

**N = 1, Fortuitous Effects, and AIDS Research**  
**by Michal Jasienski**

A recent article on xenotransplantation (R. Finn, *The Scientist*, Aug. 19, 1996, page 1) and two published responses to my commentary (M. Jasienski, *The Scientist*, March 4, 1996, page 10), which was critical of a single-subject baboon Bone-marrow transplant trial, prompt me to explicate some methodological issues further.

What insights can a single-subject study provide? While, as pointed out by J.E. Janosky (*The Scientist*, May 27, 1996, page 12), there could be some room for N = 1 studies (see e. g. H. Motulsky, *Intuitive Biostatistics*, New York, Oxford University Press, 1995), a letter by J.G. Llauro (The Scientist, July 8, 1996, page 12) unintentionally strengthens my skepticism in this matter. Llauro writes that the currents that Alessandro Volta used on himself to study electricity are "today believed sufficient to cause lethal arrhythmias on a less corpulent man than Volta." Is it then not quite fortunate for the development of science that Volta was overweight (that is, not representative of the whole population)? How many Voltas were there who were scrawny and, consequently, electrocuted? I suspect that many similar single-subject experiments gain from selective memory.

There is a deeper point, though. Any empirical science moves from general demonstrations to refinements. Single-subject demonstrations of the applicability of laws of nature rely on the subject's being roughly representative of its kind. You've seen one, you've seen them all apples falling to the ground. This is because the property we focus on (mass, rather than, say, color) has indeed the greatest bearing on the phenomenon we are trying to explain (apple's falling down). How often can we be sure, however, which properties as expressed in a John Doe are robustly representative of the responses of all mankind? Granted, it has certainly worked in the past, as Llauro correctly points out, but the lucky single subjects were representative of the human species only because the questions were about some of the most fundamental phenomena. Our knowledge becomes more and more subtle, however. Rough ideas, approximate explanations, and nonmechanistic predictions are no longer sufficient, especially in medicine.

While I am full of admiration for Jeff Getty's perseverance and fortitude in his involvement in the baboon bone-marrow transplant trial, I would wish the results of his efforts were not rendered uninterpretable by the weakness of the experimental design. I hope that the Food and Drug Administration and the medical establishment are equally determined to follow Getty's leadership with the state-of-the-art statistical methodology. A high-tech approach is a necessary, but not a sufficient, component of a successful study. Statistically sound design will always be a condition sine qua non. Alas, N = 1 is not it.

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