



ALTERNATIVE MEDICINE: HOMEOPATHY- A REVIEW

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ABSTRACT

Homeopathic remedies have been the subject of numerous clinical trials, which test the possibility that they may be effective through some mechanism unknown to science. While some individual studies have positive results, systematic reviews of published trials have failed to demonstrate efficacy. Because of the extremely high dilutions, most homeopathic remedies are, at least, harmless. However, patients who choose to use homeopathy rather than normal medicine risk missing timely diagnosis and effective treatment of serious conditions. The regulation and prevalence of homeopathy vary greatly from country to country.

Key words: Homeopathy, Alternative medicine, History.

INTRODUCTION

Homeopathy is a form of alternative medicine originated by Samuel Hahnemann, based on the idea that a substance that causes the symptoms of a disease in healthy people will cure that disease in sick people. This axiom is known as the law of similars or like cures like. Scientific research has found homeopathic remedies ineffective and their postulated mechanisms of action implausible. Within the medical community homeopathy is generally considered quackery.

In addition to symptoms, homeopaths consider a patient's physical and psychological state and life history, before consulting homeopathic reference books known as repertories to select a remedy based on the totality of symptoms as well as personal traits. Homeopathic remedies are prepared by serial dilution of a chosen substance in alcohol or distilled water, followed by forceful striking on an elastic body, called succussion. Each dilution followed by succussion is supposed to increase the remedy's potency. Homeopaths call this process potentization. Dilution usually continues well past the point where none of the original substance remains.

The low concentrations of homeopathic

remedies, often lacking even a single molecule of the diluted substance, lead to an objection that has dogged homeopathy since the 19th century: Modern advocates of homeopathy have suggested that water has a memory—that during mixing and succussion, the substance leaves an enduring effect on the water, perhaps a vibration, and this produces an effect on the patient. However, nothing like water memory has ever been found in chemistry or physics. Furthermore, the claims of homeopathy contradict pharmacological science, which shows that higher doses of an active ingredient exert stronger effects.

Homeopathic remedies have been the subject of numerous clinical trials, which test the possibility that they may be effective through some mechanism unknown to science. While some individual studies have positive results, systematic reviews of published trials have failed to demonstrate efficacy. Because of the extremely high dilutions, most homeopathic remedies are, at least, harmless. However, patients who choose to use homeopathy rather than normal medicine risk missing timely diagnosis and effective treatment of serious conditions. The regulation and prevalence of homeopathy vary greatly from country to country [1-5].

Philosophy

A homeopathic remedy prepared from marsh tea: The 15C dilution shown here exceeds the Avogadro constant, so contains no trace of the original herb. Homeopathy is a vitalist philosophy that interprets diseases and sickness as caused by disturbances in a hypothetical vital force or life force. It sees these disturbances as manifesting themselves as unique symptoms. Homeopathy maintains that the vital force has the ability to react and adapt to internal and external causes, which homeopaths refer to as the law of susceptibility (as with the law of similars this is a term of art and not a natural law, and it lacks significant scientific acceptance).

The law of susceptibility implies that a negative state of mind can attract hypothetical disease entities called miasms to invade the body and produce symptoms of diseases. However, Hahnemann rejected the notion of a disease as a separate thing or invading entity, and insisted it was always part of the living whole. Hahnemann proposed homeopathy in reaction to the state of traditional Western medicine at that time, which often was brutal and more harmful than helpful. Hahnemann coined the expression allopathic medicine, which was used to pejoratively refer to traditional Western medicine.

Law of similars

Hahnemann observed from his experiments with cinchona bark, used as a treatment for malaria, that the effects he experienced from ingesting the bark were similar to the symptoms of malaria. He therefore decided cure proceeds through similarity, and treatments must be able to produce symptoms in healthy individuals similar to those of the disease being treated. Through further experiments with other substances, Hahnemann conceived of the law of similars, otherwise known as *let like be cured by like* (Latin: *similia similibus curentur*) as a fundamental healing principle. He believed that by using drugs to induce symptoms, the artificial symptoms would stimulate the vital force, causing it to neutralise and expel the original disease and that this artificial disturbance would naturally subside when the dosing ceased. It is based on the belief that a substance that in large doses will produce symptoms of a specific disease will, in extremely small doses, cure it. Hahnemann's law of similars is an *ipse dixit* axiom, in other words an unproven assertion made by Hahnemann, and not a true law of nature [6-8].

Miasms and disease

In 1828, Hahnemann introduced the concept of miasms; underlying causes for many known diseases. A miasm is often defined by homeopaths as an imputed peculiar morbid derangement of vital force. Hahnemann associated each miasm with specific diseases, with each

miasm seen as the root cause of several diseases. According to Hahnemann, initial exposure to miasms causes local symptoms, such as skin or venereal diseases, but if these symptoms are suppressed by medication, the cause goes deeper and begins to manifest itself as diseases of the internal organs. Homeopathy maintains that treating diseases by directly opposing their symptoms, as is sometimes done in conventional medicine, is ineffective because all disease can generally be traced to some latent, deep-seated, underlying chronic, or inherited tendency. The underlying imputed miasm still remains and deep-seated ailments can be corrected only by removing the deeper disturbance of the vital force.

Hahnemann originally presented only three miasms, of which the most important was psora (Greek for itch), described as being related to any itching diseases of the skin, supposed to be derived from suppressed scabies, and claimed to be the foundation of many further disease conditions. Hahnemann believed psora to be the cause of such diseases as epilepsy, cancer, jaundice, deafness, and cataracts. Since Hahnemann's time, other miasms have been proposed, some replacing one or more of psora's proposed functions, including tuberculosis and cancer miasms.

