Letters to the Editor

Letters (~300 words) discuss material published in Science in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Editorial Retraction (I)

RECENTLY, AS A RESULT OF THE REPORT OF THE
Beasley Committee to Bell Laboratories, Lucent Technologies, several papers on which J. H. Schön was the lead author have been retracted. Another paper (1) that was published by Science was not formally analyzed by the Beasley Committee. Although we recognize that some parts of this paper may remain valid, we note that key parts depend on and cite results or methods derived from two of the already retracted papers (2, 3). We therefore advise the scientific community that the validity of all of the results in this paper cannot be established.

DONALD KENNEDY

Editor-in-Chief

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that these journals will now have a policy in which editors will screen and, if necessary, reject manuscripts submitted for publication if “an editor … conclude[s] that the potential harm of publication outweighs the potential societal benefits.”

Clearly, there are individuals, groups, and even rogue governments that might seek to use biological agents to infect and kill others as a means for political gain or as part of a general philosophy for causing terror. Most of the concerns raised about what is or is not sensitive information revolve around pathogenic microorganisms, toxins, and other factors associated with infectious diseases of humans, livestock, and plants. It is not a new problem. My quarrel is not that the editors have agreed that a course of action was necessary, but rather what they failed to say or do on the subject.

The editorials accompanying the statement have been characterized as a tactical act of good citizenship. The statement itself and the editorials are notable for their failure to provide guidelines regarding who exactly would make these decisions about publication and what constitutes a potential contribution to the activities of bioterrorists.

Some 25 years ago, guidelines were adopted by the scientific community that still apply stringent restrictions on genetic manipulation of many microbial pathogens, including the introduction of antibiotic-resistance genes into microorganisms where they do not naturally occur. These voluntary guidelines effectively halted a significant amount of research of the sort that worries government officials today.

The Recombinant DNA Advisory Committee was established to provide ongoing guidance to the scientific community on matters of genetic manipulation that might adversely impact humans, animals, or agriculture. The editors might have suggested a similar advisory committee to help individual investigators and editors with the thorny problems of research deemed to be “too sensitive” for publication. Such an advisory committee could contain experts in infectious diseases, as well as members of the intelligence community. What might constitute these elusive sensitive areas of research? The editors state, “we cannot now capture it with lists or definitions.” Sensitive information might include alterations in bacterial virulence that could defeat vaccines, accelerate a disease course, delay diagnosis, or affect drug resistance. The issue of “dual technology” (that is, technology that can be applied to beneficial medical uses as well as, in principle, to bioterrorism; for example, the development of aerosol technology to deliver pharmaceuticals or pesticides that might be used to deliver bioengineered infectious agents) is also particularly problematic.
Presumably, there may be other areas of concern. Had the editors provided guidelines, the responsibility would be taken from them as the self-appointed regulators and placed where it belongs—with individual investigators. I do not seek more regulation, but I much prefer to have it be my responsibility, rather than the responsibility of an anonymous editor who may not have the expertise to make an informed judgment.

Global infectious diseases offer a greater threat than bioterrorism to the security and economic stability of the United States and other countries (1). Recent experiences with SARS and West Nile virus punctuate this fact. In the concern to thwart bioterrorism, advisory committees and those concerned with national security must not fail to weigh the fact that the bulk of research done on pathogenic microorganisms has as its goal the defeat of infectious diseases and its medical, societal, and economic burdens. Any decision to suppress information must weigh this relative impact.

It is not too late for the editors and authors group to establish realistic guidelines and procedures to ensure that no real sensitive information is released to a handful of individuals who might misuse it. It is an issue that should be earnestly discussed by the broad community of scientists, together with those whose mission it is to guard national security.

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Response

PROFESSOR FALKOW IS A RESPECTED AND thoughtful colleague with whom I rarely disagree. By way of minimizing our differences on this matter, a few quick points: First, those of us who developed the statement believe that changes or rejections will be rare, and we will follow careful consultative processes. Second, we failed to codify guidelines because we found that the possibilities simply made too big a target. Falkow’s use of the Recombinant DNA Advisory Committee is interesting, but the spectrum of potentially hazardous outcomes was, I would argue, far narrower in that case—and therefore more guideline-friendly. Finally, his letter properly reminds us of the potential benefits of such research. That was recognized in our statement, though perhaps with insufficient emphasis. I suspect that most or all of its authors would agree that these benefits must be balanced against any potential security risk.

