

21 years of progress in homeopathy research

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A special issue of the journal '*Homeopathy*' recently marked the 21st anniversary of the book "Ultra High Dilution", published in 1994. This project – the latest output of what might be considered the "buena vista social club" of homeopathy research – featured 26 contributions from authors with diverse scientific backgrounds. In this Research in Focus article, we present highlights from these wide-ranging commentaries on developments in the field of ultra-high dilution research from 1994-2015.

Introduction

"Ultra High Dilution" was a landmark in the evolution of research in homeopathy, representing the first multi-disciplinary work to address the 'how and why' of the actions of ultra-high dilutions. For two decades, "Ultra High Dilution" was widely quoted within the research community.

In 2015, it was time to re-visit and review the 21 years of research activity since studies were collated for this publication. The original authors from 1994 (or close laboratory colleagues) were asked to contribute papers covering their research efforts, experience and insights into ultra-high dilutions (UHDs) in the period from 1994 up to 2015. This article highlights key aspects of the re-assessment conducted in 2015¹.

Controversial beginnings

In 1988, a now infamous and persistently controversial paper was published in the journal *Nature* that documented the biological effects of UHDs of histamine and antibody on basophils (a type of white blood cell involved in immunity) in an experiment known as the basophil degranulation test². This paper not only began a public scientific debate that remains unresolved today, but also raised a number of questions with great significance for homeopathy, such as: does the 'memory of water' phenomenon really exist? What is the mechanism of action of UHDs? Which experiments are reproducible between laboratories?

Immunological models

In the 2015 retrospective collection, **Bernard Poitevin**³ and **Leoni Bonamin & Paolo Bellavite**⁴ reported separately on research developments aimed at answering some of these key questions arising from the controversial beginning of UHD research.

Poitevin³ offered a commentary and overview of experimental research in the field of immuno-allergology i.e. assessing the effects of UHD homeopathic remedies (e.g. *Apis*, *Rhus tox* and *Silicea*) on inflammatory, immune and allergic responses. For example, in replications of the basophil degranulation test carried out since the 1988 paper, 11/16 gave comparable 'positive' results; 3/16 produced zero effects (i.e. no difference between test and controls); and 2/16 gave opposite or new results. While the balance of evidence is clearly in favour of a real effect of

UHDs on basophil degranulation, the need to fully elucidate the factors affecting different outcomes (e.g. sensitivity of the individual blood donor to the homeopathic remedies) remains.

Similarly, Bonamin & Bellavite⁴ provided a summary of immunological experiments presented by Madeleine Bastide (deceased) in 1994. Her approach to UHD research capitalised on the ability of the immune system to detect and respond to very low levels of specific molecules, particularly antigens and cytokines. Numerous papers have been published since 1994 using these immunological models showing the direct effects of UHDs on isolated immune cells as well as whole immune systems, including a clear benefit for infected and stressed animals. However, these observations have yet to be repeated in a multicentre study.

Digital biology

Yolène Thomas⁵ presented an overview of the evolution of "digital biology", exploring the possible ways by which information can be transferred electromagnetically between molecules without physical contact. This echoes a fundamental issue for homeopathy where it is often stated that no physical starting material persists through the dilution process used in making remedies. Thomas highlights three specific experimental models that provide a starting point for elucidating whether 'memory of water' is a real phenomenon and can add to the growing body of evidence exploring the possible mechanism of action of UHDs at the molecular and sub-molecular level.

Replication studies

Extending the commentaries of Poitevin³ and Bonamin & Bellavite⁴ on the issue of reproducibility, **Christian Endler et al.** presented a detailed bibliometric study of the overall state of replication of experimental models used in UHD research⁶. In 1994, a total of 35 studies were available describing 15 experimental models: 70% of the repetition studies yielded comparable results, 25% produced a zero result and 5% an opposing result. Interestingly, similar results were found for replication studies available up to 2015: of 126 studies describing 28 experimental models, 70% yielded comparable results, 20% a zero result and 9% opposing results.