Hahnemann's miasm theory remains disputed and controversial within homeopathy even in modern times. In 1978, Anthony Campbell, then a consultant physician at the Royal London Homeopathic Hospital, criticised statements by George Vithoulkas claiming that syphilis, when treated with antibiotics, would develop into secondary and tertiary syphilis with involvement of the central nervous system. This conflicts with scientific studies, which indicated penicillin treatment produces a complete cure of syphilis in more than 90% of cases. Campbell described this as a thoroughly irresponsible statement that could mislead an unfortunate layman into refusing orthodox treatment.

The theory of miasms has been criticized as an explanation developed by Hahnemann to preserve the system of homeopathy in the face of treatment failures, and for being inadequate to cover the many hundreds of sorts of diseases, as well as for failing to explain disease predispositions, as well as genetics, environmental factors, and the unique disease history of each patient [9-12].

Remedies

Homeopathic practitioners rely on two types of reference when prescribing remedies: materia medica and repertories. A homeopathic materia medica is a collection of drug pictures, organised alphabetically by remedy, that describes the symptom patterns associated with individual remedies. A homeopathic repertory is an index of disease symptoms that lists remedies associated with specific symptoms.

Homeopathy uses many animal, plant, mineral, and synthetic substances in its remedies. Examples include arsenicum album (arsenic oxide), natrum muriaticum (sodium chloride or table salt), Lachesis muta (the venom of the bushmaster snake), opium, and thyroideum (thyroid hormone). Homeopaths also use treatments called nosodes (from the Greek nosos, disease) made from diseased or pathological products such as fecal, urinary, and respiratory discharges, blood, and tissue. Homeopathic remedies prepared from healthy specimens are called sarcodes.

Some modern homeopaths have considered more esoteric bases for remedies, known as imponderables because they do not originate from a substance, but from electromagnetic energy presumed to have been captured by alcohol or lactose. Examples include X-rays and sunlight. Today, about 3,000 different remedies are commonly used in homeopathy.[citation needed] Some homeopaths also use techniques that are regarded by other practitioners as controversial. These include paper remedies, where the substance and dilution are written on pieces of paper and either pinned to the patients' clothing, put in their pockets, or placed under glasses of water that are then given to the patients, as well as the use of radionics to prepare remedies. Such practices have been strongly criticised by classical homeopaths as unfounded, speculative, and verging upon magic and superstition [13-16].

Preparation

Mortar and pestle used for grinding insoluble solids, including quartz and oyster shells, into homeopathic remedies. In producing remedies for diseases, homeopaths use a process called dynamisation or potentisation, whereby a substance is diluted with alcohol or distilled water and then vigorously shaken by 10 hard strikes against an elastic body in a process homeopaths call succussion. Hahnemann advocated using substances that produce symptoms like those of the disease being treated, but found that undiluted doses intensified the symptoms and exacerbated the condition, sometimes causing dangerous toxic reactions. He therefore specified that the substances be diluted, due to his belief that succussion activated the vital energy of the diluted substance and made it stronger. To facilitate succussion, Hahnemann had a saddle-maker construct a special wooden striking board covered in leather on one side and stuffed with horsehair. Insoluble solids, such as quartz and oyster shell, are diluted by grinding them with lactose (trituration) [17].

Dilutions

Three logarithmic potency scales are in regular use in homeopathy. Hahnemann created the centesimal or C scale, diluting a substance by a factor of 100 at each

stage. The centesimal scale was favored by Hahnemann for most of his life. A 2C dilution requires a substance to be diluted to one part in 100, and then some of that diluted solution diluted by a further factor of 100. This works out to one part of the original substance in 10,000 parts of the solution. A 6C dilution repeats this process six times, ending up with the original substance diluted by a factor of $100-6=10^{-12}$ (one part in one trillion or 1/1,000,000,000,000). Higher dilutions follow the same pattern. In homeopathy, a solution that is more dilute is described as having a higher potency, and more dilute substances are considered by homeopaths to be stronger and deeper-acting remedies. The end product is often so diluted as to be indistinguishable from the dilutant (pure water, sugar or alcohol).

Hahnemann advocated 30C dilutions for most purposes (that is, dilution by a factor of 1060). In Hahnemann's time, it was reasonable to assume the remedies could be diluted indefinitely, as the concept of the atom or molecule as the smallest possible unit of a chemical substance was just beginning to be recognized. The greatest dilution reasonably likely to contain even one molecule of the original substance is 12C [18].

Some homeopaths developed a decimal scale (D or X), diluting the substance to ten times its original volume each stage. The D or X scale dilution is therefore half that of the same value of the C scale; for example, 12X is the same level of dilution as 6C. Hahnemann never used this scale, but it was very popular throughout the 19th century and still is in Europe. This potency scale appears to have been introduced in the 1830s by an American homeopath, Constantine Hering. In the last ten years of his life, Hahnemann also developed a quintamillesimal (Q) or LM scale, diluting the drug 1 part in 50,000 parts of diluent. A given dilution on the Q scale is roughly 2.35 times its designation on the C scale. For example, a remedy described as 20Q has about the same concentration as a 47C remedy.

Critics and advocates of homeopathy alike commonly attempt to illustrate the dilutions involved in homeopathy with analogies. Hahnemann is reported to have joked that a suitable procedure to deal with an epidemic would be to empty a bottle of poison into Lake Geneva, if it could be succussed 60 times. Another example given by a critic of homeopathy states that a 12C solution is equivalent to a pinch of salt in both the North and South Atlantic Oceans, which is approximately correct. One-third of a drop of some original substance diluted into all the water on earth would produce a remedy with a concentration of about 13C. A popular homeopathic treatment for the flu is a 200C dilution of duck liver, marketed under the name *oscillococcinum*. As there are only about 10⁸⁰ atoms in the entire observable universe, a dilution of one molecule in the observable universe would be about 40C. *Oscillococcinum* would

thus require 10320 more universes to simply have one molecule in the final substance. The high dilutions characteristically used are often considered to be the most controversial and implausible aspect of homeopathy [19-22].

