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LETTERS TO THE EDITOR

The continuing mystery of the Memory of Water

Sir,

I read with a great interest the special issue about the Memory of Water. I began to work on that subject with Dr Benveniste in 1981 and I cooperated with him until 1991. To complement Thomas's article,[1] I think that some details connected with this story can be also important for future of the research on the high dilutions effect and homeopathy.

The first detail seems without importance, but it may be more significant than it appears: it concerns the origin of the expression 'memory of water'.[2] It was not published first in Le Monde, but in another French daily paper, 'l'Humanité', which first used this metaphor the 30th May 1988 'L'homéopathie a peut-être une base scientifique: la mémoire de l'eau'. The title of the article published in Le Monde the 30th June 1988, just before the publication of Nature the 1st July 1988 was 'La mémoire de la matière' (the memory of matter). It is interesting to note this detail because several of the hypotheses proposed in this Special Issue of Homeopathy concern the role of components other than water which are present during the process of dilution and agitation of high dilutions, such as silica, or dissolved gases.

Other details relative to the history, to the replicability and to the hypothesis may be interesting to complement the articles published in the special issue.

1. *About the history of memory of water, the origin of the work is complex, both before the publication in Nature in 1988 and before the beginning of digital biology*

In 1980, Jacques Benveniste was the Director of INSERM (Unit 200), whose the theme of research was the Immunopharmacology of allergy and inflammation. He was well known for his work on paf-acether. In 1980, I wrote my thesis, as a student in Immunology, in this unit. I worked on the effect of paf-acether on free radicals production by the polymorphonuclear neutrophils[3] (PMN). At the same time, I studied Homeopathy at the *Centre Homéopathique de France* and I had begun to test the effect of medicines such *Apis mel.*, *Belladonna*, *Ferrum Phos.* on PMN activity in another laboratory while studying for a diploma of the Pasteur Institute in 1979. I showed Benveniste some preliminary results in 1981. I was at the same time in contact with Dr Michel Aubin, Director of Research of the Laboratoires Homéopathiques de France (LHF). We organised a meeting at the beginning of 1982 and decided to study the effect of some homeopathic medicines on experimental models of inflammation and allergy. The same year, Benveniste, who was official advisor of the new minister of research, was contacted by the Dr Belon, on behalf of the Boiron company. In 1983, contracts were signed between INSERM and two homeopathic companies:

- Boiron: Study of the high dilutions of histamine and paf-acether on basophils and mast cells.
- LHF: Study of the effects of various homeopathic medicines on inflammatory and allergic processes, including neutrophil activation, metabolism of macrophages, basophil degranulation and other models such as platelet activation.

At the end of 1983, the results were sent as reports or submitted for presentation to congresses:

- In February 1984, I sent Boiron a report about the effect on basophil activation of a mixture Histamine-Paf-acether.
- In September 1984, the results of two studies were presented at a congress (Forum des Jeunes Chercheurs), about the inhibitory effect of *Apis mel.* on basophil activation[4] and of *Belladonna* and *Ferrum phos.* on oxygen radical production by PMN.[5] Then, between 1986 and 1988, three publications about basophil activation[6,7] and metabolism of macrophage[8] were obtained in peer reviewed journals, as Thomas mentions.

In 2002, we synthesised the studies[9] conducted at INSERM U200 from 1983 to 1988 (Table 1).[a]

So, it is clear that the work about 'memory of water' was born of the will to study the biological effect of homeopathic medicines. Besides, the publication of Nature in 1988[10] was dedicated to Dr Aubin.

The article sent to Nature in 1987, and eventually published the following year concerns the direct activation of basophils by anti-IgE high dilutions, not the inhibitory effect of histamine or *Apis mel.* on basophil activation. The reasons for this choice are complex: technical (it seems easier), strategic (the influence of Nature but also of the journal Le Monde was important), and psychological. In 1987, an article on the inhibitory effect of high dilutions of histamine had also been submitted to Nature, but was not accepted. The studies about histamine effect, conducted by Sainte-Laudy and Belon, were published in other scientific journals; they are well known in the homeopathic community.

Regarding the machines for digital biology, we were in touch in June 1988 with Dr Attias at INSERM U

[a]Rapport quadriennal d'activité 1982–1985 (p 13 et 94) et 1985–1998 (pp 57–59) de l'INSERM U 200.

Table 1 Effect of various homeopathic medicines on inflammatory cells: basophils, mast cells, macrophages, PMN, platelets

Basophils; mast cells	*Apis mel.*, *Poumon Histamine*, histamine, phospholipases
Lymphocytes	*Mercurius cor.*, *Phytolacca*: no positive results.
Macrophages	*Silicea*, *Tuberculinum*
Platelets	*Crotalus*, *Lachesis*: no positive results
PMN	*Apis mel.*, *Belladonna*, *Bryonia*, *Ferrum phos.*, *Silicea*

(Contracts INSERM-LHF 1983–1988).

200 and later at his office, he demonstrated the MORA machine. Later, Citro's machine, (Citro was a physician from Turin), was used at the Benveniste' laboratory (see reference 11). With regard to the contact with physicists, Jacques Benveniste met Del Giudice in March 1988, in Bermuda, at a scientific meeting where E. Davenas and I were also present. In the last months of 1988, we had a meeting with Preparata and Cyril Smith. I was also involved in a project of research with Prof. Ludwig in Germany and tried to develop cooperation with Ludwig, Del Giudice, Smith and some French physicists. But the management of the Boiron company decided in July 1989 to stop all funding of fundamental research projects on high dilutions. Fortunately, it was possible to carry on the cooperation with Demangeat in MNR studies starting in 1986.

