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a scientist, a doctor and a lithium champion

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Mogens Schou (1918-2005): a scientist, a doctor and a lithium champion.

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In November this year, we marked the 100th anniversary of the birthday of Mogens Schou, the great Danish clinical and basic scientist and a true giant of lithium research and treatment. Mogens Schou did more than anybody else in the world to establish lithium therapy, and without his assiduousness lithium may well have been forgotten. To commemorate his achievements a special symposium was organized in Copenhagen dedicated to lithium and the life time contributions of Mogens Schou. The celebration took place on November 23, 2018, the day before Mogens Schou's actual birthday. During the symposium, Janusz Rybakowski highlighted the scientific achievements of

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Mogens Schou, Marylou Selo focused on what he meant for patients. Gin Malhi evidenced lithium as the king of mood stabilizers. Rasmus Licht positioned lithium in the management of acute mania and Lars Kessing discussed the clinical use of lithium: why, when and for whom.

Mogens Schou was born in Copenhagen in 1918. His father, Hans Jacob Schou (1887-1952) was a reputed Danish psychiatrist, who is regarded by many as the organizational founder of modern Danish psychiatry. Schou senior served as the director of various psychiatric institutions from 1922 onwards. Mogens Schou's brother had manic-depressive illness.

Mogens Schou graduated with a degree in medicine from Copenhagen University in 1944, and then undertook training in clinical psychiatry, experimental biology, and neurochemistry. Although a qualified doctor, from 1951 until the end of his life he was associated with the Aarhus University Psychiatric Hospital in Risskov but served as the Head of the Psychopharmacology Research Unit from 1956-1988.

For more than half a century he immersed himself in research examining all aspects of lithium therapy. He conducted research of the highest quality, and among lithium researchers, Mogens Schou was undoubted "Primus Inter Pares". With his co-workers, he was the first to perform many pioneering and pivotal studies that informed clinical practice with invaluable clinical observations on lithium therapy. Despite his passion for research, Mogens Schou was above all devoted to the care of his patients the vast majority of whom received lithium.

In 1952, Mogens Schou gave lithium for the first time to a manic patient. This occurred three years after the Australian psychiatrist John Cade had reported lithium's potential antimanic action. In 1954, Schou and his colleagues published the first controlled study on lithium's effectiveness in patients experiencing mania. When it was performed over half a century ago, the study was kind of unusual as the researchers used a neutral preparation (placebo) for comparative purposes to show the real effect of lithium, which was not well known at that time. The study included 38 patients in a manic state among whom 30 had "clear" affective symptoms. Twelve of these patients showed spectacular improvement while fifteen showed some improvement and three showed no effect at all. During therapy, the concentration of the drug in blood serum was systematically established, and in six patients, also in the cerebrospinal fluid. It was found that concentrations of lithium ion in the serum remained within 0.5 to 2 mmol/l, which was an important element for further research on relations between the concentration of lithium in serum and its clinical effectiveness and toxic symptoms [1]. Three years later Mogens Schou summed up his research and the entire

contemporary knowledge concerning pharmacology, biochemistry and clinical effects of lithium in an extensive article published in "Pharmacological Reviews".

In the early 1960s, the first reports appeared pointing on a possible prophylactic effect of lithium therapy on manic and depressive recurrences. They came from England (Geoffrey Hartigan) and Denmark (Paul Christian Baastrup). Following this, Mogens Schou, together with this Danish colleague, performed a mirror-image study of lithium prophylaxis on eighty-eight patients with unipolar and bipolar affective disorder. They found that the average duration of mood disorders (mania or depression) within a year before lithium administration was 13 weeks while during a year on lithium it was shortened to the average of two weeks.

The year 1968, exactly a half of century ago, was marked by Mogens Schou's important clinical observations and studies. For the first time, the adverse effect of lithium on thyroid function (goiter) was described, based on findings in a large group of 330 lithium-treated patients [2]. Also, a study on renal handling of lithium elucidated the mechanism of renal lithium reabsorption (occurring in the proximal tubule) and its relationship to sodium reabsorption. This discovery provided a plausible explanation of lithium toxicity with sometimes fatal outcome in subjects receiving lithium as a salt substitute which occurred around the 1940/1950's. Also, the first comprehensive description of lithium poisoning was published, based on eight cases, with a characterization of prodromes, clinical picture, outcomes as well as suggested management.

