

Lecture Series

Immunology and Homeopathy. 1. Historical Background

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Homeopathy was born as an experimental discipline, as can be seen from the enormous amount of homeopathic data collected over more than two centuries. However, the medical tradition of homeopathy has been separated from that of conventional science for a long time. Conventional scientific wisdom dictates that homeopathy should have no effect above placebo but experiments on ultra-high dilutions of solutes together with some clinical data suggest the intriguing possibility that it might do in some circumstances. Today, an osmotic process between disciplines, previously seen as in conflict, is facilitated because over the last few decades homeopathy has initiated the methods of current medical science and a substantial number of experimental studies—at molecular, cellular and clinical levels—are available. One area of dialogue and of common progress is that of inflammation and immunity, probably because these are closely related to the traditional 'vital force' of the body's self-healing power. In a series of papers we review the historical origins of homeopathy, the laboratory and animal models related to the field of immunopharmacology, the clinical evidence in favor and against the use of homeopathy in the inflammatory diseases and the hypotheses regarding its action mechanism(s). Finally, we will enlighten the specific characteristics of the homeopathic approach, which places great emphasis on identifying a cure for the whole organism.

Keywords: Hahnemann – Hippocrates – history of medicine – homeopathy – immunotherapy – isotherapy – nosodes – Paracelsus – similia principle

The majority of substances have more than one action; the first is a direct action, which gradually changes into the second, which I call its indirect secondary action. The second is generally the opposite of the first C.F.S. Hahnemann, 1796

Introduction

The main principle of homeopathy, a unique scientific system of medicine established by Samuel Hahnemann two centuries ago, is that of 'similia' or 'simile' (similarity), which means 'let likes be cured by likes'. In other words, when a substance is capable of inducing a series of symptoms in a healthy living

system, low doses of the same substance can cure these symptoms under certain circumstances ('similia similibus curentur'). About 200 years have passed since the original interpretation of the principle of similarity. During this period, medicine evolved as never before and homeopathic theories and pharmacopoeias have also been scientifically investigated, albeit slowly with considerable delay in comparison with those of conventional medicine. However, the fundamental nucleus of homeopathy has been little discussed. Similarity is frequently considered unscientific because the statements of Hahnemann or other homeopaths are not supported by documentary proof. The various principles of similarity, Hahnemann as a scientist, Hahnemann's homeopathy, various 'homeopathic' innovations such as electro-homeopathy and various types of alternative therapy including herbal medicine have been indescribably confused, and this has led to conclusions being drawn on the basis of summary subjective judgments. Unless these sources of confusion are constantly and

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Figure 1. Jenner vaccinating a child with cow smallpox.



Figure 2. C.F.S. Hahnemann (1775–1843).

completely acknowledged and corrected, little progress can be made in clarifying the concepts of homeopathy or the principle of similarity.

Immunology is the study of the structure and function of the immune system, the complex and integrated group of organs, tissues, cells and cell products such as antibodies that, by differentiating self from non-self, defend the body against infection or disease and neutralize potentially pathogenic cells or substances. This branch of biomedicine initially found resistance in differentiating from more traditional medical disciplines such as pathology and physiology, recent decades have witnessed an extraordinary development.

Western immunology and homeopathy both began at the end of the eighteenth century: the first of Jenner's smallpox vaccinations (Fig. 1) were given at the same time that the German physician Samuel Hahnemann (Fig. 2) was conducting his first homeopathic 'provings'. The first organic enunciation of the fundamentals of homeopathy was made by Hahnemann in 1796: 'One imitates nature, which sometimes cures chronic diseases by adding another disease, and then uses in the (preferably chronic) disease a drug that is capable of exciting another artificial disease as similar as possible to the natural disease to be cured: *similia similibus*' (1, cited in ref. 2, p. 52).

The profound analogies between homeopathic thought and immunology are due to the fact that the whole of homeopathic theory is substantially based on the principle of regulating endogenous systems of healing, the best known of which is certainly the immune system and its neuroendocrine integrations. A significant example of a pioneer of immunology with an open mind towards the new homeopathic theories was Emil Von Behring (Fig. 3), who wrote:

The mechanisms of action of my anti-toxin therapy are still unclear, although many authors say that the



Figure 3. E.A. Von Behring (1854–1917).

diphtheria and tetanus anti-toxins can be clearly understood on the basis of Ehrlich's lateral chain theory. (...) Despite all of the scientific speculations and experiments of anti-smallpox vaccinations, Jenner's discovery remained a relatively isolated episode in medicine until Pasteur connected its origin with a principle that cannot be better characterized than by Hahnemann's word: homeopathic. What else causes epidemiological immunity in a sheep vaccinated against anthrax, if not the influence previously exercised by a micro-organism having similar characteristics to those of fatal anthrax? And what

technical term appropriately defines this influence exercised by a similar micro-organism if not the word of Hahnemann: homeopathy? [Behring, *Beitrag zur Experimentellen Therapie*, H. 2, 26, 1906, cited in (2), p. 125]

In 1912 he wrote ‘Hahnemann principle, according to our present way of thinking, was not bad at all’ and ‘The concept that the sick person reacts differently to medications than the healthy one, which had to be established empirically by therapeutic trials, also played a role in Hahnemann’s thinking’ (3). Hahnemann’s principles of homeopathy were not totally new as traces of them can be found throughout the history of medicine.

The ‘Magical’ Simile

The principles underlying homeopathy can be traced to roots dating back even further than those of immunology (2,4,5). Mankind has always wondered how to identify remedies capable of curing diseases. In the pre-scientific era, empiricism based on chance observations, and trial and error, was probably the most widely used approach, accompanied by various forms of oral or written tradition. In many other cases, the sick relied (and still do among some primitive people) on the intuition of individuals judged to be particularly endowed with divine or natural powers: healers, shamans, witch-doctors and so on. However, there was also another line of thought that, often in a marginal manner, has accompanied various medical cultures in different epochs: the identification of particular ‘resemblances’ between remedies and the diseases they were thought to be able to cure. The first examples of treating ‘like with like’ can be found in the papyrus of Ebers (1500 BC): ear diseases treated with ear extracts, headache with fish heads, blindness with the eyes of a pig.

