Allergy and Allergic Disorders: Homeopathic Leaders

10

Introduction

The word, allergy, derives from the Greek "allos" (other) and "ergon" (action, energy, or reactivity

The term "allergy" was introduced into medicine in 1906 by Clemens von Pirquet, a pediatrician with an interest in immunity. By introducing a term that denotes the concept of altered biological reactivity, his aim was (1) to draw together a group of conditions that were caused by altered host responsiveness and (2) to describe the nature of the seemingly parallel process of immunity and hypersensitivity [1].

While today allergies and allergic disorders are understood to be common and still on the rise, for a long time, they were regarded as rare and mainly confined to upper socioeconomic groups. For most of the nineteenth and part of the twentieth century, allergy was poorly understood, although this did not in any way stifle vigorous debate about its nature, causes, and treatment.

Many individuals contributed to the growing knowledge base of allergies, and homeopathy can claim two members of this pioneering group: Charles Harrison Blackley and L. Grant Selfridge. Also to be noted briefly is the work of Gregory Shwartzman, a non-homeopathic physician who obtained his medical degree in Brussels and became professor of bacteriology at the New York Homeopathic Medical School between 1923 and 1926, where he began to build his research career before moving to Mount Sinai Medical Center. His initial association with a homeopathic establishment is of some historical interest. Today, Shwartzman is recognized for his pioneering work in anaphylaxis and typhoid vaccination, and his name lives on eponymously in the Shwartzman reaction. At NYHMC, Shwartzman experimented with bacteriophage (a virus that infects bacteria) at dilutions in the range of 10^{-9} (i.e., corresponding to low-potency homeopathic doses) and found them to be capable of producing bacteriolysis under anaerobic conditions [2].

Charles Blackley

Blackley (1820–1900) practiced medicine between 1835 and 1900 and is credited as the first to demonstrate that seasonal hay fever is caused by pollen, along with a number of other important discoveries (Fig. 10.1). Blackley was born in Bolton, England; he received little education and at an early age was apprenticed to a firm of engravers. However, ambition led him to pursue further education through evening classes in chemistry, botany, physics, microscopy, and Greek. From his studies of chemistry, Blackley became intrigued with the fact that a disproportionately small quantity of enzyme was able to catalyze the

Fig. 10.1 Charles Harrison Blackley. English general practitioner who discovered pollen as the cause of hay fever (Image by courtesy of Stephen Holgate, MD)

J. Davidson, *A Century of Homeopaths*,
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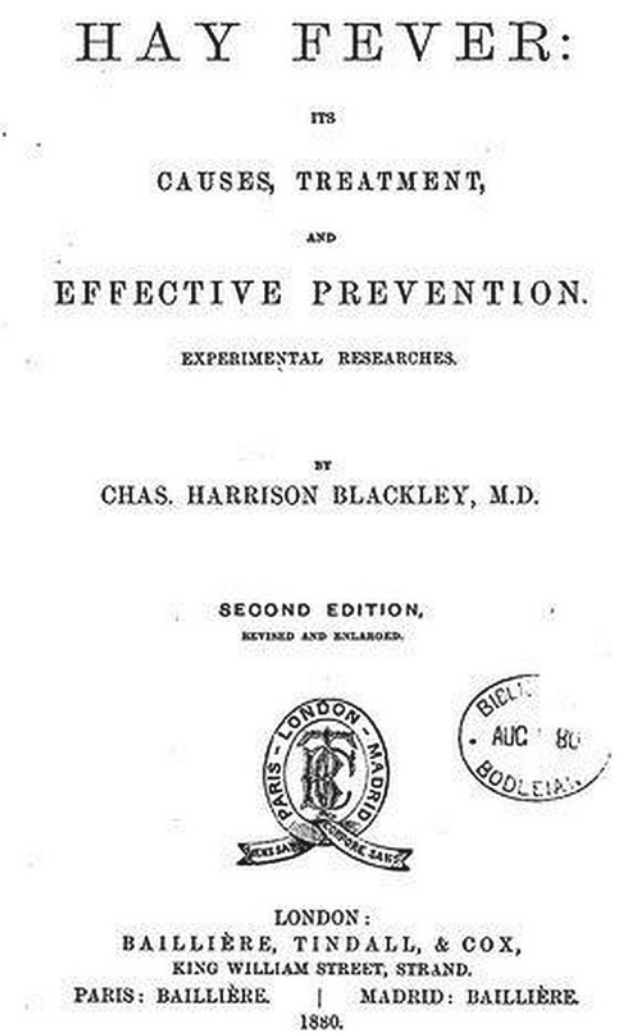
conversion of large amounts of one substance into another, a phenomenon that may have been relevant to his subsequent interest in homeopathy. It is also likely that his personal experience as the patient of a local homeopath gave further impetus to this interest [3]. His fascination with allergies, specifically hay fever, was almost certainly the result of being a hay fever sufferer.