However, in the same year, a strong backlash against lithium prophylaxis took place lead by the British psychiatrists Barry Blackwell and Michael Shepherd. Their criticism appeared in an article published in the Lancet and was titled "Prophylactic Lithium. Another Therapeutic Myth?". The article questioned the validity of the findings on lithium's effectiveness and requesting double-blind trials on this issue. Subsequently, eight such placebo-controlled trials in which Mogens Schou exercised a significant initiative were performed in Europe (in Denmark and the UK) and the USA between 1970–1973. The patients were required to have at least two recurrences of the illness in the two years preceding lithium treatment. Most of these studies employed a method comparing the course of illness in a group in which lithium was discontinued and replaced with placebo with a group which continued to receive lithium (discontinuation design). Recurrence of illness was defined as a deterioration requiring psychiatric hospitalization or commencing regular antidepressive or antimanic treatment. Analysis of all this research showed that the percentage of patients in whom recurrences of depression or mania occurred were significantly lower while receiving lithium for two years (on average 30%) than while receiving placebo (on average 70%) [3].

In his promulgation of lithium therapy, Mogens Schou was most interested in how such a therapy influences the various aspects of the life of patients. Bipolar disorder is overrepresented among artists, and he was the first to examine the issue of the effect of lithium prophylaxis on artistic creativity. From 24 artists treated with lithium due to bipolar disorder, 12 reported an increase in their artistic productivity, six a slight decrease and six noted no change at all [4].

As lithium therapy can be administered in pregnancy, Mogens Schou was an initiator of the Register of Lithium Babies forty-five years ago. The clinical observations to date have shown that using lithium in pregnant women with a mood disorder, especially those previously treated with this drug, shows a favorable risk/benefit ratio in favor of lithium.

Mogens Schou was extremely dedicated to the best clinical practice of lithium therapy. Since 1980, successive issues of Mogens Schou's book "Lithium Treatment of Manic-Depressive Illness" were published. This is a practical guide to lithium therapy for doctors, patients, and their families. The successive revised editions appeared in 1983, 1986, 1988 and 1993. The 6th edition was titled "Lithium Treatment of Mood Disorders" [5].

Mogens Schou, together with Bruno Müller-Oerlinghausen from Berlin, and Paul Grof from Ottawa were the Founding Fathers of the International Group for the Study of Lithium-Treated Patients (IGSLI), founded in 1988. In the 1990s the group published seminal papers showing a favorable influence of lithium on the decrease of mortality and prevention of suicidal behaviors. Since its conception, the group has been meeting yearly, and the most recent meeting, the 32nd IGSLI conference, took place in Santiago (Chile). The participants had the possibility to visit the Atacama Desert where a significant part of the world's lithium resources production is located. Lithium is extracted from stone and brine on location.

Between 1990-1994 the journal "Lithium" was published. Mogens Schou was on the editorial board and became the author of the first scientific article in the journal. It was on lithium and treatment-resistant depression. After many years, lithium augmentation of antidepressants has become the best evidenced pharmacological strategy in treatment-resistant depression. Some researchers even regard it as the second main indication for lithium use (after preventing mood recurrences) in mood disorders).

Mogens Schou authored over 500 lithium-related papers and book chapters and was the recipient of numerous prestigious awards. Among them, the International Scientific Kitty Foundation Award (shared with John Cade) (1974), John Cade Memorial Award (1982), Albert Lasker Clinical Medical Research Award (1987), International Society of Lithium Research's Prize for Lifetime

Achievement (1995), C.I.N.P's Pioneers in Psycho-pharmacology Award (2000), and NARSAD Lifetime Achievement Award (2004). He was twice nominated to Nobel prize in medicine and physiology.

With the foundation in 1999 of the International Society of Bipolar Disorders (ISBD), Mogens Schou was nominated as its honorary president. Since 2001, Mogens Schou's awards have been given for exceptional achievements in the field of research, educational activity and organizational and media activity and advocacy in the field of bipolar affective disorder at the society's annual international conferences. Among the IGSLI members, the Mogens Schou scientific awards were conferred to Paul Grof, Martin Alda and Janusz Rybakowski, and the advocacy and media award to Marylou Selo.

From 23–25 September 2005, Mogens Schou participated in the 19th IGSLI conference that took place in Poznań. Despite age-related limitations, he was quite pleased that he could actively participate; it was during this conference that he presented one of his new research proposals. It concerned the issue of lithium for prophylaxis of unipolar depression where he suspected a significant efficacy, especially among so-called "hidden bipolars". Over the years a growing number of controlled studies have been published, confirming that lithium has prophylactic effectiveness in unipolar depression and recently, a report from Finland on the basis of an observational study showed that lithium monotherapy is the pharmacological treatment associated with the lowest risk of psychiatric hospitalizations in patients with severe unipolar depression.

There was no sign then that several days after the Poznan IGSLI conference Mogens Schou would come to the end of his busy lithium-oriented life. Among a plethora of praising obituaries, Samuel Gershon, the first Editor-in-Chief of "Bipolar Disorders" noticed: Although Mogens Schou's contribution to the field will leave a permanent and lasting legacy, the loss of his humanity and personal commitment to science and patient care are irreplaceable.

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