

Johan Schioldann: History of the Introduction of Lithium into  
Medicine and Psychiatry  
Birth of modern psychopharmacology 1949

**Part II**

**Renaissance of lithium therapy. Birth of modern psychopharmacology 1949**

**Chapter 24. Cade's first lithium patient, W.B.:  
a paradigm of lithium therapy**

Cade recorded his observations on ten manic patients on system case cards, later deposited by his wife in the Medical Museum of the University of Melbourne.<sup>1021</sup> The 1949 paper contains edited case vignettes of each of these patients, and some information is contained in their respective case files.

According to these documents, Cade conducted his clinical trial between 29 March 1948 and 11 February 1949.<sup>1022</sup> The last date recorded in the 1949 paper was March 4, 1949 (case 9). However, it cannot be established when he submitted his paper to the Medical Journal of Australia, or for that matter his equally important paper from 1947, as the Journal does not hold editorial records relating to that time.<sup>1023</sup>

Cade's description of the first manic patient to receive lithium, W.B., epitomises its striking anti-manic effect as well as its toxic properties.

In 1983 (and 1999) Brian Davies of Melbourne published W.B.'s case history based on his original medical record.<sup>1024</sup> Johnson also included parts of it in his book.<sup>1025</sup> However, the present author has not been able to retrieve this record, whereas the medical records of the other patients have been sighted.<sup>1026</sup>

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<sup>1021</sup> MHM00985 Card: original record cards of lithium treatment by John Cade, 1948-1950 (17 items), MHM00986 Card: original record cards of J. Cade's guinea pig experiments, c. 1950 (4 items): 'no details of his experiments with lithium salts are on the cards'.

<sup>1022</sup> Cade, 1949 & Case Cards.

<sup>1023</sup> 'Medical Journal of Australia', Joanne Elliot, personal communication, 5.5.2004.

<sup>1024</sup> Davies B.: 'The first patient to receive lithium'. Aust. NZ. J. Psychiatr. 1983;17:366-8, reprinted *ibid.* 1999;33, Suppl.:S32-34. Haigh G.: 'Matter over Mind'. The Bulletin (Australia) December 21, 2004–January 11, 2005:91–95.

<sup>1025</sup> Johnson, *op. cit.*, 1984:37–41, 1999:217–219.

<sup>1026</sup> The present author, in October 2000, had access to the original case files held by Archival Services, Department of Human Services, Victoria, Australia (Mrs Brenda Le Grand, Mrs Carolyn Stephens)—a 'reception file' on W.B. was retrieved but not his case file proper.

W.B., born in 1899, had a history of manic-depressive illness from 1916, and over the years required several admissions to psychiatric hospitals for mania (though in 1934 he was hospitalised for ‘melancholic depression’). In 1943 he was admitted to Bundoora Psychiatric Hospital at Melbourne, in a state of mania. He remained under the auspices of this hospital until his death in May 1950.

From Davies’s article it can be inferred that the first case file entry by Cade was made on 24 February 1946, ‘as were all subsequent notes’.<sup>1027</sup> Cade, returning from convalescence after his captivity at Changi, had commenced duties at the Bundoora Hospital the month before.

The first case file entry, 24 February 1946, notes that W.B.’s mental state has remained unchanged over the last two years. He is chronically euphoric: excitable, restless and has no power of concentration whatever; so lacking even momentary attention that questions usually fail to interrupt his flight of ideas. He is dirty and destructive; noisy both day and night. A rubbish gatherer and petty pilferer. Frequently impulsive [...]

On physical examination he appeared ‘in good physical health’. One month later, ‘the mental state has not improved’. Therefore, on 29 April 1946 W.B. was given a course of electroconvulsive treatment. One month later, Cade recorded that W.B.

‘has had nine ECT treatments. Remarkable improvement’—he ‘is now quiet, clean and tidy in his appearance, well behaved and an excellent and willing worker, contrasting strongly with his previous restless, destructive, interfering state a few weeks ago’.

The patient was then sent on leave for several months. However, by September 1946 he had relapsed. He became ‘euphoric, restless, destructible and [showing] flight of ideas’. Therefore, on 27 September 1946 he had another course of five ECT treatments. One month later (no date given) Cade recorded that ‘[W. B.] seems to have reached his mental optimum with this sort of treatment’, ‘but [he is] still rather uncertain and lacking in judgement’. One month later (no date given) Cade recorded that W. B. ‘has been slowly deteriorating, becoming more restless, untidy and erratic’. Over the next two months no improvement occurred. In December 1947 Cade recorded that W.B. had been ‘in a state of chronic mania all this year’.

