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Statistics of Ancestral Roots

My comment reported in Constance Holden's News Focus article "Were Spaniards among the first Americans?" (19 Nov., p. 1467) was a general, not a specific, comment on Walter Neves' interpretation of the hominid skeleton Luzia. Nevertheless, Neves' comment (*Science's* Compass, Letters, 11 Feb., p. 974) that he and his colleagues have "almost 15 specimens dated between 8500 and 11,500 years ago" is no contradiction of my statement in Holden's article that variation within (and, I should have said, intergradation between) racial groups today is so great that it is impossible to identify an individual's roots on the basis of sparse skeletal evidence. Multivariate statistics won't offset small sample sizes. Whether analysis is based on 1, or 15, or 30 individuals spread out over a 3000-year period, any attempt to assign them to a race is spurious: they do not constitute a

population, and there is not enough evidence to point conclusively to any original homeland or to affinities (other than coincidental ones) between them and modern Australians or Africans.

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A Question of Permanence

Scientific literature has a definite structure, a connectivity matrix consisting of citations from one article to previous articles. This structure was recognized by *Science* 45 years ago (1). In fact, *Science* took a leadership role by publishing several articles dealing with the literature (2-4). Publishers of online journals, however, do not seem to appreciate this inherent structure.

In Floyd E. Bloom's Editorial "Lunch selections expanding" (4 Feb., p. 801), he refers to the *British Medical Journal* policy of allowing authors to make changes in their online articles. Although this policy may be innocuous in itself, in the same category as meeting presentations, it would be disastrous to the literature

structure if these ephemeral articles are allowed to be cited. The inherent value of paper journals is that they cannot be changed once published. Any changes must be made in a subsequent publication. That way, an author citing an article can be assured that the information referred to in it does indeed exist exactly as it was read. If articles are ongoing works in progress, the utility of the published literature breaks down.

Articles may be cited many decades after they have been published (5). Meta-analyses are based on the permanence of their underlying articles. Current concern over such matters as peer review and format pale into insignificance if the basic integrity of the literature structure is lost.

Science has advanced because of its literature structure. Online journals certainly have many advantages over paper, but they must also preserve the basic advantage of paper—its immutability. Citation networks differ from hyperlinks, a point scientific publishers must keep in mind. I'm concerned that students today are getting the impression that if information is not available online, it doesn't exist. On the other hand, we old-timers think that if something is not published on pa-

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per, it doesn't exist. We need to reconcile these divergent views.

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Clinical Research

The Policy Forum by Ralph Snyderman and Edward W. Holmes, "Oversight mechanisms for clinical research" (*Science's Compass*, 28 Jan., p. 595), is a positive addition to the growing debate concerning the state of clinical research and the problems that have accompanied human experimentation over the years (1). Snyderman and Holmes correctly point out the complex array of duplicate regulations and the problems inherent in complying with multiple regulations and their interpretations. The Food and Drug Administration, Office for Protection from Research Risks (OPRR), and institutional review boards (IRBs) often offer their own interpretations of the regulations, and it may be difficult to discern how they envision specific regulations to be implemented. There are additional issues that were not elucidated by Snyderman and Holmes, yet are central to the field of regulation and proper conduct of clinical investigation.

For example, a major weakness in our efforts to protect patients from the risks inherent in participation in clinical trials is the informed consent process. No regulation, however detailed, will improve this process until potential participants are fully informed of what they are volunteering for, and until methods for improving the entire process are developed and studied. Emphasis on the informed consent form, and not on the process of continuing education of study participants in the nature of the study and their role in it, will result in continued focus on a piece of paper, to the detriment of establishing true informed consent.

Another problem is that the IRB is not just another university or hospital committee. The IRB is mandated by law to perform certain specialized tasks. It has regulatory authority and must adhere to specific regulations. Members need to be educated in the proper conduct of their work, and this has been woefully inadequate (2). Sufficient resources need to be provided to the IRB (2), and members need to realize that the activities of an IRB member differ from those of members of other committees. The recent OPRR actions against the IRBs of several respected academic medical centers (3) support the recognition of the IRB as a special activity

in the medical center and university.

Snyderman and Holmes identify "ethics of physicians being remunerated by pharmaceutical companies" as an important conflict of interest. However, proper conduct of clinical investigation requires time and effort, for which investigators should be compensated. Moreover, such compensation in the academic setting invariably goes to the investigator's section or department and not to his or her personal bank account. The conflict inherent in institutional faculty reviewing grants that may deliver millions of dollars of support, not to mention the accompanying prestige, to the institution that employs the members of the IRB is another conflict that needs to be addressed.

Finally, the stress inherent in a physician functioning as both a health care provider and a principal investigator of a clinical study has been acknowledged (4), yet no satisfactory resolution has been proposed. The two roles are irreconcilable, because the aims of each of these positions are in direct conflict. Creative solutions that incorporate sufficient safeguards for human rights and participant protection are urgently needed.

As clinical investigation engages more of the general population and a significant number of those in the health care system, there is an urgency to more completely develop the dialogue within the medical community and the population at large. Our efforts to ensure ethical conduct of experimentation with humans need to catch up with the incredible advances in science.

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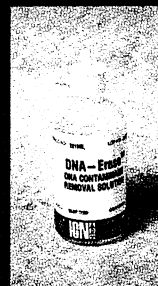
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CORRECTIONS AND CLARIFICATIONS

Letter: "Luzia is not alone" (*Science's Compass*, 11 Feb., p. 974). In two instances the word "million" was inadvertently added to human skeleton ages during editing. The oldest human skeleton found in the Americas dates from 11,000 to 11,500 years ago, and the 15 specimens referred to in the last paragraph date between 8500 and 11,500 years ago.



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