Attempting to treat a disease by administering the agent capable of causing it or transmitting it is one of the most general acquisitions of empirical medicine. Numerous primitive medicines used to cure the effects of snake venoms by repeatedly inoculating them or materials extracted from the venom apparatus of snakes. In the Far East the Chinese practiced a form of preventive smallpox vaccination both by wearing the clothes worn by a smallpox victim in the full suppuration phase of the disease and by inhaling dried smallpox pustules after storing them for 1 year. Pliny claimed that the saliva of a rabid dog can afford protection against rabies. Dioskurides of Anazarbo recommended that hydrophobia sufferers eat the liver of the dog that bit them. Aetius of Antioch recommended eating the meat of the viper that had just bitten you. In the seventeenth century the Irishman Robert Fludd cured the victims of consumption with dilutions of their own sputum after suitable preparation.

Equally primitive and often elaborate applications of the same principle could be found in many pharmacopoeias until the last century. The reasoning is sometimes elementary: swallow human stones in cases of calculosis but,

also here, the connection is obscure in the light of current knowledge. It is well known that King Mithridates VI (132–163 BC) is said to have taken small quantities of poisons and toxins to protect himself against the repeated attempts made to poison him. Native Americans wear a headdress of eagle feathers partly to underline their prowess as hunters and partly for decorative purposes, but the custom is also based on a belief that the sight, speed, courage and other desirable characteristics of the eagle can be magically acquired. The magical transfer of the courage of a killed enemy to the victor by means of the ingestion of organs (the heart) also explains some aspects of cannibalism.

The ‘Simile’ of Hippocrates

By means of highly acute observations made without sophisticated instruments but still valid today, the school of Hippocrates understood that many of the phenomena of a disease are attempts at cure and suggested imitating them: this is the Hippocratic ‘simile’ (Fig. 4). The most frequently cited assertions are:

The pains (complaints) will be removed by means of their opposite, each according to its own characteristics. Thus, heat corresponds to a hot constitution that has been made ill by the cold, and so on for the others. Another way of removing pain is the following: a disease develops by means of its like and is cured by means of the use of its like. Thus, what causes urinary tenesmus in health cures it in disease. Cough is caused and cured by means of the same agent, as in the case of urinary tenesmus. Another method: the fever causing the development of inflammation will be caused and cured by the same agent. At other

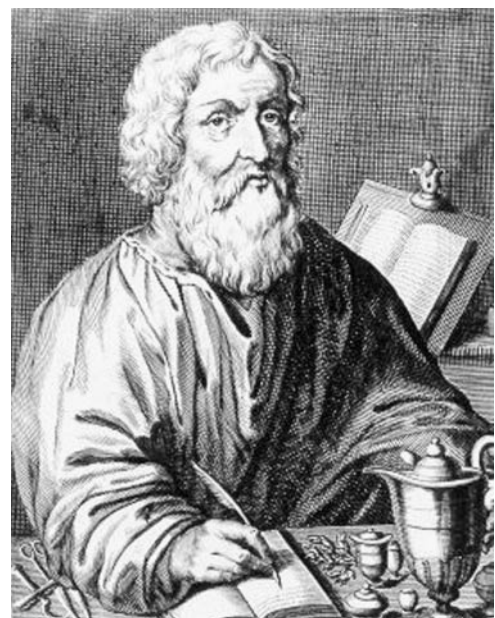


Figure 4. Hippocrates (470–367 BC).

times, it will be cured by the opposite of its cause.
 [Littre's *Oeuvres Completes d'Hippocrates*, VI, 334,
 Paris, 1839, cited in (2), p. 9]

It is particularly worth mentioning that Hippocrates did not adopt a dogmatic or ideological position, but saw both approaches ('similarity' and 'opposition') as potentially useful. Prognostic interest, a great capacity for controlled observation, the rejection of fanciful tendencies and other characteristics unmistakably distinguish this from magic.

Without going into the whole of Hippocratic medicine, it must be said that his doctrine is permeated by the concept of natural healing. Nature ('physis') is the healer of disease. 'Physis' is an expression of life, not a special energy; it is unconscious or similar to instinct; it prevails over physiological and mechanical processes; it combats disease; it is frequently incomplete and must be assisted by a doctor. It is likely that no thought has had a more profound effect on medicine than Hippocrates' observation that the manifestations of disease consist of two groups of events: the first being the direct effects of the damage, the second the reaction of repair. The corollary to this is that the direct effects must be removed whenever possible, but the reparative reaction must be promoted in order to imitate nature. Hippocrates considered many pathophysiological phenomena as being fundamentally 'defensive': fever, skin eruptions and others. In line with this pathophysiological conception, physicians must make a distinction between useful and harmful symptoms by stimulating the former and blocking the latter. Using typical Greek conciseness, Hippocrates formulated what can legitimately be considered one of the fundamental rules of therapy: nature is the primary physician and the first duty of medicine is 'to do no harm'.

The 'Simile' of Paracelsus

One further representative of this line of thought was P.T. von Hohenheim, also known as Paracelsus (Fig. 5). His works, which were first published in Basel in an almost complete version of 11 volumes between 1589 and 1591, contain a mixture of genial intuitions and ingenuities; profound clinical observations and strange affirmations concerning the influence of celestial bodies; new pharmacological observations and convinced assertions as to the truth of alchemical and magical concepts (6). Among other things, Paracelsus proposed the 'doctrine of signatures' ('signa naturae') according to which the therapeutic properties of different remedies were 'similar' to—and could be deduced from—the external appearance of plants and minerals: red remedies for blood diseases, sharply pointed leaves for the pain caused by stab wounds, iris-colored *Eufrasia* for eye diseases, topaz against jaundice (because both are yellow) and so on. In this way, 'magical similarity' was re-exhumed in an empirical and intuitive manner without any scientific understanding or experimental proof.

However, not all of the work of Paracelsus was 'magical': he had many important intuitions and made a number of empirical



Figure 5. P.T. von Hohenheim (Paracelsus) (1494–1541).

observations that were to form the basis for a large number of medical applications in subsequent centuries. For a long time, the following citation was considered one of the most significant anticipations of the 'simile' as seen by homeopathy: 'What causes jaundice also cures jaundice. That is, the good and the bad lie in the same thing: the bad causes jaundice but, if you separate the good, it becomes an efficacious remedy against jaundice. . . Since the drugs that cure paralysis must come from the substances that cause it. . . This is the way to understand the curative powers of minerals. . . What may be harmful in our hands can be transformed into a medicine' [Paracelsus, *Miners Diseases*, IX, 481, cited in (2), p. 13]. There is also a certain harmony with the concepts concerning drug doses that were subsequently adopted by homeopaths, since according to Paracelsus medicines must be administered not on the basis of their weight, but according to criteria that go beyond simple weight.

