

## What is Homeopathy? An Introduction

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## 1. ABSTRACT

Homeopathy is based on the idea of ‘let like be cured by like’. It was founded by Samuel Hahnemann in the late 18th century, although similar concepts existed earlier. Homeopathy became popular in the 19th century in part because of its success in epidemics but declined during most of the 20th century. Its popularity increased in the late 20th and early 21st centuries in many parts of the world. Homeopathy is controversial because of its use of highly dilute medicines. There is a significant body of clinical research including randomised clinical trials and meta-analyses of such trials which suggest that homeopathy has actions which are not placebo effects. Cohort, observational and economic studies have yielded favourable results. There are several schools of homeopathy. Systems which use homeopathic medicines based on symbolism and metaphor are not homeopathy. Despite the long history of scientific controversy, homeopathy has proved resilient and is now geographically widespread. There is a significant body of scientific evidence with positive results. Homeopathy is an anomaly around which deserves further investigation.

## 2. INTRODUCTION

Homeopathy (also spelt homoeopathy; Greek homoios = same or similar, pathos = suffering) is a system of medicine based on the idea of ‘let like be cured by like’, in Latin: ‘similia similibus curentur’. It was founded by the German physician Samuel Christian Friedrich Hahnemann (1755-1843) in 1796 with his seminal ‘Essay on a new curative principle for ascertaining the curative power of drugs with a few glances at those hitherto employed’ (1). Hahnemann did not use the adjective ‘homeopathic’ until 1807, and the noun homeopathy appeared for the first time in the first edition of his magnum opus, the *Organon of Medicine*, published in 1810. The *Organon* eventually ran to 6 editions, the last of which was published nearly 80 years posthumously in 1921 (2).

Coincidentally 1796 was the same year that Edward Jenner first vaccinated against smallpox. It also coincided with the period of so-called ‘Heroic Medicine’ which advocated treatments including bleeding and purging in ‘doses: as large as the patient could tolerate and sometimes larger, resulting in the death of the patient.

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Heroic medicine originated in the work of John Brown (1735-1788), but had many influential advocates, including Benjamin Rush (1745-1813), a signatory of the American Declaration of Independence. A reaction against heroic medicine may, in part, explain the adoption by homeopaths of increasingly small doses.

Early in his career Hahnemann became so disillusioned with the practice of medicine that he abandoned it, instead earning his living as a translator. It was while translating, in 1790 'A treatise of Materia Medica', by Brown's mentor, William Cullen that he made his first, crucial observation. In a footnote he recorded his disagreement with Cullen's elaborate theoretical explanation of the effects of Peruvian Bark, the bark of *Cinchona officinalis*, also known as China, the source of quinine. This was the first effective treatment for malaria, then endemic in parts of Europe. According to Cullen, its effects were due to its 'tonic effects on the stomach'. Hahnemann expressed his disagreement in typically forthright terms, and went on to experiment on himself: 'I took for several days, as an experiment, 4 drams (about 35 grams) of good China twice a day'. He developed 'all those symptoms which for me are typical of intermittent fever' (3). This was the empirical 'Newton's Apple' of homeopathy.

The roots of homeopathy are thus empirical, and some historians of medicine (notably Harris Coulter) have analysed the history of medicine in terms of dialectic between the holistic 'Empirical' and reductionist 'Rationalist' trends of thought. Both are to be found in the Hippocratic corpus. The empirical school developed through the thought of Celsus through Paracelsus, van Helmont, Sydenham, Laennec and Hahnemann, while the Rationalist school is represented by Galen, Boerhaave, Brown, Virchow and Bernard. According to Coulter, at least in the United States, the Rationalist school is now dominant, and this has led to a crisis in medicine including its costs and the high prevalence of iatrogenic disease.

### 2.1. Homeopathy and allopathy

Hahnemann delineated two main approaches to medical treatment: the homeopathic and the allopathic or enantiopathic method (based on 'contraria contrariis': opposites oppose). It was Hahnemann who coined the words homeopathy and allopathy. The latter term is now sometimes, incorrectly, used to refer to all conventional medicine.

In the 'Essay on a new curative principle...' he describes three fundamental approaches to the treatment of disease. The first, 'to remove or destroy the fundamental cause' is 'the most elevated'. The second, in which 'symptoms were sought to be removed by medicines which produced and opposite condition', he was strongly opposed to, going on to say 'I beseech my colleagues to abandon this method (contraria contrariis) in chronic diseases' Concluding that 'nothing then remains but to test the medicines we wish to investigate on the human body itself' (4).

References to both these methods of treating disease can be found in the Hippocratic corpus, for

instance: 'Diseases are cured by opposites; for every disease there is something proper; so, for what is warm by nature, but sickened by cold, there is something to warm it up, and so on. This is another way: by similar (homoia) means a disease arises and by administering similar things health is restored from sickness; for instance the same which causes strangury that wasn't there before, when it is there, will make it stop. Likewise coughing arises, like strangury, and it stops by the same things.' (5). The ideas of homeopathy were also prefigured by the Swiss physician Theophrastus von Hohenheim (1493-1541), better known as Paracelsus, who said, for instance 'all substances are poison, there is none which is not a poison, it is the dose which distinguishes a poison from a medicine'(6).

