Concluding Thoughts

Samuel Hahnemann has been characterized as a "sower of seed ...[which] fell on widening circles" [1]. Some of these seeds have grown into veritable trees and others perhaps into healthy shrubs, as shown by the many individuals described in the previous pages. Some seeds, too, fell on stony ground. On balance, however, medicine has undoubtedly benefited from the homeopathic impulse and in a variety of unexpected ways.

Not only did Hahnemann bring about a new system of therapeutics, but through the industry of his followers in the United States, his system gave rise to a number of progressive medical schools, which were among the first to admit women, minorities, and the disabled. They pioneered in other ways too, for example, by introducing longer curricula, courses in public health and radiology, formal anesthesia training, and advances in surgical practice. Some outstanding research was also stimulated, and one of the first endowed academic research units in the United States was established at a homeopathic school as the direct result of a benefactor who was pleased with the care given to her husband. Hahnemann's concern for public health and medicine's societal responsibilities was translated into action by the several homeopathic physicians who entered politics and public health. The collective impact of these homeopaths will be summarized.

Perhaps what stands out above all else is the moral force that homeopathy expressed through its female practitioners (and some of its male practitioners), who devoted themselves to reform, social justice, and care of the poor and oppressed in a manner that calls to mind the healing legacy of medieval monastic orders and the Knights Hospitaller [2, 3]. It is difficult to imagine any group of physicians that has come closer to fulfilling the core mission of medicine: to relieve suffering for all human beings, no matter what their station in life. By their actions, these homeopaths embodied Mahatma Gandhi's maxim of "Be the change you want to see in the world."

For much of the nineteenth and early twentieth centuries, homeopathy attracted physicians with reformist inclinations.

Among the large number of women described in Chap. 3, Clemence Lozier is the most notable in US medicine, while Emily Stowe in Canada and Maria Estrella in Brazil stand out in their respective countries. Harriet Clisby's name lives on today through the WEIU/Crittenton Women's Union. Laura Towne is considered to have been a primary force in keeping the Gullah culture alive, and several women homeopaths led the fight for women's suffrage, such as Anna Shaw, Leila Bedell, and Mary Safford Blake. Other homeopaths who battled for healthcare among minority groups included the first Native American medical graduate, Charles Eastman, who attempted to bridge the divide between Native and white American cultures and improve the welfare of the Indian population; similarly, Solomon Fuller, Walter Crump, and Geraldine Burton-Branch led trailblazing efforts on behalf of healthcare and medical training opportunity for African-Americans. Bayard Holmes was yet another pioneering homeopath. James Cocke, blind from infancy, graduated first in his class and serves to inspire that that no barrier could stand in the way of fulfilling one's ambition.

Homeopaths have played a crucial role in advancing the growth of medical specialties, most notably anesthesiology, cardiac surgery, urology, and ophthalmic surgery, particularly through individuals at Hahnemann Medical College, Philadelphia, and the New York Homeopathic Medical College between the 1890s and 1940s. The disciplines of pathology and physiology were also indebted to the efforts of certain individuals working in Boston and New York schools during their homeopathic eras, while the work of Robert Dudgeon and Edward Cronin Lowe in Britain should not be discounted. The growth of allergy as a medical specialty was stimulated by the careful studies of Charles Blackley in England and later by Grant Selfridge in the United States, who organized one of the earliest professional allergy societies; Charles Millspaugh was the first to treat hay fever by desensitization with grass pollen.

Homeopathically trained physicians left an enduring mark in psychiatry, notably Charles Menninger, founder of the Menninger Clinic, Solomon Fuller for his work on dementia, Winfred Overholser as an administrative and forensic psychiatrist, Clara Barrus for her studies on mental illness in women, and the teaching and administration in Boston by Emmons Paine, Frank Richardson, and Henry Pollock. Two homeopathic asylum doctors (Selden Talcott and Samuel Worcester) were regarded highly enough to appear as expert witnesses at the trial of a presidential assassin.

Surgery has been enriched by the original work of many physicians who trained at homeopathic medical schools. These include the pioneers Charles Bailey (cardiac surgeon), Ralph Lloyd (ophthalmologist), William Helmuth, and Israel Talbot (general surgeons).

In the realm of education and academic administration, three homeopathic graduates stand out: Ira Remsen as president of Johns Hopkins University, Marcus Kogel as dean of New York Medical College, and Charles Cameron as dean of the reinvented Hahnemann Medical College.

