did not discover the fact. Lazear did discover a method to produce experimental cases of the disease, without which Reed would not have been able to stage his experiments. Reed must be held responsible for the loss of Lazear's notebook, officially entrusted to him; it has never been found.

The January 1984 *Scientific American* recalls in "50 and 100 Years Ago" that in January 1884 Carlos Finlay published an article on microscopic observations of the proboscis of the mosquito and insisted on its ability to transmit yellow fever: this was 13 years before Reed wrote his first scientific paper on hog cholera.

Reed was vacationing in Point Sublime, Pennsylvania, while his associates, Carroll and Lazear, as well as Soldier Dean, contracted yellow fever through the bite of an infected mosquito. Even after Lazear's death, Reed wrote that these cases "proved nothing." For his return to Havana, he asked that he be given personal quarters in the "non-infected area" of the post.

Reed listed his associates as coauthors of his Preliminary Report and mentioned that Finlay had given them ova of a mosquito. However, he did not point out that the eggs were of the specific culprit that Finlay had discovered, out of numerous species, as the one capable of transmitting yellow fever and the one with which Finlay had made 105 inoculations of human volunteers. Reed could have rendered proper homage to the man who for 18 years had struggled to have his truth accepted. Neither did he give credit to Lazear for his transcendental technological contribution.

Carroll, Reed's protégé and devoted assistant, carried out additional experiments in Havana, in which the American nurse Clara Maass lost her life. Carroll actively and persistently protested the excessive credit given to Reed; he insisted that, if only one member of the U.S. Army Board was to have been singled out, it should have been Lazear. Carroll's daughter, the late Ethel McClung, graciously permitted me to catalog her father's papers; they contain interesting items, but not, as I had hoped, Lazear's notebook.

Reed appears to have not been satisfied with the comfortable position of those who are credited beyond measure; he initiated subtle innuendos that were repeated to his advantage. As he read Lazear's notebook, he became excited and wrote to his wife: "Lazear contracted the disease by letting a mosquito bite him . . . in order to test *our theory*" (emphasis mine). He also contributed to the myth of Finlay as a whimsical country doctor.

William Gorgas, an important protagonist of this saga, gave public credit to Finlay: "his inspiration was laughed at, his theory was mistaken for the fanciful illusion of a tropical imagination. . . I cannot pronounce his name with due reverence." Upon publication of these remarks, Reed wrote to Gorgas: "I know you did not intend to say it, but somehow, I suppose being back in Havana, you feel it your duty to honey-fuggle the simpering old idiot." In response to these incredible remarks, Gorgas, true to his reputation as a southern gentleman, forcefully reiterated his view of Finlay's genius, that his selection of the *Stegomyia* (*Aedes aegypti*) was the best piece of medical reasoning to be found anywhere.

My article on Lazear is listed among Norman's references, and he states that Franklin and Sutherland relied on my article for key information. Thus, I feel obligated to reveal my sources: with one exception, all of the relevant facts in my article and the quoted ones in this letter can be substantiated and extended in Walter Reed's own alma mater, in the *Hench Yellow Fever Collection*, to which I was graciously introduced by William Bean. The one exception, Reed's letter to Gorgas (31 January 1902), with the invidious remarks about Finlay, is to be found in the Denver Medical Society Library.

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There is no dispute about the central "revelation" in Franklin and Sutherland's account of the yellow fever work: Lazear carried out the key early experiments, and Reed relied on Lazear's notebook to write the first Preliminary Report of the yellow fever board. Neither is there any question about Finlay's pivotal role. As I said in my article, Finlay published his mosquito theory nearly two decades before the Reed board began its work; by "a piece of brilliant deduction" he singled out the right mosquito; and he provided the board with ova for its experiments.

del Regato maintains Reed did not give Finlay sufficient homage in the Preliminary Report. The Report actually stated that the theory was "first advanced and ingeniously discussed by Dr. Carlos J. Finlay, of Havana, in 1881." It expresses "sincere thanks" to Finlay for discussing his work with the board and providing ova "of the variety of mosquito with which he had made his several inoculations." It says that "we have not space to refer, at length, to the various interesting and valuable contributions made by Finlay to the mosquito theory," but lists several of his papers. And, finally, it concludes that the board's observations "must excite renewed interest in the mosquito-theory of the propagation of yellow fever, as first proposed by Finlay."

In his response to Reed, Gorgas affirmed his respect for Finlay, as del Regato states, but went on to say: "You are the great man in the matter. His [Finlay's] theory would have remained an idle dream except for your work."

Franklin and Sutherland contend that Lazear's key discovery was not the 12-day incubation period, but the finding that yellow fever is contagious only in the early stages of the disease. Ironically, as I mention in my article, Reed failed to mention the critical contagious period in the Preliminary Report, and it was not listed among the 11 conclusions in the Additional Note, published in February 1901. Earlier experiments failed because the mosquitoes did not bite patients in the early stages *and* incubate the virus

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for at least 12 days. No "Reed scholar" I encountered believes Lazear could not understand his own notes.

Lazear is certainly not the first junior researcher who did key work for which the head of the research team is remembered. Reed's supporters maintain, however, that Reed helped plan the experiments and provided the definitive proof with his controlled studies. In his firsthand account, for example, Truby says that Reed and the board discussed mosquito studies with two visiting English researchers in July and showed them the board's facilities for raising the insects. This was some time before Reed left for the United States. The board also discussed human experimentation and the need to volunteer themselves before Reed departed.

Franklin and Sutherland build up their case against Reed by vividly reconstructing events with telling details. When asked the sources for some of these details, Sutherland said they did not go back to documents from the period but relied on other accounts, including del Regato's, and used some "extrapolation." As I said in my article, it is sometimes difficult to tell where established fact ends and imaginative reconstruction begins.—COLIN NORMAN

Formaldehyde Risk Assessment

The published version of our response to William R. Havender's comments on formaldehyde (Letters, 11 May, p. 556) contains two inadvertent misstatements that should be corrected for proper interpretation. The "further argument on linearity" (second column, first full paragraph) is inappropriately attributed to Havender. It is we who make the argument that the "best estimate" dose-response functions for genotoxic carcinogens may well be linear at low doses, not he. Further, the formula for saturable Michaelis-Menton enzyme kinetic and transport processes is incorrectly stated. The correct form of the second line of this equation is as follows:

$$(\sim \text{low } [S])\ V_{max}[S]/K_m$$

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(Continued from page 1092)

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