

EIR Science & Technology

The case of the missing molecule

John Grauerholz, M.D., reports on Dr. Jacques Benveniste and colleagues' astounding experimental results, and the scientific witchhunt provoked against Benveniste.

In addition to the AIDS epidemic, which threatens to repeat the devastation of the 14th-century Black Death, another relic of the Dark Ages has reappeared. For those who missed the first performance of the Holy Inquisition, the editors of Britain's *Nature* magazine staged a rerun for the benefit of those scientists who might be guilty of thinking, and uttering, forbidden ideas.

The initial event in this auto-da-fé was the publication of an article describing the biological effects of highly diluted solutions of antibodies on human white blood cells, in the June 30, 1988 issue of *Nature* magazine. This was accompanied by an editorial entitled, "When to believe the unbelievable" and, ironically, a News and Views column, "Can a Greek Tragedy be avoided?" The editorial referred to the results reported in the paper, titled "Human basophil degranulation triggered by dilute antiserum against IgE." The significance of the News and Views column will become evident later.

The paper reported on research conducted at the INSERM 200 laboratory at Université Paris-Sud by Dr. Jacques Benveniste and his colleagues, and subsequently confirmed at three other laboratories in Milan, Toronto, and Rehovot, Israel. The data indicated that highly diluted solutions of antibodies retained their ability to stimulate a reaction by certain white blood cells even at dilutions at which antibody molecules are no longer present.

That these results were highly upsetting to *Nature* is evident from the accompanying editorial.

"Inexplicable observations are not always signs of the supernatural.

"There is no objective explanation of these observations—for there is no evidence of any other kind to suggest

that such behaviour may be within the bounds of possibility. Indeed, during the long period since this article was first submitted to *Nature*, it is plain that Benveniste has been as puzzled by the data he reports. On many occasions, he has responded to referees' suggestions at great inconvenience to himself. When told, for example, that the experiments should be repeated at an independent laboratory, he arranged for this to be done.

"Certainly there can be no justification, at this stage, for an attempt to use Benveniste's conclusions for malign purposes—homeopathic medicine, for example.

"But, those of supernatural inclinations will protest, is it not grossly unfair that science should put aside, even temporarily, some surprising and unexpected observations (such as these) while apparently welcoming others which are no less surprising (such as the recent suggestion that there may be a 'fifth force' between material objects)? The explanation is simple, but perhaps for that reason, not widely understood. It is entirely possible for physicists to welcome the notion of the fifth force because it would be a novel happening which could nevertheless be accommodated within the accepted framework of science. Benveniste's observations, on the other hand, are startling not merely because they point to a novel phenomenon, but because they strike at the roots of two centuries of observation and rationalization of physical phenomena. Where, for example, would elementary principles such as the Law of Mass Action be if Benveniste is proved correct?"

Obviously, the implications of these results are perceived as threatening to a view of science which has become hegemonic over the past 200 years. They are, in other words, "unorthodox," which is to say, they contradict "right opin-

ion,” which is the meaning of ortho (= right)-doxy (= doctrine or opinion).

These particular results were so unorthodox that *Nature*, which initially received the paper on Aug. 24, 1987, did not accept it for publication until June 13, 1988. During this time, the experiments were rerun at a number of other laboratories by request of the referees reviewing the paper. In addition, Benveniste repeatedly requested *Nature* to send representatives to the laboratory to observe the experiments and redo them during this period.

Nature finally agreed to publish the paper in its July 14, 1988 issue, after a visit by an investigative committee was to have been made to evaluate Benveniste's laboratory. Then, *Nature* decided to publish the article, which had been accepted on June 13, 1988, on June 30, 1988, which may be some sort of speed record for publication of a paper in a major journal. The investigative committee was to come after publication.

Now, it might seem a bit odd that after taking nearly a year to accept a paper for publication, *Nature* could not have waited two more weeks until its investigative committee had finished its work. Especially since there were such serious reservations about the results. As *Nature* itself had noted, Benveniste himself was puzzled by the results and had sought assistance in finding an explanation for them.