In the post-Paracelsian period, the 'simile' was often mentioned, but usually in reference to magical practices. Typical authors are Porta, who attempted to apply the doctrine of signatures to the whole botanic world (examples include the use of hairy plants for scalps, beautiful plants to improve personal appearance, 'happy' plants, 'sad' plants, etc.), and Schroder who presented related ideas, such as the fact that the leaves of *Hepatica triloba* resemble the liver [citations in ref. (2), p. 16]. One true predecessor of Hahnemann was Stoerck (7) (1731–1803), who in the 1760s published a series of works on the treatment of diseases with poisons according to the principle of similars. This author made a highly significant statement: 'If stramonium causes illness in someone who is sound in mind by inducing mental confusion, why should we not try to establish whether it can give mental health to someone who is confused or whose senses are altered by disease? If it cures someone affected by spasms, why should we not investigate whether it causes the spasms?' [cited in ref. (2), p. 19].

Hahnemann

Christian Frederick Samuel Hahnemann was born on April 10, 1755 in Meissen, Germany, graduated in Medicine from Erlangen University in 1779, and died in Paris in 1843 after a long and adventurous life. Although he worked in many fields of chemistry, pharmacology and medicine, he has passed into history as the founder of homeopathy, of which he is still unanimously acknowledged as being the greatest authority.

The first reflection of Hahnemann concentrated on the fact that two diseases may interact in very particular ways in the same individual, with one temporarily or permanently taking the place of another. One example is the well-known alternation of eczema and asthma as chronic expressions of an allergic constitution. Hahnemann studied the less known lasting replacement of one disease by another and, for example, observed that a chronic skin rash disappeared after the onset of measles. He wondered what it was that led to this difference between temporary and permanent replacement, and became convinced that the latter occurred when the two diseases had similar symptoms.

His next step was to try to apply this finding in a systematic and therapeutic manner. As he was also an expert in chemistry, he was familiar with many of the symptoms caused by toxic agents and aware of the fact that a number of naturally occurring diseases closely resemble symptoms owing to intoxication: e.g. the intoxication induced by *Belladonna* resembles scarlet fever; that induced by quinine resembles malaria; and that induced by arsenic resembles cholera. It did not take him long to combine the idea of the replacement of similar diseases with that of the replacement induced by 'artificial' intoxication: for example, he tried to use low doses of *Belladonna* to treat patients with scarlet fever and of arsenic to treat cholera. He intuitively understood that it was possible to discover specific remedies for a number of diseases, and therefore sought other potentially advantageous drugs and tested their 'pathogenic' power in healthy volunteers. After a long series of experiments on himself, his family and the medical students who followed his ideas, Hahnemann arrived at the first generalization of his thought in 1796 and then its overall description in the treatises called 'Organon', 'Chronic Diseases' and 'Materia Medica', which were published in various editions during the first decades of the nineteenth century.

Little by little, Hahnemann refined his homeopathic ideas. For example, he discovered that diseases other than cholera could be cured by small doses of arsenic provided that they had other common 'characteristics of arsenic'. However, not all cholera patients responded to arsenic, but required another remedy depending on their individual symptoms. He thus changed the current nosological schema of medical thought by introducing the concepts of drug-specific pathogenesis and disease-specific individual status. He then noted that patients apparently cured by means of homeopathy could suffer a recurrence of the same disease or be affected by another, and drew the conclusion that permanent cure could only be achieved by selecting the remedy on the basis of other

criteria, including the patient's constitutional and psychological characteristics, as well as previous diseases.

Hahnemann interpreted his 'simile-based' therapy as the result of a reactive process that we would now call homeostatic or, better, homeodynamic: 'If, in the case of a chronic disease, you give a medicine whose primary direct action corresponds to the disease itself, its secondary indirect action exactly represents the state of the body it is desired to obtain...' (1). The fundamental points of Hahnemann's 'simile' can be summarized in Table 1. In other words, according to Hahnemann the 'vital energy' alone is not sufficient to combat the disease. By giving a remedy that resembles the disease, this instinctive natural force (in analogy to the hippocratic 'physis') is driven to increase its energy to a point at which it becomes stronger than the disease itself, which finally disappears.

Hahnemann also claimed that diluting the remedies in a particular manner ('potentiation' obtained by the extensive succussion of serial dilutions) not only reduced or abolished their toxic effects, but also paradoxically increased their curative power, which is still one of the most controversial aspects of homeopathy. Another highly criticized aspect is the theory of the 'psora' and the 'miasmas', by means of which Hahnemann tried to describe the diseases of his time.

However, it is necessary to point out that Hahnemann never claimed that homeopathy was the only guide to therapy, but often said that the primary method of treatment ('the highest to be pursued') is to remove the fundamental cause of the disease. He called this the 'real way' or 'causal therapy' and, rather than contesting its value, doubted the possibility of applying it. It must be remembered that he lived between the end of the eighteenth and the beginning of the nineteenth century.

The application of Hahnemann's theory of 'simile' not only requires a scrupulous study of 'Materia Medica' (a compendium of the symptoms caused by the various substances in normal human beings), but also of the symptoms and pathophysiological characteristics of each individual patient:

We must, on the one hand, first precisely understand the essential characteristics and incidental manifestations of the diseases of the human body and, on the other, the effects purely due to the use of drugs: that is, their essential characteristics and the incidental symptoms of the specific artificial diseases they induce (as a result of differences in dose, form, etc.). In this way, by choosing a remedy capable of causing an artificial disease that is very similar to a given natural disease, we will be able to cure the most obstinate of diseases (1).

As we have already mentioned and as is only logical, further discoveries and applications have gradually added themselves to the initial concepts and groundrules. Among these, particularly worthy of note are 'isopathy' and the introduction of the use of the so-called 'nosodes'.

