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Obituary

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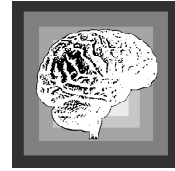
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Obituary

Mogens Abelin Schou (1918–2005) – half a century with lithium

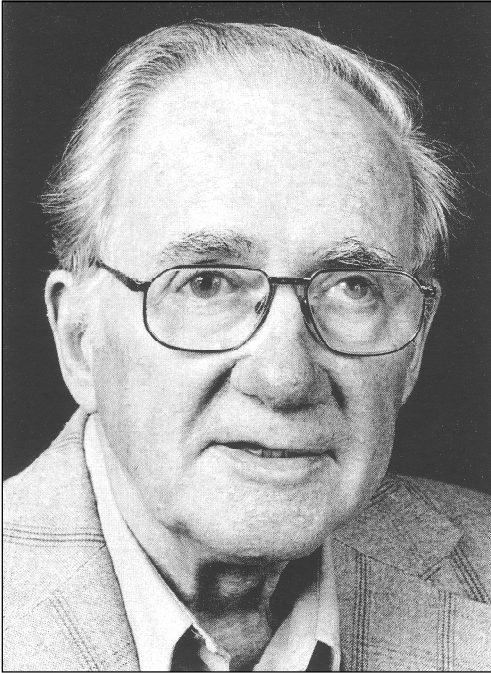
JOHAN SCHIOLDANN*

Mogens Schou, the most prominent of the pioneers of modern lithium therapy, passed away on 29 September 2005. He was 86 years old. A couple of days before, he had returned home from an IGSLI (International Group for the Study of Lithium-Treated Patients) meeting in Poland. He succumbed to pneumonia, having managed to finish a last manuscript just hours before.

Schou was born in Copenhagen in 1918. His father, Hans Jacob Schou, an influential figure in Danish psychiatry, adopted the notion of a biological basis of affective disorders from his countryman, Carl Lange, one of the early era lithium pioneers (Schioldann, 2001), and established a research laboratory to study the possible biochemical and physiological changes in manic-depressive illness (Schou, 2005). This interest was also driven by the occurrence of manic-depressive illness in the Schou family. *Mirabile dictu*, Mogens Schou (1989), in his own words, 'chose to study medicine with a specific view to do research on manic-depressive illness'. He graduated in medicine from the University of Copenhagen in 1944, and after some years in clinical psychiatry he studied experimental biology under Herman Kalckar (Copenhagen), and under Heinrich Waelsch (New York), a pioneer of neurochemistry. Also, Rolf Gjessing (Norway), known for his work on periodical catatonia, and his countryman, the famous Erik Strömngren (Risskov; see Schioldann & Sand Strömngren, 1996), should be counted among his early mentors.

Eventually, in 1951 Strömngren drew the attention of his 'brilliant' research assistant, Schou (Johnson, 1984), to the Australian publications on the

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MOGENS SCHOU

(photo given to the author by M. Schou)

antimanic action of lithium by John F. Cade (1949) and by C. H. Noack and E. M. Trautner (1951). However, Schou found these studies, although revolutionary, to be 'insufficiently stringent'. He therefore designed a protocol for a trial that was partly open, partly randomized and placebo-controlled. In fact, according to David Healy (1997), it was one of the first, if not the first, of its kind in psychopharmacology.

Together with Strömngren, Niels Juel-Nielsen and Holger Voldby, Schou now selected, treated and observed a cohort of manic patients, whom he had allocated randomly to lithium or placebo. The trial, published in 1954, fully confirmed Cade's revolutionary discovery (Schou *et al.*, 1954). As the lithium historian Neil F. Johnson wrote (1984): '[Schou's trial] was to prove a major turning point, not

only in the fortunes of lithium therapy, but twentieth-century psychiatry as a whole: it heralded, in fact, the second era of lithium in medicine.' The antimanic effect of lithium therapy had become evidence-based.

Intriguingly, Eliot Slater, then an assistant editor of *Journal of Mental Science* (now *British Journal of Psychiatry*) had assessed Schou's manuscript and suggested it be sent it to 'a more out-of-the-way journal', i.e., *Journal of Neurology, Neurosurgery and Psychiatry*, as he 'did not think much of this report about an unknown drug' (Healy, 1998).

Over the next decade, with never-abating energy and zeal Schou agitated internationally for the introduction of lithium in the treatment of mania – an uphill battle – assisted in this endeavour by Alec Coppen, Nathan Kline and Samuel Gershon.

Moreover, by 1964, independently of one another, G. P. Hartigan, Poul Chr. Baastrup and Schou had made sporadic observations which were suggestive of lithium also having *prophylactic* properties in manic-depressive illness (Schou, 2005). Subsequently, Baastrup and Schou followed up these fascinating observations in a non-blind lithium trial. They found the outcome so significant that they concluded that 'lithium is the first drug demonstrated as a clear-cut prophylactic agent against one of the major psychoses' (Baastrup

& Schou, 1967), and with great foresight Schou wrote to Cade (1966) that 'I should not be astonished if studies based on the observations with lithium would eventually lead to a real break-through in the control of manic-depressive psychosis'.