Hahnemann was rooted in enlightenment thought, taking the 'Battle cry of the Enlightenment', *Aude Sapere* ('dare to know'), popularised by Immanuel Kant as his personal motto. He was a vitalist, as were most doctors of his time, seeing health and disease as a derangement of the life force, the *vis medicatrix naturae*. At various points in the *Organon*, he describes health in terms of a "harmonious course of life". But he also saw health as a result of struggle, describing many pathogenetic influences against which the organism has to defend itself. These include physical, climatic, and geographical to mental and emotional influences but also a recognition that living transmissible entities might be involved. At Hahnemann's time most micro-organisms were unknown, and he used terms such as contagion and miasm.

His thinking also included an autocratic vital force supplying life and order, enabling perception and self-preservation. He also saw health as providing the potential for moral and intellectual growth. He was a freemason and not religious in the conventional sense, but he saw the practice of medicine as a sacred duty. He also favoured self-care, writing many pamphlets and articles intended for the public on hygiene, dietetics, and life style etc (7).

Hahnemann's concept of 'chronic miasms' was a relatively late development to deal with chronic disease which did not respond, or responded only temporarily, to treatment. He believed that all chronic diseases originated in one (or sometimes a combination of) three chronic miasms. These miasms are living, transmissible entities, by far the most common was psora, which Hahnemann related to 'the itch'. It is not clear exactly what he meant by 'the itch', but he believed psora to underlie a very wide range of chronic disease. Many homeopathic medicines are listed as 'anti-psoric', the most important being Sulphur. The other two chronic miasms are 'sycosis' which relates to hypertrophy, skin warts and condylomas etc, the most important antisycotic medicine is Thuja, and Syphilis (although not in the sense it is currently understood). 'Syphilis' is characterised by ulceration and destructive changes, the most important anti-syphilitic medicine is Mercurius (8). Various modifications of the theory of chronic miasms have since been proposed. But it has never been accepted by all homeopaths, and is not essential to homeopathic practice.

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### 2.2. Homeopathic pathogenetic trials

But without doubt it was Hahnemann's insistence on basing medicine on empirical data, derived from human experiments that constitutes his greatest contribution, and is the keystone of his work. It follows logically from the Similia principle that, if one wants to know what a substance may cure, one must first know what it can cause. In order to understand the effects of drugs on healthy humans, Hahnemann conducted volunteer experiments, and Homeopathy is the first form of medicine that aspired to base itself purely on empirical clinical trial evidence.

As Hahnemann himself acknowledged, he was not the first to propose testing drugs on healthy volunteers – this had been proposed by the Swiss naturalist Albrecht von Haller (1708-1777) – but Hahnemann was the first to propose the systematic use of medicines on such data. But he was insistent on empirical evidence and fiercely critical of symbolic, metaphorical and metaphysical approaches such as the 'Doctrine of Signatures':

'...the mere suppositions of our superstitious forefathers, who had childishly enough asserted certain medicinal substances to be the remedies of certain diseases, merely on account of some external resemblance of those medicines with some...[signature], or whose efficacy rested only on the authority of old women's tales, or was deduced from certain properties that had no essential connexion with their fabulous medicinal powers...' (9).

'I shall spare the ordinary school the humiliation of reminding them of the folly of those ancient physicians who, determining the medicinal powers of crude drugs from their signature, that is from their colour and form...but I shall refrain from taunting the physicians of the present day with these absurdities, although traces of them are met with in the most modern treatises on materia medica.' (10).

Hahnemann himself conducted a total of 99 'pruefungen' (tests) of a wide range of substances on healthy individuals, and published these in his *Materia Medica Pura* and *Chronic Diseases*. Pruefung is traditionally translated into English as 'proving', but the more recent term homeopathic pathogenetic trial (HPT) is more apt. Significant numbers of HPTs have been published subsequently since Hahnemann's time: a systematic review of the English, German, Spanish, French, Portuguese and Dutch language literature between 1945 to 1995, found 156 HPTs on 143 medicines, involving 2815 volunteers (11).

HPTs are not the only source of prescribing information, the other main sources are toxicology and clinical experience, sometimes referred to as 'ab usu in morbis' (from use in disease). Phosphorus, for instance is an important homeopathic medicine associated with a large toxicological literature, including chronic industrial exposure. Similarly for other toxic substances used in homeopathy, for instance arsenic or *Nux vomica* (which contains strychnine). Considerable numbers of symptoms recorded in the homeopathic materia medica cannot be traced to HPTs or toxicological sources, and these originate

from clinical experience. In many cases their provenance is not clear, and this has been a cause for concern.

TF Allen's 12 volume *Encyclopedia of Pure Materia Medica* published between 1874 and 1879 collects provings of 730 substances, most of them of plant origin, but including for instance mercury and 12 of its salts, and includes two volumes of therapeutic index or repertory (12).

### 3. DEVELOPMENT OF HOMEOPATHY

Homeopathy rapidly gained popularity in Europe in the first half of the 19th century, this seems to have been due to two main factors: its success in some high profile cases and in epidemics (13). For instance the famous violinist Paganini and the great naturalist Charles Darwin, among other prominent individuals, spoke highly of homeopathy. Darwin was initially very sceptical about high dilutions, but derived great benefit from treatment by Dr James Gully, a homeopath and hydrotherapist. Subsequently Darwin conducted experiments on the effects of highly dilute Ammonium phosphate on the carnivorous plant *Drosera* (14, 15).