Table 1. Essential principles of classical homeopathy

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- Potentially therapeutic substances must be tested carefully in healthy subjects in order to document their 'pure', direct effects: this is the basis of the medical matter
 - The remedy capable of causing a similar state in a healthy subject causes a counter-reaction in a patient that is stronger than the pathological stimulus of the disease itself
 - The disease must be studied as a whole (and not only in terms of its main symptom or pathology) in order to ensure that it and the drug interact in a global manner; the choice of the remedy must be based on the complex of individual symptoms rather than on the name of the disease
 - The dose must be the minimal effective dose and therefore adjusted on the basis of individual sensitivity
 - Homeopathy empirically maintains that the dose should be higher in the case of acute diseases affecting specific organs, whereas chronic diseases that are more sensitive to pharmacological stimulation should be treated with high dilutions ('potencies') separated by much longer intervals
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Isotherapy and Nosodes

One of the earliest and most notable innovations of homeopathy, mentioned even in the later editions of the *Organon*, is isopathy or isotherapy. The term was probably coined by the veterinarian Wilhelm Lux (8) somewhere around 1831–33: after starting to treat his animals with the homeopathic method, he became convinced that every contagious disease bears within itself the means whereby it can be cured. He observed that the technique of dilution and dynamization of a contagious product (bacterium, virus or infected secretions, and organic material) would put such a product in a position to exert a therapeutic action on the disease resulting from the contagion. The law of similars 'Similia similibus curentur' thus becomes 'Aequalia aequalibus curentur' or the law of sameness.

Three authors dominate the history of isopathy (2), and all three were homeopaths: Constantine Hering, Wilhelm Lux and Denys Collet. Constantine Hering (Fig. 6) was born in Saxony in 1800 and became an assistant to the surgeon Robbi, who entrusted him with the task of writing a book for him confuting homeopathy once and for all, as had already been requested by the publisher Baumgartner. After taking a closer look at Hahnemann's works, Hering was not only intrigued, but ended up by defending Hahnemann and coming out in favor of the new method. Hering contributed a great deal to homeopathy, but above all it is to him that we owe some drug provings and the preparation of homeopathic remedies from pathological excretions and secretions, which he terms 'nosodes'. Originally this term denoted any remedy extracted from pathological excretions or secretions obtained from human subjects or animals. Animal poisons were included in this definition, so much so indeed that Hering was the first to 'prove' 'Lachesis' (venom of the bushmaster snake, the first nosode in history, later to become a homeopathic remedy to all intents and purposes) and the rabies 'poison'. Convinced that every disease contains within it its own remedy and prophylaxis, he extended his studies to the scabies 'virus', extracting the alleged 'virus' from blisters from a subject with well developed scabies.

**Figure 6.** C. Hering (1800–80).

Hering also maintained that products of the human body and the various parts of the body in the healthy state all have a preferential action on the corresponding diseased parts, and as early as 1834 he advised the use of diluted and dynamized homologous organs ('iso-organotherapy') (9). Finally, he assumed that the chemical elements exerted a particular action on those organs in which they were mainly contained. His studies and papers on minerals and salts preceded the work of Schüssler on biochemical salts.

The second great isopath was the veterinarian Joseph Wilhelm Lux, born in Silesia in 1776. Lux was appointed Professor of Veterinary Science at the University of Leipzig in 1806, and his work constituted a landmark in the history of veterinary medicine. From 1820 onwards he was familiar with Hahnemann's works and applied the new method in veterinary medicine, becoming a staunch advocate of veterinary homeopathy. In 1831 Valentin Zibrik asked him for a homeopathic remedy for distemper and anthrax. As he knew of no homeopathic remedies for these epidemics at the time, his advice was to replace the homeopathic 'similar' (i.e. the drug prescribed on the basis of the symptoms) with a 30c dilution of a drop of nasal mucus from an animal with distemper and a 30c dilution of a drop of blood of an animal with anthrax, and get all the animals suffering from distemper and anthrax, respectively, to take them. He was thus the first to create the strain called *Anthracinum*. In 1833 Lux (8) published the results obtained in a booklet entitled *Isopathik der Contagionen*, in which he claimed that all contagious diseases bear within their pathological phenomena and products their own means of cure. Moreover, Lux also extended the principle to substances that had become iatrogenic as a result of abuse, so that a method which was originally used only in contagious diseases was also applied to non-contagious illnesses. Isopathy

provoked endless arguments in the homeopathic circles: other nineteenth century relevant physicians who employed isopathy were Stapf, Rademacher (founder of 'organotherapy'), Brown-Séguard, Arnold, Veith, while Griesselich, Berridge and others disapproved this method because the isopathic substances were rarely subjected to proving and were not prescribed on the basis of symptom similarity as in the original Hahnemann's method (9,10).

After this early period of expansion, the new method ran into continuous and increasingly severe criticism, so much so that isopathy went into decline for several years, even within the homeopathic community. Only a few solitary practitioners went on using isopathic remedies. It was Father Denys Collet, a doctor and Dominican friar born in 1824, who eventually brought isopathy back onto the scene. In 1865 he witnessed a homeopathic healing which convinced him to devote himself to the new method. He rediscovered isopathy alone and after several decades of practice published a book entitled *Isopathie, Méthode Pasteur par Voie Interne* at the age of 74 (11). According to Collet, there are three ways of healing, namely allopathy, homeopathy and isopathy, all of which are useful depending on the clinical indications. In addition, he distinguishes between three types of isopathy: (i) 'Pure isopathy', which uses secretion products from the patient to cure the same disease. (ii) 'Organic isopathy', which cures the diseased organs with dynamized derivatives from healthy organs. (iii) 'Serotherapeutic isopathy' or 'serotherapy' (dilutions of hyperimmune serum). The book also contains 42 personal observations and the rules of isopathic pharmacopraxis, which is the starting point for a substantial renewal of the method.

