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Samuel Hahnemann (1755–1843), founder of the homeopathic school, began the systematic serial dilution and succussion of his medicines around 1814.¹ Since then the homeopathic materia medica has often been thought of as an elaborate collection of placebos, and it has long been known that placebo-controlled tests of homeopathy took place as early as the mid-1830s.² A likely origin for this development in the history of clinical evaluation can be found in reports of two linked hospital-based trials of homeopathy that took place in Russia a few years earlier.

The homeopath in both trials was a Dr Herrmann, who received a 1-year contract in February 1829 to test homeopathy with the Russian military.³ The first study took place at the Military Hospital in the market town of Tulzyn, in the province of Podolya, Ukraine.⁴ At the end of 3 months, 164 patients had been admitted, 123 pronounced cured, 18 were convalescing, 18 still sick, and six had died. The homeopathic ward received many gravely ill patients, and the small number of deaths was shown at autopsy to be due to advanced gross pathologies. The results were interesting enough for the Russian government to order Herrmann to the Regional Military Hospital at St Petersburg to take part in a larger trial, supervised by a Dr Gigler. Patients were admitted to an experimental homeopathic ward, for treatment by Herrmann, and comparisons were made with the success rate in the allopathic wards, as happened in Tulzyn. The novelty was Gigler's inclusion of a 'no treatment' ward where patients were not subject to conventional drugging and bleeding, or homeopathic dosing. The untreated patients benefited from baths, tisanes, good nutrition and rest, but also:

'During this period, the patients were additionally subjects of an innocent deception. In order to deflect the suspicion that they were not being given any medicine, they were prescribed pills made of white

breadcrumbs or cocoa, lactose powder or saleg infusions, as happened in the homeopathic ward.'³ (page 415)

The 'no treatment' patients, in fact, did better than those in both the allopathic and homeopathic wards. The trial had important implications not just for homeopathy but also for the excessive allopathic drugging and bleeding that was prevalent. As a result of the report, homeopathy was banned in Russia for some years, although allopathy was not.

Within a couple of years of publication, placebo drugs became fashionable in clinical evaluation, sometimes in comparison with homeopathy, sometimes on their own, later as controls for allopathic treatments. A well-known opponent of homeopathy, Carl von Seidlitz, witnessed the St Petersburg trial and wrote a hostile report.⁵ He then conducted a homeopathic drug test in February 1834 at the Naval Hospital in the same city in which healthy nursing staff received homeopathically-prepared vegetable charcoal or placebo in a single-blind cross-over design.⁶ Within a few months, Armand Trousseau and colleagues were giving placebo pills to their Parisian patients; perhaps in the belief that they were testing homeopathy, and fully aware they were testing a placebo response.^{7,8} A placebo-controlled homeopathic proving took place in Nuremberg in 1835 and even included a primitive form of random assignment—identical vials of active and placebo treatment were shuffled before distribution.⁹ Around the same time in England, Sir John Forbes treated a diarrhoea outbreak after dividing his patients into two groups: half received allopathic 'treatment as usual' and half got bread pills. He saw no difference in outcome, and when he reported the experiment in 1846 he added that the placebos could just as easily have been homeopathic tablets.¹⁰ In 1861, a French doctor gave placebo pills to patients with neurotic symptoms, and his attitude is representative: he called the placebo 'orthodox homeopathy', because, as he said, 'Bread pills or globules of Aconitum 30c or 40c amount to the same thing'.¹¹

The interest in substituting placebos for active drug treatments in clinical evaluation from the 1830s onwards is well known. However, the extract from the St Petersburg report quoted above hints at a more complex story. Apparently, 'no treatment' patients received placebos, 'as happened in the homeopathic ward'. This mystifying phrase

is not explained or mentioned again. Why did the homeopathic patients receive placebo, when homeopathy was being tested?

The answer can be found in Herrmann's report of his earlier trial.⁴ The Tulzyn patients were hard-bitten Russian soldiers, who expected 'heroic' drugging and bleeding. We are told they lacked confidence in the innocuous homeopathic powders and their scepticism was not reduced by the doses of unmedicated lactose Herrmann prescribed in between the single doses of active medicine. In using placebos as part of day-to-day homeopathic practice, Herrmann was following Hahnemann's guidelines published between 1810 and 1830. Homeopaths were expected to prescribe placebo as a wash-out when discontinuing allopathic medication, and at the beginning of homeopathic treatment, to identify 'placebo responders'. It was also frequently used in longer-term case management, because the single rarely-repeated doses of active medicines used in homeopathy were believed to produce misleading psychosomatic responses.¹²

This little-known aspect of homeopathic practice has been passed down in some form or other as part of formal training in the discipline until the present day. A detailed history of placebos in homeopathic clinical evaluation and practice can be found elsewhere.¹³ Methodologically, Hahnemann's guidelines seem closest to modern trials to determine optimal therapy in single patients,¹⁴ although homeopaths gave placebos single-blind, and without randomization of treatment periods. Whatever we may think of it now, the practice contrasts strongly with the traditional palliative use of therapeutic placebos when active treatments were unavailable or ineffective, and with the all-or-nothing placebos in parallel-group clinical trials, where patients typically receive either placebo or active treatment, but not usually both. The St Petersburg trial is probably the moment that homeopathic within-treatment placebos began to be used as external controls, as became the norm in clinical trials more than a century later.

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