Dilution debate

Not all homeopaths advocate extremely high dilutions. Many of the early homeopaths were originally doctors and generally used lower dilutions such as 3X or 6X, rarely going beyond 12X. The split between lower and higher dilutions followed ideological lines. Those favoring low dilutions stressed pathology and a strong link to conventional medicine, while those favoring high dilutions emphasised vital force, miasms and a spiritual interpretation of disease. Some products with such relatively lower dilutions continue to be sold, but like their counterparts, they have not been conclusively demonstrated to have any effect beyond that of a placebo.

Proving

Hahnemann experimented on himself and others for several years before using remedies on patients. His experiments did not initially consist of giving remedies to the sick, because he thought that the most similar remedy, by virtue of its ability to induce symptoms similar to the disease itself, would make it impossible to determine which symptoms came from the remedy and which from the disease itself. Therefore, sick people were excluded from these experiments. The method used for determining which remedies were suitable for specific diseases was called proving, after the original German word Prüfung, meaning test. A homeopathic proving is the method by which the profile of a homeopathic remedy is determined. At first Hahnemann used undiluted doses for provings, but he later advocated provings with remedies at a 30C dilution, and most modern provings are carried out using ultradilute remedies in which it is highly unlikely that any of the original molecules remain. During the proving process, Hahnemann administered remedies to healthy volunteers, and the resulting symptoms were compiled by observers into a drug picture. The volunteers were observed for months at a time and made to keep extensive journals detailing all of their symptoms at specific times throughout the day. They were forbidden from consuming coffee, tea, spices, or wine for the duration of the experiment; playing chess was also prohibited because Hahnemann considered it to be too exciting, though they were allowed to drink beer and encouraged to exercise in moderation. After the experiments were over, Hahnemann made the volunteers take an oath swearing that what they reported in their journals was the truth, at which time he would interrogate them extensively concerning their symptoms.

Provings have been described as important in the development of the clinical trial, due to their early use of simple control groups, systematic and quantitative procedures, and some of the first application of statistics in medicine. The lengthy records of self-experimentation by homeopaths have occasionally proven useful in the development of modern drugs: For example, evidence that nitroglycerin might be useful as a treatment for angina was discovered by looking through homeopathic provings, though homeopaths themselves never used it for that purpose at that time. The first recorded provings were published by Hahnemann in his 1796 *Essay on a New Principle*. His *Fragmenta de Viribus* (1805) contained the results of 27 provings, and his 1810 *Materia Medica Pura* contained 65. For James Tyler Kent's 1905 *Lectures on Homoeopathic Materia Medica*, 217 remedies underwent provings and newer substances are continually added to contemporary versions.

Though the proving process has superficial similarities with clinical trials, it is fundamentally different in that the process is subjective, not blinded, and modern provings are unlikely to use pharmacologically active levels of the substance under proving. As early as 1842, Holmes noted the provings were impossibly vague, and the purported effect was not repeatable among different subjects [23-38].

Physical, mental, and emotional state examination

Homeopaths generally begin with detailed examinations of their patients' histories, including questions regarding their physical, mental and emotional states, their life circumstances and any physical or emotional illnesses. The homeopath then attempts to translate this information into a complex formula of mental and physical symptoms, including likes, dislikes, innate predispositions and even body type.

From these symptoms, the homeopath chooses how to treat the patient. A compilation of reports of many homeopathic provings, supplemented with clinical data, is known as a homeopathic *materia medica*. But because a practitioner first needs to explore the remedies for a particular symptom rather than looking up the symptoms for a particular remedy, the homeopathic repertory, which is an index of symptoms, lists after each symptom those remedies that are associated with it. Repertories are often very extensive and may include data extracted from multiple sources of *materia medica*. There is often lively debate among compilers of repertories and practitioners over the veracity of a particular inclusion.

The first symptomatic index of the homeopathic *materia medica* was arranged by Hahnemann. Soon after, one of his students, Clemens von Bönninghausen, created the *Therapeutic Pocket Book*, another homeopathic repertory. The first such homeopathic repertory was Georg Jahr's *Symptomenkodex*, published in German

(1835), which was then first translated to English (1838) by Constantine Hering as the Repertory to the more Characteristic Symptoms of Materia Medica. This version was less focused on disease categories and would be the forerunner to Kent's later works. It consisted of three large volumes. Such repertories increased in size and detail as time progressed.

Some diversity in approaches to treatments exists among homeopaths. Classical homeopathy generally involves detailed examinations of a patient's history and infrequent doses of a single remedy as the patient is monitored for improvements in symptoms, while clinical homeopathy involves combinations of remedies to address the various symptoms of an illness [29,30].

Homeopathic pills

Homeopathic pills, homeopathic remedy *osillococcinum*. Homeopathic pills are made from an inert substance (often sugars, typically lactose), upon which a drop of liquid homeopathic preparation is placed.

Active ingredients

The list of ingredients seen on remedies may confuse consumers into believing the product actually contains those ingredients. According to normal homeopathic practice, remedies are prepared starting with active ingredients that are often serially diluted to the point where the finished product no longer contains any biologically active ingredients as that term is normally defined. James Randi and the 10:23 campaign groups have demonstrated the lack of active ingredients in homeopathic products by taking large overdoses. None of the hundreds of demonstrators in the UK, Australia, New Zealand, Canada and the US were injured and no one was cured of anything, either.