An important factor in the rise of homeopathy was its success in the epidemics, particularly of cholera, which swept Europe during the 19th century. Homeopaths were much more successful in saving lives than their conventional counterparts. While in some conventional hospitals up to 74% of the patients died, in homeopathic settings the figure was 4–11% (16). Homeopaths and the public usually attributed these successes to homeopathic treatment but historical analyses and modern data raise the question of whether the difference in outcomes (of which there is little doubt) was due to homeopaths curing their patients, or conventional physicians killing theirs! The mainstay of conventional treatment of Cholera at that time was bloodletting, rehydration was not used (17). A modern study of homeopathy in cholera showed no difference in death rates between homeopathy and placebo, because there were no deaths (18).

In the early 19th century homeopathy spread widely around the world: it was introduced to the USA by German immigrants, most notably Dr Constantin Hering (1800-1880), who moved to Philadelphia PA in 1833. Dr. John Martin Honigberger (1795-1869), physician to Maharaja Ranjit Singhji of the Punjab, was the first to practice homeopathy in India, in 1839. The Frenchman Benoit Mure (1809-1858) introduced homeopathy to Brazil, founding the Instituto Homeopático do Brasil in Rio de Janeiro in 1843, and later introduced it to Egypt.

The fates of homeopathy in the USA and India contrast sharply. In the USA, the Flexner Report on medical education was written by the Abraham Flexner and published in 1910. At that time "modern" medicine faced vigorous competition from osteopathy, eclectic medicine, naturopathy and homeopathy and other schools of medicine. The Flexner Report resulted in the closure of almost all the 'alternative', including homeopathic, medical

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schools (as well as the 'negro' and women's medical colleges). This was followed by a sharp decline in the number of doctors practising homeopathy (19). Some osteopathic medical schools were able to comply with Flexner's recommendations and now teach from a rationalistic, medicalised perspective.

### 3.1. Homeopathy worldwide

By contrast in India in 2009 there were 178 homeopathic medical colleges of which 35 were government institutions. There were over 200,000 registered homeopaths with approximately 12,000 graduating every year. There were over 300 homeopathic hospitals and more than 8000 homeopathic dispensaries (20). Elsewhere in the world homeopathy is widespread, for instance the European Commission estimated in 1997 that 29% of European citizens had used it. It is also widely practised in Latin America, and its use is growing in North America. It is officially recognized by the government in countries in Latin America (Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, Mexico), Asia (India, Pakistan, Sri Lanka) and Europe (Belgium, Bulgaria, Hungary, Portugal, Romania, Russia, United Kingdom). In some of these countries, homeopathy is integrated into the national healthcare systems (Brazil, India, Mexico, Pakistan, Sri Lanka and the United Kingdom) (21).

Despite the controversies which have long surrounded it, homeopathy is popular in diverse regions of the world including the Indian subcontinent, parts of Latin America, and Western Europe. In other regions it has experienced seemingly terminal declines, for instance the United States during most of the 20th century and Eastern Europe and Russia during the communist period, only to rise again at the end of the 20th century. And its use is growing in regions as different as South Africa and Japan. It is clear that what has sustained homeopathy above all is not scientific evidence, but the fact that it is, and remains, popular with patients (22).

Qualifications of practitioners vary widely: in some countries, such as India, they can have qualifications exclusively in homeopathy, or they may train in homeopathy following professional qualification as a health professional (doctor, dentist veterinarian etc) In most European and Latin American countries homeopathy can only be practised by such health professionals, but in other regions it may be practised by CAM practitioners without a full conventional medical education (e.g. Heilpraktikers in Germany; statutorily regulated CAM practitioners in Australia, Denmark, Iceland, Norway and South Africa; Naturopathic Doctors in some US states and Canadian provinces). Homeopathic practice by unregulated practitioners is permitted in a number countries (e.g. Finland, Ireland, Netherlands, Sweden, United Kingdom) (23).

Countries including Brazil, France, Germany, India and the USA have officially recognised homeopathic pharmacopoeias and European Commission has issued Directives aimed at harmonising registration procedures for homeopathic products, and quality standards for homeopathic medicinal products are increasingly

incorporated into the European Pharmacopoeia. The World Health Organisation has published guidelines on safety issues in the preparation of homeopathic medicines (24).

## 4. CONTEMPORARY HOMEOPATHIC PRACTICE

Several distinct types of homeopathy are used in practice. The main types are 'individualized' or 'classical' homeopathy, 'clinical' homeopathy, 'drainage' and the related concept of homotoxicology, and isopathy. In individualized homeopathy typically a single homeopathic medicine is selected on the basis of the total 'symptom picture' displayed by a patient, including mental, general and constitutional features. In clinical homeopathy, one or more homeopathic medicines are administered for standard clinical situations or conventional diagnoses – sometimes several homeopathic medicines are combined in a fixed ('complex') formulation. Isopathy is the use of homeopathic dilutions of allergens or causative infectious or toxic agents. Homotoxicology founded by HH Reckeweg and homeopathic drainage introduced by Antoine Nebel and Léon Vannier, are related approaches. Disease is interpreted as intoxication or auto-intoxication and an expression of the defensive effort of the organism and detoxification is achieved with homeopathic medicines.