At the age of 35, Blackley changed his career path and enrolled in the Pine Street Medical School in Manchester, graduating as member of the Royal College of Surgeons (MRCS) in 1858. He settled in the nearby town of Holme as a general practitioner. Although trained as an allopathic doctor, Blackley incorporated homeopathy into his practice and later in his career became heavily involved in homeopathic affairs by editing the *Manchester Homoeopathic Observer* and serving as president of the British Homoeopathic Society. In 1874, Blackley made a significant detour and obtained a doctorate of medicine from the University of Brussels. Although his MRCS degree served as a legitimate passport into medical practice, it has been suggested by Taylor and Walker that the Brussels MD degree conferred a greater measure of scholarship, which could have been significant to Blackley because adherents of homeopathy were look at askance by the allopathic medical community. It is believed that on at least one occasion, his homeopathic allegiance resulted in the withdrawal of an offer to collaborate on a hay fever study.

In Blackley's day, debates about hay fever and related allergic conditions focused on their causes, frequency, epidemiology, and treatment. There were different notions as to what caused hay fever, which was initially termed *catarrhus aestivus* (summer catarrh) by Bostock in 1827 and then "hay asthma" by the poet Robert Southey, who suffered from the condition. The term "hay fever" was introduced in 1828 [4]. Simultaneously, hay fever came to the attention of a famous London consultant physician, John Elliotson (1786–1868), who in 1831 affirmed his belief that the condition was caused by grass flowers, most likely the pollen. However, Elliotson never demonstrated this was so and encountered serious problems of credibility with his colleagues when he advocated hypnosis as a form of anesthesia. Thus, for their beliefs, Blackley and Elliotson were marginalized by the medical community and their insights about hay fever failed to receive due attention, with the result that knowledge of its cause was retarded by almost 50 years [5].

In order to pursue the possible cause of hay fever, Blackley commenced a series of painstaking and systematic experiments in 1859, which continued over at least the next 15 years. As he lamented in his book, their slow progress was due to difficulty taking time off from his practice in the summer months. He described the results of many of his experiments in his 1873 book *Experimental Researches on the Cause and Nature of Catarrhus Aestivus (Hay-Fever or Hay-Asthma)* [6], as well as in a second book in 1880 (Fig. 10.2). Blackley experimented on himself since he was unable to find a patient willing to devote the time. He administered pollen from over 100 species of grass and flowers by different routes to the nasal mucosa, larynx and throat, conjunctiva, tongue and lips, and upper and lower limbs. He took the precaution of including an inactive control substance for comparison. Blackley observed reactions of different intensities but they all pointed to grass pollen as the cause of his symptoms, which included itching, nasal discharge,


HAY FEVER:

ITS

CAUSES, TREATMENT,

AND

EFFECTIVE PREVENTION.

EXPERIMENTAL RESEARCHES.

BY

CHAS. HARRISON BLACKLEY, M.D.

SECOND EDITION,

REVISED AND ENLARGED.

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1880.

