Letters

HIV Infection in the Laboratory

In their report "Risk of human immunodeficiency virus (HIV-1) infection among laboratory workers," Stanley H. Weiss *et al.* (1 Jan., p. 68) make repeated reference to "concentrated virus." We wish to remind readers that concentration of an infectious agent is far less important than its pathogenicity. The strain that has infected two laboratory workers to date is presumed to be a strain of HIV-1, designated HTLV III_B whose clinical origins are obscure. Another strain of HIV-1 called LAV, with a genome virtually identical to HTLV III_B (*1*), was isolated from an individual who is still alive and reported well at least 6 years after the initial isolation (*2*). It may be, therefore, that the pathogenicity of these particular strains is low. However, this does not mean that individuals will only become infected by large amounts of virus, but rather that only a few virus particles will succeed in being infectious. Any laboratory worker exposed to any amount of virus is at risk, whether the virus is "concentrated" or not.

We heartily concur that all laboratory workers should receive quarterly testing and suggest both a sensitive enzyme-linked immunosorbent assay (ELISA) and a Western blot in conjunction with appropriate counseling and confidentiality of test results. The beneficiaries of testing will be not only laboratory workers themselves but their loved ones.

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Response: Our focus on potential exposure to "concentrated" virus arose because of the fact that both the worker reported in the cohort study and the second worker shared laboratory procedures in different settings that involved the handling of large volumes of concentrated virus (*1*). It is well recognized from infectivity studies that potential human pathogens vary in their infectious dose. Thus some agents require fewer than ten infectious organisms to result in a human infection while others require significantly larger doses (for example, more than 10^6 infectious organisms). For HIV the number of particles needed to cause infection in humans has not been quantified, but it would not appear to be one of the more infectious agents to which health care and laboratory workers are exposed. This is evidenced by the failure in numerous studies to document "casual" household transmission, the rarity of infections resulting from parenteral inoculation in the hospital setting, and the fact that, in our cohort, among the ten workers experiencing parenteral exposure to potentially infectious apparatus, none seroconverted, although the second worker who did seroconvert, who was not in our cohort, did experience parenteral exposure (*1–3*). It is recommended that biosafety level 3 practices and containment be followed for HIV, since it is a dangerous human pathogen. In our report we emphasized certain biosafety practices to prevent inapparent exposures or unnecessary risk resulting from the use of glass or sharp instruments, in agreement with the concerns of Fox and Fox for careful biosafety practice.

With regard to the speculation about laboratory strain variation and disease pathogenicity, HTLV-III_B differs from the LAV strain by 144 nucleotides (*4*), and HTLV-III_B has a polymorphic variant of the *R* gene different from that shared by LAV and ARV (*5*). Whether there are less pathogenic strains of HIV, as suggested from the follow-up of Clavel's LAV patient and in vitro correlates of the original 48 HIV isolates (*3*), or whether host or other factors explain different rates of disease progression, remains to be established. While the strain isolated from the laboratory worker was indistinguishable from a subclone of HTLV-III_B, it is noteworthy that this T lymphocyte–adapted laboratory strain could be isolated only from monocyte-macrophages of the individual (*1*). Careful molecular analysis of the isolates from the worker are under way to search for subtle changes in the nucleotide sequence of the virus that may explain this altered tropism. The difference between LAV and HTLV-III_B is significantly greater than that between HTLV-III_B and the isolate from the laboratory worker. Thus, if even subtle mutation can result in changes in tropism or pathogenicity, or both, then the apparent lack of pathogenicity noted for LAV may not be relevant for HTLV-III_B.

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Historiographic Distinctions

In his review (8 Jan., p. 198) of my book *Darwin and the Emergence of Evolutionary Theories of Mind and Behavior* (*1*), John Greene states: "Human nature has dimensions that escape, and must forever escape, the abstractions of science." I rather believe there is no other way to knowledge than the kind of thinking that drives science. On several points of fact and logic, though, I believe Greene has attempted an alternative.

Greene writes that "Richards fails to distinguish" between considerations that led Lamarck and Darwin to adopt an evolutionary theory and those that led them to advance certain mechanisms to explain species change. The distinction, a standard one, I most assuredly made, and precisely in those terms he suggests I neglected (*1*, pp. 47–48 and 79–81). I even referred to Greene's own theory about what led Lamarck to his initial formulation (*1*, p. 47). Greene's remarks about Herbert Spencer, a figure who quickly polarizes historians of biology, epitomize the difficulties I have with his review. Greene quotes me as praising Spencer's entire philosophical-scientific system—with the implication that anyone would be foolish to do so. But the truncated quotation he uses refers only to Spencer's ethical notions, especially of justice and altruism (*1*, p. 303). Greene writes that "Spencer himself eventually admitted that his ethical principles and social theory did not require evolutionary biology as a foundation" and uses this supposed admission to rebut my argument that Spencer's ethical ideas determined his evolutionary theory. I do not know on what grounds Greene bases this statement. In an earlier essay, he surmised: "The truth of the matter is that [Spencer's] social ideal had never really been grounded in biological science, much as he liked to pretend that it was" (*2*). A historian's surmise about Spencer is quite different from "Spencer himself eventually admitted. . . ." (Another assertion attributed to Lamarck is, I believe, a surmise.) The last phrase in the quotation from his essay indicates that at the time Greene himself believed Spencer never "eventually admitted. . . ." Moreover, in Spencer's last major ethical work, *Principles of Ethics* (1893), which I discussed at length, he explicitly sought to derive his basic moral principles from evolutionary laws. In a way, Greene's series of counterclaims is beside the point. My primary thesis in the chapters on Spencer was not that his ethics depended on his evolutionary theory; it was that his evolutionary theory depended on his ethics. It is a simple error to render these two relations of dependency as logically equivalent.