While the lack of active compounds is noted in most homeopathic products, there are some exceptions such as Zicam Cold Remedy, which is marketed as an unapproved homeopathic product. It contains a number of highly diluted ingredients that are listed as inactive ingredients on the label. Some of the homeopathic ingredients used in the preparation of Zicam are *galphimia glauca*, histamine dihydrochloride (homeopathic name, *histaminum hydrochloricum*), *luffa operculata*, and sulfur. Although the product is marked homeopathic, it does contain two ingredients that are only slightly diluted: zinc acetate (2X = 1/100 dilution) and zinc gluconate (1X = 1/10 dilution), which means both are present in a concentration that contains biologically active ingredients. In fact, they are strong enough to have caused some people to lose their sense of smell, a condition termed anosmia. This illustrates why taking a product marked homeopathic, especially an overdose, can still be dangerous because it may contain biologically active ingredients, though as discussed previously, most

homeopathic preparations contain no active ingredients. Because the manufacturers of Zicam label it as a homeopathic product (despite the relatively high concentrations of active ingredients), it is exempted from FDA regulation by the Dietary Supplement Health and Education Act of 1994 (DSHEA).

Related practices

Isopathy

Isopathy is a therapy derived from homeopathy invented by Johann Joseph Wilhelm Lux in the 1830s. Isopathy differs from homeopathy in general in that the remedies, known as nosodes, are made up either from things that cause the disease or from products of the disease, such as pus. Many so-called homeopathic vaccines are a form of isopathy.

Flower remedies

Flower remedies can be produced by placing flowers in water and exposing them to sunlight. The most famous of these are the Bach flower remedies, which were developed by the physician and homeopath Edward Bach. Although the proponents of these remedies share homeopathy's vitalist world-view and the remedies are claimed to act through the same hypothetical vital force as homeopathy, the method of preparation is different. Bach flower remedies are prepared in gentler ways such as placing flowers in bowls of sunlit water, and the remedies are not succussed. There is no convincing scientific or clinical evidence for flower remedies being effective.

Veterinary use

The idea of using homeopathy as a treatment for other animals, termed veterinary homeopathy, dates back to the inception of homeopathy; Hahnemann himself wrote and spoke of the use of homeopathy in animals other than humans. The FDA has not approved homeopathic products as veterinary medicine in the U.S. In the UK, veterinary surgeons who use homeopathy belong to the Faculty of Homeopathy and/or to the British Association of Homeopathic Veterinary Surgeons. Animals may be treated only by qualified veterinary surgeons in the UK and some other countries. Internationally, the body that supports and represents homeopathic veterinarians is the International Association for Veterinary Homeopathy. The use of homeopathy in veterinary medicine is controversial; the little existing research on the subject is not of a high enough scientific standard to provide reliable data on efficacy. Other studies have also found that giving animals placebos can play active roles in influencing pet owners to believe in the effectiveness of the treatment when none exists.

Electrohomeopathy

Electrohomeopathy was a 19th century practice combining homeopathy with electric treatment.

Evidence

Homeopathy Claims Proponents claim that illnesses can be treated with specially prepared extreme dilutions of a substance that produces symptoms similar to the illness. Homeopathic remedies rarely contain any atom or molecule of the substance in the remedy.

The medicinal claims of homeopathy are unsupported by the collective weight of modern scientific research. There is an overall absence of sound statistical evidence of therapeutic efficacy, which is consistent with the lack of any biologically plausible pharmacological agent or mechanism. Abstract concepts within theoretical physics have been invoked to suggest explanations of how or why remedies might work, including quantum entanglements, the theory of relativity and chaos theory. However, the explanations are offered by nonspecialists within the field, and often include speculations that are incorrect in their application of the concepts and not supported by actual experiments [31-33].

Plausibility

The extreme dilutions used in homeopathic preparations usually leave none of the original substance in the final product. The modern mechanism proposed by homeopaths, water memory, is considered implausible in that short-range order in water only persists for about 1 picosecond. Existence of a pharmacological effect in the absence of any true active ingredient is inconsistent with the observed dose-response relationships characteristic of therapeutic drugs (whereas placebo effects are non-specific and unrelated to pharmacological activity). The proposed rationale for these extreme dilutions – that the water contains the memory or vibration from the diluted ingredient – is counter to the laws of chemistry and physics, such as the law of mass action.

High dilutions

The extremely high dilutions in homeopathy preclude a biologically plausible mechanism of action. Homeopathic remedies are usually diluted to the point where there are no molecules from the original solution left in a dose of the final remedy. Homeopaths contend that the methodical dilution of a substance, beginning with a 10% or lower solution and working downwards, with shaking after each dilution, produces a therapeutically active remedy, in contrast to therapeutically inert water. Since even the longest-lived noncovalent structures in liquid water at room temperature are stable for only a few picoseconds, critics have concluded that any effect that might have been present from the original substance can no longer exist. No evidence of stable clusters of water molecules was found when homeopathic remedies were studied using nuclear magnetic resonance.

Furthermore, since water will have been in contact with millions of different substances throughout its history, critics point out that water is therefore an extreme dilution of almost any conceivable substance. By drinking water one would, according to this interpretation, receive treatment for every imaginable condition. For comparison, ISO 3696: 1987 defines a standard for water used in laboratory analysis; this allows for a contaminant level of ten parts per billion, 4C in homeopathic notation. This water may not be kept in glass as contaminants will leach out into the water.

Practitioners of homeopathy contend that higher dilutions produce stronger medicinal effects. This idea is inconsistent with the observed dose-response relationships of conventional drugs, where the effects are dependent on the concentration of the active ingredient in the body. This dose-response relationship has been confirmed in myriad experiments on organisms as diverse as nematodes, rats, and humans. Since the least amount of a substance in a solution is one molecule, a 30C solution would have to have at least one molecule of the original substance dissolved in a minimum of 1,000 [or 1060] molecules of water. This would require a container more than 30,000,000,000 times the size of the Earth.

