

Malaria Vaccines

It was with great surprise that I read the description of our work in your correspondent Jeremy Cherfas' article "Malaria vaccines: The failed promise" (News & Comment, 26 Jan., p. 402). Our 1987 paper (1) reported the results of a malaria vaccine trial in monkeys, not humans, while our 1988 paper (2) reported the results of a malaria vaccine trial in humans. Both of our papers showed good protection against infection. The trial carried out last spring by Bill Collins and his associates in the Malaria Branch of the Centers for Disease Control in Atlanta, Georgia, was in monkeys, not humans.

Perhaps Cherfas was misinformed, but what Collins describes as "slight differences" between our monkey trial (repeated several times by our group with results similar to those we published in 1987) and his monkey trial were described in a report (3) to the World Health Organization's Lindsay Martinez as follows: "We feel that the most likely explanation for the different serologic responses in animals immunized with the peptide mixtures in Atlanta and Colombia was a problem with the peptide—BSA conjugation procedure. This probably also explains the lack of protection in the two groups of animals immunized with a mixture of 3 peptides in Atlanta."

Perhaps most disturbing is the statement by Cherfas that "Patarroyo has not given up. . . . [T]here is 'tremendous excitement' in Venezuela and Colombia. . . . [but] few scientists outside those countries share wholeheartedly in that enthusiasm." This implies that no one believes good science can be carried out in developing countries. In our view, science exists only in two forms—good or bad; and good science, like truth, is based on facts. Our clinical trials in humans are under way, and their results should settle the issue.

MANUEL ELKIN PATARROYO
Director, Instituto de Immunología,
Hospital de San Juan de Dios,
Bogotá, Colombia

REFERENCES

1. M. E. Patarroyo et al., *Nature* **328**, 629 (1987).
2. M. E. Patarroyo et al., *ibid.* **332**, 158 (1988).
3. G. H. Campbell, T. K. Ruebush II, W. E. Collins, personal communication.

Cherfas states that "In two trials of different vaccines only one of nine subjects was protected—and even that case is suspect." As the senior investigators who ran the trials, we can attest that one of three volun-

teers immunized with a synthetic peptide conjugate vaccine (NANP)₃-TT was protected against sporozoite challenge (1), and one of six immunized with a recombinant vaccine FSV1 was protected (2). Andy Waters, a molecular biologist who was not involved in either clinical trial, is cited as suggesting that an allergic reaction to the vaccine was responsible for the subsequent protection against malaria. We are unaware that persons can be protected from a sporozoite challenge by virtue of an allergic reaction stimulated 12 months previously and think it is far more likely that specific vaccine-induced ant sporozoite immunity was responsible. This interpretation of the results is supported by the fact that, in both clinical trials, the vaccinated individuals had significantly longer prepatent intervals than did unimmunized control subjects, which indicates that vaccination stimulated some degree of ant sporozoite activity, albeit a level that was completely protective in only two of the nine vaccinees. We believe these results provide evidence that biologically relevant ant sporozoite antibodies can be stimulated by subunit vaccines.

Furthermore, in contrast to what is stated in the article, there are no data demonstrating any significant variation in the central repeat region of the *Plasmodium falciparum* circumsporozoite protein. This apparently invariant region remains an excellent target for protective antibodies. A major challenge is to design vaccines that consistently induce higher concentrations of such antibodies.