Although Greene generously appraises

the significance and scope of my study, it is clear we differ greatly on the historical reconstruction of 19th- and 20th-century biology. Readers should not be left with the impression that my argument teeters on the faulty supports he alleges.

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Response: I hope that the readers of my review of Richards' book understand that I consider it an important, if controversial, work—"well-researched, thought-provoking, ably argued, and highly readable." If I did not catch the drift of his argument in every detail, it was not for want of trying. Obviously, Richards and I disagree in many respects in our interpretation and evaluation of Herbert Spencer, and in all respects about the omnicompetence of science. So be it. Spencer's reservations about the relevance of evolutionary theory to his ethical maxims may be found in the preface to the second volume of his *Principles of Ethics*. I hope readers will be motivated to read both Richards and Spencer and form their own judgments on the issues raised in this exchange of opinions.

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Primate Research and "Psychological Well-Being"

Thank you for Constance Holden's informed article about the status of laboratory animal regulations (News & Comment, 13 Nov., p. 880). The 1985 amendment to the Animal Welfare Act requires the U.S. Department of Agriculture (USDA) to develop standards for physical environments that promote "the psychological well-being of laboratory primates." Last spring, USDA's Animal and Plant Health Inspection Service (APHIS) assembled a national advisory group to review regulations it was considering for adoption. The group included nationally recognized behavioral scientists and veterinarians with first-hand experience in primate husbandry and research. They analyzed the proposal and returned a much-revised version that APHIS will presumably take into serious consideration as it redrafts regulations to implement the 1985 law.

APHIS faces the problem that, while biomedical researchers are willing and eager to change their facilities to improve the psychological well-being of laboratory primates, they want reasonable assurance that the changes mandated will in fact have the desired effect. There are essentially no scientific data to support more specific requirements for single housing of laboratory primates than now exist in USDA and National Institutes of Health guidelines.

Eventually, four features of single cage housing are reasonable candidates for regulation to promote psychological well-being: cage size, opportunities for social contact, exercise, and cognitive stimulation. Cage size is the most salient target for arbitrary revision. Even minor changes in U.S. cage size standards translate into millions of dollars of investment in new and renovated hardware. There is now considerable public and congressional support for upgrading laboratory primate facilities, but arbitrary changes in cage dimensions that have no effect on the well-being of the animals can rapidly squander that support. APHIS needs to know the threshold cage dimensions at which the most commonly used laboratory primates evidence stress, the cage sizes that the animals "prefer," and the strength of those preferences.

Second, while behavioral scientists generally agree that social deprivation can compromise the psychological well-being of primates, it has also been established that frequent change in group composition is stressful (*1*) and can produce disease in macaques (*2*). In laboratories where animals only stay for a limited time, no physical contact may be better for psychological well-being than enforced contact with ever-changing strangers. What are the critical time parameters? Are there simple ways to identify compatible partners? Similarly, it must be established whether exercise and cognitive stimulation reduce stress in adult laboratory primates. How consistently do they respond to opportunities for exercise and other forms of stimulation?

These questions can be answered by relatively straightforward experiments. Physiological measures of stress and behavioral techniques for testing preferences and motivational intensity exist for assessing the influence of such factors on psychological well-being.

The necessary studies should be done in a few qualified laboratories before all of the several hundred primate laboratories in the United States are required by federal regulation to build facilities and adopt the husbandry routines necessary to ensure that every laboratory primate has such experiences.

Since the term "psychological well-being" entered the federal regulatory lexicon, at least four national meetings of professional biomedical, veterinary, and animal welfare societies have focused on the issue of laboratory primate housing and husbandry. The key questions are being delineated, and several laboratories have initiated pertinent research. Let us hope that arbitrarily restrictive regulations do not arrive before the answers.

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Census Undercount Recommendation

Marjorie Sun's News & Comment article (29 Jan., p. 456) quotes former Census Advisory Committee (CAC) chair Benjamin King as saying that the American Statistical Association advisory group recommended in April 1987 that the Census Bureau "should plan to provide adjusted counts after the legal requirement dates, if necessary, so we can know as much as we can about the undercount."

However, the complete CAC recommendation stated, "*Should* the determination in May be that adjustment is feasible, *and if* subsequent analyses support that decision, the Bureau should plan to provide adjusted counts after the legal requirement dates for apportionment and redistricting, if necessary. If the Bureau does decide to adjust, we recommend that it view the adjusted estimates as generally superior to the census counts in planning its data release program" (emphasis added).

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Erratum: In Mark Crawford's News & Comment article "Superconductor funds flat" (4 Mar., p. 1089), Robert J. Birgeneau was reported to have had his grant cut to $4.4 million. That National Science Foundation grant actually covers the Massachusetts Institute of Technology's Materials Research Laboratory and supports 40 faculty members. Birgeneau's personal grant was reduced from $125,000 in 1987 to $122,000 for this year.