In the politico-legislative arena, measures to protect patient rights and improve safety in drug development were undertaken by two homeopathic senators, and in England, an important resource for complementary medicine was preserved through the intervention of a senior member of parliament, who was a homeopathic physician. In the public health sector, health departments in San Francisco, Los Angeles, Washington, New York State and City, and Puerto Rico communities were all led at various times by homeopaths. John Hayward and John Drysdale, who were part of the domestic sanitation movement in England, concerned themselves with the question of home design and improved ventilation as factors to reduce disease.

Otto Guttentag put bioethics on the medical map shortly after World War II; William Dieffenbach, Francis Benson, John Mallory Lee, and Emil Grubbé were prominent innovators in radiology; Oscar Auerbach and Charles Cameron conducted groundbreaking work in cancer research; Matthias Roth and George Taylor introduced massage into medicine, and Diocletian Lewis developed a system of gymnastics which was widely adopted.

Finally, homeopaths have produced their share of villains. Although George Simmons put the AMA on a strong footing, his professional and personal life was tarnished by scandal. Other ne'er-do-wells included murderers (Luc Jouret and Hawley Crippen), perpetrators of license scams (Robert Reddick), promoters of dubious treatments (Edwin Pratt, Albert Abrams, William Koch), and some who aligned themselves with Nazi policies which attempted to subordinate personal health needs to those of the state (Karl Koetschau and Hans Wapler).

In appraising the legacy of many of these physicians, it is not difficult to accept that they contributed to medical progress, but in very few cases was it under the banner of homeopathy. Any search for traces of homeopathy in the practice of modern medicine would disappoint those hoping to find it – there are few, but they are not altogether absent. The

concept of sensitization is rooted in homeopathic thought, which stressed from the early days that diseased patients were often more sensitive to treatment effects than were healthy subjects. The unanswered question, even today, is how sensitive can a diseased individual, body tissue, or organ be? And related to that question, we may ask how low can the dose be taken while preserving a therapeutic effect? There are recent studies showing that picogram and nanogram doses of some medicines can be effective. These units correspond, respectively, to milligram dilutions of 10-9 and 10⁻⁶, doses common in homeopathy, but which orthodox medicine has so much difficulty accepting, yet on occasion has embraced them as though homeopathy had never existed [4]. Nicholls [5] has pointed out that, for several decades, British medicine actually incorporated many homeopathic remedies into its pharmacopeia, as, for example, in Ringer's authoritative Handbook of Therapeutics, which in its first edition acknowledged medicine's debt to homeopathy, but

Persecution Against Homeopaths

subsequently deleted any reference to this provenance.

The reason why homeopathy has failed to make overt inroads to medicine is obvious - it has forever been met with resistance and prejudice - allopathy has not made room for it. Examples of persecution are legion, although it is beyond the scope of this book to go into detail on that matter. However, such persecution should be regarded as one of medicine's more shameful chapters - in some other walks of life, such behavior would be illegal. Even when distinguished and decorated scientists, such as Luc Montagnier and Jacques Benveniste, have turned their sights towards homeopathy or kindred concepts, the scientific community accuses them of being unhinged, and it is not long before the witch-hunt begins. In the 1990s, a bizarre scenario unfolded in the case of George Guess, a competent and well-qualified family physician in North Carolina who chose to practice homeopathy. For no sound reason, the state licensing board awakened long-dormant ghosts of the past by unaccountably pursuing him and ordering that he either relinquish his license or give up practicing homeopathy and revert to orthodox medicine. This occurred in spite of the board's acknowledgement that Dr. Guess was a competent practitioner whose only "crime" was that of using homeopathy. After long and costly litigation with appeals and counter-appeals, Dr. Guess left North Carolina for Virginia, where he still practices. One local consequence of the Guess affair was that public opinion became so stirred up that legislation followed which made it possible to practice homeopathy and other forms of alternative medicine without fear of persecution by the state licensing authority simply on the grounds that such practice was not customary. Curiously, about 20 years after the Dr. Guess ruckus, the same state licensing board elected a doctor of osteopathy

(D.O.) as its president, and one of the tasks he placed on his presidential agenda was to chip away at discrimination against osteopaths [6]. He noted that, even as of 2009, one large hospital system refused to recognize osteopathic board certification as equivalent to the allopathic certification.

The medical legacy of homeopaths is broadly based, as described in the preceding chapters. There are the few instructive cases of distinguished academic homeopaths practicing in the mid-twentieth century, at a time when it had become impossible to conduct homeopathic practice and research in medical schools. The experience of these individuals seemed to be that modern medicine with its magic bullets had rendered homeopathy irrelevant, although with the growth of antibiotic resistance, some of these wonder drugs are beginning to lose their luster.