DEIRDRE HERRINGTON
Center for Vaccine Development,
University of Maryland School of Medicine,
Baltimore, MD 21201

STEPHEN L. HOFFMAN
Malaria Program,
Naval Medical Research Institute,
Bethesda, MD 20892

MYRON M. LEVINE
Center for Vaccine Development,
University of Maryland School of Medicine

DANIEL M. GORDON
Department of Immunology,
Walter Reed Army Institute for Research,
Washington, DC 20307

REFERENCES

1. D. A. Herrington et al., *Nature* **328**, 257 (1987).
2. W. R. Ballou et al., *Lancet* **i**, 1277 (1987).

It is true that the promise of a malaria vaccine seems as distant in 1990 as it did in 1985, if not more so. However the same is also true of many areas of biotechnology. Attempts to find the elusive malaria vaccine should certainly be subjected to scrutiny and, where necessary, shortfalls highlighted and admitted. The public has a right to be

kept thoroughly informed about the progress being made when its money is made available for such research. But to concentrate purely on the "failure" to find a vaccine is to overlook the huge contribution that the "search" has made to the understanding of the basic biology of the parasite and the nature of its interaction with the host immune system. For instance, selective pressure on the circumsporozoite (CS) protein results not in myriad sequence variation but instead in limited changes focused on small, distinct regions of the protein which have been shown to elicit immune responses. This, when allied with our increasing knowledge of host genetics and immune effectors, suggests that a CS-based vaccine holds more promise than it did 5 years ago.

Cherfas uses a fragmentary quote of mine to imply the complete failure of the CS protein vaccine trials. While I do not have perfect recall of our conversation, I remember also enthusing about progress in the field. An individual exhibiting an allergic response may clear a challenge of parasites for one of two reasons, either because of a specific ant sporozoite response or a non-specific reaction. I believe that I made these two options clear to Cherfas. If not, then I would like to take this opportunity to do so. It would have been quite simple to confirm the facts with one of the authors of the study.

The vaccination against malaria is one of the most complicated biological puzzles that man has attempted to solve. If it seems that the public has been misled into believing that it would be a simple process, then that is indeed unfortunate. It would be unfair to the scientists involved to ignore that the last 5 years have produced a much more detailed picture of the object of that challenge.

A. P. WATERS
Laboratory of Parasitic Disease,
National Institute of Allergy and
Infectious Disease,
Bethesda, MD 20892

Light Bending: Prediction and Theory

Stephen Brush (Articles, 1 Dec., p. 1124) gives an interesting account of the shifting importance of light bending as evidence for relativity. He appears, however, to have mixed this up with the question of falsifiability, apparently because of Popper's report of being led to the notion by Einstein's prediction of light bending prior to observation of the effect.

The central historical facts seem to be two. First, in the early days of relativity, scientists were substantially more impressed

by the orbit of Mercury than by light bending, although the latter was discovered only after having been predicted from the theory. Second, as subsequent attempts to explain light bending along Newtonian lines failed, scientists came to regard light bending as carrying greater evidential weight. The lesson is that empirical evidence for a new theory counts more heavily when it cannot be handled by, but bears on principles central to, existing theory. The basic point has, of course, been familiar since Kuhn's discussion of anomalies in 1962, but Brush provides an important example which makes clear that merely forecasting a new phenomenon by itself provides only weak support for a new theory.

Thus, Brush shows Popper was wrong in his interpretation of the importance of light bending, but it should be plain that this has nothing to do with the soundness of the falsifiability criterion. A theory so flexible that one can always find a way to explain any phenomenon, whether before or after the fact, is not scientifically interesting or useful. However, this criterion does not demand prediction of novel phenomena in advance. In short, the question of falsifiability concerns the nature of acceptable theory in natural science, whereas the issue of prediction of novel phenomena in advance has to do with the historical process of theory change.

THOMAS P. WILSON
Department of Sociology,
University of California,
Santa Barbara, CA 93106

Brush's use of the word "fact" (for example, "subsequent evaluations of [Einstein's] theory in the technical literature do not seem to give greater weight to the prediction of novel facts than to the persuasive deduction of known facts") undercuts his argument. Since the word "fact" implies immutable truth, use of phrases such as "known facts" undercuts such statements as "observations are not intrinsically more reliable sources of knowledge than theories. . . ." More appropriate words than "fact" would include "observation," "data," and "theory," which imply incompleteness and falsifiability.

