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Welcome to the Spring 2021 edition of *Physiology News*

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Cover image: The Iron Lung ward at Rancho Los Amigos Hospital, c. 1953. From: http://www.fda.gov/cber/summaries/cent092302pp.htm

Obituary: Otto F Hutter 1924 – 2020

Otto F Hutter

Honorary Member Otto Hutter died peacefully, aged 96, on 22 November 2020 at his home in Bournemouth. First elected to The Society in 1953, he was the then longest serving member.

Otto's research work focused on nerve and muscle electrophysiology. His reputation was established early when, with Wolfgang Trautwein, he first revealed the electrical changes responsible for the slowing and speeding of cardiac pacemaker rate by vagal or sympathetic innervation (Fig.1). His parallel enthusiasm for, and innovations in, teaching were recognised by The Society naming its annual teaching prize, the Otto Hutter Physiology Teaching Prize, in his honour.

Otto was born to a Jewish family on 29 February 1924 in Leopoldstadt, central Vienna. His happy childhood included attending the Zwi Perez Chajes *Gymnasium*. However, the *Anschluss*, the annexation of Austria by Nazi Germany in March 1938, signalled shattering changes. When just 14, a chance meeting with a friend on the Marienbrücke over the Danube Canal near his home encouraged him to register for the *Kindertransport* evacuation. He became number 359 of the 360 children on the train that left in December 1938, despite his having no familial or personal connections in the UK. Otto retained that *Kind 359* ticket all his life.

From December 1938, Otto was fostered by the Blaxill family in Colchester. Letters from his father reinforced his aspiration for a strong education rather than "learning a trade", otherwise typical at age 14. He secured one of just two refugee scholarships generously sponsored by the Old Boys Association of Bishop's Stortford College, opting for the Science Sixth Form. In 1942, considering himself "not robust enough" for the Pioneer Corps, the only option for a refugee, he took up "essential war work" at the Wellcome Physiological Research Lab (WPRL) in Beckenham, south-east London. There he worked on standardising insulin and testing penicillin for pyrogen. He was able to continue science studies on evenings and weekends at the then Chelsea Polytechnic and Birkbeck College. He also attended a lecture course called Chemical Transmission in the Nervous System given by Sir Henry Dale at the Royal Institution. Whilst at WPRL, he met Yvonne who was to become his wife of 70 years.

At the end of the Second World War, the grim truth of the loss of almost all his family became clear. Just from Otto's home street, Lilienbrunngasse in Vienna, some 493 Jewish men, women, and children had died in the Holocaust.

From 1946, Otto took the BSc Honours Physiology course at University College London (UCL), followed by a Sharpey PhD Fellowship there under Sir Charles Lovatt Evans (remembered in the *Physiology News* article Otto completed just before his death: Hutter, 2020). Lovatt Evans' lecture-demonstration teaching method was to prove a major influence on Otto.

Otto's early research investigated tetanus toxin on neuromuscular transmission. During these experiments, a cat nipped his fingertip. Weeks later a threatening adenopathy developed in one arm. It resisted the antibiotics then available, but eventually yielded miraculously to massive doses of potassium iodide, an ancient last-ditch remedy.

Otto was then appointed Lecturer at UCL. A 2-year Rockefeller Travelling Fellowship at Stephen Kuffler's lab at Johns Hopkins University in Baltimore began in 1953. He worked initially with another visitor, Werner Loewenstein. He met Otto Loewi at Woods Hole, recalling that "when animated, as [Loewi] often was, he spoke in a mixture of Austro-German and English which I could comprehend well enough". Loewi's suggestion that Otto should read Gaskell's work from the 1880s on the tortoise heart was pivotal.

His work with another visitor, Wolfgang Trautwein from Heidelberg, was iconic. In what most would consider very early microelectrode work (Bretag, 2017), they studied the cardiac pacemaker potential in frog and tortoise hearts. (At that time microelectrodes were hand-pulled from capillary glass over a Bunsen burner and much of the necessary electronic equipment was constructed by the experimenters themselves). Hutter and Trautwein revealed the pacemaker potential slowing and speeding under the influence of vagal or sympathetic nerve stimulation, respectively (as well as by the neurotransmitters those nerves release).