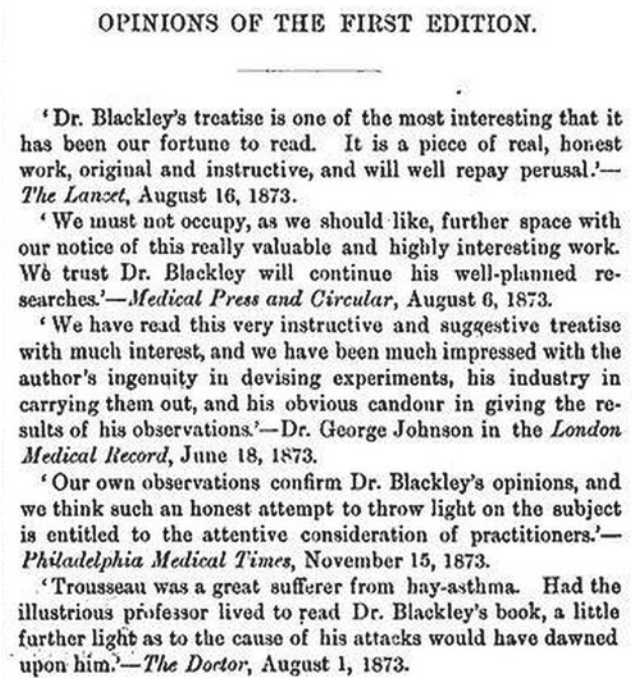
Fig. 10.2 Title page of Hay Fever: Its Causes, Treatment and Experimental Researches. 2nd Edition. 1880 (Image in the public domain)

swelling, and even asthma. After challenge with higher doses, more severe symptoms emerged, including rapid heartbeat, fever, and sweating up to 48 h in duration. Some reactions were extraordinarily severe, as shown by the appearance of a wheal ½″ high and over 2″ round following injection of pollen into the skin of his arm. As pointed out by Hurwitz, by using the diagnostic scratch and mucous membrane tests, Blackley may be credited for anticipating by 25 years their more widespread use in medicine. From his experiments, Blackley concluded that pollen was the cause of seasonal hay fever.

Blackley's next goal was to ascertain whether a relationship existed between atmospheric pollen content and symptom severity. To answer this question, in the summer months of 1866, he devised some intricate experiments in which he attached a glass-slide apparatus to kites flown at different altitudes between 500 and 2,000 ft, from which he collected pollen samples. Symptom intensity was found to correlate with pollen count. He also found that rainy and cool weather brought about a reduction in the pollen count and in his symptoms.

The results from all of these experiments were published in his 1873 book on the causes and nature of hay fever, which drew favorable attention from the press and from certain prominent people, including Charles Darwin, with whom Blackley engaged in correspondence. Darwin found Blackley's work to be "ingenious and profoundly interesting" [7]. The *Lancet* gave a favorable review to Blackley's book as being "one of the most interesting that it has been our fortune to read" [8], but the reviewer quite reasonably concluded that since the findings were based on one subject, it would be necessary to replicate them (Fig. 10.3). In 1929, Bosden Leach, writing in the *British Medical Journal*, characterized Blackley as "the first who brought extensive experimental evidence to show that pollen is the one cause of hay fever … (that he was) looked upon as somewhat of a faddist – a man who played with grass – … (that he was) certainly not sufficiently recognized in England." Leach observed that more enquiries were received from America about Blackley than from Britain at that time [9].

Blackley made other observations relevant to hay fever. He conjectured that the low rate of hay fever in farmers, who were in frequent contact with grass, could reflect the buildup of immunity ("insusceptibility"). He also asserted that a "nervous temperament" was one predisposing factor for hay fever and that hay fever increased in incidence as population patterns shifted from rural to urban and as life became increasingly competitive [6, p. 159]. He created what is perhaps the first pollen counter to measure the quantity of pollen in relation to symptoms of hay fever (Fig. 10.4). In affirming the causative role of pollen, Blackley had ruled out other possible candidates, such as ozone, coumarin, dust, light, and heat.



OPINIONS OF THE FIRST EDITION.