Park is also quoted as saying that, to expect to get even one molecule of the 'medicinal' substance allegedly present in 30X pills, it would be necessary to take some two billion of them, which would total about a thousand tons of lactose plus whatever impurities the lactose contained. The laws of chemistry state that there is a limit to the dilution that can be made without losing the original substance altogether. This limit, which is related to Avogadro's number, is roughly equal to homeopathic potencies of 12C or 24X (1 part in 1024). Scientific tests run by both the BBC's Horizon and ABC's 20/20 programs were unable to differentiate homeopathic dilutions from water, even when using tests suggested by homeopaths themselves.

Efficacy

The effectiveness of homeopathy has been in dispute since its inception. One of the earliest double blind studies concerning homeopathy was sponsored by the British government during World War II in which volunteers tested the efficacy of homeopathic remedies against diluted mustard gas burns. No individual preparation has been unambiguously demonstrated to be different from placebo. The methodological quality of the primary research was generally low, with such problems as weaknesses in study design and reporting, small sample size, and selection bias. Since better quality trials have become available, the evidence for efficacy of homeopathy preparations has diminished; the highest-

quality trials indicate that the remedies themselves exert no intrinsic effect.²⁰⁶ A review conducted in 2010 of all the pertinent studies of best evidence produced by the Cochrane Collaboration concluded that the most reliable evidence – that produced by Cochrane reviews – fails to demonstrate that homeopathic medicines have effects beyond placebo.

The fact that individual randomized controlled trials have given positive results is not in contrast with an overall lack of statistical evidence of efficacy. A small proportion of randomized controlled trials inevitably provide false-positive outcomes due to the play of chance: a statistically significant positive outcome is commonly adjudicated when the probability of it being due to chance rather than a real effect is no more than 5%—a level at which about 1 in 20 tests can be expected to show an effect even though there is none. Furthermore, trials of low methodological quality (ie ones which have been inappropriately designed, conducted or reported) are prone to give misleading results. In a systematic review of the methodological quality of randomized trials in three branches of alternative medicine, Linde et al. highlighted major weaknesses in the homeopathy sector, including poor randomization [34,35].

A related issue is publication bias: researchers are more likely to submit trials that report a positive finding for publication, and journals prefer to publish positive results. Publication bias has been particularly marked in complementary and alternative medicine journals, where few of the published articles (just 5% during the year 2000) tend to report null results [118]. Regarding the way in which homeopathy is represented in the medical literature, a systematic review found signs of bias in the publications of clinical trials (towards negative representation in mainstream medical journals, and vice-versa in complementary and alternative medicine journals), but not in reviews.

Systematic reviews and meta-analyses of efficacy

Both meta-analyses, which statistically combine the results of several randomized controlled trials, and other systematic reviews of the literature are essential tools to summarize evidence of therapeutic efficacy. Early systematic reviews and meta-analyses of trials evaluating the efficacy of homeopathic remedies in comparison with placebo more often tended to generate positive results, but appeared unconvincing overall. In particular, reports of three large meta-analyses warned readers that firm conclusions could not be reached, largely due to methodological flaws in the primary studies and the difficulty in controlling for publication bias. The positive finding of one of the most prominent of the early meta-analyses, published in *The Lancet* in 1997 by Linde et al., was later reframed by the same research team, who wrote:

The evidence of bias [in the primary studies] weakens the findings of our original meta-analysis. Since we completed our literature search in 1995, a considerable number of new homeopathy trials have been published. The fact that a number of the new high-quality trials ... have negative results, and a recent update of our review for the most original subtype of homeopathy (classical or individualized homeopathy), seem to confirm the finding that more rigorous trials have less-promising results. It seems, therefore, likely that our meta-analysis at least overestimated the effects of homeopathic treatments.

In 2002, a systematic review of the available systematic reviews confirmed that higher-quality trials tended to have less positive results, and found no convincing evidence that any homeopathic remedy exerts clinical effects different from placebo.

In 2005, *The Lancet* medical journal published a meta-analysis of 110 placebo-controlled homeopathy trials and 110 matched medical trials based upon the Swiss government's Program for Evaluating Complementary Medicine, or PEK. The study concluded that its findings were compatible with the notion that the clinical effects of homeopathy are nothing more than placebo effects [36,37].

A 2006 meta-analysis of six trials evaluating homeopathic treatments to reduce cancer therapy side-effects following radiotherapy and chemotherapy found that there was insufficient evidence to support clinical efficacy of homeopathic therapy in cancer care.

A 2007 systematic review of homeopathy for children and adolescents found that the evidence for attention-deficit hyperactivity disorder and childhood diarrhea was mixed. No difference from placebo was found for adenoid vegetation, asthma, or upper respiratory tract infection. Evidence was not sufficient to recommend any therapeutic or preventative intervention, and the delay in medical treatment may be harmful to the patient.

The Cochrane Library found insufficient clinical evidence to evaluate the efficacy of homeopathic treatments for asthma, dementia, or for the use of homeopathy in induction of labor. Other researchers found no evidence that homeopathy is beneficial for osteoarthritis, migraines or delayed-onset muscle soreness.

Health organisations such as the UK's National Health Service, the American Medical Association, and the FASEB have issued statements of their conclusion that there is no convincing scientific evidence to support the use of homeopathic treatments in medicine.

Clinical studies of the medical efficacy of homeopathy have been criticized by some homeopaths as being irrelevant because they do not test classical homeopathy.[131] There have, however, been a number of clinical trials that have tested individualized homeopathy. A 1998 review found 32 trials that met their

inclusion criteria, 19 of which were placebo-controlled and provided enough data for meta-analysis. These 19 studies showed a pooled odds ratio of 1.17 to 2.23 in favor of individualized homeopathy over the placebo, but no difference was seen when the analysis was restricted to the methodologically best trials. The authors concluded that the results of the available randomized trials suggest that individualized homeopathy has an effect over placebo. The evidence, however, is not convincing because of methodological shortcomings and inconsistencies. Jay Shelton, author of a book on homeopathy, has stated that the claim assumes without evidence that classical, individualized homeopathy works better than nonclassical variations [38,39].

