The mustard gas experiments done by the British Homoeopathic Society for the Ministry of Home Security, 1941–1942

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Introduction

Following its military use during World War I, mustard gas was found to be not only a skin irritant, causing the well-known signs of blistering and conjunctivitis, but also a powerful cytotoxin that could compromise immune function by attacking blood-cell production in the bone marrow.\textsuperscript{1,2} The renewed threat of chemical attacks in the early years of World War II meant that research into prevention and treatment of mustard gas lesions assumed a high priority in the UK.

The Ministry of Home Security asked homeopaths if they had any scientific evidence that homeopathic mustard gas ‘potencies’ could prevent or act as antidotes to the effects of the poison. In reply, the Council of the British Homoeopathic Society regretted that there was no scientific evidence of efficacy, but informed the Ministry that homeopathic physicians were calling for ‘gas potencies’ to be prepared for use in the event of a gas attack. The Council’s reply to the Ministry included a research proposal for trials if the Government provided support.

The homeopaths’ decision to propose controlled trials appears to have been influenced by the Society’s President, John Paterson. He had been active in homeopathic clinical research in Glasgow,\textsuperscript{3,4} and he was confident that homeopathy would survive testing, despite the concern of some members of the Council that ‘negative’ results might jeopardise homeopathy’s position in the projected National Health Service.\textsuperscript{5} After receiving comments on the proposal from its scientific advisors, the Ministry agreed to co-operate, and the Society set up a ‘Gas Research Committee’, headed by Paterson and W. Lees Templeton, to coordinate the work of teams in Glasgow and London.

Homeopathic (Greek \textit{homoios}, similar) medicines are usually prepared from natural substances that provoke symptoms in healthy people like those seen in disease. For the intense itching, blistering and sores caused by mustard gas, a homeopath might prescribe poison oak (\textit{Rhus toxicodendron}) or Spanish fly (\textit{Cantharides}), for example. Another homeopathic approach, known as isopathy (Greek \textit{isos}, same), treats the effects of a poison or other substance with the same substance in dilution. Both approaches were used in the mustard gas trials.

As directed by the Ministry, the trials were done under carefully controlled conditions.\textsuperscript{6} The use of unbiased allocation to comparison groups, placebos to blind volunteers and those assessing the effects of treatment, and independent statistical analysis were all rare in the early 1940s. It is unclear whether these features of the studies resulted from the Ministry’s scientific advisers or from Paterson. The Ministry supplied a 10% solution of mustard gas in benzene, a 2-mm diameter drop to be applied to each volunteer’s forearm. Preparation of the skin, the area affected, surgical dressings and room temperature were all standardised. The outcome measured in all the trials was the visual assessment of lesions seven days after application.

The Glasgow trials

The experiments in Glasgow used blocked allocation to either isopathic potency or control. Coded vials of tablets were laid out on a table containing either Mustard gas 30 c (that is, the 30th centesimal potency, prepared by the London Homoeopathic Laboratories from the Ministry’s solution) or an identical placebo. After signing consent forms, male volunteers from the Ralston District Home Guard arranged themselves into pairs matched approximately by age and physique. One from each matched pair of volunteers then chose any vial, and the other member of the pair took a vial with a serial number either directly above or below the first vial chosen. This implies that alternation to potency or control had been used to assign serial numbers to the vials.
Immediately after a volunteer had swallowed his first dose from his assigned vial, a drop of mustard gas solution was applied to his forearm. All participants received a four-week clinical diary to record the state of the blister and subsequent stages, and a photograph was taken on day 7. These records were used to categorise the lesions as either superficial (skin intact) or deep (breach of surface).

Paterson reported that the first 12 cases showed no deep lesions in the treatment group, and no superficial lesions in the placebo group. A further 28 volunteers were then tested. No matching was attempted and no account of the allocation procedure was reported. Among these 28 volunteers, 12 superficial and two deep lesions were seen after isopathic potency compared with two superficial and 12 deep lesions after placebo.

The Ministry suggested retesting the same volunteers after the lesions had healed, so 13 of them took part in a further experiment approximately four weeks later. The method of allocation to isopathic potency or placebo was not clear in the report, and the analysis difficult to interpret. The Committee thought the Glasgow trials showed promise, but the Ministry regarded them as ‘inconclusive and hardly worth consideration’.

The London trials

Undeterred by the Ministry’s response, the committee went ahead with larger trials at the London Homoeopathic Hospital, directed by Templeton. Volunteers for the trials came at first from the Missionary School of Medicine and then from the general public. One hundred and thirty-nine of them were assigned to take one of several reputed homeopathic burns medicines (Rhus toxicodendron, Kali bichromicum, Opium and Cantharides), or Mustard gas 30c, after exposure. Details of the method of assignment to treatment or placebo control are not reported, but the dispensing pharmacists who prepared the medicines concealed the allocation code until after outcome measurements had been completed. A second series of 101 cases tested Variolinum 30c and Rhus-tox 30c taken after exposure, as well as Mustard gas 30c and Rhus-tox 30c given 14 days before exposure. Altogether there were 127 medicated cases versus 113 controls, which suggests that blocked allocation was not used in London.

Precautions against unblinding were more stringent than they had been in Glasgow. Two medical observers, blind to treatment allocation, inspected and graded each lesion on a three-point scale of superficial, medium or deep, and excluded cases if they could not agree on the depth of lesion.

The results of the London studies were sent for independent analysis to the Scientific Computing Service Ltd., which analysed each medicine versus control separately, as well as the combined total of 240 cases. A report signed by HO Hartley concluded that ‘all potencies taken together provide a sample of sufficient size to detect any beneficial effects and the verdict of the statistical test, known as a chi-square test of significance, is that there is certainly an indication of a beneficial effects of the drugs in general—there is a definite shift of frequency towards the group “Medium” and “Superficial”, whilst in the controlled (sic) group, frequencies are pretty even. This shift in frequency is tested by the chi-square test’. This yielded a value of 8.44, which was statistically significant.

Forty years later a statistician and a homeopathic researcher looked again at the statistics, analysing the total of 40 Glasgow cases for the first time. They concluded that the differences between isopathic potency and placebo in favour of the former were very unlikely to have been due to chance. As far as the experiments in London were concerned, they commented that use of the chi-square test was unsuitable for analysing the small numbers in some of the many subgroups, and that a single larger placebo group would have been more efficient.

Discussion

When the London data were submitted to the Ministry in 1942, it had already dismissed the Glasgow trials. The homeopaths were still waiting for the government to respond when they published the final report as a supplement to the May 1943 issue of the British Homoeopathic Journal. When pressed, the Ministry rejected the London results on the grounds that the experimental technique must have been flawed. This was despite the design including the use of placebo controls, blind outcome assessment and independent statistical testing.

It is probably futile to speculate why the government asked for evidence, co-operated in obtaining it, but then rejected it. The pressures of war or staff changes might have contributed. Medical advisers might have been concerned about the professional repercussions of collaboration with homeopaths. Statisticians might have thought trials needed many more cases to achieve reliable conclusions. Whatever the reasons, some of the methodological safeguards adopted in the homeopathic mustard gas trials would gradually become expected features of trial design over subsequent decades.
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