'Dr. Blackley's treatise is one of the most interesting that it has been our fortune to read. It is a piece of real, honest work, original and instructive, and will well repay perusal.'—*The Lancet*, August 16, 1873.

'We must not occupy, as we should like, further space with our notice of this really valuable and highly interesting work. We trust Dr. Blackley will continue his well-planned researches.'—*Medical Press and Circular*, August 6, 1873.

'We have read this very instructive and suggestive treatise with much interest, and we have been much impressed with the author's ingenuity in devising experiments, his industry in carrying them out, and his obvious candour in giving the results of his observations.'—Dr. George Johnson in the *London Medical Record*, June 18, 1873.

'Our own observations confirm Dr. Blackley's opinions, and we think such an honest attempt to throw light on the subject is entitled to the attentive consideration of practitioners.'—*Philadelphia Medical Times*, November 15, 1873.

'Trousseau was a great sufferer from hay-asthma. Had the illustrious professor lived to read Dr. Blackley's book, a little further light as to the cause of his attacks would have dawned upon him.'—*The Doctor*, August 1, 1873.

Fig. 10.3 Book reviews of Blackley first book, *Experimental Researches on the Causes and Nature of Catarrhus Aestivus*. 1873 (Image in the public domain)

In addition to these discoveries, Blackley explored the relationship between symptoms and dose. While his work seems quite clearly supportive of pollen effects at homeopathic dose, this aspect of his work was not so well recognized. In a paper published in 1882 [10], Blackley assembled evidence that extremely low doses could, in general, be biologically active and that this applied to pollen sensitivity. He initially referred back to work with the enzyme diastase which, it was found, could convert 40,000 times its weight of starch into sugar. He then reviewed Darwin's work with insectivorous plants, such as *Drosera rotundifolia*, in which quantities of ammonia phosphate as low as 1/20,000,000th of a grain (one grain, often abbreviated as "gr." = 60 mg) could exert physiological action in the leaf glands of this plant. Darwin admitted incredulity to himself at this finding, likening it to the application of one drop of the salt to a 31 gallon cask of water and still finding biological activity. A dilution this great is definitely in the homeopathic range, that is, 10^7 or 7X. In his paper, Blackley derived a calculation that showed that 1/2,000,000th gr. of pollen could bring on hay fever symptoms, a dilution that represents a homeopathic quantity of around 6X.

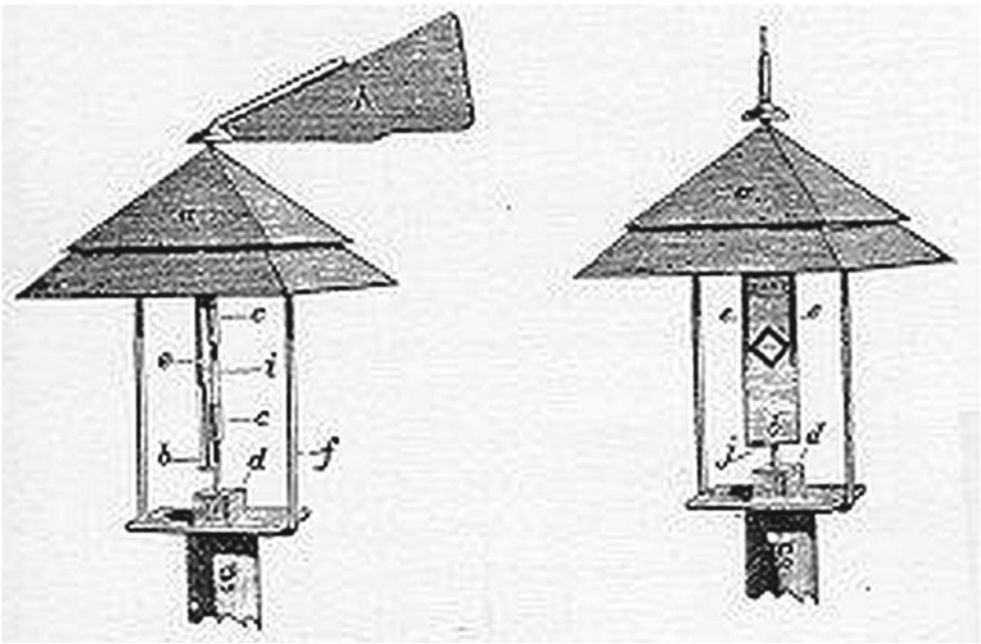


Fig. 10.4 Blackley's pollen counter – the first of its kind (Image in the public domain)