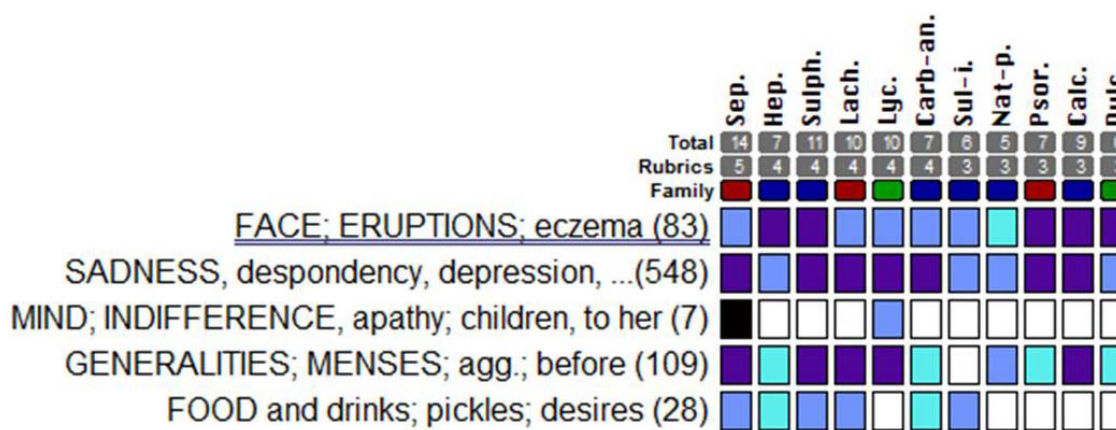
Anthroposophic medicine, an approach founded by R Steiner and I Wegmann integrating conventional medicine with the influence of soul and spirit, often uses homeopathic medicines although not usually on the basis of similarity.

### 4.1. Individualised homeopathy

Individualised homeopathy, as the name implies, involves a high degree of individualisation, such treatment is frequently 'constitutional' sometimes described as 'treating the patient, not the disease'. Most practitioners who use this form of homeopathy use a repertory, this is essentially an index of symptoms and homeopathic medicines associated with them, now usually in the form of a computer program. Individualisation implies that two patients with the same conventional diagnosis might receive entirely different treatments.

Three domains are considered: the 'locals', 'mentals' and 'generals'. It is sometimes said that reliable prescription requires a 'tripod' comprising one clear symptom from each of these domains. The 'locals' are usually the symptoms of the condition of which the patient complains, but may include other incidental or 'collateral' symptoms which the patient has, but which are not the primary motive for the consultation. 'Modalities': any factor which improves (ameliorates) or causes it to get worse (aggravates) it. 'Complete symptoms' with location (including radiation or extension), sensation (for instance character of the pain), modalities, and concomitants are considered particularly valuable. Context is also important: symptoms which are unusual in the context are considered particularly important.

However for individualised homeopathy, the local symptoms are often relatively unimportant compared



**Figure 1.** Individualised homeopathy for eczema. NK was a 42 year old woman who presented with eczema, worst on the face. She felt very depressed in the premenstrual period, and had an unusual food craving: she liked acidic tastes. Sepia 30c 2 pills twice a week was prescribed with an excellent result. Repertorisation: the depth of the colour indicates the strength of association between a symptom and homeopathic medicine. Sepia (Sep) is very strongly associated (grade 4) with the symptom MIND; indifference, apathy, children, to her, but less strongly (grade 2) with FACE: ERUPTIONS; eczema. The latter symptom is ‘underlined’, increasing its weight in the analysis.

to the other domains: mental and general. ‘Mental’ symptoms are the psychological attributes of the patient including relatively fixed or constitutional traits and variable psychological states such as mood, anxiety, irrational fears or phobias. ‘Generalities’ are the general characteristics of the patient: these again include relatively fixed physical characteristics such as physical build and habitus, and also such things as a susceptibility to cold, sleep pattern, perspiration etc.

The data gathered from the history and examination is then synthesised into a ‘picture’, with greater weight given to unusual (in the context) symptoms and strong or unusual mental or general features. The symptoms may be then be repertorised. (see Figure 1).

An individualised homeopathic prescription consists of one or at most a few medicines. Typically a ‘constitutional’ medicine, prescribed mostly on the basis of mental and general features, in a relatively high dilution (30c or higher), at relatively low frequency

**4.2. Clinical homeopathy**

The other major school of homeopathy is clinical homeopathy, also known as pluralist homeopathy. Clinical homeopathy has its origins in France (where Hahnemann lived for the last twelve years of his life), but is now widespread. The basic principles are common to all forms of homeopathy: medicines are prescribed on the basis of similarity between the symptoms they provoke when ingested either accidentally or in a homeopathic proving.

The materia medica is similar in clinical and individualised homeopathy, but clinical homeopathy places greater emphasis on pathology and the use of particular medicines in particular pathologies, and less to mental and constitutional characteristics. The dilutions prescribed are usually lower: dilutions such as 5 and 9cH are used and dilutions above 30cH rarely used.