Explanations of perceived effects

Science offers a variety of explanations for how homeopathy may appear to cure diseases or alleviate symptoms even though the remedies themselves are inert. The placebo effect — the intensive consultation process and expectations for the homeopathic preparations may cause the effect. Therapeutic effect of the consultation - the care, concern and reassurance a patient experiences when opening up to a compassionate caregiver can have a positive effect on the patient's well-being. Unassisted natural healing — time and the body's ability to heal without assistance can eliminate many diseases of their own accord. Unrecognized treatments — an unrelated food, exercise, environmental agent or treatment for a different ailment, may have occurred. Regression toward the mean — since many diseases or conditions are cyclical, symptoms vary over time and patients tend to seek care when discomfort is greatest, they may feel better anyway but because the timing of the visit to the homeopath they attribute improvement to the remedy taken. Non-homeopathic treatment — patients may also receive standard medical care simultaneous with homeopathic treatment, and the former is responsible for improvement. Cessation of unpleasant treatment — often homeopaths recommend patients stop getting medical treatment such as surgery or drugs, which can cause unpleasant side-effects; improvements are attributed to homeopathy when the actual cause is the cessation of the treatment causing side-effects in the first place, but the underlying disease remains untreated and still dangerous to the patient. Lifestyle changes — homeopaths often recommend diet and exercise, as well as limitations in alcohol or coffee consumption and stress reduction, all of which can increase health and decrease symptoms [40].

Effects in other biological systems

While some articles have suggested that homeopathic solutions of high dilution can have statistically significant effects on organic processes including the growth of grain, histamine release by

leukocytes, and enzyme reactions, such evidence is disputed since attempts to replicate them have failed.

In 1987, French immunologist Jacques Benveniste submitted a paper to the journal *Nature* while working at INSERM. The paper purported to have discovered that basophils, a type of white blood cell, released histamine when exposed to a homeopathic dilution of anti-immunoglobulin E antibody. The journal editors, sceptical of the results, requested that the study be replicated in a separate laboratory. Upon replication in four separate laboratories the study was published. Still sceptical of the findings, *Nature* assembled an independent investigative team to determine the accuracy of the research, consisting of *Nature* editor and physicist Sir John Maddox, American scientific fraud investigator and chemist Walter Stewart, and James Randi. After investigating the findings and methodology of the experiment, the team found that the experiments were statistically ill-controlled, interpretation has been clouded by the exclusion of measurements in conflict with the claim, and concluded, we believe that experimental data have been uncritically assessed and their imperfections inadequately reported. James Randi stated that he doubted that there had been any conscious fraud, but that the researchers had allowed wishful thinking to influence their interpretation of the data [41].

Ethics and safety

As homeopathic remedies usually contain only water and/or alcohol, they are thought to be generally safe. Only in rare cases are the original ingredients present at detectable levels. This may be due to improper preparation or intentional low dilution. Instances of arsenic poisoning have occurred after use of arsenic-containing homeopathic preparations. Zicam Cold remedy Nasal Gel, which contains 2X (1:100) zinc gluconate, reportedly caused a small percentage of users to lose their sense of smell; 340 cases were settled out of court in 2006 for 12 million U.S. dollars. In 2009, the FDA advised consumers to stop using three discontinued cold remedy products manufactured by Zicam because it could cause permanent damage to users' sense of smell. Zicam was launched without a New Drug Application (NDA) under a provision in the FDA's Compliance Policy Guide called Conditions Under Which Homeopathic Drugs May be Marketed, but the FDA warned Zicam via a Warning Letter that this policy does not apply when there is a health risk to consumers [42].

The lack of convincing scientific evidence supporting its efficacy and its use of remedies without active ingredients have led to characterizations as pseudoscience and quackery, or, in the words of a 1998 medical review, placebo therapy at best and quackery at worst. Jack Killen, acting deputy director of the National Center for Complementary and Alternative Medicine,

says homeopathy goes beyond current understanding of chemistry and physics. He adds: There is, to my knowledge, no condition for which homeopathy has been proven to be an effective treatment. Ben Goldacre says that homeopaths who misrepresent scientific evidence to a scientifically illiterate public, have ...walled themselves off from academic medicine, and critique has been all too often met with avoidance rather than argument. Homeopaths often prefer to ignore meta-analyses in favour of cherry picked positive results, such as by promoting a particular observational study (one which Goldacre describes as little more than a customer-satisfaction survey) as if it were more informative than a series of randomized controlled trials [43]. Referring specifically to homeopathy, the British House of Commons Science and Technology Committee has stated: In the Committee's view, homeopathy is a placebo treatment and the Government should have a policy on prescribing placebos. The Government is reluctant to address the appropriateness and ethics of prescribing placebos to patients, which usually relies on some degree of patient deception. Prescribing of placebos is not consistent with informed patient choice - which the Government claims is very important - as it means patients do not have all the information needed to make choice meaningful.