In attempting to explain how such infinitesimal doses could produce clinically evident effects, Blackley (1882) understood that it was not the result of "ordinary chemical affinity" and that "it does not derive its marvelous endowments from its material substance." He believed that the stimulating granular matter contained potential energy that became charged at the moment the stimulus was brought into contact with the responding tissue. In his speculations, Blackley anticipated the direction taken by more recent theoreticians in trying to explain the mechanisms of action of homeopathy.

One might be tempted to dismiss Blackley's findings on the infinitesimal dose were it not for later work by Noon and Freeman [11, 12]. In 1911, these consultant physicians reported on the use of hypodermic pollen desensitization, or pollen vaccination as they sometimes named it, to treat hay fever. In their clinic at St. Mary's Hospital in London, Noon and Freeman used initial doses of Timothy grass (*Phleum pratense*) as low as 1/1,000,000 dilution, that is, in the amount of 1/1,000,000 g, or 1 microgram (μg). Half a century later in the practice of sublingual immunotherapy [13, 14], nanogram (ng) doses of house dust mite allergen were found to produce an effect, which are again within the "infinitesimal" dose range described by Blackley, corresponding to homeopathic dilutions of 6–9X.

Grant L. Selfridge

While Blackley's major contribution to allergy lays in the careful experiments that helped him to identify the cause of hay fever, another homeopath from a later generation contributed in different ways, less through science (although that was not altogether neglected) and more by shaping the new medical specialty of allergic diseases. Grant Selfridge (1863–1951) received his medical training at Hahnemann Medical College in San Francisco and joined the California State Homeopathic Medical Society. Although on record as attending its meetings, it is not clear how much he used homeopathy in his own clinical practice. He first became aware of pollen as a factor in hay fever through friendship with Dr. Joseph Goodale of Boston, a pioneering allergy researcher. Selfridge later specialized in otolaryngology, allergy, and nutritional medicine; he is reputed to have been the first surgeon in San Francisco to perform a tonsillectomy [15, p. 126]. Known for using salty language and frequent swear words when he encountered difficult cases of deafness, he earned the moniker of "the little Goddamn," so named as there was another San Francisco surgeon who had already secured a reputation as "the big Goddamn." Selfridge ultimately went on to achieve national fame, being cited in *Time* magazine in 1939 for his use of vitamin B to treat deafness [16].

Similar to anesthesiology and other nascent branches of medicine, allergy had not yet evolved into a recognized specialty during the 1920s, and Grant Selfridge was one of the first to change that. Along with two colleagues, Albert Rowe and George Piness, he established the Western Society for the Study of Hay Fever, Asthma, and Allergic Diseases in 1923 and was elected its first president. As this regional society increasingly drew members from a wider catchment area, it metamorphosed into the American Association for the Study of Allergy (AASA). In turn, the AASA amalgamated with its Eastern counterpart, the Society for the Study of Asthma and Allied Disorders, to form the American Academy of Allergy. These associations all played a pivotal

role in establishing allergy as a scientifically and medically credible specialty.

Selfridge's role has been described by Cohen [17], who saw Selfridge as the senior and most forceful personality of the three founders. His impact was clearly visible during his terms as the first and second president of the Western society between 1923 and 1925 and then for the ensuing 5 years as a director of the organization. Perhaps because Selfridge resigned his membership in 1932 due to other interests related to the use of vitamin B, Cohen believes that later generations of allergy specialists never sufficiently recognized his achievements in establishing allergy as a medical specialty. Another initiative taken by Selfridge was his attempt to set up a governmental institute of nutrition in San Francisco; although this was not immediately successful, ultimately, such an institute came about and evolved into a component part of the National Institutes of Health in Bethesda.