Clinical homeopaths typically prescribe regimes involving several homeopathic medicines (hence the alternative term ‘pluralist’), prescribed for different aspects of the health problem. These are usually prescribed in a cycle with a lower dilution medicine taken daily or more frequently and other medicines taken weekly or other frequencies. Clinical homeopaths pay greater attention to the conventional medical diagnosis and relatively less to the ‘constitution’ than individualised homeopaths.

In clinical homeopathy the approach is similar to that taught in conventional medical colleges. This includes the physical signs detected by physical examination, imaging or lab tests: general signs and symptoms which stem from the general systemic response of the person: fever, loss of weight, sweating, thirst, asthenia etc; aetiologic signs as revealed by biological analysis such as infections, or abnormal biochemistry etc.

Homeopathic medicines are generally prescribed in the 5C to 30C range. Dose regime is from several times a day for acute medicines to once weekly for chronic conditions. Consultations are designed to be completed within the space of a normal clinic visit of 30-60 minutes.

**4.3. Complex homeopathy**

Complex homeopathy refers to the use of combined homeopathic medicines which incorporate several different homeopathic medicines in a single dose. These are often sold under trade names which suggest their use, often direct to the public. (see Figure 2).

**4.4. Drainage and homotoxicology**

Drainage and Homotoxicology are related concepts which originate in the first half of the 20th century, part of the distinction is linguistic: Homotoxicology was founded by the German physician Hans-Heinrich Reckeweg (1905-1985), while the concept

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Allium cepa 3c, Apis mellifica 6c, Belladonna 6c, Eupatorium perfoliatum 3c, Gelsemium sempervirens 6c, Kalium bichromicum 6c, Nux vomica 3c, Phytolacca decandra 6c, Pulsatilla 6c.

**Figure 2.** The formula of Coldcalm (Boiron) marketed for control of common cold and similar minor upper respiratory problems.

Aconitum napellus 3x, Arnica montana, radix 3x, Belladonna 4x, Bellis perennis 2x, Calendula officinalis 2x, Chamomilla 3x, Echinacea purpurea 2x, Hamamelis virginiana 2x, Hepar sulphuris calcareum 8x, Hypericum perforatum 3x, Mercurius solubilis 8x, Millefolium 3x, Symphytum officinale 8x

**Figure 3.** The formula of Traumeel tablets (Heel) an antihomotoxicological complex marketed for temporary relief of muscular and joint pain, sports injuries and bruising.

of drainage was introduced by the French-speaking Swiss doctor, Antoine Nebel (1870-1954) and the French homeopathic physician Leon Vannier (1880-1963).

Drainage is based around the concept of (auto-)intoxication, Nebel and Vannier considered toxins to be of three main categories: Exogenous including external environmental, dietary and psychological influences, endogenous mostly toxins arising from microbial infections and autogenous toxins: those generated by the subject himself and transmitted by heredity. Homotoxicology interprets disease as an expression of the defensive effort of the organism against pathogenic toxins and detoxification with homeopathic medicines. Homotoxins include physical agents such as weather, climate and radiation; chemical factors including environmental pollutants; biological factors including infectious agents, allergens and endogenous intermediate metabolites; psychosocial factors including stress and personality disorders. (see Figure 3).

### 4.5. Anthroposophical medicine

Anthroposophic medicine, an approach founded by Rudolph Steiner and Ita Wegmann integrates conventional medicine with the influence of soul and spirit. 'Formative forces' are a key concept in anthroposophy. They are classified into four types: those found in fixed, inorganic systems (crystals etc); those which evolve over time, typical of plants; those which include an element of 'inwardness', typical of animals and the fourth, typical of man which, in addition to the three previous types of formative force, includes the ability to perceive general laws and to reflect. In addition to homeopathy, anthroposophic doctors use many other substances, the best known are Mistletoe preparations for cancer.

### 4.6. Metaphorical and symbolic prescribing

More controversial in their claim to be homeopathy are certain 'new' doctrines which describe themselves as homeopathy but in which substances are prescribed, not on the basis of similarity between the symptoms they cause in healthy people and those of a patient, but through metaphor, symbolism or the Doctrine of Signatures. Prescriptions are based on metaphorical

similarity: for instance patients who require a remedy made from a mineral express themselves with words relating to structure and solidity or lack thereof, medicines made from snake venoms are associated with malice and deceit and so on.

Although they use substances prepared in the homeopathic manner, these systems lack the defining characteristic of homeopathy: similarity. Homeopathy is based on similitude between the effects a substance can cause in a healthy organism and the symptoms suffered by a sick person. The pathogenetic effects are determined by homeopathic pathogenetic trials, toxicological data and clinical experience. These systems substitute metaphor and symbolism for pathophysiological similarity.

Metaphorical thinking has a long history in medicine, it is best known in the Doctrine of Signatures, which claims that the healing properties of plants can be known from analogies between their physical characteristics and those of a disease or part of the body. The doctrine of signatures and other forms of symbolic and metaphorical thinking are not homeopathy, and were explicitly criticised by Hahnemann (9, 10). The prescribing of highly diluted substances on metaphorical or symbolic grounds is not homeopathy.

