Chapter 20. The revived passion of *Nature* for high dilutions

"Our results contain a source of variation for which we cannot account"

One would have thought that *Nature* had turned over a new leaf on "Benveniste's affair". It was the case indeed for any result from the laboratory of Clamart. Nevertheless, the works of other scientists on high dilutions were obviously considered by *Nature*. The condition, of course, was that their conclusions should be in keeping with the editorial team of the journal. [1]

Indeed, early December 1993, an article signed by researchers of London (J. Hirst, N.A. Hayes, J. Burridge, F.L. Pearce and J.C. Foreman, of *University College London*) was published in *Nature*. The article was a remake of the article on high dilutions of 1988. Its conclusion was – one could expect it – at the opposite of the article of 1988.

Strangely, as an ultimate ceremony of purification, the journal once again used the famous unusual column entitled *Scientific Paper* and the title of the article was the same as the one in 1988, but under a negative form. Except the layout of the journal which changed between these two dates, the comparison of both titles, with a 5-year interval, is eloquent:

Nature June 28th, 1988


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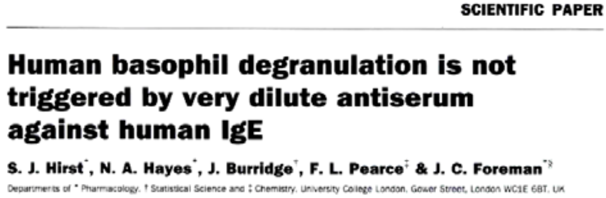
Human basophil degranulation triggered by very dilute antiserum against IgE

E. Davenas, F. Beauvais, J. Amara*, M. Oberbaum*, B. Robinzon†, A. Miadonna‡, A. Tedeschi†, B. Pomeranz§, P. Fortner§, P. Belon, J. Sainte-Laudy, B. Poitevin & J. Benveniste||

Nature December 9 th, 1993


SCIENTIFIC PAPER

Human basophil degranulation is not triggered by very dilute antiserum against human IgE

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The only bibliographical reference quoted in the article of Hirst *et al* was the article of *Nature* of 1988. The article of 1991 in the *Comptes Rendus de l'Académie des Sciences* was ignored contrary to the most elementary scientific and academic rules.

The method used to present the results was the same as for the investigation report of 1988: the conclusion was given at the beginning so that the reader saves time.. Indeed, having looked at the title in the negative form, the reader knew, from the first paragraph onwards, the conclusion of the article:

> "We have attempted to reproduce the findings of Benveniste and co-workers […]. The results were contrary to conventional scientific theory and were not satisfactorily explained. Following as closely as possible the methods of the original study, we can find no evidence for any periodic or polynomial change of degranulation as a function of anti-IgE dilution. Our results contain a source of variation for which we cannot account, but no aspect of the data is consistent with the previously claims."

The readers who pursued the reading beyond the title and the first paragraph were sureley noy many to do so. Furthermore, the article was rather unclear and it was necessary to be extremely motivated to be able to understand all the experimental details. It is what we will do in the next chapter and, in particular, we will try to decipher what the authors meant by this mysterious "source of variation" that they could not explain. In the present chapter, we describe only the circumstances of the publication of this article and its consequences.

Of course, in this issue of *Nature* there was not any question of a possible on-site inquiry with diligent investigators and self-proclaimed "experts". Because the data fitted the "expected" results, it was – in the logic of goat and unicorn as developed by J. Randi – naturally useless. Indeed, with the article of Hirst *et al*, one was obviously in the case of the goat. As for the unicorns (namely, effects of high dilutions), everybody "knows" that they do not exist. One would then wonder, if these results were totally expected, why were they published in *Nature* which is always parsimonious of its editorial space.

When fair play is not British any more

J. Benveniste was furious. After the refusal of the article cosigned with A. Spira, it was a new affront of *Nature* which took advantage of its position of power. J. Benveniste noted that the experimenters introduced numerous technical variations which could jeopardize the success of the experiment. To better understand the reported results, in particular to understand what was this strange "source of variation", he requested in writing to J. Burridge, the statistician of the team, and to the other authors, to quickly communicate the raw data of the counts of basophils to him in order to analyze these results and then to send an appropriate answer to *Nature*:

> "Professeur Spira and myself ask you to kindly communicate the raw data corresponding to the recent Nature article by the fastest means available, including using our telecopy […] or sending a computer disquette. We are ready to send you our data of the 1991 C. R. Acad. Sciences and to come to London to compare our data with yours." [2]

J. Benveniste pursued his letter by criticizing the modifications of the original protocol and the absence of reference to the article of the *Comptes Rendus*. The answer at the request of J. Benveniste arrived only on January 11th although the letter was dated December 14th. It was signed by all authors of the article:

> "We are really only prepared to give our raw data to an independent, professional statistician. The raw data was offered to the reviewers of our Nature paper. We have no comments to make on the methodology except to say that that we followed as closely and carefully as was possible the method in your original Nature paper;
>
> We do not accept that there has been any misrepresentation, in our article, of your Nature paper.
>
> We conducted our study at the request of the Research Council for Complementary medicine. We do not intent to pursue any further investigation and, as far as we are concerned, our contribution is complete and the matter closed." [3]

J. Benveniste immediately and briefly answered that "Prof. Spira, an independent professional statistician, is awaiting the data" while specifying that "there are 14 points of discrepancies between our methods and yours." [4]

Of course, J. Benveniste and A. Spira newer saw the raw data. J. Benveniste drafted nevertheless with A. Spira an answer to *Nature* resuming each of the litigious points. The answer of J. Maddox to these comments arrived on… July 22nd and a letter of J. Benveniste, B. Ducot and A. Spira was finally published on August 4th, that is eight months after the article of Hirst *et al.* A text of J. Maddox (unsigned) accompanied the response of J. Benveniste. In his text, J Maddox reminded that many "discoveries" have never been reproduced and have now been abandoned. He ended by:

> "It is unfortunate, and a little sad, that Benveniste and his colleagues do not appreciate the parallel. Correctly, Hirst *et al* did not conclude in their article that Benveniste was mistaken, but merely that their reasonable test of his conclusion failed to support it." [5]

And if, one more time, the key for reading of J. Maddox prevented him to see an unexpected aspect of the results of Hirst *et al* (well hidden in the article, admittedly)?

Notes of end of chapter

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[1] In 1989, in an unsigned editorial, *Nature* returned on "the affair" at the moment when the direction of Inserm decided the fate of the Unit 200. The author of this editorial – J. Maddox apparently – noted: "*Nature* in the past year has been sent for publication a single paper reporting similar observations with a different system, now with its authors for further clarification, but may well have discouraged others by its treatment of Benveniste's contribution" (Can heresy be real? *Nature*, July 13th, 1989, p. 82).

With a disarming frankness, the editorial writer thus recognized that the "treatment" of high dilutions by *Nature* could indeed have dissuaded other researchers to undertake research in this field or to submit their results to *Nature*. We will see in this chapter that all scientists were not "discouraged" if their conclusions were at the opposite of those of J. Benveniste.

[2] Letter of J. Benveniste to J. Burridge and other coauthors of December 9th, 1993.

[3] Letter of S.J. Hirst, N.A. Hayes, J. Burridge, F.L. Pearce and J.C. Foreman to J. Benveniste of December 14th, 1991.

[4] Letter of J. Benveniste to S.J. Hirst of January 11th, 1994.

[5] Replication defined. *Nature*, August 4th, 1994, p. 314.