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Dean ME. The homeopathic mustard gas trials of 1941–42

Commentary on: British Homoeopathic Society (1943). Report on mustard gas experiments (Glasgow and London). *British Homoeopathic Journal* 33: 1–12.

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Following its military use during the First World War, 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 able to compromise immune functioning by attacking blood-cell production in the bone-marrow (Kurmbahaar 1919). The renewed threat of chemical attacks in the early years of the Second World War meant that research into methods of prevention and treatment of mustard gas lesions assumed a high priority in the UK.

As part of the research effort, homeopathic clinicians collaborated with the Ministry of Home Security in a series of clinical trials at the homeopathic hospitals in Glasgow and London in 1941–42. Homeopathic (Greek *homios*, similar) medicines are usually prepared from natural substances that can produce a clinical analogue of the presenting symptoms. For the intense itching, blistering and sores caused by mustard gas, a homeopath might prescribe poison oak (*Rhus toxicodendron*) or Spanish fly (*Cantharides*). Another homeopathic approach, known as isopathy (Greek *isos*, same), involves medicines prepared from the same causal agent that they are used to treat. Both methods were used in the mustard gas trials.

The trials took place under carefully controlled conditions. The Ministry supplied a 10% solution of mustard gas in benzene, a 2 mm drop of the solution to be applied to each volunteer's forearm. Preparation of the skin, area affected, surgical dressings, and room temperature were all standardized, as were the age, sex and physique of the participants as far as possible. The outcome measured in all the trials was the visual assessment of lesions 7 days after application.

The isopathic experiments in Glasgow used a simple method of blocked randomization. Coded vials of tablets were laid out on a table, alternately containing Mustard gas in the 30th centesimal potency or an identical placebo. The first of each pair of volunteers (males from the Home Guard) was instructed to choose any vial, and the second then took any serial number immediately above or below the first. Immediately after swallowing the tablet, a drop of mustard gas solution was applied. Visual inspection and photographic records were used to categorize the lesions as either superficial (skin intact) or deep (breach of surface). According to the Medical Officer, the first 12 cases showed no deep lesions in the treatment group, and conversely no superficial lesions in the placebo group. However, the measurements of the skin lesions by the subjects themselves suggested that the Medical Officer may not have been blind (in only 4 of 6 pairs did the treated person have the smaller lesion). Further volunteers were tested, with similar results, although the report is unclear whether the tabulated 'summary of 28 cases' represents new cases or includes the original 12. Approximately 4 weeks later, 13 of the tested volunteers took part in a fresh experiment, also randomized and placebo-controlled. This led potentially to 4 groups: placebo–treatment, treatment–placebo, placebo–placebo, and treatment–treatment. The results seemed to confirm those found in the first series, and only superficial lesions were seen in the treatment–placebo group 5 weeks after receiving the preventive treatment. The editorial commentary that this was 'remarkable' seems optimistic however since there were only 3 cases.

The London trials took place soon afterwards, with the help of volunteers from the Missionary School of Medicine and the general public. Mustard gas and several reputed homeopathic burns treatments (*Rhus toxicodendron*, Kali

bichromicum, Opium, Variolinum and Cantharides), all 30c, were screened as potential treatments, given after volunteers were exposed to mustard gas solution. Although details of the randomization method are missing from the report, unequal numbers received treatment (127) or control (113) suggesting that simple pairing was not used. Precautions against unblinding were more stringent than in Glasgow. The dispensing pharmacists who prepared the medicines took no part in the experiments, and concealed the randomization code until after the experiments were completed. Two Medical Officers, blind to treatment allocation, visually inspected and graded each lesion on a 3-point scale of superficial, medium or deep, and excluded cases if they could not agree on the depth of lesion. The different outcome scale, and doubts about the reliability of the visual assessment in Glasgow, ensured only the London figures were included when H.O. Hartley of the Statistical Computing Service analysed the results for each medicine separately and for all groups combined. The combined analysis of 240 cases showed a statistically significant result favouring homeopathy ($X^2 = 8.44$). Mustard gas ($X^2 = 3.58$) and Rhus-tox ($X^2 = 5.24$) approached significance on their own, despite the small numbers involved (23 and 21 respectively).

A second London series retested Rhus-tox as a treatment, and also investigated the preventive effects of Mustard gas, Variolinum (smallpox nosode) and Rhus-tox given as prophylactics, 14 days before exposure. According to Hartley, the efficacy of Rhus-tox as a treatment was 'definitely established' ($X^2 = 7.04$), especially when the results from series 1 and 2 were combined ($X^2 = 11.78$), and the preventive efficacy of Mustard gas was 'confirmed' ($X^2 = 10.39$).

Forty years later, it was pointed out that the original analysis may have underestimated the efficacy of homeopathic Kali-bich in the first London series, because the placebo group in that experiment was untypical (Owen and Ives 1982). A single larger placebo group would have been a more efficient control increasing the number of participants available to be assigned to each of the test medicines. The pooling of results from separate medicines is also suspect. In spite of these weaknesses, the London mustard gas trials contained many of the methodological safeguards and requirements that would eventually be expected in clinical trials. These include concealed randomization to treatment or control, blinded dual evaluation of outcomes, and independent statistical testing.

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