FIGHTING LAMARCK'S SHADOW

BY SUSAN WEST

This story is not about what you're going to think it's about. It's about some experiments that, on first reading, you're going to think are evidence for that emotion-charged black sheep of evolutionary theory — Lamarckism, commonly called the inheritance of acquired characteristics. They aren't. They are, however, possible evidence for a new and significant means of altering genetic material. But the slight scent of Lamarckism that the experiments give off, if picked up by overly sensitive noses, may obscure the importance of the findings. In fact, there are indications that this has happened. So let's set the record straight.

In May 1980, Reginald M. Gorczynski and Edward J. Steele, at that time both at the Ontario Cancer Institute in Toronto, published the results of experiments in which male mice that had been made tolerant to foreign antigens passed that tolerance on to a large proportion of their offspring. As described in their paper, which appeared in the PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, newborn mice were made tolerant to antigens from another strain of mice by the common technique of repeated injections of spleen, bone marrow and lymphoid cells from the second strain. The mice were judged to be "tolerant" to the foreign antigens when cells taken from their spleens did not respond — produce cytotoxic lymphocytes—when exposed to spleen cells from the second mouse strain. Exposure to spleen cells from other strains, however, elicited a normal immunological response. When the mice were 8 weeks old, 10 tolerant males were randomly selected and mated to nontolerant females. Nontolerant females were used to avoid the possibility of transferring tolerance-inducing factors through the milk or placenta. When the response of these progeny was tested, 60 percent were found to be tolerant to the antigens to which their fathers had been exposed. When this generation of mice was mated, either with siblings or with non tolerant mice, about 50 percent of the offspring showed either no response or a diminished response to the foreign antigens. Neither the first- nor the second-generation mice were exposed to the foreign antigens before they were tested for tolerance, indicating that they must have received tolerance from their fathers.

In the Feb. 19 NATURE, Steele, now at the Clinical Research Centre in London, and Gorczynski report an extension of this work. Using similar techniques, the researchers made another batch of mice tolerant to antigens from *two* different mouse strains. Again, a large percentage of the first- and second-generation offspring showed tolerance to the antigens to which their fathers had been made tolerant. In addition, some of the offspring were tolerant to only one set of antigens, while others were tolerant to both, indicating that the two traits had been passed on independently.

Sound Lamarckian? On the surface — in that the experiments deal with the inheritance of characteristics picked up during an animal's lifetime — it does. Jean-Baptiste de Lamarck, a 19th century biologist who made substantial contributions to comparative anatomy and the classification of invertebrates, is infamous for his speculations on evolutionary change. He believed that new environments require new needs that organisms try to meet by developing new habits that eventually modify their parts cumulatively and permanently. The well-worn example of this is that the forelegs and necks of giraffes lengthened gradually as a result of the animals' habit of browsing trees. Later, Lamarck's speculations were taken out of their very general context and applied to fields of which he had no conception.

> The results of a recent set of experiments risk being overshadowed by an ancient debate

The advent of neo-Darwinism — the theory that parents can transmit only what they have inherited and that evolution occurs by the natural selection of random mutations that are not related to environmental stresses — polarized the evolutionary camp. The battle was joined, spiced by a variety of celebrated incidents, including August Weismann's chopping the tails off 20 generations of mice to see if a tailless mouse would be born and, as recounted in Arthur Koestler's *The Case of the Midwife Toad,* the sabotaged experiments and subsequent suicide of Austrian biologist Paul Kammerer. Such is the emotional baggage that the experiments of Gorczynski and Steele carry.

But according to Gorczynski, Lamarckism need not be invoked to explain their results. The mechanism they suggest, which was first proposed in a 1979 book by Steele, is an adaptation of two well-accepted biological theories. One deals with the way in which the immune system works: The body constantly produces a wide variety of lymphocytes, each capable of producing a specific antibody. In true Darwinian fashion, natural selection, in the form of the appropriate antigen, chooses which lymphocytes will proliferate. At this point, the second theory comes into play.

