An extraordinary discovery that should revolutionize biology

by Laurent Rosenfeld

On June 30, the British science magazine *Nature* (Vol. 333, dated June 30, 1988, pp. 816-818.) published an article by the team of Prof. Jacques Benveniste, head of the INSERM 200 laboratory, the French institute of medical research. This groundbreaking work concerns "Human basophil degranulation triggered by very dilute antiserum against IgE."

The dilutions in question are homeopathic types of dilution, at which there is, in principle, no molecule of the antiserum left in the solution. These results, which have already been reproduced by four other teams internationally, should revolutionize all our knowledge of biology, chemistry, and physics, especially our knowledge of the function of the immune system.

Benveniste and his colleagues investigated the ability of progressively more dilute solutions of antibodies to cause the loss of histamine-containing granules in white blood cells, called basophils. The solutions were prepared by a process known as serial dilution, in which a tenth part of one solution is diluted with nine parts of water and mixed thoroughly. A tenth part of this new solution is then mixed with nine parts of water, and so on. This results in dilutions of 1/10, 1/100, 1/1,000 and so forth.

Based on the molecular weight of the antibody molecule and the initial concentration, once a dilution of 1 part in 10^{14} had been reached, less than one molecule of antibody was present in the system. Yet, activity was still present at dilutions of 1 part in 10^{120}!

The activity was measured by microscopic examination of the basophils for loss of staining of the histamine granules. Not only were low dilutions (below the point at which antibody molecules could be present) capable of producing the effect, but the effect appeared, then disappeared, then reappeared in a periodic fashion as the dilution process continued.

Similar periodic waves of degranulation of basophils were seen with other substances. However, water in which such molecules had not been present at one time did not produce the effect. In other words, even though the molecule might not be present at the high dilution, it had to have been present at a lower dilution in order for the high dilution effect to occur. In addition, vigorous agitation of the solution was necessary for the effect to appear at high dilution.

Shock to the scientific establishment

The idea of "key-molecules" and "lock-molecules" which presently dominates the field of immunological research should, in this light, be completely revised. In a popular article published in *Le Monde,* Benveniste stated, "Our procedure consists in dipping the key of a car in the Seine river in Paris, and picking up some water in Le Havre [at the mouth of the Seine, 100 miles down the river], and using it to start up the same automobile, and not another one."

In fact, this image is inadequate: Dipping the key in Paris and picking up the water in the Gulf of Mexico would give a better idea of the process, and yet, one still very much inferior to the reality.

The discovery so shakes the currently accepted textbook views of the field that *Nature,* which had received this paper on Aug. 24, 1987, took until June 13, 1988 to clear it for publication. Only then did the referees reviewing the article finally accept it, after several other teams were asked to repeat the experiments, and even then, with two "editorial reservations."

The abstract reads as follows:

"When Human polymorphonuclear basophils, a type of white blood cell with antibodies of the immunoglobulin E (IgE) type on its surface, are exposed to anti-IgE antibodies, they release histamine from their intracellular granules and change their staining properties. The latter can be demonstrated at dilutions of anti-IgE that range from 1×10^{-2} to 1×10^{-120}; over that range, there are successive peaks of degranulation from 40% to 60% of the basophils, despite the calculated absence of any anti-IgE molecules at the highest dilutions. Since dilutions need to be accompanied by vigorous shaking for the effects to be observed, transmission of

the biological information could be related to the molecular organization of water."

So, what Professor Benveniste has done is to obtain an allergic reaction with basically pure water which had been in contact with a specific allergen, but could not possibly have still contained any molecule of that allergen.

High levels of dilution

His procedure is parallel to the one followed in homeopathy. Take an allergen such as, for example, bee venom, and mix it with 10 times as much pure water, and shake strongly; take some of this mixture, mix with 10 times as much pure water, and shake again; and just follow the same procedure 10, 20, 50, or 100 times. Obviously, the concentration of the original allergen falls by a factor of 10 at each step of the process.

A basic law of physics says that one molecule-gram of water (18 grams) contains 6.022×10^{23} (Avogadro's number) molecules, which means that after having repeated the decimal dilution operation about 24 times (what is called in homeopathy a "12CH" dilution, or a 10^{-24} dilution), there is little chance of one molecule of the original allergen remaining, let alone after the operation is repeated up to 120 times, i.e., the dilution of 1×10^{-120} at which Benveniste's team still found an allergic reaction.

This is like pouring a glass of whiskey into a gallon of water, taking a glass of that and pouring it into another gallon of water; and after repeating the operation 60 times, getting drunk on the end product. If that worked, Seagram's would go bankrupt very quickly!

To give an idea of what a 10^{-120} dilution is, it is estimated that there are only about 10^{28} molecules of water in the universe, and that there are about 10^{60} atoms in the universe. So, the dilution is like mixing one molecule with the universe, and taking one molecule of the mix and mixing it again with the universe.

A rigorous procedure

The experimental procedure was entirely rigorous, and has been checked and counterchecked by several different teams in Israel, Italy, and Canada, all with the same result. Before deciding to publish these incredible results, which most scientists deemed impossible, but yet, conceded were done according to the most rigorous rules, *Nature* even demanded that Benveniste hire a special officer to control the "double-blind" procedure for interpretation of the results.