This mutability is the basis of the superiority of science as an explanatory-predictive system—scientists' observations and theories can be progressively corrected by scientists' further attempts at explanation and prediction, that is, there is a knowledge feedback loop. The use of "fact" to describe an observation or theory undercuts the system's strength by making a dynamic process into something static.

BERNARD BERGMANN
Departments of Psychiatry and Psychology,
University of Chicago, Chicago, IL 60637

Brush notes that the initial surprise over gravitational light bending—and the initial power of this result in support of Einstein's general relativity theory—soon dissipated when alternative explanations of the phenomenon were tested. This may be an example of what psychologists have studied as "hindsight bias"; uncertain events are rated less surprising after they occur than the same events are rated before they occur (1). It appears that physicists initially reacted to light bending in terms of its prospective surprise value, but moved easily to a reduced surprise in retrospect. If they did not go so far as to say they "knew it all along," many were soon a long way from admitting they "never would have guessed it" (2).

CLARK MCCAULEY
Department of Psychology,
Bryn Mawr College,
Bryn Mawr, PA 19010

REFERENCES

1. B. Fischhoff, *J. Exp. Psychol. Hum. Percep. Perform.* 1, 288 (1975).
2. S. Hoch and G. Lowenstein, *J. Exp. Psychol. Learn. Mem. Cognit.* 15, 605 (1989).

Response: Wilson says that the criterion of falsifiability "does not demand prediction of novel phenomena in advance." Although some philosophers of science agree with him, others do not. My reading of the Popper texts cited in my article is that Popper himself does (most of the time) demand novel prediction [see, for example, (1, p. 117)] and that this was the reason for his original objection to Darwinian theory (1, p. 340). In any case that is the interpretation that has been widespread in the popular scientific literature and has been used to denigrate the scientific legitimacy of evolutionary biology, psychoanalysis, and so forth.

Bergmann dislikes my use of the word "fact" because it implies "immutable truth." I agree that scientists should try to use other words suggesting vulnerability to revision. As a historian I observe that scientists do talk as if light bending and the advance of Mercury's perihelion are "facts."

STEPHEN G. BRUSH
Department of History and
Institute for Physical Science and Technology,
University of Maryland,
College Park, MD 20742-2431

REFERENCES

1. K. Popper, *Conjectures and Refutations* (Basic Books, New York, 1962).

Water Temperatures

In a helpful and informative article about



The Human Genome Organisation Nominations for Membership

HUGO is an international organisation of scientists. Its major objective is the coordination of human genome research, with a view to encouraging collaboration between scientists and avoiding unnecessary duplication of effort. Its other objectives include making the exchange of data and materials as easy as possible. It also plans to encourage debate on the social and ethical impact of human genome projects.

Membership is by election, after nomination either by five HUGO members or by HUGO Council. The Council has decided that it wishes to widen the membership: in particular, it hopes to include people in cognate areas of research such as information technology, scientists working on other genomes, and those involved in assessing the ethical impacts. It also wishes to broaden the geographical base and would particularly like to hear from people outside North America and Western Europe.

The principal criterion for nomination is active involvement in human, or other, genome research as evidenced by academic appointments in a relevant department, or employment in a research institution or company doing relevant work, and by a publication record.

Persons interested in becoming members of HUGO are invited to write to the address below enclosing **two** copies of each of the following:

- a brief up-to-date *curriculum vitae*
- a list of *not more than 6* key publications
- 2 letters of support

Applications must be received by **Friday 18 May 1990**.

ONLY APPLICATIONS CONTAINING ALL THE ABOVE WILL BE CONSIDERED. NO CORRESPONDENCE ABOUT INCOMPLETE APPLICATIONS CAN BE ENTERED INTO.

Applications will be acknowledged only on specific request *and* if a self-addressed label is enclosed.

HUGO
President's Office
Imperial Cancer Research Fund
P O Box 123, Lincoln's Inn Fields
London WC2A 3PX
UK