In the twentieth century two works devoted entirely to nosodes have been published: the first in 1910 by H.C. Allen (12), entitled *The Materia Medica of the Nosodes*. The second is by the Frenchman O.A. Julian (13), who first published *Materia Medica der Nosoden* in German in 1960, later to come out in two French versions, one in 1962 entitled *Biothérapeutiques et Nosodes* and the other in 1977 entitled *Traité de Micro-Immuno-thérapie Dynamisée* (14). The above-mentioned book by O.A. Julian in 1960 was a success in Germany, where it revived the study of nosodes. In particular, R. Voll accorded therapy with nosodes a central role in his diagnostic-therapeutic procedure called electroacupuncture-organometry, and H.H. Reckeweg (15), the founder of homotoxicology, made extensive use of nosodes and immunomodulators in his biotherapy. The use of the nosode *Meningococcinum* as prophylaxis of meningitis was suggested by others (16).

Subsequent Developments of Homeopathy

The rapid initial spread of homeopathy was probably due, on the one hand, to the fact that the orthodox medicine of Hahnemann's day and age was still extremely backward and lacked truly effective therapeutic remedies, and, on the other, to the distinct superiority of homeopathy in treating the various

epidemics of typhoid fever, cholera and yellow fever which raged across Europe and America in the 1800s (17–19).

Homeopathic medicine has undergone substantial ups and downs in its historical development. The rapid early boom throughout the world in the nineteenth century and its immense popularity were due to the fact that the other modes of medicine practiced at that time often used rather crude and painful means for a cure. A survey of the periodicals and other literature of the first decades of the nineteenth century reveals that in the medical practice among physicians of the orthodox persuasion the most common methods of treatment were bloodletting, sulfur, camphor, calomel and mineral medicines, mostly mercurial salts (20).

However, this rapid spread was followed by a head-on clash with orthodox medicine, which stopped homeopathy in its tracks and then led to its progressive decline, particularly in Western countries, where in some cases it all but disappeared. Over the past few decades, however, we have been witnessing a steady recovery of homeopathic practice, even in very advanced countries such as France, Germany, and Italy.

Hahnemann, right from the outset, found himself faced with stern opposition from colleagues and even more so from the apothecaries, who felt that he was undermining the foundations of their profession: since he was recommending the use of small doses and was against multiple prescriptions, this new medicine was perceived as a serious threat to their profits. Moreover, he was accused of dispensing his own medicines and administering them to his patients, which was illegal at the time. He was thus arrested in Leipzig in 1820, convicted and forced to leave the city. He then obtained special permission from Grand Duke Ferdinand to practice homeopathy in the town of Köthen, where he continued to work, write, and instruct his followers who were swiftly increasing in numbers and spreading their wings further afield. At his death (1843), homeopathy was known in all European countries (except Norway and Sweden), as well as in the United States, Mexico, Cuba and Russia, and not long after his death it reached India and South America. It was first introduced into Italy in 1822 thanks to G. Necker who founded the Neapolitan School.

By the middle of the nineteenth century, there were a large number of homeopathic journals, clinics, hospitals, societies and pharmacies; homeopathic physicians could be found throughout the world; and more than 20 faculties of homeopathic medicine were founded in the United States. However, there were many controversies between the Hahnemann school and the other trends of twentieth century medicine, particularly in Germany. Furthermore, homeopathy itself also began to develop different tendencies and conflicts, such as that between physicians who used albeit diluted ponderal doses and those who insisted on extremely diluted/dynamized preparations; that between those who gave only single medicines and those who gave combinations; or that between those who combined homeopathic and conventional medicines and those who relied exclusively on homeopathic remedies.

Homeopaths had separated into two groups even before the death of Hahnemann: one group considered itself the representative of pure Hahnemann homeopathy, and recognized the founder as the ultimate authority; the others formed a group of 'scientific homeopaths' who acknowledged Hahnemann as a brilliant innovator, but did not consider him infallible or hesitate to question his opinions. The 'scientific' conception of homeopathy that developed during the nineteenth and early twentieth century (2) was largely due to the efforts of this second group of homeopaths, who encouraged the greatest theoretical and experimental progress.

Early attempts to investigate the principle of similarity on the experimental ground can be traced back to the years around the end of nineteenth century, when H. Schulz published a series of papers that examined the activity of various kinds of poisons (iodine, bromine, mercuric chloride, arsenious acid, etc.) on yeast, showing that almost all these agents have a slightly stimulatory effect on yeast metabolism when given in low doses (21,22). He then came into contact with the psychiatrist R. Arndt and together they developed a principle that later became known as the 'Arndt-Schulz law', stating that weak stimuli slightly increase biological responses, medium and strong stimuli markedly raise them, strong ones suppress them and very strong ones arrest them (23). Similar observations were reported by several other authors in the 1920s and from their findings one can conclude that the occurrence of inverse, or biphasic, effects of different doses of the same substance was known before the era of molecular medicine (24–27).

This phenomenon is now well recognized in cell biology, with a number of explanation at the molecular level (e.g. different receptors for the same substance having different ligand affinities and triggering transduction pathways) and in immunology, where the systemic and local responses are known to depend on the dose in a complex way (e.g. foreign antigens may sensitize the host but low doses of the same substance may suppress the system if administered by oral route). We will go back to these concepts in a subsequent paper dealing with the scientific models of the similia principle. The delayed recognition of the possible contribution of homeopathic ideas to mainstream medical science and, insistent attacks of some homeopaths against allopathy are at least partially responsible for the rejection of homeopathy by the majority of modern physicians and academic circles.

It is generally agreed that one of the greatest physicians in Germany at the time of Hahnemann was Christoph Wilhelm Hufeland (1762–1836), a rich and magnanimous physician who was a friend of Goethe and Schiller (Fig. 7). He was a pioneer of medical journalism and dedicated his *Journal der Praktischen Arzneikunde* (which he edited for 40 years and which subsequently took his name) to the correction of the medical deviations of his time. Although being a leading representative of 'official' medicine, he also dealt extensively with the developments of homeopathy. His works include



Figure 7. C.W. Hufeland (1762–1836).

many references indicating his openness to homeopathic ideas, such as:

The first reason inducing me to write is the fact that I considered it incorrect and unworthy of science to ridicule or persecute the new doctrine of homeopathy. . . I find suppression and despotism in science repugnant; here, the only rule should be freedom of spirit, basic research, the confutation of hypotheses, the comparison of observations, adherence to facts and not to personalities. (..) Homeopathy must necessarily be contested if it intends to present itself as a general principle of every therapy. In fact, if this affirmation were to be taken literally, it could seem to be the grave of all sciences and human progress. (..) But homeopathy is valid as a field of observation and, instead of being repudiated, should be used as a special method of cure, subordinate to the higher concepts of rational medicine. On the basis of my personal observations, I am convinced that it can render a service not rarely, but sometimes in a highly striking manner, particularly after the failure of other treatments. (..) I am not in favor of homeopathy, but of the inclusion of a homeopathic method in rational medicine. I would not speak of homeopathic physicians, but of physicians that use the homeopathic method at the right time and in the right place. [Hufeland, *System der Prakt. Heilkunde*, 1830, cited in (2), p. 146]