That there was a different agenda than the search for truth became evident when the composition of the committee became known. It was to consist of John Maddox, the editor of *Nature*, James (“The Amazing”) Randi, a professional magician, and Mr. Walter Stewart, an investigator of scientific “fraud.”

Mr. Randi, a highly talented professional magician, has carved out a reputation for himself as a debunker of so-called “paranormal,” or as the editors of *Nature* would put it, “supernatural” phenomena. One of Mr. Randi's targets was Uri Geller, the Israeli mystic, about whose alleged psychic powers *Nature* had once published an article which drew some criticism. Mr. Randi's forte is detecting the sorts of sleight of hand which escape the usual scientifically trained observer.

Mr. Stewart is a National Institutes of Health scientist who is one of a group of scientific “bounty hunters,” whose qualifications were best described by Mr. Maddox: “They have no substantial scientific published record of their own—they are self-appointed keepers of the scientific conscience.” Even more interesting, Mr. Stewart was one of the referees of Benveniste's paper, who, with the raw data and statistics in his hands, cleared the paper for publication.

Conspicuously absent from the group was any scientist with actual laboratory experience in the area in question. When Dr. Benveniste became aware of the composition of the committee, he experienced a well-justified apprehension. His apprehension was borne out in spades by subsequent events.

This intrepid group of “ghostbusters” descended upon Benveniste's laboratory to exorcise the malign spirits of high aqueous dilution, once and for all. Unfortunately, during the first three days of the Inquisition, the high dilution degranulation effect occurred in three out of the four trials and in the other trial degranulation did not occur even at high concentrations of the antibody, indicating a problem with that particular specimen as opposed to a statistical variation in the method. The samples were examined “blind,” that is to say, that the identity of the particular sample was unknown to the person analyzing the sample.

Mr. Stewart then declared these results “valueless” and proceeded to alter the experimental procedure in order to obtain a trial in which the effect did not occur. In order to facilitate this, Mr. Randi employed his talents as a professional magician to distract the laboratory technician assigned to observe Mr. Stewart while he prepared the samples for analysis. Having obtained one such trial, he and his fellow truth seekers then packed their bags and issued a report, reeking with innuendos of incompetence and willful misconduct on the part of Benveniste and his laboratory staff.

In true inquisitorial fashion, Mr. Maddox then offered not to print the report if Dr. Benveniste would recant his heresy. Dr. Benveniste declined this kind offer and wrote a response to the report, which was published along with the report in the July 28, 1988 issue of *Nature*.

The report concluded that Benveniste's results were not to be believed because they were not reproducible and were “based chiefly on a series of experiments which are statistically ill controlled, from which no substantial effort has been made to exclude systematic error, including observer bias, and whose interpretation has been clouded by the exclusion of measurements in conflict with the claim that anti-IgE at ‘high dilution’ will degranulate basophils.”

This all sounds very damning until you consider that Mr. Randi apparently detected no sleight of hand on the part of the laboratory personnel, and in fact, used his own abilities on that score to help Stewart produce a trial that did not work after three that did. As for the statistics, Stewart had them in hand when he refereed the paper. If they were so bad, why was the paper cleared for publication without informing Benveniste of the problem beforehand? What about the other laboratories where the effect was reproduced? It is hard to escape the conviction that a precommitment to get a certain result was greater on the part of the investigating team than on the part of Benveniste's group.

Now, these results may represent an artifact, an uncontrolled condition or practice in a given laboratory, or they may not. If they do, it is common to at least four laboratories in different parts of the world, and may be affecting other studies in these and other laboratories. If so, an effort to identify it is vital to ensure the accuracy of other such assays in these laboratories. Such an effort would require one or more experienced laboratory scientist with background and

expertise in the particular techniques and equipment being used.

From the composition of the investigating team, however, it is obvious that the gameplan was to document fraud, and when that failed, the fallback was a series of scattershot accusations and innuendos. In retrospect, it would appear that a decision was taken to rush the article into print and then print a devastating attack as the most effective method of destroying not only it, but Benveniste and his collaborators, and the general line of research into high dilution effects.