## 5. SCIENTIFIC ISSUES RAISED BY HOMEOPATHY

### 5.1. ultramolecular dilutions

Homeopathy remains one of the most controversial forms of complementary and alternative medicine. Throughout its history of over 200 years it has been the focus of debate, often heated, with strong opinions for and against expressed. As long ago as 1846 John Forbes denounced homeopathy as 'ludicrously absurd' and an 'outrage to human reason', and any effect of homeopathy therefore impossible (25). While more recently it has been claimed that "Accepting that infinite dilutions work would subvert more than conventional medicine; it wrecks a whole edifice of chemistry and physics" (26). Homeopathy has been described as 'implausible' and this has been used as a justification for scepticism concerning the claimed results of clinical trials of homeopathy (27,28).

Central to the controversy surrounding homeopathy is the lack of a 'plausible' mechanism of action for the very high dilutions often used in homeopathy. Hahnemann initially used doses similar or somewhat smaller than those used in contemporary conventional medicine, but he gradually reduced the size of his doses to include 'ultramolecular dilutions' which are the focus of most of the argument. Homeopathic medicines are now used in both low dilutions, where the original substance is materially present, and in high dilutions, in which material quantities of the starting substance are much less likely to be present.

Dilutions are prepared by a process known as potentization which involves repeated dilutions, usually in steps of 1:10 or 1:100, with succussion (vigorous shaking) between each dilution. Dilutions are denoted for instance

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5x (in the Anglo-American convention) or 5dH (European convention) for the 5th decimal (i.e. 5 times 1:10 dilutions) or 30c/cH for the 30th centesimal (1:100 dilutions). 'H' denotes the Hahnemannian method, in which clean glassware (test tube and pipettes) is used for each step of dilution (29). This remains the most widely used dilution scale, but other dilutional scales are also used.

The value of Avogadro's constant, the number of particles (atoms or molecules) in a mole of a pure substance, is  $6.022 \times 10^{23}$ . Thus dilutions above 23x/dH or 12c/cH (corresponding to dilutions of  $10^{-23}$  and  $10^{-24}$  respectively) are very unlikely to contain a molecule of the starting substance. Homeopathic medicines in which a molecule of the starting substance is unlikely to be present are referred to as 'ultramolecular' or ultra low dilutions (ULD), or BRAN (Beyond the Reciprocal of Avogadro's Number).

Classical pharmacological actions ('classical pharmacological action' is defined as interaction between pharmacologically active molecules and receptors) have been reported with dilutions as high as  $10^{-22}$  mol/L and frequently with dilutions of  $10^{-17}$  –  $10^{-18}$  (30). By definition dilutions beyond the 'molecular threshold' cannot have classical pharmacological actions. Many homeopathic medicines are of biological origin, and consist of complex mixtures of molecules often of unknown molecular weight and concentration.

It is important to remember that the first principle of homeopathy is that of similarity, and in this area there is substantial overlap with other areas of science including hormesis (the stimulatory or beneficial effects of small doses of toxins) rebound effects, dose-dependent reverse effects and paradoxical pharmacology (31, 32, 33, 34, 35, 36, 37).

The recent concept of 'postconditioning hormesis' refers to a small stimulus exerting a beneficial effect after a biological system has experienced a harmful stress of similar nature (38). These phenomena have in common that they are secondary, reverse or paradoxical effects of drugs and toxins in living organisms as a function of dose or time.

The scientific issues raised by homeopathy can be classified as follows:

1. Do homeopathic medicines have effects that are not placebo effects?
2. Does homeopathy provide benefit in terms of effectiveness and cost-effectiveness?
3. Is homeopathy safe?
4. Can substances diluted beyond the Avogadro limit have effects in living systems?
5. How are such effects mediated?
6. Do substances cure diseases or syndromes similar to those that they cause?

Questions 4-6 are addressed by other papers in this issue, I discuss questions 1-3 below.

## 5.2. Do homeopathic medicines have clinical effects which are not placebo?

Systematic reviews and meta-analyses of randomized controlled trials (RCTs) sometimes known as 'Type 1' evidence are considered the strongest form of clinical evidence. A number of systematic reviews and meta-analyses of homeopathy as a whole and for specific conditions or of particular homeopathic medicines have been published.

### 5.2.1. Systematic reviews of homeopathy as a whole

Most comprehensive systematic reviews and meta-analyses conclude that homeopathy differs from placebo. A meta-analysis published in *The Lancet* in 1997 included 186 placebo-controlled studies of homeopathy, from which data for analysis could be extracted from 89. The overall mean odds ratio for these 89 clinical trials was 2.45 (95% confidence interval, 2.05–2.93) in favour of homeopathy. The main conclusion was that the results "were not compatible with the hypothesis that the effects of homeopathy are completely due to placebo" (39).

Another such publication identified 184 clinical trials and meta-analysed the placebo-controlled RCTs, in the 17 which had a predefined primary outcome measure. These included 2001 patients. It concluded that there was strong evidence that homeopathy was more effective than placebo, but concluded that "the strength of this evidence is low because of the low methodological quality of the trials" (40).