Beyond ethical issues and the integrity of the doctor-patient relationship, prescribing pure placebos is bad medicine. Their effect is unreliable and unpredictable and cannot form the sole basis of any treatment on the NHS. The National Center for Complementary and Alternative Medicine of the United States' National Institutes of Health states: Homeopathy is a controversial area of CAM because a number of its key concepts are not consistent with established laws of science (particularly chemistry and physics). Critics think it is implausible that a remedy containing a miniscule amount of an active ingredient (sometimes not a single molecule of the original compound) can have any biological effect—beneficial or otherwise. For these reasons, critics argue that continuing the scientific study of homeopathy is not worthwhile. Others point to observational and anecdotal evidence that homeopathy does work and argue that it should not be rejected just because science has not been able to explain it. On clinical grounds, patients who choose to use homeopathy in preference to normal medicine risk missing timely diagnosis and effective treatment, thereby worsening the outcomes of serious conditions. Critics of homeopathy have cited individual cases of patients of homeopathy failing to receive proper treatment for diseases that could have been easily diagnosed and managed with conventional medicine and who have died as a result and the marketing practice of criticizing and downplaying the effectiveness of mainstream medicine. Homeopaths claim that use of

conventional medicines will push the disease deeper and cause more serious conditions, a process referred to as suppression. Some homeopaths advise their patients against immunisation. Some homeopaths suggest that vaccines be replaced with homeopathic nosodes, created from biological materials such as pus, diseased tissue, bacilli from sputum or feces. While Hahnemann was opposed to such preparations, modern homeopaths often use them although there is no evidence to indicate they have any beneficial effects. Cases of homeopaths advising against the use of anti-malarial drugs have been identified. This puts visitors to the tropics who take this advice in severe danger, since homeopathic remedies are completely ineffective against the malaria parasite. Also, in one case in 2004, a homeopath instructed one of her patients to stop taking conventional medication for a heart condition, advising her on 22 June 2004 to Stop ALL medications including homeopathic, advising her on or around 20 August that she no longer needed to take her heart medication, and adding on 23 August, She just cannot take any drugs – I have suggested some homeopathic remedies I feel confident that if she follows the advice she will regain her health. The patient was admitted to hospital the next day, and died eight days later, the final diagnosis being acute heart failure due to treatment discontinuation [41].

In 1978, Anthony Campbell, then a consultant physician at The Royal London Homeopathic Hospital, criticised statements made by George Vithoulkas to promote his homeopathic treatments. Vithoulkas stated that syphilis, when treated with antibiotics, would develop into secondary and tertiary syphilis with involvement of the central nervous system. Campbell described this as a thoroughly irresponsible statement that could mislead an unfortunate layperson into refusing conventional medical treatment. This claim echoes the idea that treating a disease with external medication used to treat the symptoms would only drive it deeper into the body and conflicts with scientific studies, which indicate that penicillin treatment produces a complete cure of syphilis in more than 90% of cases.

A 2006 review by W. Steven Pray of the College of Pharmacy at Southwestern Oklahoma State University recommends that pharmacy colleges include a required course in unproven medications and therapies, that ethical dilemmas inherent in recommending products lacking proven safety and efficacy data be discussed, and that students should be taught where unproven systems such as homeopathy depart from evidence-based medicine. Edzard Ernst, the first Professor of Complementary Medicine in the United Kingdom and a former homeopathic practitioner, has expressed his concerns about pharmacists who violate their ethical code by failing to provide customers with necessary and relevant information about the true nature of the homeopathic

products they advertise and sell: My plea is simply for honesty. Let people buy what they want, but tell them the truth about what they are buying. These treatments are biologically implausible and the clinical tests have shown they don't do anything at all in human beings. The argument that this information is not relevant or important for customers is quite simply ridiculous [42].

Regulation and prevalence

Homeopathy is fairly common in some countries while being uncommon in others; is highly regulated in some countries and mostly unregulated in others. It is practised worldwide and professional qualifications and licences are needed in most countries. Regulations vary in Europe depending on the country. In some countries, there are no specific legal regulations concerning the use of homeopathy, while in others, licences or degrees in conventional medicine from accredited universities are required. In Germany, to become a homeopathic physician, one must attend a three-year training program, while France, Austria and Denmark mandate licences to diagnose any illness or dispense of any product whose purpose is to treat any illness. Some homeopathic treatment is covered by the public health service of several European countries, including France, the United Kingdom, Denmark, and Luxembourg. In other countries, such as Belgium, homeopathy is not covered. In Austria, the public health service requires scientific proof of effectiveness in order to reimburse medical treatments and homeopathy is listed as not reimbursable but exceptions can be made; private health insurance policies sometimes include homeopathic treatment. The Swiss government, after a 5-year trial, withdrew homeopathy and four other complementary treatments in 2005, stating that they did not meet efficacy and cost-effectiveness criteria, but following a referendum in 2009 the five therapies are to be reinstated for a further 6-year trial period from 2012. The Indian government recognises homeopathy as one of its national systems of medicine, and a minimum of a recognised diploma in homeopathy and registration on a state register or the Central Register of Homoeopathy is required to practice homeopathy in India [43].

In the United Kingdom, MPs inquired into homeopathy to assess the Government's policy on the issue, including funding of homeopathy under the National Health Service and government policy for licensing homeopathic products. The decision by the House of Commons Science and Technology Committee follows a written explanation from the Government in which it told the select committee that the licensing regime was not formulated on the basis of scientific evidence. The three elements of the licensing regime (for homeopathic products) probably lie outside the scope of the select committee inquiry, because government

consideration of scientific evidence was not the basis for their establishment, the Committee said. The inquiry sought written evidence and submissions from concerned parties.

In February 2010 the House of Commons Science and Technology Committee concluded that: In the Committee's view, homeopathy is a placebo treatment and the Government should have a policy on prescribing placebos. The Government is reluctant to address the appropriateness and ethics of prescribing placebos to patients, which usually relies on some degree of patient deception. Prescribing of placebos is not consistent with informed patient choice – which the Government claims is very important – as it means patients do not have all the information needed to make choice meaningful.

Beyond ethical issues and the integrity of the doctor-patient relationship, prescribing pure placebos is bad medicine. Their effect is unreliable and unpredictable and cannot form the sole basis of any treatment on the NHS. In July 2010 the newly appointed UK Secretary of State for Health deferred to local NHS on funding homeopathy. A nineteen page document details the Government's response, and it states that our continued position on the use of homeopathy within the NHS is that the local NHS and clinicians, rather than Whitehall, are best placed to make decisions on what treatment is appropriate for their patients - including complementary or alternative treatments such as homeopathy - and provide accordingly for those treatments. The response also stated that the overriding reason for NHS provision is that homeopathy is available to provide patient choice by February 2011 only one third of PCTs still funded homeopathy.