DONALD KENNEDY
Editor-in-Chief

Ethnic Differences and Disease Phenotypes

IT IS DIFFICULT TO DETERMINE WHETHER diseases are similar across different ethnic groups, because of the paucity of clinicopathological studies in non-Caucasians. This has led to a fundamental although flawed assumption in epidemiological cross-cultural comparisons of disease that clinically defined disorders are similar in cause and outcome across ethnic groups. A recent Report (“Genetic structure of human populations,” N. A. Rosenberg et al., 20 Dec., p. 2381) describes a genetic approach to define distinct populations and shows that it is possible to dissect out five genetically identifiable groups. Genetic techniques such as this will facilitate the definition of ethnic groups based on genomic variation and enable scientists to test the hypothesis that diseases have divergent clinical features between these groups. However, there is already growing evidence that ethnicity modulates disease via genetic background.

Neurodegenerative diseases are clinicopathologic entities almost exclusively defined in Caucasian populations. It is often forgotten that these diseases are biological processes, not symptom clusters, and it is equally important to remember that diagnoses are descriptive predictors of course and natural history, not scientific absolutes (1). As reports of monogenic disease in different ethnic groups increase, the range of disease phenotype also increases. Spinocerebellar ataxia (SCA) 3 in Caucasians typically presents as an ataxia syndrome (2), and coexisting parkinsonism is at the edge of the phenotypic range (3). In contrast, in people of African origin, ataxia with parkinsonism is common (2), and pure ataxia and clinically typical Parkinson’s disease (4–6) represent the edges of the disease spectrum. SCA2 mutations usually present with a pure ataxia syndrome in Caucasians (7), but in many Chinese families, a phenotype that is almost indistinguishable from Parkinson’s disease occurs (8–10). Likewise, the clinical phenotype of Dentatorubropallidolysian Atrophy in Japanese and European populations and that of Haw River syndrome in African Americans were disparate enough to hide the fact that these diseases were caused by the same mutation (11, 12). Finally, presenilin mutations, described widely in Caucasian and Japanese patients, usually cause a dementia in which memory loss predominates (13), but in the sole reported example of a presenilin mutation occurring in an African kindred, personality changes and disinhibition were an early feature (14). In these examples, genetic background is the...
Although we might expect the burden of neurodegenerative disease to be similar between ethnic groups, the clinical diagnoses may differ. Given this, it is to be expected that diseases such as Alzheimer’s disease and Parkinson’s disease, whose diagnosis is based on consensus criteria derived from analysis of Caucasians, may seem to have lower rates of disease in other populations because the clinical criteria have been fine-tuned to exclude all similar diseases in the defining population.

Of great importance are the therapeutic implications inherent in these differences; patients with similar clinical phenotypes might need different treatments if that phenotype has an entirely different cause. What is required are genetic, epidemiologic, and pathologic investigations of neurodegenerative disease in different populations. In these investigations, it will be inappropriate to apply consensus criteria derived from the analysis of Caucasian populations uncritically; rather, criteria will have to be rederived in different racial groups. Such investigations, despite their challenges from a design standpoint, are essential if we are to achieve appropriate diagnosis and treatment for non-Caucasian and Caucasian populations alike.

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Studying Traditional Chinese Medicine

In Dennis Normile’s article on traditional Chinese medicine (TCM) (“The new face of traditional Chinese medicine,” News Focus, 10 Jan., p. 188), Wallace Sampson maintains that relying on the traditional Chinese medicinal texts for hints to effective remedies for specific diseases is wishful thinking: “Those empirical obser-
vations on herbs are unreliable, fanciful, false, [and] irrelevant.” He does not cite any papers to back up this statement.

Such broad, unsupported claims are harmful to unbiased investigations into TCM. A number of recent studies support the efficacy and safety of some TCM herbal formulas. In addition, they have shown that these remedies worked effectively in some instances in which conventional Western therapies failed or proved to be insufficient to provide a palliative cure. For example, a randomized, nonblind, controlled clinical trial conducted in Japan showed that sho-saiko-to, an extract of seven Chinese herbs, helps prevent liver cancer in patients with cirrhosis (1). This is apparently the first treatment in any medical system that offers such benefits. Two double-blind, placebo-controlled clinical trials were performed in Britain to evaluate the effect of Zemaphyte, a preparation of 10 herbs used by TCM practitioners for treating certain kinds of skin disease. In both studies, the formula produced impressive responses in treating severe, widespread atopic eczema that was resistant to conventional steroid therapies (2, 3).

In addition, we should point out that herb enthusiasts are not the only ones who think that screening misses the point. Some Western-trained scientists have long expressed the view that the benefits of TCM drugs often come as a result of synergistic interactions of multiple ingredients [e.g., (4, 5)]. In the cases mentioned above, available data suggest that the composite formulas have greater efficacy than single ingredients, hardly a novel idea to chemists. The researchers who investigated sho-saiko-to noted that it is difficult to explain its benefits as the effect of a single ingredient (1). Preliminary study also indicates that there was no single active herb in Zemaphyte and that the complete combination of 10 herbs was needed to achieve the desired clinical results (6). It follows that the reductionist approach of isolation of a single bioactive compound is not always appropriate for TCM.

References