In 2005, Shang et al. published a controversial meta-analysis comparing 110 placebo-controlled trials of homeopathy and 110 trials of conventional medicine. Homeopathy and conventional medicine showed a similar positive treatment effect overall. The results of 14 larger higher quality trials (8 homeopathy, 6 conventional medicine) were analysed. The authors' conclusion was that there was "weak evidence for a specific effect of homeopathic remedies, but strong evidence for specific effects of conventional interventions. This finding is compatible with the notion that the clinical effects of homeopathy are placebo effects."

This meta-analysis was criticised for its opacity, including the failure to cite the papers on which its conclusions were based, absence of sensitivity analysis, and failure to adhere to the QUOROM guidelines for reporting of systematic reviews (41, 42). Subsequently a reconstruction has found that it was heavily skewed by a single trial on muscle soreness in long-distance runners, that its results were very sensitive to the definition of 'larger' sample sizes, and there was great heterogeneity between the trials, concluding that the results were less definite than purported (43, 44).

### 5.2.2. Systematic reviews of randomized clinical trials for particular conditions

The following systematic reviews focused on particular clinical situations or homeopathic medicines have been published. Twelve of these 26 reviews included positive conclusions for homeopathy:

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- \* Adverse effects of cancer treatments (45).
- \* Allergies and upper respiratory tract infections including otitis media (46, 47).
- \* Childhood diarrhoea (48).
- \* Fibromyalgia (49).
- \* Influenza (50).
- \* Post-operative ileus (51).
- \* Rheumatic diseases (52).
- \* Seasonal allergic rhinitis (hay fever) (53, 54, 55).
- \* Vertigo (56).

Eight reviews were inconclusive (generally due to lack of high-quality evidence):

- \* Anxiety (57).
- \* Chronic asthma (58).
- \* Dementia (59).
- \* Depression (60).
- \* Headache and migraine treatment (61).
- \* HIV/AIDS (62).
- \* Induction of labour (63).
- \* Osteoarthritis (64).

The other 6 reviews have concluded there was little or no evidence for homeopathy:

- \* Ailments of childhood and adolescence (65).
- \* Attention deficit hyperactivity disorder (66).
- \* Cancer (67).
- \* Delayed-onset muscle soreness (68).
- \* Headache and migraine prevention (69).
- \* Insomnia (70).

### 5.2.3. Randomized controlled clinical trials (RCTs)

A review of RCTs in homeopathy published between 1975 to 2002 found 93 studies comparing homeopathy with placebo or other treatment (71). Positive effects of homeopathy were found in 50. The evidence favoured a positive treatment effect of homeopathy in: allergic rhinitis, childhood diarrhoea, fibromyalgia, influenza, pain, side effects of radio-/chemotherapy, sprains, and upper respiratory tract infection. Reviewing 12 systematic reviews of homeopathy for specific medical conditions, Jonas et al. reached similar conclusions: homeopathy may be effective for allergies, childhood diarrhoea, influenza and postoperative ileus, but not for treatment of migraine, delayed-onset muscle soreness or prevention of influenza (72).

Single RCTs of homeopathy have been conducted in clinical areas including asthma, life-threatening sepsis, and stomatitis induced by cancer chemotherapy, chronic fatigue syndrome, premenstrual syndrome, post-partum bleeding, and Arnica for various clinical conditions (73-80).

In some clinical situations, both RCTs and clinical observational studies have been conducted, providing a fuller picture of the possible role of homeopathy. Such areas include upper respiratory tract and ear infections in children, attention deficit hyperactivity

disorder (ADHD), and homeopathy for symptoms related to cancer treatment (81-88).

Reilly's group has published an impressive series of trials of isopathy for respiratory allergies including hayfever, perennial rhinitis and allergy, including a meta-analysis (46, 89, 90, 91) To date there has been no independent positive replication of these findings. However other studies of isopathy of different design have not yielded positive results (92, 93).

Another model with independent replication is Arnica 30x to prevent delayed-onset muscle-soreness. The results of two studies in the Oslo marathon have been pooled, and a small but significant effect on muscle soreness, but none on muscle enzymes, was shown (94) However, a larger scale study replication was negative (95). But the results of three linked studies of Arnica 30x in different types of knee surgery have yielded a positive result (96).

In another area the apparently contradictory results of replications may be explicable by methodological differences. Two placebo-controlled RCTs of homeopathy for Attention Disorder Hyperactivity Disorder were published at about the same time and were superficially similar. However, closer scrutiny reveals important differences in prescribing between the two studies: only one of the five most frequently prescribed homeopathic medicines was the same in the two studies (97,85) One of these studies was in fact a study of treatment withdrawal (85). The optimum treatment was determined, then after improvement had occurred, randomly and blindly replaced with placebo, then resumed. The patients deteriorated when on placebo. It took a mean of three attempts to find the effective homeopathic medicine. If this study had randomized the patients at the first homeopathic prescription, its results too would have been negative (98).

### 5.3. Economic evaluation

Cost effectiveness studies suggest that integration of homeopathy is associated with better outcomes for equivalent costs. These studies were of 'quasi-experimental' design (i.e. different treatments were compared, but patients were not randomly assigned to the different treatments).

