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# James Crichton Browne and controlled evaluation of drug treatment for mental illness

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There are very few 19th-century examples of attempts to test treatments given to people with mental health problems. Indeed, the situation up until World War II has been described as ‘a world of desperate remedies. Then the attendant’s role was akin to a zookeeper’s: feeding, scrubbing, and forcibly treating hundreds of “demented” patients. The psychiatric workforce was largely cut off from surgical and physician colleagues, was of poor quality, and was readily mocked.’<sup>1</sup> There are a few exceptions to this general rule, however, and the 1872 report by James Crichton Browne (1840–1938) of the effects of conium for people with mania is one such example.<sup>2–4</sup>

Sir James Crichton Browne lived a long productive life during which he was not shy of confronting authorities, cultures and dogmas.<sup>5</sup> In 1866, not long after he qualified in medicine and at the young age of 25, he was made medical director of the West Riding Lunatic Asylum, Wakefield, Yorkshire, England. Crichton Browne improved the environment of the hospital, its record-keeping and academic culture, and he established laboratories for anatomy, neuropathology and histology, and for research using animals. The treatments given under his supervision avoided use of restraint, but employed diversion and occupational therapy as well as many neuroactive drugs, often after Crichton Browne had tested them on himself.<sup>6</sup>

Crichton Browne founded two journals – *Medical Reports* and *Brain*, a journal that quickly attracted international interest and continues today as a leading journal in neurology. *Medical Reports* (1871–1876) commented on a wide range of neuropsychiatric topics. For example, clinical photography, a research technique which had been pioneered by Crichton Browne, was described in the journal and was warmly acknowledged by Charles Darwin

in 1872. Jellinek<sup>6</sup> has noted that the six volumes of *Medical Reports* contained ‘optimistic but unconvincing papers’ on treatment trials by juniors, on madness, depression, organic brain disease and epilepsy, with drugs (some parenterally) and agents then known to have some effect on the nervous system – alcohol, morphine, cannabis, hyoscine, ergot, conia, nicotine, chloral, ether, nitrous oxide, and electricity, all recorded as inspired by Crichton Browne.<sup>6</sup>

Conium was the drug featured in Crichton Browne’s 1872 paper in *The Lancet*. It is a genus of two species of flowering plants, by far the most familiar of which – and most likely the one used by Crichton Browne – is *Conium maculatum* (Hemlock or Poison Hemlock). It contains alkaloids, the most toxic of which is coniine. This causes death by blocking neuromuscular junctions in a similar way to curare. Ingestion of Poison Hemlock in any quantity can result in respiratory collapse and death – as the ancient Greeks knew well.<sup>7</sup> Nevertheless, Poison Hemlock had been used by physicians of ancient Greece and Persia for sedation, for its antispasmodic properties, and for arthritis.<sup>8</sup>

Crichton Browne’s *Lancet* article on conium was published in three separate issues,<sup>2–4</sup> and uses most of its 75 column inches to express contrary opinions to those of Henry Maudsley, Crichton Browne’s predecessor at the Wakefield Asylum and pioneer of British psychiatric care. Maudsley had suggested that recovery of people with mania may be retarded by use of sedatives and that putting ‘nerve-cells of the patient’s brain into chemical restraint’ ... ‘does not really benefit them’. Crichton Browne disagreed. To support his argument he reports a study undertaken in 1870–1871.

Twelve consecutive people with mania were treated with remedies such as bromide of potassium,

*cannabis indica*, chloral and digitalis. These people were 'recovered and discharged' after an average duration of hospital stay of 150 days. Twelve more people with mania were then consecutively treated with conium, and their stay averaged only 102 days. From the brief clinical descriptions of 10 of these people, they could well have been suffering from what would be diagnosed today as bipolar affective disorder, currently mania or hypomania, although some may have had organic co-morbidity. Crichton Browne noted the considerable difference in duration of stay compared with the earlier series; stated that use of conium was the cause; and suggested that early intervention with conium might even decrease the need for admission to the asylum. At the end of the paper, he expresses a wish to have an opportunity to describe the results of treating 'certain mental diseases' with a combination of conium and opium/hyoscyamus.

It is possible that conium may indeed be of value for people with bipolar disorder who are currently manic: it has been used for people with psychiatric problems for hundreds of years.<sup>9–11</sup> However, Crichton Browne's study is a long way from proving this, and it must be remembered that conium is potentially lethal. The difference between a 'therapeutic' and toxic dose is very slight.<sup>10</sup> Judged by today's standards, Crichton Browne's evaluation of conium has many methodological problems. The comparison groups were not randomized and there is no suggestion of how selection bias might have been avoided. Decisions about length of hospital stay could have been prey to observer bias (it seems unlikely that Crichton Browne was disinterested in the findings). Even though the periods in hospital did seem different, with such a small study is possible that there was no statistically significant difference between the

two averages (especially if data had been skewed, as seems likely). Even if the difference between the comparison groups had been statistically significant, it could still have been due to chance, or have been 'cherry-picked' from the many analyses that had been undertaken by Crichton Browne and his team. In other words, they invited replication.

All that said, *The Lancet* paper does show that Crichton Browne was forward-thinking. He argued for drug treatment of mania and used a control group in his assessment of conium. He used 'real-world' outcomes, understandable to this day; and he conceptualized early-intervention and preventative treatment in the community – all signs that he was attempting to move psychiatry towards fairer means of evaluating its treatments.

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