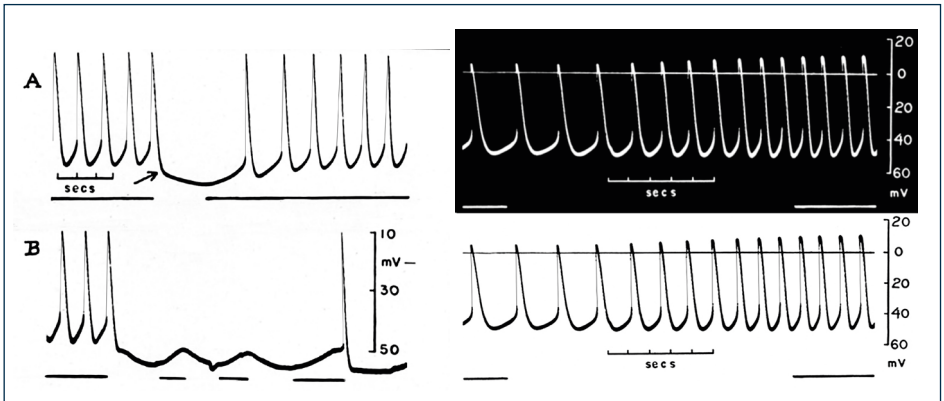

Figure 1. Two key figures from Hutter & Trautwein, 1956: see original paper for detail. Reversed black/white from originals, "rising phases slightly retouched". *Left:* The rate of firing of action potentials (APs) of frog sinus venosus pacemaker cells is slowed or even stopped, by stimulation of the vagus nerve (gaps in line below trace). Repolarisation is faster and "diastolic" membrane potential is more negative during vagal stimulation. *Right:* Original above, revised version below. Rate of firing is increased by stimulating the sympathetic supply (gap in line below trace). APs rise and fall more steeply, AP peak is higher and diastolic potential more negative than control. (Atropine present to block vagal effects).

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The Hutter lab, Glasgow, 1980.

Otto Hutter during Oral History interview, Tilli Tansey's office, 1996.

The inability of the camera system to capture the fast-rising phase of action potentials reinforces the experimental challenges of the time (see Fig. 1). But the images they secured now grace virtually every medical and physiological textbook – albeit too often in near-cartoon versions.

Otto's subsequent studies (back at UCL) of the underlying mechanisms furthered his interest in potassium and anion conductance channel properties, notably in skeletal muscle, expanding this field considerably. His students there were SM Padsha and Denis Noble. A key finding was of the substantial chloride conductance of skeletal fibres; their outward rectification and the inward rectification of K^+ conductance were successfully quantified. The much lower Cl^- conductance of cardiac muscle was also revealed: the rank order of foreign anion permeability in cardiac muscle proved to be the reverse of that in skeletal muscle. In 1961, Otto transferred to Wilhelm Feldberg's Division at the MRC's National Research Institute in Mill Hill: Anne Warner was his PhD student. Here he continued studying actions of various anions, formaldehyde and pH on sarcolemmal K^+ and Cl^- conductances.

In 1971 Otto fulfilled his wish to return to academia when appointed Regius Professor of Physiology at Glasgow University. His research moved on, studying the Graafian follicle (with Colin McCaig), adenosine actions on the sinus venosus (with Andy Rankin), deploying techniques of noise analysis and patch clamp (with Tom DeCoursey, John Dempster, Francis Burton). Computer-based data acquisition and analysis were introduced early to support his work and that of others in his department. In later years at Glasgow, he returned to simpler experiments on sarcolemmal vesicles in work relevant to muscular dystrophy (with Francis Burton, Jim Nichol, Douglas Bovell), yielding information on mechanical properties and water permeability. Otto sustained his deep scholarship of Cl^- and K^+ conductances, giving a masterly review of the topic to a spell-bound audience of early career researchers at the 2016 Physiological Society annual conference in Dublin (Hutter, 2017).

In parallel with his research, around 1966 Otto persuaded The Society to support practically orientated short courses for school teachers, marking the beginnings of The Society's Education Subcommittee. He also became involved with the International Union of Physiological Sciences (IUPS), first as Commission Chairman and then on its Council. During a 12-year stint, he pioneered the Educational Workshops that became a feature of IUPS Congresses. He also convened special workshops in (then) developing countries, such as a patch-clamp workshop at the Shanghai Institute of Physiology in 1983, led by Dick Tsien. The Society's *Otto Hutter Physiology Teaching Prize*, founded in 2009, recognised these endeavours.

"Those fortunate enough to experience his small-group teaching remember being challenged but greatly enthused"

Otto was a gifted and dedicated teacher, taking that aspect of professorship seriously. Lecturing to 250 medical or science students demands a major performance. He would remark, "If you're not nervous before a lecture, you're not taking it seriously enough!". Those fortunate enough to experience his small-group teaching remember being challenged but greatly enthused. He pioneered the use of sophisticated instrumentation for large junior labs. In the mid 1970s, a set of 32 identical, oscilloscope-based workstations were resourced, designed and constructed (Eadie *et al.*, 1974). Thus, lab groups of 32 student pairs could simultaneously complete hands-on work in core physiology practicals, enabling several hundred medical, science and dental students to learn by doing each week. Then, in the mid 1980s, the system was replaced in an early move to computerisation, deploying so-called BBC micro-based workstations (Edmondson *et al.*, 1987; Orchardson *et al.*, 1989). Well-equipped and -staffed departmental electrical and mechanical workshops were supported by his advocacy, vital both for research and for teaching with a substantial practical content.