According to Cade’s *case card*, W.B. suffered from chronic mania of about 5 yrs duration. Fair but temporary improvement after ECT 2 years ago. Since Nov. 46 has completely reverted to his usual state—noisy, restless, untidy & mischievous. [undated]

Subsequently, according to Davies’s survey, W.B. *was commenced on lithium citrate* gr(ains) 10 t.d.s. [29 March 1948], after a few days increased to gr. 40 t.d.s. This was followed by Cade’s comment that ‘[W.B.] commenced to vomit with nocturnal

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<sup>1027</sup> cf. Johnson, 1984, op. cit., pp.40, 154.

enuresis but his mental state was improving. Dosage reduced and replaced with lithium carbonate gr. 5 b.d.' - the case card notes identical information:

W.B. act. 51.  
Chronic mania of about 5 yrs duration. Fair but temporary improvement after ECT. 2 yrs ago. Since W.B. has completely reverted to his usual state - noisy, restless, untidy & mischievous.  
29/3/48. Commenced lithium citrate mixture gr x tds after a few days increased to gr xx tds & then for a few days to gr ~~xx~~ xl tds - commenced to vomit & ep nocturnal enuresis. Mental state improving. Dosage reduced & still sensitive so discontinued & replaced with capsules of  $\text{Li}_2\text{CO}_3$  gr v. b.d.  
5/5/48. Has been in 17 ward for about 10 days, and after steadily settling down, now has appeared perfectly normal both to my observation & that of his relatives for over a week. Continues on  $\text{Li}_2\text{CO}_3$  gr v b.d. in capsules.  
14/5/48. Continues well. 20/5/48. Continues well.  
29/5/48. A little unsettled today. Discontented that he has not been able to go home (housing difficulty).  $\text{Li}_2\text{CO}_3$  incr. to gr x tds.  
30/5/48. Settled down again.  
3/6/48.  $\text{Li}_2\text{CO}_3$  reduced to gr v. tds. Well. 7/6/48. Well.

**Figure 13.** From John Cade's case cards with details of W.B., his first patient to receive lithium. Reproduced courtesy of the Medical History Museum, the University of Melbourne. Editor's note: image has been adjusted to remove patient's full name.

### Case file 1 May 1948

Remarkable improvement in the last four weeks. He now appears to be quite normal - a diffident, pleasant, energetic little man.

### Case card 5 May 1948

Has been in A ward for about 10 days and after steadily settling down, now has appeared perfectly normal both to my observation & that of his relatives for over a week. Continues on [lithium carbonate] gr V b.d. in capsules.

### Case cards, 14 May 1948 and 20 May 1948

Continues well.

### Case card 29 May 1948

'A little unsettled today. Discontented that he has not been able to go home (housing difficulty). [Lithium carbonate] incr[eased] to gr. x t.d.s.'. The following day 'settled down again'.

### Case card 3 June 1948

[Lithium carbonate] reduced to gr. v tds. Well.

*Case card 7 June 1948*

Well.

*Case card 9 June 1948*

[Lithium carbonate] incr. to gr. x tds.

*Case card 14 June 1948*

Very well. More self-confidence.

*Case card 25 June 1948*

[On Trial Leave] for week-end. Improved still further.

*Case card 29 June 1948*

Very well. [Lithium carbonate] reduced to gr. v tds.

*Case card 2 July 1948*

[On Trial Leave] 5 days.

*Case card 8 July 1948*

[Return from Trial Leave] —v[ery] well.

### **Case file 9 July 1948**

It was noted that the improvement had been maintained, and he was discharged on 'indefinite trial leave'.

*Case card, same day*

W.B. was to continue 'lithium carbonate gr. V tds'.

### **Case file 24 July**

It was reported that he was back at work (at his old firm), and was taking lithium carbonate gr. 5 b.d.

*Case card, same day*

Seen this A.M. V[ery] well.

### **Case file 11 September 1948**

It was recorded that he was 'very well mentally and continues at work'.

*Case card, same day*

Off colour for a few days [with] dyspepsia.

### **Case file 13 November 1948**

It was recorded that 'he was well and working but had stopped his lithium 6 weeks previously'.

*Case card, same day*

Seen today. Well. Working. Discontinued [lithium carbonate] about 6/52 ago. Some vomiting recently—put on mixt. by local M.O.—No trouble since. Has lost no wt. & sleeping extremely well. To report in 3/12.

### **Case file 24 November 1948**

The patient's son-in-law had written a letter informing Cade that W. B. had become excitable and argumentative after a trivial row.