2. *The problem of the 'scientific committee' of Nature and the problem of the replication of the results published in Nature are complex. In May 1988, when Jacques Benveniste announced to us that Nature accepted the publication, a central question was raised: why Nature decided to send a committee after the publication, not before*?

I have copies of all the letters exchanged between Nature and Benveniste in 1987 and 1988. It appears very clearly that Maddox was annoyed with Benveniste and that he tried to 'trap' him. About this very complex story, I can only briefly testify about the facts in which I participated directly.

It is certain that the deputation sent by Nature was not scientifically correct, although Sir John Maddox was very polite and sometimes sympathetic. But it is also true that there were difficulties in reproducing the activation by anti-IgE high dilutions before the publication and after. For instance, in July 1988 during the week which followed the visit of the scientific committee, Davenas worked on the system with Benveniste and me; we quickly realized that she could not reproduce the positive experiments and that there were technical problems. I told Jacques that it was better to work with discretion and Elisabeth Davenas was of the same opinion.

During the two years which followed, some positive results were obtained by Davenas, but other experimenters did not obtain the same positive results on anti-IgE activation (see reference 12). This fact, not reported in the version published in the *Comptes Rendu d'Académie des Sciences*,[13] had been made clear in the articles sent in 1990 to Nature and Science (and refused by these journals). Such an operator effect seems not have been observed during the study of inhibitory effect by *Apis mel* or histamine. It is not possible to explain this fact. There was no fraud at INSERM U 200 and Elisabeth Davenas was a very conscientious experimenter. I wrote an article on that subject,[14] after the publications of a series of articles in Le Monde in 1997. I had also some exchanges about this problem with Michel De Pracontal who wrote in 1990 a book about the memory of water: 'Les Mystères de la mémoire de l'eau'.[15] In this book, he was rather in favour of the effect of the high dilutions, but with the evolution of controversy he became increasingly skeptical and wrote, ten years later, about a 'scientific imposture'.[16] I tried to demonstrate that an experimenter could obtain some non reproducible results without fraud.

To sum up, I am convinced, when I read all the results obtained from 1986 to 1991, that the activation of basophils by anti-IgE high dilutions was dependent on the origin of the blood and of the immunological state of the donor. We were not sufficiently rigorous on this point in 1988. But I agree with Yolène Thomas on the role of subtle human operator's effects, suggested in 1991 and observed recently in the study of Jonas about digital biology.[17]

Are there any simple solutions? It is scientifically possible to try to replicate the experiments conducted with anti-IgE and *Apis mel.*, as published in 1988 and 1991 with the new method of flow cytometry. It is also possible to replicate the protocol used in digital biology on activation of human neutrophils.[18] But, at least in France, it is not politically easy.

More generally, some interesting hypotheses are developed in this Special Issue of *Homeopathy*. We discussed the possible role of silica in 1987, and also the role of free radicals and hydrogen bonds.[19] Some new studies, coming perhaps from physicists, will shed some complementary light on the very mysterious story of memory of water, story which began before the Nature publication and which will surely continue a long time after.

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Memory of water and blinding

Sir,

As one of the co-authors of the "famous" article in *Nature* in 1988[1] on high dilutions and a former member of the Benveniste's team, I would like to comment the recent article *"The history of the Memory of Water"* by Yolène Thomas.[2] She reports some of the problems with reproducibility encountered during the "memory of water" experiments, and suggests that uncontrolled parameters (eg electromagnetic pollution or quality of water) were most probably responsible when poor results were obtained. I do not fully agree with this presentation of the events. Indeed, the difficulties of reproducibility were quite atypical and did not appear to result from a weak "signal" among a noisy background. This was obvious with the experiments on isolated heart and with the coagulation experiments. The main issue was that in some circumstances, "effect" and "no effect" were randomly distributed regardless their origin (negative or positive samples).

The strangeness of these disturbances was particularly highlighted during the demonstrations that J. Benveniste organized regularly with the isolated heart system to convince other scientists of the reality of the phenomenon. These demonstrations were generally performed in two steps. In a first step, negative and positive samples were produced (high dilutions, samples of "informed water" or digital files) and were blinded with a code by an observer not belonging to the Benveniste's team. Some negative and positive samples were kept unblinded. In a second step, Benveniste's team tested all samples (blinded and unblinded). When all measurements were complete, the results were sent to the observer and the code was broken.

In these demonstrations, the biological effects (and absence of effect) were usually clear-cut. However, the results of blinded samples were almost always at random and did not fit the expected results: some "controls" were active and some "active" samples were without effect on the biological system. We could indeed hypothesize that active samples had been "erased" by external influence. It is however more difficult to explain how inactive samples had been transformed into "active samples". And we are unable to explain why the open samples (positive and negative samples), prepared and tested at the same time as blinded samples, gave systematically correct (ie expected) results.

It is difficult to summarize these numerous and disturbing experiments in a few lines, but I have described them in details in a recent book that tells the whole "memory of water" story.[3] This can be read free on Internet (www.mille-mondes.fr): despite the successive technical improvements of the different experimental systems, the weirdness persisted. Taking these experiments as a whole, it appears that the results reflected more the expectations of the experimenters (and of the lab team) than supposed properties of the samples.

These strange results culminated with the DARPA experiments performed in 2001 on the coagulation