Trichard et al. compared two treatment approaches ('homeopathic' vs. 'antibiotic' strategy) used by French GPs with and without in the management of recurrent acute rhino-pharyngitis in children (99,100). The GPs who integrated homeopathy in their practice had significantly better results for similar cost. A study based in a public sector clinic in Italy and using data from the official Prescription Archive documented a large reduction in drug costs for patients receiving homeopathic treatment compared to patients who did not (101).

Witt and colleagues compared homeopathic and conventional GPs' outcomes in 493 patients with chronic diagnoses commonly treated in general practice (102, 103). The conclusion was that, after correction for differences



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between groups, patients who sought homeopathic treatment had better outcomes for similar cost. The same group conducted cohort study comparing homeopathic and conventional treatment of eczema in children. The two groups had similar improvements in perception of eczema symptoms (assessed by patients or parents) and disease-related quality of life (104).

### 5.4. Observational studies

The clinical areas in which RCTs of homeopathy have been conducted do not match well with those for which it is used in practice. Reasons for this include model simplicity (for instance isopathic treatment of allergies has been investigated because it is a simple model), expediency and commercial motives. In practice homeopathy is frequently used for clinical problems, for instance dermatological or gastrointestinal conditions where there is little or no RCT evidence. But observational studies look at what happens to patients who receive homeopathic treatment. A comprehensive observational study at the Bristol Homeopathic Hospital included over 6,500 consecutive patients with over 23,000 attendances in a 6-year period (105) 70% of patients reported improved health, 50% major improvement. The best treatment responses were reported in childhood eczema or asthma, and in inflammatory bowel disease. A study at a public sector clinic in Italy yielded similar results (106).

In a prospective, multi-centre cohort study in Germany and Switzerland, 73% of 3,709 patients had 8-year follow-up data. The most frequent diagnoses were allergic rhinitis and headache in adults, and atopic dermatitis and recurrent infections in children. Disease severity decreased and quality of life improved significantly ( $p < 0.001$ ) between baseline, 2 years and 8 years (107).

A 500-patient survey at the Royal London Homoeopathic Hospital showed that many patients were able to reduce or stop conventional medication following homeopathic treatment. The size of the effect varied between diagnoses: for skin complaints, for example, 72% of patients reported being able to stop or reduce their conventional medication; there was no reduction for cancer patients. Safety considerations were an important motive for patients to seek homeopathic treatment (108). In these surveys, many of the patients were suffering from difficult-to-treat 'effectiveness gap' conditions (109).

These studies were uncontrolled, so the extent to which the effects are due to differential dropout, spontaneous improvement, regression to the mean, life-style changes, placebo or context effects etc is unknown.

### 5.5. Safety

The available evidence suggests that patients' confidence in the safety of homeopathy is justified: the hazards from homeopathic products are modest in comparison with those of conventional medicine (110). A systematic review of the safety of homeopathy, including a search of the English-language literature between 1970 and 1995, came to the following conclusions: homeopathic

medicines may provoke adverse effects, but these are generally mild and transient; adverse effects of homeopathy are under-reported; there are cases of 'mistaken identity' where herbal medicines were described as homeopathic (111). The main risks associated with homeopathy are indirect, relating to the prescriber rather than the medicine (112). In two studies, adverse reactions were observed in approximately 2.7% of the patients; in a third study, 7.8% of homeopathy patients had adverse reactions, compared to 22.3% in the corresponding group receiving conventional treatment (113, 114, 115).

Homeopathic 'aggravation' (or healing reaction): temporary deterioration on starting homeopathic treatment associated with a good long term prognosis is widely described in the homeopathic literature (116,117). A systematic review of double blind randomized trials of homeopathy found no clear evidence of their occurrence but case series have reported rates of aggravation ranging from 2.68% to 24% (114, 118, 119).

## 6. CONCLUSIONS

Homeopathy is a system of medicine based on the idea of 'let like be cured by like'. Its main principle is that of similitude, but the controversial aspect of homeopathy is its use of high 'ultramolecular' dilutions. Other important concepts include holism and idiosyncrasy. The founder of homeopathy, Samuel Hahnemann was insistent that the similarity should be established on the basis of pharmacology or toxicology or human volunteer experiments known as provings or homeopathic pathogenetic trials.

Homeopathy spread widely in the 19th century as a result of its success in epidemic diseases and the endorsements of prominent individuals, in many parts of the world, and particularly the United States it experienced a sharp decline for most of the 20th century but its use has increased worldwide since the late 20th century. It is regulated and recognised in a number of countries worldwide.

Homeopathy is highly controversial because of its use of 'ultramolecular' medicines, diluted beyond Avogadro's number and for this reasons has been criticised and sometimes been the object of polemics. Yet there is a body of clinical evidence which although not conclusive suggests that homeopathy does indeed have 'real' (ie not placebo) clinical effects. There is a large 'credibility gap' surrounding homeopathy due to its use of very dilute medicines. However a number of animal and in-vitro studies now seem to support the concept that such dilutions might have physiological effects. There is some modern empirical and theoretical physical and physico-chemical work which suggests a basis for such actions.

Despite the long history of scientific controversy surrounding homeopathy and despite periods of apparently terminal decline, homeopathy has proved resilient and is now geographically widespread. There is a significant and growing body of scientific endeavour around homeopathy

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which has generated some challenging results. It is, at least a scientific anomaly around which there is no consensus and therefore deserving of further investigation.

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