*Case card, same day*

S. in law in letter states [W.B.] has become excitable & argumentative after trivial row last Sun[day] 21/11. Pt. written to, to come for interview on 27/11 & recommence [lithium carbonate].

### **Case file 29 November 1948**

Lithium restarted.

*Case card, same day*

Seen this A.M.—quiet & rational but a bit uneasy.

### **Case file 15 December 1948**

The patient did not take lithium carbonate regularly.

*Case card, same day*

S. in law writes—irritable, not taking med[ication] regularly.

### **Case file 30 January 1949**

The patient's 'relatives say that he has been irritable, sleepless and restless and they do not think he is taking his medication regularly, if at all'. On examination: 'he was not too bad. Rather garrulous, mild distractibility and flight of ideas, consequently his account of himself is unreliable. He was restarted on lithium carbonate gr. 10 t.d.s.'

*Case card, same day*

to have [lithium carbonate] gr. x [...] as from this evening.

**Case file 7 February 1949**

No improvement so far. Quite well behaved and not euphoric or restless, but erratic with flight of ideas.

*Case card, same day*

[Notes identical information].

*Case card 8 February 1949*

SI[ightly] euphoric, rather restless.

**Case file 12 February 1949**

He 'appears considerably more settled but there has been some retching. He is more settled and doing useful odd jobs'.

*Case card, same day*

[Notes identical information].

*Case card 13 February 1949*

More settled, useful odd jobs & messages.

**Case file 16 February 1949**

The patient was 'approximately normal and his lithium carbonate was reduced to gr. 5 t.d.s.'.

*Case card, same day*

[Notes identical information].

**Case file 18 February 1949**

He was 'normal again'.

*Case card, same day*

[Notes identical information].

**Case file 3 March 1949**

The patient 'continued well with occasional biliousness'.

*Case card, same day*

[Notes identical information] lithium carbonate reduced to gr. v b.d.

For comparison, Cade's *published* vignette of W.B. in his 1949 paper reads as follows:

W.B., a male, aged fifty-one years, who had been in a state of chronic manic excitement for five years, restless, dirty, destructive, mischievous and interfering, had long been regarded as the most troublesome patient in the ward. His response was highly gratifying. From the start of treatment on March 29, 1948, with lithium citrate he steadily settled down and in three weeks was enjoying the unaccustomed surroundings of the convalescent ward. As he had been ill so long and confined to a chronic ward, he found normal surroundings and liberty strange at first. Owing to this, as well as to housing difficulties and the necessity of determining a satisfactory maintenance dose, he was kept under observation for two months. He remained perfectly well and left hospital on July 9, 1948, on indefinite leave with instructions to take a maintenance dose of lithium carbonate, five grains twice a day. The carbonate had been substituted for the citrate as he had become intolerant of the latter, complaining of severe nausea. He was soon back working happily at his old job. However, he became more lackadaisical about his medicine and finally ceased taking it. His relatives reported that he had not had any for at least six weeks prior to readmission on January 30, 1949, and was becoming steadily more irritable and erratic. He ceased work just before Christmas. On readmission to hospital he was at once started on lithium carbonate, ten grains three times a day, and in a fortnight had again settled down to normal. The dose of carbonate was then reduced to five grains three times a day, and in a further two weeks to five grains twice a day. He is now (February 28, 1949) ready to return to home and work.

According to Johnson's summary of W.B.'s case file, in February 1950 he had required readmission, as over the preceding week he had developed temperature rise, dyspepsia, nocturnal vomiting, diarrhea and bradycardia. However, his mental state remained good - such that he could return to his hostel.

On 8 March 1950, according to his case card, W.B. was still experiencing 'dyspepsia, anorexia & vomiting. Still bradycardia', and 'He is becoming mentally unsettled tho[ugh] not yet euphoric, talking nonsense. Behaviour not yet erratic', Cade proceeding to write:

*Lithium discontinued.* Under all circumstances it seems that he would be better off as a care-free restless case of mania rather than the dyspeptic, frail, little man he looks on adequate lithium.

Subsequently, according to the case card on 28 March 1950, W.B. was 'rapidly reverting to his manic phase & forgetting his dyspepsia', and on 12 May 1950, being the last entry on the case card, W.B. 'has continued manic-restless, euphoric, noisy, dirty, mischievous, destructive, flight of ideas', and as 'this state seems as much a menace to life as any possible toxic effects of Li.: recommenced Li cit[rate] gr xx tds today'.

Johnson's summary of the case file has that the treatment started to calm him almost immediately; but within a week (by 19 May 1950) lithium was ceased again as W.B. became semi-comatose and had three fits. On 22 May he was 'in extremis' and died the next day.