After retirement, Otto continued to publish reviews and opinion pieces, often with letters in *The Times* on science or Israel's politics. He had sustained his love of gardening at a flat at Kilchattan Bay, Isle of Bute. Soon after the millennium, he and Yvonne moved to Bournemouth to be nearer to family, to continue gardening and to give talks on bioscience topics to lay audiences. His scholarship of Judaism grew further. His identity as a Holocaust survivor became more prominent: he gave several lectures and attended reunions. In 1996 he was interviewed for The Society's Oral History series (see Hutter, Tansey and Rosenberg, 1996). In 2001, with Bernard Wasserstein

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at Glasgow University, Otto established the prestigious Annual Holocaust Memorial Lecture series. Remarkably, at the age of 94, he gave the 18th lecture himself to a sell-out audience (Hutter, 2018). He had meticulously researched the varied careers, or sad fates, of nearly all his 37 school classmates from 1938. He sustained a large network of correspondents to the end. By the time of his death, he had family in the UK, Israel and Australia with 27 great-grandchildren. Otto became an Israeli citizen in 2018.

Professionally, Otto was first and foremost a gifted scientist. He had enormous powers of concentration and dedication to envisage and execute complex experimental work and then to conduct the thorough analysis of the data that followed. The authors, as well as many others fortunate enough to have known him, now retain fond memories of: the sheer energy he always had; his lively mind; the joy he took in helping those less gifted to understand; his attention to details; his enthusiasm; the pleasure he took in whatever he was attending to, be it world-class science or his garden; his deep love and pride in his family; his respect for his Jewish heritage; his wide scholarship; the lively twinkle that never left his eye; the ready smile; the charming anecdote; and his impeccable memory for facts, names and faces.

Otto was fond of quoting the Talmudic sages. His life and work surely fulfilled the counsel of Rabbi Tarphon: "You are not required to complete the task, but neither are you free to desist from it".

Otto Hutter was elected to The Society in 1953, Honorary Member, 1991, served on the Editorial Board of The Journal of Physiology (1961–1966), The Society Committee (1968–1972).

Written by David Miller, University of Glasgow, UK, and Denis Noble, University of Oxford, UK.

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Obituary: Jan Lännergren 1939 – 2020

Jan Lännergren

Jan Lännergren grew up in Stockholm and completed his medical training at the Karolinska Institutet, Sweden. After compulsory military service as a medical officer, he returned to the Karolinska Institutet and in 1967 he presented his PhD thesis entitled "Mechanical activity of twitch and slow muscle fiber in *Xenopus laevis*" with Bernhard Frankenhaeuser as his supervisor. Aside from sabbaticals with Andrew F Huxley at University College London, UK, with Russel Close at the Australian National University, Canberra, and with Willem van der Laarse at Free University Amsterdam, Netherlands, Jan spent the majority of his career at the Karolinska Institutet, where he became a Professor of Physiology in 2000.

Jan was a perfectionist in his approach to research. Fuelled by strong freshly brewed coffee and a pipe, later replaced by nicotine chewing gum, he spent weeks refining muscle fibre dissection and recording chambers, stimulators, and amplifiers. His designs, albeit highly complex, turned out to be infinitely robust and some of his muscle chambers and stimulators are still in use more than 30 years after they were built. His constant search for perfection ensured that the experiments performed were of the highest quality, but the downside was that this slowed his research output. Thus, his major results remain valid and are still quoted. Luckily, this was before the modern era where the presumed importance of data is assessed by extensive, and sometimes irrelevant, statistical analyses.

Jan's work is influential in that he demonstrated the feasibility of using mechanically dissected, single, intact muscle fibres from amphibians and mammals to address fundamental physiological questions. An early research interest of his was properties of different muscle fibre types, and in muscle of clawed frogs (*Xenopus laevis*), he described contractile properties of five different fibre types and related these to their myosin composition. Thereafter, his major research interest was muscle fatigue and recovery; his research team, which includes the authors of this obituary, revealed several cellular mechanisms, ranging from decreased activation to impaired function, of the contractile machinery.

Jan was an engaged and popular teacher who spent hours producing the perfect slides for a lecture, only to replace them the following year. He was the major driving force behind a popular Swedish physiology textbook, which is still used by numerous students each year. Outside of work, Jan enjoyed running and, in the winter, skating on the natural ice of the archipelago outside Stockholm. Later in life he and his second wife, Britta Wingård, were part of a competitive veteran quiz team and enjoyed playing golf and travelling. He is survived by his wife Britta, three children, and three grandchildren.

Written by Håkan Westerblad and Joseph Bruton, Karolinska Institutet, Sweden.

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