The exact procedure is as follows.

Various substances were used at different stages of the work, especially goat anti-human IgE (Fc) antiserum, monoclonal anti-human IgE antibodies, specific antigen in allergic patients, phospholipase A2 from bee venom or porcine pancreas, Na+ (sodium) ionophore monensin (up to 90% degranulation at 1×10^{-30} M th) and the Ca++ (calcium) ionophores A23187 and ionomycin (1×10^{-38} Mth). At each step of the dilution process, the mixture was thoroughly mixed for 10 seconds using a vortex.

In the end, a cell suspension was added, containing white cell enriched plasma from venous blood donated by healthy donors. Samples were incubated 30 minutes, stained, and the red-stained basophils (i.e., non-degranulated basophils) were counted under the microscope by several operators (who, of course, did not know which kind of samples they were working on: The samples were labeled according to blind, double-coded procedures).

Serial dilutions were performed in such a way as to rule out experimental errors: For example, "Pipette tips and glass micropipettes were discarded between each dilution." And various other checks were performed. Chemical and physical methods were used to check that the actual dilution did follow the theoretical pattern, thereby checking that no accidental polluting of a very diluted sample by a much less diluted sample occurred.

The implications

In sum, chemically pure water "remembers" the allergen with which it was once mixed. Benveniste hypothesizes that water keeps some form of the *electromagnetic configuration of the geometrical structure* of the allergen. Furthermore, it appears that if the mixed substance is frozen and thawed, or heated at a temperature of 70° to 80°C, or submitted to ultrasound, then the effect disappears, and also that the "shaking" of the mix is necessary at every step of dilution.

This would confirm the idea that there is a need for the substance to "print" its structure onto the water, and then a need for the mixed water to in turn "print" its structure at the next dilution test; if something is done to break this structure, such as freeze-thawing or heating the water, then the structure is lost.

Investigations of the physical and chemical nature of the entity active in the solution at high dilutions give the following extremely interesting results:

"1) The importance of agitation in the transmission of information was explored by pipetting dilutions up and down ten times and comparing with the usual 10s[econd]-vortexing. Although the two processes resulted in the same dilution (degranulation at 1×10^{2} and 1×10^{3} were superimposable whatever the dilution process), degranulation did not occur at high dilutions after pipetting. Ten-second vortexing was the minimum time required, but vortexing for longer (30 or 60 s[econds]) did not increase high-dilution activity. So transmission of the information depended on vigorous agitation, possibly inducing a submolecular organization of water or closely related liquids. 2) The latter is possible as ethanol and propanol could also support the phenomenon. In contrast, dilutions in dimethylsulphoxide did not transmit the information from one dilution to the other, but increasing the proportion of water in dimethylsulphoxide resulted in the appearance and increment of the activity at high dilutions.

3) Heating, freeze-thawing, or ultrasonification suppressed the activity of highly diluted solutions, but not the activity of several active compounds at high concentrations. A striking feature was that molecules reacted to heat according to their distinctive heat sensitivity, whereas all highly diluted solutions ceased to be active between 70 and 80°C. This result suggests a common mechanism operating at high dilution, independent of the nature of the starting molecule.

"Therefore we propose that none of the starting molecules is present in the dilutions beyond the Avogadro limit and that specific information must have been transmitted during the dilution/shaking process. Water could act as a 'template' for the molecule, for example, by an infinite hydrogen-bonded network, or electric and magnetic fields."

Background

Although considered some sort of maverick by his peers in the scientific community, Benveniste is not a homeopathy freak out to prove that it indeed works. He is interested in these phenomena and wants to study them, but is not at all the type to fake results.

In fact, on March 5, 1988, he published in *The Lancet,* an article on work proving that two well-known homeopathic drugs, Opium 15CH and Raphanus 5CH, had no effects on the clinical conditions for which they were supposed to work. This would tend to indicate that he is interested in scientific data, and not ideology.

Homeopathy is based on three assumptions: 1) high dilutions of the effective substance have as much of an effect as (or even more than) the original substance; 2) shaking the substance at each dilution is a necessary step for the effect to occur; 3) contrary to the normal medical dogma (*contraria contrariis curantur*, i.e., formally, if a patient is constipated, you solve the problem by something that induces diarrhea), homeopathy says that by prescribing a substance which has an effect similar to the pathology, there is a kind of immunization effect; the body somehow learns to fight the disease.

Benveniste's findings vindicate, at least theoretically, the first two assumptions, which most "rationalist" scientists believe to be a scientific heresy, and the third one seems to make sense (it is the basis of vaccinations, serotherapies, etc.), at least in certain circumstances. Yet, the way homeopathy is usually performed is, at the very least, extremely questionable.

For example, without entering into many details, the way "similarity of effects" is used for defining a treatment is less than rigorous. Hence, Benveniste's other findings, reported above, on Opium 15CH and Raphanus 5CH.

In fact, the main point of this discovery is not that it confirms homeopathy, but that it shakes the very foundations of prevailing biochemistry, biology, and even physics. It confirms the importance of expanding investigations in the field of optical biophysics, in order to achieve a more sophisticated understanding of the living process.