In the case of Conrad Wesselhoeft, his later writings on infectious disease make no mention of homeopathy. The exact reasons are open to conjecture: unwillingness by mainstream journals to countenance it, or ambivalence about Wesselhoeft's homeopathic past and the need to downplay it in order to prosper in the changing world of medicine. It is therefore possible that such homeopathic allegiance went underground and never truly disappeared, as we have seen with Fuller and Menninger. As to Thomas McGavack and Linn Boyd, although they were active in homeopathy until around 1940, their later writings also made very little mention of homeopathic treatment. Boyd was probably the last to conduct substantial homeopathic research and practice in a medical school, which he continued well into the 1930s with drug provings on NYMC medical students and animal model experiments.

The homeopathic impulse was more evident in the humanitarian side of medicine – patient rights, bioethics, disparities on healthcare, and healthcare legislation, all aspects of medicine that are as important as the scientific. These humanitarian values were upheld by the founder of homeopathy, which may explain why progressive people were attracted to the specialty. Although homeopathic medical schools were often slighted and regarded as inferior, they produced many high achievers. One has to regret the passing of these schools; the presence of an "alternative" system of medicine perhaps proved more a boon than a bane to medical progress. Even though therapeutic innovations were comparatively few in the narrow sense of homeopathic remedies, a vigorous homeopathic community provided a constant stimulus to think out of the box and challenge established prejudices.

The Evidence for Efficacy: Does Homeopathy Work?

Although this is not a book on homeopathic research, failure to touch on the subject could be seen as an important omission, so a brief overview will be presented. Firstly, the general topic of evidence will be discussed.

Basic Rules of Medical Evidence: Some Brief Considerations

In the preface, I shared a personal anecdote about Dr. Ernest Hawkes and his family of Liverpool homeopaths. Let us revisit this family to illustrate a fundamental point about medical evidence. In 1906, Ernest Hawkes' father, Alfred Hawkes, compared death rates from measles in four regular Liverpool hospitals to the number of deaths in the outpatient homeopathic practices of Hawkes' two sons. The author observed a combined death rate of 6.7 % from conventional treatment in the four hospitals and a death rate of 4 % from 466 outpatients managed homeopathically [7]. While one might be tempted to conclude that deaths from the homeopathic sample were about 40 % lower, such a conclusion would be unwarranted for the following reasons: (1) the samples differed and it is possible that those admitted to hospital were more severely ill than those in the homeopathic group, (2) it is unclear whether patients who were treated homeopathically by other doctors would have done so well (i.e., a "doctor" effect), (3) it is not stated how the four regular hospitals were chosen and whether they were representative of all city hospitals, and (4) the demographic characteristics may have differed, for example, the homeopathic outpatients may have been from a higher socioeconomic group and contained more private patients.

In order to show if homeopathy truly reduced the mortality of measles, it would have been necessary to balance the two groups beforehand so that they were as identical as possible, apart from the method of treatment. Another modification would have been to compare inpatients treated each way, or to compare outpatients, but not to mix them up, as was done by Hawkes, whose report could be construed as a comparison of inpatient vs. outpatient management as much as one of homeopathy vs. allopathy.

Such principles were not understood at the time, but today any claims made for a treatment must be supported by means of randomized, double-blind, controlled trials. In the following paragraphs, the results of such trials for homeopathy will be summarized.

Major Reviews of Homeopathy

Between 1991 and 2005, three research groups published comprehensive reviews of homeopathy in major medical journals. These reviews all examined whether homeopathy was superior to placebo in randomized, placebo-controlled, double-blind trials, a method that has been the bread and butter of drug testing in medicine for over 50 years. Homeopathy was evaluated as a general method of treatment for a wide range of conditions, which obscures the possibility that its efficacy could be more effective for some diseases than for others, or that certain types of homeopathy could be better than others, but it still answers an important question about the general method of homeopathy. Leaving that reservation aside, it is salutary that all the reviews found superiority for homeopathy, although they did not reach the same conclusions.

In the first review, Kleijnen et al. concluded positively that they would be prepared to accept that homeopathy was effective "if only the mechanism of action was more plausible" [8]. Such a conclusion conflates two different questions of whether a treatment works and how it works. While medicine has not generally had a problem accepting uncontroversial treatment even when its mechanism of action was unknown (e.g., aspirin, nitroglycerin, and digitalis), this seems to have become an issue in the case of homeopathy, which has been expected by opponents to deliver stronger proof of efficacy than other types of treatment. In other words, the standards of proof were arbitrarily expected to be higher. Anti-homeopathic critics have consistently failed to recognize that much homeopathy is practiced with material doses of drug (e.g., picogram and nanogram amounts), and, as such, there is no sound reason to adopt a higher set of research standards.