Based on work by Howard Temin of the University of Wisconsin in Madison, naturally occurring RNA viruses in the cell are known to capture intracellular RNA sequences and carry them into other body cells where that RNA is copied by reverse transcriptase into DNA, which in turn could be incorporated into the cell's genome. Steele and Gorczynski suggest that if the capture of RNA sequences by the viruses is random and if there is a great supply of a particular type of RNA about — such as that belonging to a newly selected and rapidly proliferating lymphocyte — then it stands a greater chance of "capture." Next, their scheme requires that the virally pirated RNA sequences be coopted by the DNA of the germ cells — the eggs and sperm — so that they can be passed to the next generation. It is known that such RNA viruses can infect germ line cells, Temin said in an interview, so that such a scenario is not far-fetched. In fact, Temin has previously suggested just such a scheme as a means, in addition to the accepted mode of random chromosomal mutation, that new information is introduced into the genes.

Rather than being Lamarckian, the "whole concept is based on Darwinian selection at a cellular level," says Gorczynski. Beyond this statement, according to Gorczynski, the researchers see no need to enter the Lamarckist-Darwinist dogfight. Notably, no mention is made in either paper of Lamarck, and Gorczynski discusses the issue only reluctantly, sticking to the phrase, "the inheritance of acquired tolerance."

But others won't let it go away. While most response from their colleagues has been positive, says Gorczynski, they have encountered negative reactions from persons who "are not prepared to retain an open mind." Much of the problem arises from those who still see the issue as an either-or proposition. "Those people who would like to believe Lamarck would say this is concrete scientific evidence for it," Gorczynski says, while the extreme Darwinians cannot accept it. The researchers' interpretation lies at neither pole: "We believe that on the long-term, gross level, Darwinism holds true but ... at the individual level this is evidence for other means of [genetic] change."

The tendency to polarize discussion of the research — and possibly obscure its importance — is evident in some published accounts of Gorczynski and Steele's work. In the Aug. 28, 1980, NATURE, for example, an editorial by R. B. Taylor of the University of Bristol Medical School that describes the May 1980 PNAS paper is titled "Lamarckist revival in immunology." Similarly, a second editorial accompanying the researchers' Feb. 19 NATURE article

is titled "Too soon for the rehabilitation of Lamarck." While both editorials address the scientific aspects of the research, the urge to throw the research into the Lamarck-Darwin fray is clear. "It will be time enough to worry about the rehabilitation of Lamarck when and if the data now reported are independently confirmed," concludes the Feb. 19 editorial.

What risks being lost in all this is what the experiments seem to be illustrating. Says Temin: "They are a very interesting set of reports, indicating a possibly new phenomenon. The most exciting interpretation is that they may be an example of a different sort of genetic influence, but it is also possible that they may have just discovered something new about cellular immunology." While the experiments appear to be explainable in terms of an influence of RNA viruses on DNA content — a system that would push aside random mutations as the only natural means of altering DNA — they are not a direct test of that model, Temin cautions. "Right now we just have a phenomenon," he says, "and we need to confirm that the phenomenon exists." If it indeed exists, he continues, then it remains to be determined if it is a function of genetics or of immunology.

Other researchers are already trying similar experiments. According to Gorczynski, one group at the facility where Steele now works repeated the first experiments, but used different cells in the test for responsiveness to the foreign antigens and concluded that the results could not be reproduced. In another set of experiments, researchers at Portland State University Medical School are using a similar approach but looking directly at the animal's ability to make a specific antibody instead of the more indirect cellular response used by Gorczynski and Steele.

Among the questions raised by Gorczynski and Steele's work, says researcher Gerrie A. Leslie, who is conducting these experiments with Anwyl Cooper-Willis and Joan Olson, is exactly what is being transmitted to the offspring. It is possible, he says, that the antigen itself has found its way into the germ cells and has induced the tolerance response without actually altering the genome. Noting that the percentage of tolerant individuals decreases with each generation, Gorczynski agrees with this possibility and adds that it is also possible that the RNA virus has been incorporated into the germ cells but not into the genome or that the tolerant message requires more than one gene to become stably integrated. All of these possibilities require further experimentation, Leslie stresses, and he eschews the Lamarckian overtones that he fears may prevent scientists from addressing the central question of the research. "I'm not convinced that inheritance like this occurs," he says, "but we can't just ignore the experiments. We have to do something rather than stick our heads in the sand and deny that the results exist." □

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