Unfortunately, the history of medicine during the second half of the nineteenth and, particularly, the twentieth century was characterized by bitter struggles between the 'official' and

'alternative' medical worlds that made vain these hopes of Hufeland. As a result of an irrational policy of reciprocal excommunication, the two disciplines failed to develop any common points for a long time and continued along their own separate and often conflicting ways. With some exceptions (e.g. the German school), homeopaths have failed to scrutinize homeopathic concepts and theories in relation to conventional biology and immunology, possibly because they feel that any reductionist scientific approach is incapable of interpreting the greatness of their 'art'.

Opposition to the Development of Homeopathy

In the nineteenth century homeopathy was immensely popular in the United States where major figures such as Hering, Kent and Farrington were practicing. Homeopathy was taught at Boston University and at the Universities of Michigan, Minnesota and Iowa. By the turn of the century as many as 29 homeopathic journals were being published. The year 1844 marked the founding of the American Institute of Homeopathy, which thus became the first American national medical society.

Despite this, strong organized opposition was soon forthcoming from 'orthodox' medicine, which viewed the growth of homeopathy as a major threat: homeopathy was calling into question the very philosophical basis, clinical methodology and official pharmacology of orthodox medicine. Right from the very beginning the new approach embodied a strong critical attitude towards the use of conventional medicines, which were judged to be harmful, toxic and counterproductive for the practice of homeopathy, in that they were all based on suppression of symptoms. What is more, good homeopathic practice called for a long apprenticeship and individualization of treatment, both of which demanded more time than physicians were normally prepared to give their patients.

The year 1846 marked the foundation of the American Medical Association (AMA), one of the first objectives of which was to combat homeopathy: homeopaths could not be members of the AMA, and AMA members were not allowed even to consult a homeopath, the penalty for this being expulsion from the Association; legal recognition was denied to graduates with diplomas from universities with full professors of homeopathy on their academic boards. In 1910, a classification of American medical schools was drawn up (the Flexner Report) on the basis of criteria which assigned high ratings to schools which placed the emphasis on a physicochemical and pathological approach to the human body and strongly penalized the homeopathic approach (9,19,20,28). The homeopathic colleges obviously obtained poor ratings, and as only the graduates of schools with high ratings had their qualifications recognized, this was a mortal blow to the teaching of homeopathy. Of 22 homeopathic colleges operating in 1900, only two were still teaching homeopathy in 1923. By 1950 there was not a single school in the United States teaching

homeopathy and it was estimated that there were only about a hundred practicing homeopaths, almost all over 50 years of age, throughout the United States. For similar reasons, there was also a parallel decline in homeopathic practice in Europe in the early decades of the twentieth century.

We should not conclude, however, that the decline of homeopathy was due to only political and economic reasons. At least two other factors played a decisive role, namely the internal struggles within homeopathy itself and the new major scientific and pharmacological discoveries. As regards the splits in the homeopathic world, there were disputes between the various schools over dilutions (high or low potencies), over single or multiple prescriptions, and over whether prescribing should be based on total symptoms or on the main disease present. The various different schools developed their own organizations, hospitals and journals, thus making it very hard even for doctors seriously interested in learning about homeopathy to get their bearings in this field.

A severe blow to homeopathic theory was delivered by the chemical sciences and in particular by the law formulated by Amedeo Avogadro (Fig. 8), that was published initially as a hypothesis in 1811 and then tested experimentally by Millikan in 1909 (29): as is well known, this law establishes that one mole of any substance contains 6.02254×10^{23} molecular or atomic units. As a result, a simple calculation demonstrated that dilutions of any substance beyond 10^{24} ($\sim 24\times$ or $12c$ in homeopathic terms) presented an increasingly remote chance of containing even only a single molecule or atom of the original compound. From this it was obviously but a short step to ridiculing the use of homeopathic medicines, and



Figure 8. A. Avogadro (1776–1856).

homeopaths were branded by their adversaries as being on a par with some kind of esoteric sect. Such opinions have continued to be voiced virtually unaltered up to the present day.

The decisive factor, however, permitting conventional scientific medicine to prevail over homeopathy was its own development as a science capable of identifying the causes of many diseases and as a source of effective techniques and technologies for curing them. Lister's discoveries in the antiseptic field and the development of anesthesiology greatly increased the success, indications and popularity of surgery. While chemistry, physiology and pathology were making giant strides in the theoretical sphere, the discovery of vitamin and hormone replacement therapies and, above all, the advent of antibiotics, analgesics and anti-inflammatory drugs enabled orthodox therapy to demonstrate its practical superiority. The possibility of interpreting pathological phenomena rationally on the basis of a scientifically validated model of the human body and the availability of chemical, physical or technological means capable of repairing defects detected with the utmost precision by increasingly sophisticated and reliable instruments was (and is) altogether too attractive and convincing a prospect to allow scope for exploring alternatives based on outdated and mysterious theories.

Homeopathy Revival

As we have already stated, the enormous progress of conventional medicine in this century has reinforced the opinion that allopathic treatment by means of 'opposites' is the only effective form of treatment and, generally speaking, has also strengthened the view that it is only a question of time before a treatment is found for every disease. The great epidemics of infectious diseases have been defeated by a combination of improvements in living conditions, hygiene, vaccinations and antibiotics. Our knowledge of disease due to vitamin, enzyme or hormone deficiencies has furnished new weapons in the struggle against diseases such as pernicious anemia, dwarfism and diabetes. If it were not for the problem of finding donors, transplants would already be routine therapy for a sizeable number of diseases. Cortisone and its derivatives are solving many problems of immune hypersensitivity. Recent developments in molecular biology give us good reason to believe that not even the genetic sphere will be able to escape our manipulative capability.