Six years after the Kleijnen review, Linde et al. [9] analyzed a different series of studies and found that their results were incompatible with the hypothesis that homeopathy and placebo did not differ. Homeopathy was more effective, including in the better quality trials, which was an important observation since low quality studies often favor a treatment over placebo because other influences (sources of bias) have not been adequately controlled. If higher quality trials demonstrate efficacy, then one has greater confidence that this is due to differences between treatments rather than to other factors, such as unblinding of assessors during the trial. Adding further support were two later analyses of the same data by Linde's group, which showed that good quality studies of any homeopathy [10] and of individualized homeopathy [11] exerted greater effect than placebo, although they did show that magnitude of difference diminished as study quality increased and that in one subgroup of the best studies, the treatments were equivalent: they accepted that their 1997 report may have overestimated the effect of homeopathy [12].

The third study will be described in more detail, since it has gained wide visibility. Shang and colleagues [13] compared the funnel plots in 110 studies of homeopathy vs. placebo to those of 110 conventional medicine vs. placebo. (A funnel plot shows the relation between treatment effect and study size. Larger trials are more likely to have effects that cluster near to the average effect, while small samples spread further away from the mean. Under ideal circumstances, the resulting pattern shows a distribution of effects that visually resembles an inverted funnel. Any asymmetry suggests the possibility that large effects from small sample trials are exerting undue influence on the conclusions and/or that neg-

ative studies have not been included in the analysis.) In the Shang report, there was no difference in the funnel patterns for the two kinds of study, with homeopathic and allopathic treatments both being superior to placebo. Moreover, study quality was assessed as good in 19 % of homeopathic trials, compared to only 8 % in allopathic ones, a finding that was glossed over in the paper. Rather than concluding, as did Kleijnen and Linde, that homeopathy was effective, Shang's group then picked eight top quality homeopathic studies and compared them to six conventional trials of comparable quality. But in this small subsample, the authors reportedly altered their criteria of high quality and also compared different diseases in the two groups. For example, the homeopathy group contained six conditions that were absent in the conventional group, and, vice versa, three conditions appeared in the conventional group that did not appear in the homeopathy sample [14]. In this subsample, homeopathy did not fare so well, leading the authors to opine that, in the best studies, allopathic treatments remained superior, while homeopathy failed to outperform placebo. Readers could have been further puzzled by Shang's finding that a sample of eight homeopathic trials for upper respiratory infection significantly favored remedy over placebo. Following on this particular finding, a later report by Lüdtke and Rutten showed that if Shang had analyzed their 21 allopathic respiratory infection studies, they would have found no conclusive evidence in favor of conventional treatment. So it is far from clear that Shang's results spelled "the end of homeopathy," as the editor of *Lancet* claimed [15].

Subsequent to the reviews by Kleijnen, Linde, and Shang, a health technology assessment (HTA) report was published by Bornhoft and Mattiesen, as part of the Swiss government's Complementary Medicine Evaluation Program (PEK). This report found that homeopathy was effective, safe, and most probably cost-efficient [16]. The methods used in this report (e.g., its selective inclusion of reports) have come under some valid criticism, however [17], although the editorial critical of the report has itself been criticized for inaccuracies [18]. A similar assessment by the Belgian authorities in 2011 found no evidence for efficacy of homeopathy.

While reviews such as those described above have become the cement in all evidence-based medicine, we should adopt a cautious approach and not regard them as infallible pronouncements. Ezzo and colleagues have noted that it is common for such reviews to give conflicting results, to show no effect or insufficient evidence for a treatment, and for their results to be influenced by subjective factors on the part of reviewers [19].

So what does the evidence say? Does homeopathy work? The time has not yet arrived to dismiss the practice, and even from a skeptic's point of view, it must be admitted that light still flickers. While there is room for disagreement [20], the evidence against homeopathy is not robust enough to warrant its defenestration: for that, one would need to see serial and unambiguously negative results. As Lüdtke and Rutten [21] have stated, conclusions on the effectiveness of homeopathy depend substantially on the set of trials analyzed and decisions underlying study selection; the choice of outcome parameters and their interpretation is much determined by subjective factors. Many of the same arguments that have taken place about homeopathy have been raised against other types of treatment including, for example, the effect of antidepressants. Although it is beyond argument that antidepressants are superior to placebo, positions pro and con have often been staked out in advance based on personal prejudices, and what are termed "evidence-based" treatment guidelines can be influenced by the composition of review committees and the rules they establish to organize and interpret the data.