Selfridge commissioned a comprehensive botanical survey of the western US states. The background to this survey was related to disability from seasonal allergy in a Southern Pacific Railroad Company employee who consulted with Dr. Selfridge. Selfridge quickly realized the possible economic implications for the employer if many of its employees were losing time from work because of seasonal allergies. Following the encounter with his patient, Selfridge conducted a survey to determine the number of hay fever cases in the company who reported sick each year. He learned that the number was about 500, far more than the authorities had believed. This review was succeeded by two surveys of grass, shrub, and tree pollen, the largest of which was supervised by Henry Hall, professor of botany at Stanford University, who organized the collection of pollen samples along the rail path. Hall identified those most likely to cause hay fever, and Selfridge then experimented on many of them to identify allergens and for desensitization. In his 1918 report, Selfridge described a method of testing for pollen allergy and then noted very positive results in 90 % of patients who were desensitized. His paper concluded by noting the value of (1) a careful botanical survey of local flora, (2) testing pollen extracts, (3) removing focal infections, (4) cross-disciplinary teamwork, (5) pollen therapy as the most beneficial therapy, and (6) starting treatment at least 60 days before the hay fever season begins. He also made a cogent plea for pharmaceutical companies to put patient interests ahead of commercial interests in the content of pollen preparations, many of which he found to be useless, although they were accompanied by extravagant claims [18].

Beyond his concern with allergic diseases, Selfridge was convinced that vitamin B was a contributing factor in hearing loss. In 1934, Selfridge observed that most of his deaf patients were consuming very small amounts of food that contained vitamin B, which led him to add vitamin B tablets, rice bran, or injections in over 100 patients with nerve deafness. After as few as six injections, some patients noted substantial improvement; for older patients, a longer course of treatment was necessary and recovery was rarely as good as in younger cases. While it is hard to discern the long-term effect of Selfridge's insights about vitamin B in relation to deafness, he may well have identified a true phenomenon [19]. As a result of his clinical work, he suggested to the young otolaryngologist W.P. Covell that it would be worthwhile investigating the matter further. This resulted in a publication that is still cited in today's literature, demonstrating a relationship between low levels of the vitamin B complex (B_6 and B_{12}) and other vitamins and damage to the auditory nerve in animal experiments [20]. Recent work has to some extent confirmed Selfridge's views about the relationship between vitamin B and deafness [21], and one study has found that hearing was improved by administration of vitamin B_{12} [22]. However, not all studies have supported the claims of Selfridge and Covell [23]. Among the various recommendations that have been made to preserve optimal hearing function in older adults, Johnson et al. write that "nutrients of particular importance include vitamin B_{12}, folacin, vitamin D and calcium" and that generous dietary intakes are encouraged in the elderly [24].

Homeopathy, Immunology, and Allergy: Other Considerations

While Blackley and Selfridge have been singled out, they were not the only homeopaths to carve out a place in the history of allergy and immunology.

In *A History of Medicine*, Inglis states that homeopathy can lay some claim to the paternity of immunization [25]. He quotes Emil von Behring, winner of the first Nobel Prize in medicine for his discovery of diphtheria antitoxin and renowned for demonstrating that immunization was a practical therapeutic procedure. Von Bering said that "Pasteur traced the origin of (Jenner's discovery of smallpox vaccination) to a homeopathic principle…. And by what technical term could we more appropriately speak of this influence, exerted by a similar virus, than by Hahnemann's word 'Homeopathy'? I am touching here upon a subject anathematized till very recently by medical pedantry: but if I am to present these problems in historical illumination, dogmatic imprecations must not deter me."