Highland amphibians

Endler *et al.* also reported on the experimental model where highland amphibians are exposed to UHDs of the hormone thyroxine. The multicentre study in 1994 reported a statistically significant slowing down of tadpole-to-frog metamorphosis as a result of *Thyroxine 30x* being added to the basin water (i.e. diluted 1 in 10 then vigorously shaken thirty times). This finding has been scrutinised since through replications – including a recent histological study performed by an independent team⁷ – which have shown that 9/11 studies yielded comparable results, 2/11 a zero result and none generated opposite results.

A further multicentre study performed in 1994, using *Thyroxine 30x* sealed in glass vials hung in the basin water (as opposed to the *Thyroxine 30x* being added directly to the water) also showed a decreased rate of tadpole-to-frog metamorphosis. This finding has since been replicated with 2/3 studies showing comparable results, 1/3 a zero result and none showing opposite results.

Similarly, *Cyril Smith et al.* reported on a method of monitoring resonance frequencies from *Thyroxine 30x* and subsequently exposing amphibian larvae to these frequencies as mimicked by a frequency generator⁸. In 1994, this study reported the same specific effect using frequencies seen with other routes of exposure to *Thyroxine 30x* (i.e. a decrease in tadpole metamorphosis rate). Although this challenging study has not yet been replicated or analysed further, it seems to be a promising candidate for further research in the light of today's insights and the significant body of reliable evidence now available for this amphibian experimental model.

Clinical Perspectives

Robert Mathie reported on clinical research in homeopathy⁹ as a follow-up to Max Haidvogel's contribution (Haidvogel being retired). In 1994 Haidvogel stated that while controlled clinical studies proving the efficacy of homeopathic remedies did exist, most lacked methodological quality. Research into the clinical effectiveness of homeopathy through randomised controlled trials (RCTs) has seen a marked increase in more recent times, with RCTs now being published at a rate of 1-2 per month, compared with 1-2 per year previously. From this growing body of RCT evidence we now have seven Cochrane reviews (the highest quality systematic review available for named health conditions) and six comprehensive systematic reviews with meta-analysis of homeopathy across multiple health conditions (only one of which was available in 1994). Five of these meta-analyses reached a cautiously positive conclusion that homeopathic treatment differs from placebo and one reached a negative conclusion.

In 1994, *Harald Walach* reported that, in spite of the existence of clinical trials in homeopathy, no single study had been reported at that point which tested the principle of homeopathic provings experimentally¹⁰. Provings are the foundation of homeopathic clinical practice, where a UHD is tested in healthy volunteers to see what symptoms arise, with the reasoning that the same UHD can then be used to alleviate these symptoms in a sick person. Walach responded to this challenge and embarked on a series of 9 studies of various sizes, designs and remedies with mixed and often confusing results. Ultimately, ten years later, a new triple blind, three-armed protocol with diligent daily symptom data collection and thorough statistical analysis was developed. After pilot testing of this new method, Walach *et al.* conducted two studies which were

then combined into one dataset and clearly showed more remedy-typical symptoms in the groups that had ingested the remedy than in the placebo group. This approach, when repeated in an independent study, saw the clearest result yet with two well-known remedies, *Arsenicum* and *Natrum muriaticum*. It is clear that the study of provings is a complex challenge, with many confounders that have been steadily and systematically assessed, such as the experience of the volunteers, the method of data collection and the problems of remedy-typical symptoms arising in the placebo group in an as yet unexplained non-local manner¹⁰.

Conclusion

The timely decision to revisit "Ultra High Dilution 1994" in 2015 presents a general survey of the state of UHD research highlighting new developments and insights gained from a number of experimental approaches. Areas of UHD research that have yet to be replicated and revisited deserve our full, contemporary attention for future research alongside the continuing determination to consolidate observations and search for the elusive mechanism of action of ultra-high dilution homeopathic medicines.

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