

How psychiatry was revolutionised by a treatment discovered in a shed

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In 1949, an Australian doctor discovered that lithium was an effective treatment against bipolar disease. But it almost went forgotten.

[BASIC RESEARCH](#)[6]

Today, bipolar sufferers are commonly treated with lithium, but this was not always the case.

In 1949, an Australian scientist John Cade, made a breakthrough in the development of lithium as a psychiatric treatment, which was not a recognised treatment at the time.

His discovery was published in a little known scientific journal and was almost forgotten, until the Danish scientist Mogens Schou took the case up and introduced the treatment into psychiatry.

The treatment is estimated to have saved 145 billion US dollars between 1970 and 1994 in the USA.

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Inspiration from Prisoners of War

The story begins in the 1920s when John Cade was just a young man. He was a medical consultant, and he and his brother Frank spent many hours in psychiatric departments.

The time spent among patients, gave Cade a strong understanding of mental diseases, writes WHO in a series dedicated to breakthroughs in health sciences.

Cade graduated as a doctor from the University of Melbourne at the age of 21. He got married and started a family. When the Second World War broke out, he donned his uniform and went to war.

He was promoted to major in September 1941, but soon became a prisoner of war (POW) when Singapore fell to Japan.

For three years, he lived as a POW in the Changi POW camp in Singapore and noticed that many of his fellow inmates were showing signs of psychological illness.

Many of them alternated between mania and depression, but showed no fixed pattern.

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Mental instability possibly due to poison

Cade suspected that this alternation in mental state was caused by a chemical imbalance, writes Joseph A. Schwarcz in the book “The Fly in the Ointment: 70 Fascinating Commentaries on the Science of Everyday Life.”

This led him to speculate that there could be a chemical explanation to explain the inmates alternating mental state.

Cade supposed that poison may have affected the brain and would be discharged in the sufferer’s urine.

After the war, he returned home to Australia and began to investigate his hypothesis.

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Experimented with urine and guinea pigs at home

Cade got a job at a psychiatric hospital in Melbourne. His continued curiosity in basic research led him to start experimenting to understand psychiatric diseases.

He conducted his research in his shed. But this did not hinder his ground breaking discovery.

He injected urea from patients suffering episodes of mania, schizophrenia, and melancholy, as well as that from healthy people, into guinea pigs to investigate the pharmacological effects of various toxins.

He discovered that urea from manic patients was much more lethal in small doses than urea from any of the other patients.

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Break through was pure luck

Cade’s discovery of the effect of lithium on people suffering with mania was described by many as pure coincidence.

But this criticism is misplaced, say Philip Mitchell and Dusan Hadzi-Pavlovic, authors of the WHO’s report into the history of lithium treatment.

“Such comments do not, however, acknowledge that many significant discoveries arise from keen, curious minds recognising the importance of unexpected observations during systematic research,” they write.

Cade initially mixed lithium in liquid with uric acid from the manic patients to enhance the effect in guinea pigs. Cade expected that lithium would increase the toxic effect.

But then the opposite happened. Lithium actually had a protective effect.

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Cade tested on himself

The results gave Cade faith that lithium could have a beneficial effect on patients suffering from mania, but before he could test it on people, he first had to make sure that it was safe.

So he tested it on himself in low doses, which was lucky as we know today that it can indeed be harmful at

high doses.

“Lithium treatment has a narrow therapeutic window. Take too little and it has no effect. But at blood concentrations above the therapeutic window, it has significant side effects and in the worst case you could die,” says Raben Rosenberg, head of clinic at the Amager Psychiatric Centre, Denmark.

“It’s really lucky that Cade found the successful dose first time round,” he says.

Cade then tested it on ten patients. The first to be tested was one of the most challenging patients in the hospital. But three weeks into the trial, he was calmer. And after 12 weeks, he was ready to be discharged from the hospital.

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All the odds were against lithium

Today, we know that the treatment of manic patients with lithium has saved thousands of families and patients from suffering, and in the US alone it has saved 145 billion dollars between 1970 and 1994, according to an article in Science in 1994.

But the discovery very nearly didn’t reach patients at all.

In 1949, when Cade first published his results in a scientific journal, lithium was suspected of causing death in patients suffering from heart conditions. Cade himself was not well-known in the scientific community and his results were published in a little known journal.

Most importantly, lithium was a basic element with no commercial interest in developing it as a form of treatment.

The odds were stacked against the discovery and it was in danger of slipping into oblivion.

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Danish scientists save discovery from obscurity

Luckily, the discovery was picked up by Erik Strömngren, a professor in psychiatry from Aarhus University, Denmark.

“Erik Stömngren was versatile and curious, but it’s lucky that he read Cade’s article and was made aware of lithium,” says Rosenberg.

Stömngren urged his younger colleague Schou to investigate Cade’s results. It turned out to be a crucial decision.

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International opposition to lithium treatment

Initially, there was great skepticism about the use of lithium treatments, especially in England.

“I am astonished that this young doctor was able to withstand the pressures from leading psychiatrists and continued his research on lithium,” says Rosenberg.

Instead of giving up, Schou ignored the critics and worked tirelessly to convince them of lithium's effectiveness through controlled clinical trials.

“Schou also made a huge effort to publicise the lithium research. He travelled tirelessly around the world to attend conferences. Gradually it began to have an effect,” says Rosenberg.

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Danish efforts were vital

Rosenberg has no doubt about the importance of this early basic and clinical research.

“If Strömngren had not read Cade's article, and Schou hadn't been so persistent and thorough in his work, lithium would never have been used as a psychiatric drug. It was an outstanding effort,” he says.

As a result of Schou's research, lithium ended up being approved for treatment in the US.

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International honours for Schou

The treatment was recognised throughout the world and Schou was widely recognised for his work.

“He received pretty much all the honours that you can in psychiatry. He more or less only lacks the Nobel Prize before he has received all the major awards. It was a great discovery,” says Rosenberg.

Cade's role in the discovery was also recognised on numerous occasions.

Cade and Schou received a large international research prize for their work on lithium treatment in 1974.

Several hospitals in Australia were named after Cade, following his death. And in 1980, Schou held the first Cade Memorial Lecture.

Schou remained an active researcher until his death in 2005.

Aarhus University's obituary, for Schou described how he presented research at a conference just days before his death. He was 86 years.

[Read the Danish version of this article on Videnskab.dk](#) [16]

 [A Danish psychiatrist played a crucial role in the development of lithium to treat bipolar disorders.](#)

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 [John Cade was inspired to work with mental illnesses during his three years as a prisoner of war.](#)

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 [The odds were stacked against John Cade's discovery.](#) [\(Photo: Shutterstock\)](#) [19]

 [A Danish psychiatrist played a crucial role in the development of lithium to treat bipolar disorders.](#)

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