Benveniste's heresy is not the more obvious case of "forbidden ideas," but the more profound one of having witnessed, and reported, "forbidden events."

The target of this witchhunt may appear to be homeopathy, a branch of medical practice based on the efficacy of highly diluted solutions of various drugs. But, while Benveniste is interested in phenomena occurring at high dilution, he holds no particular brief for homeopathy, and published an article in the March 5, 1988 issue of the medical journal *Lancet* reporting a study which proved that two well-known homeopathic drugs were ineffective.

The real threat represented by Benveniste's data is that they relate to the immune system, an area which so far has proved refractory to adequate explanation by molecular biology—the accepted method of “rationalization of physical phenomena” in the area of living processes. Molecular biology is based on the premise that life arose on the basis of a statistical fluke in the random interaction of molecules and rules out any higher order causal processes.

According to the late Jacques Monod, who won the Nobel prize for studies designed to squeeze the phenomena of biology into the straitjacket of information theory: “Life appeared on earth; what before the event, were the chances that this would occur? The present structure of the biosphere far from excludes the possibility that the decisive event occurred only once. Which would mean that its a priori probability was virtually zero. . . . The universe was not pregnant with life nor the biosphere with man. Our number came up in the Monte Carlo game. Is it any wonder if, like the person who has just made a million at the casino, we feel strange and a little unreal?”

To understand the relevance of this to Benveniste's work, it is necessary to return to the Greek tragedy which Mr. Maddox was so concerned to avoid. This concerned a

congressional investigation of experiments conducted in 1986 by a group headed by Dr. David Baltimore of the Whitehead Institute of the Massachusetts Institute of Technology. These experiments involved the use of transgenic mice to study variations in the formation of antibodies. Transgenic mice are formed by inserting genes of one strain of mice into the embryos of another strain of mice. This work was described by Mr. Maddox as “widely admired for its imaginativeness and productivity.”

In this case, problems arose when a postdoctoral student at the Whitehead Institute, Dr. Margaret O'Toole, testified before a congressional committee that the data published in 1986 could not be experimentally reproduced. Subsequently, Stewart, and Dr. Ned Feder, another “fraud” hunter, joined in the attack on the assays and statistical analyses used by Baltimore's group.

According to Mr. Maddox, the tragedy was that work by Dr. David Baltimore, one of the high priests of molecular biology, “which offers the particular promise of an understanding of the regulation of the immune response in the language of molecular biology, not just in the phenomenological language of immunoassays,” was being ripped to shreds by none other than Walter Stewart, among others.

That this attack was displeasing to the gods, and might have unwholesome consequences for the attackers, was stated quite bluntly by Maddox: “Although O'Toole has left research, at least for the time being, she as well as Feder and Stewart *could be hurt* by what lies ahead, even if their criticisms turn out to be correct.” (Emphasis added.)

Maddox also explained how selective rigor must be applied to orthodox research: “The chances are that the 1986 article in the dispute is flawed in some of its analyses, but that it has also demonstrated that transgenic mice are an interesting way of learning how the immune system is regulated. That process will continue, uninhibited by the errors (alleged or otherwise) in the 1986 paper. Who in ordinary circumstances, would complain of that, error [unproven] notwithstanding?”

Is it not relevant to inquire whether Maddox might have persuaded Stewart to reduce his chances of getting “hurt” by turning his “nit-picking persistence” (again quoting Maddox) onto a more acceptable target? Certainly the sweetly reasonable tolerance for Baltimore's questionable results is in sharp contrast to his personally supervised hatchet job on Benveniste.

Benveniste's heresy is not the more obvious case of “forbidden ideas,” but the more profound one of having witnessed, and reported, “forbidden events.” The gods of orthodoxy can always eliminate ideas by assassinating, physically or otherwise, those who espouse them. But natural phenomena are a consequence of that underlying lawfulness of the universe which proceeds with, to use an appropriately French term, *la belle indifférence* to the wishes of the self-styled Gods of Olympus who think they run “the system.”