Historical context

An early assertion that like cures like was made by Hippocrates about 400 BC, when he prescribed mandrake root, which produced mania, to treat mania, by prescribing a dose smaller than what would produce mania. In the 16th century the pioneer of pharmacology Paracelsus declared that small doses of what makes a man ill also cures him. but it was Hahnemann who gave it a name and laid out its principles in the late 18th century. At that time, mainstream medicine employed such measures as bloodletting and purging, used laxatives and enemas, and administered complex mixtures, such as Venice treacle, which was made from 64 substances including opium, myrrh, and viper's flesh. Such measures often worsened symptoms and sometimes proved fatal. While the virtues of these treatments had been extolled for centuries, Hahnemann rejected such methods as irrational and inadvisable. Instead, he favored the use of single drugs at lower doses and promoted an immaterial, vitalistic view of how living organisms function, believing that diseases have spiritual, as well as physical

causes. (At the time, vitalism was part of mainstream science; it wasn't completely discarded until the 20th century, with the development of microbiology, the germ theory of disease, and advances in chemistry. Hahnemann also advocated various lifestyle improvements to his patients, including exercise, diet, and cleanliness.

Hahnemann's concept

Hahnemann conceived of homeopathy while translating a medical treatise by Scottish physician and chemist William Cullen into German. Being skeptical of Cullen's theory concerning cinchona's action in intermittent fever, Hahnemann ingested some of the bark specifically to see if it cured fever by virtue of its effect of strengthening the stomach. Upon ingesting the bark, he noticed few stomach symptoms, but did experience fever, shivering and joint pain, symptoms similar to some of the early symptoms of intermittent fever, the disease that the bark was ordinarily used to treat. From this, Hahnemann came to believe that all effective drugs produce symptoms in healthy individuals similar to those of the diseases that they treat. This later became known as the law of similars, the most important concept of homeopathy. The term homeopathy was coined by Hahnemann and first appeared in print in 1807, although he began outlining his theories of medical similars or the doctrine of specifics in a series of articles and monographs in 1796.

Hahnemann began to test what effects substances produced in humans, a procedure that would later become known as homeopathic proving. These time-consuming tests required subjects to clearly record all of their symptoms as well as the ancillary conditions under which they appeared. Hahnemann saw these data as a way of identifying substances suitable for the treatment of particular diseases. The first collection of provings was published in 1805 and a second collection of 65 remedies appeared in his book, *Materia Medica Pura*, in 1810. Hahnemann believed that large doses of drugs that caused similar symptoms would only aggravate illness, so he advocated extreme dilutions of the substances; he devised a technique for making dilutions that he believed would preserve a substance's therapeutic properties while removing its harmful effects, proposing that this process aroused and enhanced the spirit-like medicinal powers of the crude substances. He gathered and published a complete overview of his new medical system in his 1810 book, *The Organon of the Healing Art*, whose 6th edition, published in 1921, is still used by homeopaths today.

Homeopathy achieved its greatest popularity in the 19th century. Dr. John Franklin Gray (1804–1882) was the first practitioner of homeopathy in the United States, beginning in 1828 in New York City. The first homeopathic schools opened in 1830, and throughout the 19th century dozens of homeopathic institutions appeared in Europe and the United States. By 1900, there were 22

homeopathic colleges and 15,000 practitioners in the United States. Because medical practice of the time relied on ineffective and often dangerous treatments, patients of homeopaths often had better outcomes than those of the doctors of the time. Homeopathic remedies, even if ineffective, would almost surely cause no harm, making the users of homeopathic remedies less likely to be killed by the treatment that was supposed to be helping them. The relative success of homeopathy in the 19th century may have led to the abandonment of the ineffective and harmful treatments of bloodletting and purging and to have begun the move towards more effective, science-based medicine. One reason for the growing popularity of homeopathy was its apparent success in treating people suffering from infectious disease epidemics. During 19th century epidemics of diseases such as cholera, death rates in homeopathic hospitals were often lower than in conventional hospitals, where the treatments used at the time were often harmful and did little or nothing to combat the diseases. From its inception, however, homeopathy was criticized by mainstream science. Sir John Forbes, physician to Queen Victoria, said in 1843 that the extremely small doses of homeopathy were regularly derided as useless, an outrage to human reason. James Young Simpson said in 1853 of the highly diluted drugs: No poison, however strong or powerful, the billionth or decillionth of which would in the least degree affect a man or harm a fly. 19th century American physician and author Oliver Wendell Holmes, Sr. was also a vocal critic of homeopathy and published an essay in 1842 entitled *Homœopathy, and its kindred delusions*. The members of the French Homeopathic Society observed in 1867 that some of the leading homeopaths of Europe not only were abandoning the practice of administering infinitesimal doses but were also no longer defending it. The last school in the U.S. exclusively teaching homeopathy closed in 1920.

Revival in the late 20th century

The Food, Drug, and Cosmetic Act of 1938 (sponsored by Royal Copeland, a United States Senator from New York and homeopathic physician) recognized homeopathic remedies as drugs. By the 1950s, there were only 75 pure homeopaths practicing in the U.S. However, in the mid to late 1970s, homeopathy made a significant comeback and sales of some homeopathic companies increased tenfold. Greek homeopath George Vithoulkas performed a great deal of research to update the scenarios and refine the theories and practice of homeopathy beginning in the 1970s, and it were revived worldwide; in Brazil during the 1970s and in Germany during the 1980s. The medical profession started to integrate such ideas in the 1990s and mainstream pharmacy chains recognized the business potential of selling homeopathic remedies [38-43].

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