Against this background, one cannot see any real scope for homeopathy, though at present its use is still spreading. This spread of homeopathy is happening in countries such as Italy, France and Germany, and parallels the renewed interest in homeopathy in many other countries throughout the world. Homeopathy is even more popular in Asia, most notably in India, Pakistan and Sri Lanka. In the United States, too, we are witnessing a revival of homeopathic practice: sales of homeopathic medicines in the USA have been growing at an annual rate of 20–25% during the 1990s.

These considerations alone should be enough to justify a greater commitment of official scientific institutions towards monitoring and clinically verifying the efficacy of therapeutic agents and measures adopted. A need is also felt for at least some teaching of the basics of homeopathy to doctors trained in universities, since, at general practitioner level particularly, patients often tend to be keenly interested in homeopathy and to ask their general practitioners for information and advice on the subject.

There may be any number of reasons for the revival of homeopathy, despite the lack of university teaching in the field and of support on the part of public health authorities (homeopathic drugs are not available on the NHS), but it can hardly be accounted for merely on commercial grounds. The main reason for the success of the so-called 'alternative' medicines lies in the fact that they offer something which today's physician is unable to provide. This can be traced, on the one hand, to the greater degree of individualization of the treatment, attention being paid to the human and psychological elements, which are becoming increasingly neglected in this era of ultra high-tech medicine; on the other hand, it is due to the awareness that many of the challenges still facing us today in the fight against disease call for a different approach from that adopted to date.

In fact, the public at large and also the medical profession itself are becoming increasingly aware that modern medicine must come up with new means and new ideas for tackling problems. These include contamination of the environment by toxic agents, ever-growing numbers of diseases induced by increasingly potent drugs themselves, degenerative diseases to which errors of diet or life-style contribute, allergies, autoimmunity and immune deficiency, large numbers of neurological and psychiatric diseases, psychosomatic disorders, and tumors. Despite undoubted progress made over the past decades in these crucial fields of medicine, despite the fact that we so often hear of new 'major breakthroughs' paving the way towards achieving a definitive cure for this or that disease, and despite the fact that our knowledge of the intimate mechanisms of the various diseases has increased enormously as a result of techniques of molecular biology, it has to be admitted that, as far as general practice and the vast majority of patients suffering from the above-mentioned diseases are concerned, the actual practical benefit of such knowledge is not exactly spectacular!

That this is not merely a commercial phenomenon is also suggested by the fact that we are witnessing a renewed interest on the part of scientists in experimental trials in this field. Studies are beginning to appear on the biological effects of homeopathic drugs, as well as studies on the so-called 'high-dilution effect', or double-blind placebo-controlled clinical trials. The debate in scientific circles is becoming increasingly heated, and many researchers are setting themselves the objective of developing reliable methods for tackling the problem.

Reilly's group has published a series of trials (30–32) describing randomized and double-blind studies of patients

with chronic allergic rhinitis or bronchial asthma treated with homeopathic immunotherapy (HIT). The studies involved administration of a 30c potency of the main allergen or (in the control group) an indistinguishable placebo. Results demonstrated a significant improvement of symptoms in the treated patients in comparison with those receiving placebo ($P = 0.0001$). This study offered proof that high homeopathic dilutions of antigens cannot be assimilated to a simple placebo. However, as underlined by the authors themselves, this does not mean that their proposed therapy is an efficacious homeopathic therapy for chronic rhinitis (also because homeopathy requires individualized treatment). These results have not yet been confirmed by independent groups; on the contrary, a paper recently published by Lewith and coworkers in the *Br Med J* describes apparently opposite results (the homeopathic medicine caused a slight but statistically significant worsening during the early phases of treatment than placebo) (33). This latter study sparked a considerable discussion in the same Journal. The reply of Reilly (34), the author of previous (positive) studies on HIT, stated that the Lewith's study was not actually a reply of their work, because the patient population, the drug administration, and the outcome measures were different. The debate on the clinical effectiveness of homeopathy is still quite hot (35–38).

We now have the results of studies that have used homeopathic remedies under well-known experimental conditions, as well as conventionally produced experimental evidence indirectly explaining homeopathic phenomena. The current scientific literature contains a substantial body of evidence and examples that may provide new insights improving our understanding of the principle of similarity and the action of small (or highly diluted) doses of medicines, particularly on the immune system and host defenses (39–45). These studies document and may clarify some of the specific aspects of the biochemical regulatory mechanisms possibly underlying the observed paradoxical phenomena. The 'simile'—brought back to its biological meaning of the inverted, or paradoxical, effects of the same or similar compounds—can operate under a number of experimental and reproducible conditions. Within the framework of our current knowledge of living systems and modern investigational techniques, it will be possible to reformulate the ancient principle with the aim of constructing reasonable models that can be tested at different biological levels, from cells to human beings.

Anyone who adopts an unprejudiced position will discover that immunology and the whole of modern biology in general can offer a considerable contribution to the understanding of homeopathy in a framework that is not very different from the conventional context. In other words, although it is true that some of the most reductionist molecular lines of modern science are ultimately incompatible with the systemic nature of homeopathic thought, it is equally true that many others are perfectly compatible.

