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OBITUARY

BCPT Basic & Clinical Pharmacology & Toxicology

Obituary

Professor Arvid Carlsson (25 January 1923 to 29 June 2018)

Arvid Carlsson was born in Uppsala, Sweden, but grew up in Lund, Sweden, because his father, Gottfrid Carlsson (1887-1964), became Professor of History at Lund University in 1925. Carlsson studied medicine at Lund University from 1941 to 1946. After his graduation, he immediately went into research. His first research topic was calcium metabolism, which he studied using radioactive isotopes, and this resulted in his doctoral thesis that was published in *Acta Pharmacologica et Toxicologica* in 1951,[1] which was the original name of Basic & Clinical Pharmacology & Toxicology (BCPT).

In the same year, he became associate professor in pharmacology at Lund University, and as detailed in his Nobel lecture,[2] the assessment committee for the position took advantage of the situation to tell him that in their view, calcium metabolism was not an appropriate topic for a pharmacologist and urged him to study something else.

Carlsson followed the advice and spent five very prolific months from August 1955 and onwards in the laboratory of the legendary Professor Bernard B. Brodie, who was the Head of the famous Laboratory of Chemical Pharmacology at the National Heart Institute of the National Institute of Health, Bethesda, Maryland, USA. Brodie was a chemist by training and a genius in developing methods to measure chemical compounds in biological tissues. Development in his laboratory of a spectrophotofluorimeter enabled him, as the first in the world, to determine serotonin levels in brain tissue. Immediately before the arrival of Carlsson, Brodie and his group had shown with this method that serotonin disappears from the brain following pretreatment with reserpine, thus linking for the first-time biochemistry, pharmacology and brain function. With the use of Brodie's instrument in Bethesda, Carlsson demonstrated that reserpine also emptied platelets of serotonin.[3]

Back in Sweden, Carlsson turned his focus to the impact of reserpine on catecholamines in different tissues, and he used the methodologies he had learned by Brodie as well as developed his own ones. This led him to the most important scientific discovery of his career. He and his collaborators performed an experiment in which they studied the impact of reserpine on catecholamines in the brain. They treated rabbits with reserpine rendering them catatonic and subsequently gave them the catecholamine precursor DOPA (3,4-dihydroxyphenylalanine), which contrary to catecholamines crosses the blood-brain barrier. With this, Carlsson observed how the animals dramatically recovered from the reserpine-induced syndrome.[4]

Dopamine was at the time considered an intermediate product in the synthesis of noradrenaline and adrenaline, but in a series of subsequent experiments, Carlsson and his group showed that dopamine is present in the brain in higher concentrations than hitherto anticipated, that dopamine disappears when animals are treated with reserpine, and that the recovery from the reserpine syndrome is intimately associated with the restoration of dopamine levels following the administration of DOPA.

Carlsson and his group were the first to demonstrate the location of dopamine in the basal ganglia, and since the reserpine syndrome bears resemblance with Parkinson's disease, he proposed that l-dopa be an effective drug in the treatment of the disease. Carlsson's idea that chemical neurotransmission is important in the brain and that dopamine is an important neurotransmitter in its own right was

initially met with much scepticism, which can be difficult to understand today.

In 1963, Carlsson reported in Acta Pharmacologica et Toxicologica that antipsychotics are antagonists of dopamine receptors.[5] As of to date, this paper[5] has been cited nearly 2000 times making it not only his most cited paper, but also the most cited paper in the 73-year history of our journal. In 1968, he discovered that tricyclic antidepressants in addition to inhibition of neuronal reuptake of noradrenaline also inhibit the reuptake of serotonin, thus laying the foundation for the subsequent development of selective serotonin reuptake inhibitors.

In 1945, Carlsson married Ulla-Lisa Christoffersson, and together they had 5 children—three boys and two girls; in their adult life, Maria and Lena became his collaborators. Together with his daughters, he developed the monoaminergic stabilizer (−)-OSU6162, which is undergoing clinical trials for a variety of neurologic conditions including mental fatigue after stroke and traumatic brain injury myalgic encephalomyelitis/chronic fatigue syndrome.[6]

Based on pridopidine, a dopamine stabilizer and a promising drug candidate for Chorea Huntington, Carlsson established a biotech company, Carlsson Research AB, which subsequently was taken over by the Danish company NeuroSearch A/S that has conducted several clinical trials on pridopidine reaching phase III.[7]

Carlsson's active career spanned more than 70 years, and his most recent paper was published in June this year!.[6] Of special interest to BCPT, he published his first 5 scientific research papers in *Acta Pharmacologica et Toxicologica,* and altogether he has published approximately 20 papers between 1946 and 1988 under BCPT's first and second name.

In 1959, Carlsson had moved from Lund to Gothenburg to become professor of pharmacology at University of Gothenburg, and this was a position he kept until his retirement in 1989. Carlsson is the greatest and most important pharmacologist of all times from the Nordic Region, and he has received numerous prestigious awards: Wolf Prize in Medicine (1979), Japan Prize (1994) and Feltrinelli International Award (1999). In 2000, he was awarded the Nobel prize in physiology and medicine together with Paul Greengard (1925-) and Eric R. Kandel (1929-).

Kim Brøsen[1]
Ulf Simonsen[2]
Ulrik Gether[3]
[1]*Department of Public Health, Clinical Pharmacology and Pharmacy, University of Southern Denmark, Odense, Denmark*
[2]*Department of Biomedicine, Pulmonary and Cardiovascular Pharmacology, Aarhus University, Aarhus, Denmark*
[3]*Molecular Neuropharmacology and Genetics Laboratory, Center for Neuroscience, University of Copenhagen, Copenhagen, Denmark*
Email: kbrosen@health.sdu.dk

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