Cade recorded as the causes of death: i) toxæmia due to lithium salts, therapeutically administered, ii) inanition, iii) chronic mania.

The case was reported to the coroner. An inquiry was undertaken at the Coroner's Court, Melbourne, on 26 October 1950. However, this added no new information.<sup>1028</sup>

Years later (in 1967, 1978 and 1979), Cade returned to the case of W.B.<sup>1029</sup> as being 'the very first manic patient ever deliberately and successfully treated with lithium salt', although according to Cade, W.B.'s treatment had not been without difficulties. These difficulties were partly due to symptoms of lithium intoxication and partly non-compliance with the drug with consequent recrudescence of his manic symptoms. *Cade never published any account that W.B. actually died of lithium intoxication.*

In light of the above, it can be argued that it was even strongly misleading when Cade characterised W.B. as a 'successful' case of lithium therapy. However, in 1949 Cade had observed striking anti-manic effects of lithium, Mogens Schou writing to him on 16 March 1963: 'That publication of yours has, as you must know, meant a good deal to my professional life'. And by 1967 it would have been a completely legitimate assessment for Cade to make as then it was not only common knowledge that Schou (and his associates) had in 1954 provided irrefutable scientific proof of lithium's anti-manic effect, but at which time Schou and Baastrup were providing evidence that lithium also had a prophylactic effect in manic-depressive illness. Thus, Schou<sup>1030</sup> wrote to Cade on 19 July 1966:

It appears that there is at present a growing interest in lithium also in the United States and in Germany, and I expect this to increase further.

It is indeed a most interesting drug you have introduced into psychiatry. The more I learn about it, the more am I intrigued by it, and I should not be astonished if studies based on the observations with lithium would eventually lead to a real breakthrough in the control of manic-depressive psychosis.

Cade<sup>1031</sup> replied to Schou two weeks later, on 5 August:

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<sup>1028</sup> 'Proceedings of Inquest [W.B.]. No. 1405. 26th October 1950, Coroner's Court Melbourne', kindly placed at the author's disposal by the former State Coroner of South Australia, Mr Wayne Chivell. The record contains a deposition by John Cade, dated 26.10.1950 (as cause of death he recorded: 1. Toxaemia due to lithium salts therapeutically administered. 2. Inanition. 3. Chronic mania).

<sup>1029</sup> Cade JF.: 'Lithium in psychiatry: historical origins and present position'. Editorial. Aust. NZ. J. Psychiatr. 1967;61-62. Cade JF.: 'The story of lithium', in Ayd FJ, Blackwell B. (eds.): 'Discoveries in biological psychiatry'. Philadelphia: Lippincott, 1970. pp.218-229. Cade JF.: 'Lithium—past, present and future', in Johnson FN, Johnson S. (eds.): 'Lithium in medical practice'. Lancaster: MTP Press, 1978. pp.5-16. Cade JF.: 'Out of the ground—lithium', in his: 'Mending the Mind. A short history of twentieth century psychiatry'. Melbourne: Sun Books, 1979. pp.65-74.

<sup>1030</sup> Kindly placed at the author's disposal by Schou. Schou, personal communication 26.3.05. This letter was also printed in: Schou M.: 'Phases in the development of lithium treatment in psychiatry,' in Samson F, Adelman G (eds.): 'The neurosciences: paths of discovery II'. Boston. Basel. Berlin: Birkhäuser, 1992. pp. 149-166 (157).

<sup>1031</sup> Kindly placed at the author's disposal by Schou. Also printed in: Schou, 1992, op. cit., p.158.



What is most impressive is your demonstration that lithium is so effective in preventing relapses of depressive as well as manic phases. This was something about which I had never been sure until I read your paper

the latter being the manuscript for Baastrup's and Schou's article on lithium prophylaxis, published in 1967.<sup>1032</sup>

This might also explain why it was that Cade, in 1967, for the first time since 1949, apart from mentioning lithium in passing in 1962 and 1964, described his discovery of lithium in print. One instance of this is in the form of an editorial he wrote for the Australian and New Zealand Journal of Psychiatry (its inaugural volume), entitled *Lithium in psychiatry: historical origins and present position*.<sup>1033</sup>

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<sup>1032</sup> Baastrup PC, Schou M.: 'Lithium as a prophylactic agent. Its effect against recurrent depressions and manic-depressive psychosis'. Arch. Gen. Psychiatr. 1967;16:162–172.

<sup>1033</sup> op. cit., 1967;1:61–62. cf. Cade JF.: 'The metabolism of melancholia'. ibid. 1967;1:23–29 (submitted 18 Aug. 1966).