However, the 'Schou-Baastrup hypothesis' was met with great resistance by British psychiatry. Thus, to Aubrey Lewis and Michael Shepherd, lithium was 'dangerous nonsense' (Wilkinson, 1993). The ensuing 'battle of lithium' was waged in the international press, for and against 'the beleaguered Danes'. Shepherd, seconded by Harry Blackwell (Blackwell, 1969; Blackwell & Shepherd, 1967), called for controlled studies, as they found the prophylaxis hypothesis to be a 'therapeutic myth', which was based on 'serious methodological shortcomings' and 'spurious claims'. Even terms such as unethical and unscientific were used (Shepherd, 1970–71). In 1968, however, Baastrup and Schou had vigorously disputed the claims of their attackers.

The ethical issue rested heavily on Baastrup and Schou for, in their opinion, to deprive their patients of lithium prophylactic treatment would expose especially those with depression to increased safety risk and thus, in accordance with the Helsinki Declaration, be ethically indefensible. Finally, after painful consideration of this ethical dilemma, they fully confirmed their prophylaxis hypothesis with a double-blind trial of prospective-discontinuation design and with random allocation of manic-depressive patients (already on lithium) to lithium or placebo. This unique trial – according to Paul Grof (1998), 'unparalleled in psychiatry' – was published in *The Lancet* in 1970 (Baastrup, Poulsen, Schou, *et al.*, 1970). Many trials internationally and with various designs corroborated this revolutionary outcome. Thus, lithium prophylaxis had also become established as evidence-based. Lithium became the first-choice mood-stabilizer in bipolar affective disorder.

Shepherd did not comment on the trial directly, whereas Blackwell (1970) found that it had 'methodological inadequacies thus rendering the evidence unreliable', a criticism that was disputed by Schou (1970). That both Shepherd and Blackwell as late as 1985 remained unrepentant is illustrated by their very critical reviews of Neil F. Johnson's excellent *History of Lithium Therapy* (1984) (Blackwell, 1985; Shepherd, 1985). The tone was blunt. Blackwell, for his part, highlighted 'some personal motives' for Schou's 'resistance to placebo-controlled studies and his evangelical belief in lithium', namely 'a number of instances of manic-depression in Schou's family', including his brother who was being treated with 'maintenance lithium' and whose results appeared as a 'miracle' (Schou's expression) to the family, making Blackwell wonder whether 'this experience and attitude may also explain the somewhat sensitive (even paranoid) response to the opposition and criticism which developed towards lithium in the late sixties'. Claims of even the most distinguished scientists, Blackwell said, 'must be subjected to controlled scrutiny to eliminate bias especially when objectivity is compromised by clinical and ethical convictions derived from treating family members'.

Most intriguingly though, Strömngren later had the opportunity to ask Shepherd, whom he knew well, why he had continued this ‘unreasonable’ and ‘denigrating’ lithium controversy (Schioldann, 1999; Strömngren, 1992). In Strömngren’s words, Shepherd ‘quite openly’ conceded that the attacks were ‘simply due to the fact that English psychiatry under the reign of Aubrey Lewis did not distinguish between psychogenic and endogenous depression, and if lithium were to be recommended against depression, all doctors in England would use it against all types of depression with the result that many patients not in need of it would only suffer damage from it – therefore lithium must be ravaged with fire and sword.’

Finally, authorities on manic-depressive illness such as Fred Goodwin and Kay R. Jamison (1990) hailed the ground-breaking discovery of lithium prophylaxis as ‘one of the most important advances in modern psychiatry’.

Schou published approximately 540 works – papers, books and book chapters – on lithium and lithium therapy. Many international awards and honours were conferred on him, for example: the International Scientific Kitty Foundation Award (shared with Cade) in 1974; the John Cade Memorial Award in 1982; the Albert Lasker Clinical Medical Research Award (the so-called ‘little Nobel Prize’) in 1987; The International Society For Bipolars’ Mogens Schou Award For Distinguished Contributions (the first recipient) in 2001; the NARSAD Lifetime Achievement Award in 2004. He held several honorary doctorates (Aix-Marseille, Munich, Praha) and honorary fellowships. In 1988, with Bruno Müller-Oerlinghausen and Paul Grof, he initiated the aforementioned distinguished International Group for the Study of Lithium-Treated Patients (IGSLI), of which he was Honorary President. Moreover, he was Honorary Lifetime President of the International Society for Bipolar Disorders.

As Pierre Pichot wrote (1983): ‘It is probable that Cade’s discovery would have been forgotten but for the persistent and systematic research of Mogens Schou’. Very similarly, Healy (2000) expressed the opinion that ‘without Schou, there must really be a question mark as to whether lithium would have survived long after its rebirth in the 1950s’. But whether or not Healy will be proven right that ‘its use may well fade away when Schou dies’ is indeed an intriguing question. Just months before his death, Schou (2005), looking back over ‘My journey with lithium’, was pleased to note ‘a recent revival of interest in and use of lithium’

Mogens Schou, a highly gifted but very complex man, achieved the exceptional. Psychiatry, medicine and millions of manic-depressive persons have much to thank him for. As Johnson (1984) put it, he was ‘the driving force behind the modern use of lithium on a worldwide scale’, finally concluding that ‘he has been responsible, more than any other single individual for bringing about what Ronald Fieve (1975) has called “the third revolution in psychiatry” . . .’, i.e., the biochemical. Thus, Schou (together with Cade and Bastrup – the three fathers of modern lithium therapy) has

inscribed his name in the history of psychiatry and medicine (Johnson, 1984; Schioldann, 2001, 2005).

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