For homeopathy, the door is not yet closed. In respect of the therapeutic contest, perhaps the Dodo-bird's words in Lewis Carroll's (real name: Charles Lutwidge Dodgson) *Alice's Adventures in Wonderland* are apposite. When the Dodo was asked who had won the Caucus race, it had trouble making up its mind and concluded that "everybody has won and all must have prizes." Such could be the verdict for homeopathy in comparison to other forms of treatment at this time.

There is also a portfolio of indirect evidence from animal and plant models that supports its activity, although of course not proving that homeopathy works as a treatment for medical disorders. Some of this secondary evidence has been replicated, including histamine H₂-receptor-mediated inhibition of basophil activation from high dilutions (10^{-32} M) of histamine, actions of aspirin as inhibitor of COX-2-mediated PGI₂ production in blood vessel endothelium, and effects of thyroxine dilutions on frog metamorphosis. This body of science has been reviewed elsewhere and will not be discussed in detail here.

The level of prejudice that exists for and against homeopathy may be insurmountable unless conscious efforts are made to examine the effect of such prejudice on rational scientific discourse. Wisdom consists, among other things, of the ability to deal with uncertainty, tolerate different perspectives, regulate emotion, develop self-understanding, and set prejudice aside [22]. A bit more sagacity on all sides of the debate would benefit everyone and help advance a more constructive, participatory, investigation of homeopathy and its place in medicine.

How Might Homeopathy Work?

Besides the question of whether homeopathy works, we may look for possible mechanisms of action, of which three offer particular appeal.

- 1. The first possibility is that remedies work according to usual pharmacological principles. For this to be the case, measurable amounts of drug would be required. If a diseased organism shows enhanced sensitivity to a drug, it is plausible that extremely low doses may have an effect. One way to demonstrate this would be to assess whether low but measurable doses are more effective than the higher dilutions that supposedly contain no drug. While the literature is sparse, one revealing analysis of the 21 best-quality trials in the Shang et al. data has shown that low molecular dose (i.e., a measurable amount of drug) was the only one of seven variables to emerge as a significant factor [21, p. 2004]. In other words, homeopathy was superior to placebo in the group of studies where material dose was used, while in those studies that used dilutions with no presumed drug content, homeopathy failed to show an effect. Other variables that could potentially have affected outcome, such as type of analysis, country of study, use of single remedy, or combination remedy, made no difference. Although the number of studies was small, this intriguing finding supports low dose homeopathy.
- 2. The above argument does not entirely dispense with high dilution homeopathy, as there have been a number of studies showing efficacy, including some good quality trials. Either this type of homeopathy works by non-pharmacological mechanisms, as has been proposed by Bell, for example [23], or a trace level of the mother tincture (original drug) remains in the dilution, which gives enough of a pharmacological stimulus to produce an effect, as was discussed in Chap. 16. At the present time, neither of these mechanisms can be discounted, and both need to be investigated further.
- A third explanation concerns the possibility that home-3. opathy of all kinds is nothing more than a good placebo. Considering that a thorough homeopathic interview takes time and can result in the patient feeling understood, there is every reason to believe that the encounter would be therapeutic - perhaps homeopathy could be classified as a form of psychotherapy with presently undetermined active ingredients. To demonstrate this third possibility, a study design would need to include the following groups: a homeopathic consultation with and without the remedy and a standard non-homeopathic consultation with and without the remedy. Such a study was conducted by Brien et al. in 56 patients with rheumatoid arthritis (RA), who had been stabilized on conventional medicine, which they continued in the trial. It was found that the homeopathic consultation produced a clinically meaningful effect on a composite RA scale and global assessment. No difference was found between the remedy and placebo groups, leading the authors to conclude that the active ingredient of homeopathy was to be found in the consultation process [24].

augment the effect of regular treatments, at least in some chronic diseases. In the Brien study, the magnitude of benefit for homeopathy was greater than what has been found for cognitive behavioral therapy. Brien's findings also suggest that the curriculum which was emphasized in homeopathic medical schools may have enhanced therapy in general.

In the last 20 years, there has been an accumulation of good quality research in homeopathy, much of which was summarized in two issues of the journal Homeopathy (October 2009 and January 2010). Research continues unabated, and it is hoped that in due course we will achieve a better grasp on the important questions about homeopathy, including its efficacy, mechanisms, indications, and method of delivery. We still cannot entirely escape from the question whether (1) Hahnemann promoted one of the biggest hoaxes in medicine; if, (2) ahead of his time, he revealed truths that show us the way to better medicine, but which we still do not yet fully comprehend; or if (3) it was a mixture of both. Meanwhile, as this book has tried to show, regardless of these questions, apart from some notable villains, homeopathically trained physicians have given medicine much to be grateful for.

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