Coulter [26] also quotes trenchantly from a speech given by von Behring to the Berlin Physiological Society in 1905, in which von Behring described having demonstrated in 1892 the immunizing property of homeopathic ("infinitesimal") doses of tetanus antitoxin and that he found the lower the dose, the better the effect. Not surprisingly, a colleague then reproved von Behring for such a comment, as it was "grist for the mill of homoeopathy" [27]. Reportedly, von Behring had been advised to suppress these 1892 experiments on account

of their propaganda value for homeopathy, and not until 13 years later, after gaining the Nobel Prize, was he to disclose this work [15, p. 117].

Charles Frederick Millspaugh

As far as hay fever and other allergies are concerned, there is evidence that a homeopath was the first to use pollen to protect against seasonal allergy. In the 1880s, Millspaugh successfully applied ragweed pollen (*Ambrosia artemisiifolia*) in the third centesimal (3C) dose to several patients with hay fever [28], antedating by over 20 years the work of Noon and Freeman. Millspaugh (1854–1923) was trained in homeopathy at the New York College, graduated in 1881, and practiced medicine for 9 years (Fig. 10.5). The first two cases were treated in 1884, when Millspaugh was working on *Millspaugh's Medical Plants*. Four more patients were reported in the *Homeopathic Recorder* (a journal of which Millspaugh was an editor) in 1889. The cures were remarkable and long-lasting. Thus, as noted by Dewey, "The first suggestion that ambrosia artemesiafolia [sic] might prove a remedy of value for in hay fever comes from a homeopathic physician" [29]. Around 1890, Millspaugh gave up medical practice for a career in botany and became one of the country's most distinguished botanists. His 1887 publication, *American Medicinal Plants*, has been referred to as "one of the monumental works in its line" [30]. Millspaugh spent a brief 3 years as professor of botany at the University of West Virginia, yet bequeathed an enduring legacy with its herbarium and his botanical survey of that state. From 1894 until his death, he was the Curator of Botany the Field Museum of Natural History in Chicago, where he assembled a large collection of valuable materials that would eventually make the field a foremost center of taxonomic research. Many honors were bestowed upon Millspaugh, including the naming of some plants (the *Millspaughia* and *Neomillspaughia* genera), fellowship of the American Association for the Advancement of Sciences, and honorary fellowship of the Mexican and Brazilian colleges of medicine.

Fig. 10.5 Charles Millspaugh. Possibly the first to use low-dose treatment for pollen allergy. Source: Eve Watson Schutze (Image by permission. Author E.F. Sherr. By permission University of Chicago Press)

Of further importance is the more recent work by Reilly and colleagues at the Glasgow Homoeopathic Hospital. In a series of small, well-designed, and carefully conducted studies, they have affirmed the benefit of homeopathic pollen treatment or, more accurately, "isopathic" treatment, since the exact same substance that causes the disease is given to treat it. In summary, over the course of a 15-year period, Reilly's group has conducted four placebo-controlled double-blind trials of homeopathically prepared allergen at 30C vs. placebo for atopic disorders. In other words, the 30C potency ensured that no material trace of the original allergen was believed to be present. The 253 subjects in the four studies suffered, respectively, from hay fever (studies 1 and 2), asthma (study 3), and allergic rhinitis (study 4). Homeopathy proved superior to placebo in every study on some (but not all) outcome measures. Two conclusions can be drawn from this work, even conceding that the studies, as with all clinical trials, had their flaws. Firstly, they provide evidence of benefit for one type of homeopathy, isopathy (i.e., use of the toxin or "cause" of the illness), in the treatment of certain allergic states. Secondly, it is important that Reilly's group replicated their findings in several studies. Replication is a basic requirement of experimental therapeutics, and medical research does not always do well in reproducing positive findings [31]. In 2009, the reported success rate for promising new drugs in phase II (i.e., drugs that initially yielded positive results) was a low 18 % [32]. Although not all trials attempting to replicate Reilly's work have

yielded positive results [33], we may still be inclined to agree with Reilly's appraisal that his repeated positive findings are incompatible with the belief that ultramolecular isopathy is a placebo [34].

While the Reilly studies clearly provide no final answers, they keep the flame burning and pose intriguing questions concerning efficacy and mechanism of action of high-potency homeopathy, especially in relation to allergic disorders.

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