References

- Hahnemann CFS. Versuch über ein neues Princip zur Auffindung der Heilkräfte der Arzneisubstanzen (Essay on a new principle for ascertaining the curative powers of drugs, and some examinations of the previous principles). *Hufelands J* 1796;2:391–439.
- Boyd LJ. *A Study of the Simile in Medicine*. Philadelphia: Boericke and Tafel, 1936.
- Behring E. *Gesammelte Abhandlungen. Neue Folge*. Bonn: Marcus and Weber, 1915.
- Bellavite P, Signorini A. *The Emerging Science of Homeopathy*. Berkeley, CA: North Atlantic Books, 2002.
- Coulter H. *Divided Legacy, vol. II. The Origins of Modern Western Medicine: J.B. van Helmont to Claude Bernard*. Berkeley, CA: North Atlantic Books, 1977.
- Coulter H. *Divided Legacy, vol. I. The Patterns Emerge, Hippocrates to Paracelsus*. Washington: Center for Empirical Medicine, 1975.
- Stoerck A. *Libellus quo demonstratur: stramonium, hyosciamus, aconitum, non solum tuto posse exhibere usu interno hominibus, verum et ea esse remedia in multis morbis maxime salutifera*. Vienna: Trattner, 1761.
- Lux W. *Isopathie der Contagionen*. Leipzig: Ed Kollmann, 1833.
- Coulter H. *Divided Legacy, vol. IV. Twentieth-Century Medicine: The Bacteriological Era*. Berkeley, CA: North Atlantic Books, 1994.
- Griesselich L. *Handbuch zur kenntnis der homoeopathischen oder specifischen heilkunst*. Karlsruhe: Malsch und Vogel, 1848.
- Collet T. *Isopathie, methode Pasteur par voie interne*. Paris: Bailliere, 1898.
- Allen H. *The Materia Medica of the Nosodes*. Philadelphia: Boericke and Tafel, 1910.
- Julian OA. *Materia Medica der Nosoden*. Ulm Donau: Haug, 1960.
- Julian OA. *Traité de micro-immunotherapie dynamisée (biotherapiques nosodes)*. Paris: Librairie Le Francois, 1977.
- Reckeweg HH. *Homotoxikologie. Ganzheitsschau Einer Synthese der Medizin*. Baden-Baden: Aurelia Verlag, 1981.
- Castro D, Nogueira G. Use of the nosode meningococcinum as a preventive against meningitis. *J Am Inst Homeopath* 1975;68:211–9.
- Shepherd D. *Homeopathy in Epidemic Diseases*. Rustington, Sussex: Health Science Press, 1967.
- Gibson S, Gibson R. *Homeopathy for Everyone*. Harmondsworth: Penguin Books Ltd, 1987.
- Ullman D. *Discovering Homeopathy: Medicine for the 21st Century*. Berkeley: North Atlantic Books, 1991.
- Coulter H. *Divided Legacy, vol. III. The Conflict Between Homeopathy and the American Medical Association*. Berkeley, CA: North Atlantic Books, 1982.
- Schulz H. Über die Theorie der Arzneimittelwirkung. *Virchows Arch* 1877;108:423–34.
- Schulz H. Über Hefegifte. *Arch Fuer Physiol* 1888;42:517–41.
- Martius F. Das Arndt-Schulz Grundgesetz. *Muench Med Wschr* 1923;70:1005–6.
- Koetschau K. The type effect hypothesis as a scientific basis for the simile principle. *J Am Inst Homeopath* 1930;23:207–95.
- Wilder J. *Stimulus and Response: The Law of Initial Value*. Bristol: Wright, 1967.
- Stebbing ARD. Hormesis: the stimulation of growth by low levels of inhibitors. *Sci Total Environ* 1982;22:213–34.
- Oberbaum M, Cambar J. Hormesis: dose-dependent reverse effects of low and very low doses. In: Endler PC, Schulte J (eds) *Ultra High Dilution*. Dordrecht: Kluwer Academic Publishers, 1994;5–18.
- Ullman D. The mainstreaming of alternative medicine. *Healthc Forum J* 1993;36:24–30.
- Majerus M. A critical appraisal of scientific arguments regarding basic research in homeopathy: a comprehensive examination of the francophone literature. *Berl J Res Hom* 1991;1:301–24.
- Reilly DT, Taylor MA, McSharry C, Aitchinson T. Is homeopathy a placebo response? Controlled trial of homeopathic potency, with pollen in hayfever as model. *Lancet* 1986;2:881–6.
- Reilly DT, Taylor MA, Beattie NG, Campbell JH, McSharry C, Aitchison TC, et al. Is evidence for homeopathy reproducible? *Lancet* 1994;344:1601–6.
- Taylor MA, Reilly D, Llewellyn-Jones RH, McSharry C, Aitchison TC. Randomised controlled trial of homeopathy versus placebo in perennial

- allergic rhinitis with overview of four trial series. *Br Med J* 2000;321:471–6.
33. Lewith GT, Watkins AD, Hyland ME, Shaw S, Broomfield JA, Dolan G, Holgate ST. Use of ultramolecular potencies of allergen to treat asthmatic people allergic to house dust mite: double blind randomised controlled clinical trial. *Br Med J* 2002;324:520.
 34. Reilly D. Randomised controlled trials for homeopathy. When is useful improvement a waste of time? Double positive paradox of negative trials. *Br Med J* 2002;325:41.
 35. Jonas WB, Kaptchuk TJ, Linde K. A critical overview of homeopathy. *Ann Intern Med* 2003;138:393–9.
 36. Linde K, ter Riet G, Hondras M, Melchart D, Willich SN. Characteristics and quality of systematic reviews of acupuncture, herbal medicines, and homeopathy. *Forsch Komplementarmed Klass Naturheilkd* 2003;10:88–94.
 37. Shang A, Huwiler-Müntener K, Nartey L, Jüni P, Dörig S, Sterne JA, et al. Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homeopathy and allopathy. *Lancet* 2005;366:726–32.
 38. Caulfield T, Debow S. A systematic review of how homeopathy is represented in conventional and CAM peer reviewed journals. *BMC Complement Altern Med* 2005;5:12.
 39. Bastide M. Immunological examples on ultra high dilution research. In: Endler PC, Schulte J (eds). *Ultra High Dilution*. Dordrecht: Kluwer Academic Publishers, 1994, 27–33.
 40. Grange JM, Denman AM. Microdose-mediated immune modulation. A possible key to a scientific re-evaluation of homeopathy. *Br Hom J* 1993;82:113–8.
 41. Bellavite P, Lussignoli S, Semizzi M, Ortolani R, Signorini A. The similia principle. From cellular models to regulation of homeostasis. *Br Hom J* 1997;86:73–85.
 42. Bellavite P, Andrioli G, Lussignoli S, Bertani S, Conforti A. Homeopathy in the perspective of scientific research. *Ann Ist Super Sanita* 1999;35:517–27.
 43. Eskinazi D. Homeopathy re-revisited: is homeopathy compatible with biomedical observations?. *Arch Intern Med* 1999;159:1981–7.
 44. Khuda-Bukhsh AR. Towards understanding molecular mechanisms of action of homeopathic drugs: an overview. *Mol Cell Biochem* 2003;253:339–45.
 45. Guajardo G, Wilson J. Models for explaining the homeopathic healing process: a historical and critical account of principles central to homeopathy. *Homeopathy* 2005;94:44–8.

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