

# Joseph Larner

Pharmacology chairman who held a lifelong research interest in the mechanisms of insulin activity

Joseph Larner (b 1921; q Columbia University, New York City, 1945), died from metastatic melanoma on 28 January 2014.

Six Nobel prize winners were key figures in Joseph Larner's long medical research career, during which he helped unlock secrets of the mechanisms of insulin activity with the objective of developing better treatments for diabetes.

As a young doctoral student in the early 1950s he learnt the basics of research in the St Louis laboratory of Carl and Gerty Cori, the husband and wife team who were awarded the Nobel Prize in Physiology or Medicine in 1947. In the same lab, he was also mentored by Earl Sutherland, who won his Nobel Prize in Physiology or Medicine in 1971. A decade later, in the 1960s, Larner spent a sabbatical year working in the Cambridge University lab of Fred Sanger, winner of Nobel Prizes in Chemistry in 1958 and in 1980.

And in 2011, two Nobel prize winners were among hundreds of scientists, faculty colleagues, students, friends, and family who gathered at the University of Virginia School of Medicine to celebrate Larner's 90th birthday. One was Alfred Gilman, who won the Nobel prize in 1994. The other was Ferid Murad, awarded the Nobel prize in 1998. Both had earlier worked under Larner, who was the long time chairman of Virginia University's pharmacology department.

Larner spent more than half a century studying the mechanism of insulin action—work that provided insight into the cause, diagnosis, and cure of non-insulin-dependent diabetes mellitus.<sup>1</sup>

Philip Cohen, of the Medical Research Council's protein phosphorylation and ubiquitylation unit at the University of Dundee in Scotland, says that Larner's main contribution to science was "making the key initial observations about how insulin switches on glycogen synthase, the enzyme that catalyses the rate limiting step in the conversion of glucose 1-phosphate to glycogen, the major storage form of glucose in the body." Cohen adds that this was the first enzyme shown to become activated in response to insulin.

Cohen, who recognises Larner's early work in a paper he coauthored in 1997 on insulin signal transduction,<sup>2</sup> says that Larner contributed three specific observations during the 1960s. He showed that incubating muscle



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with insulin induces an increase in the activity of glycogen synthase;<sup>3,4</sup> that insulin induces a loss of covalently bound phosphate from glycogen synthase, which converts it to a form with higher catalytic activity;<sup>5</sup> and that a protein kinase activated by the "second messenger" cyclic adenosine monophosphate (cAMP) can attach phosphate to glycogen synthase in vitro, thereby suppressing its activity.<sup>6</sup>

Larner continued his research into insulin and diabetes for the rest of his life. He was an author on more than 330 research papers, including one published in the month after his death.<sup>7</sup>

Joseph Larner was born in Brest-Litovsk, at the time a part of Poland but now in Belarus. Later that year Larner's parents left Poland with their infant son for the USA, where they had relatives. "It was a good opportunity to improve one's life," says Larner's son, Andrew Larner, a professor of biochemistry and molecular biology at Virginia Commonwealth University.

The family settled in New Jersey. Every morning before going to school Larner helped his parents open the family business—a candy and liquor store in Newark.

After graduating with a degree in zoology at the University of Michigan in 1942, Larner studied medicine at Columbia University in New York, earning his medical degree in 1945. After a nine month internship at the University of Chicago, he was inducted into the US Army Medical Corps. He was assigned to the Army Chemical Corps Chemical Warfare Center at Edgewood Arsenal, where he authored his first research paper.<sup>8</sup>

After completing army service, he studied chemistry at the University of Illinois, earning

a masters in 1949. He then moved to the Cori laboratory in St Louis at Washington University, where he worked mostly with Gerty Cori and earned his PhD in chemistry in 1951. Larner later wrote a biographical memoir of Gerty Cori for the National Academy of Sciences.<sup>9</sup>

He spent four years as an assistant professor at the University of Illinois. He then moved to the pharmacology department at Case Western Reserve University in Cleveland to work under Earl Sutherland, his former Cori lab mentor. In 1969 Larner was named chairman of the pharmacology department at Virginia University, serving until his retirement in 1990 to emeritus status.

"He built up the best pharmacology department in the USA," says Cohen. "He clearly had an eye for spotting talent and recruited numerous outstanding young scientists as assistant and associate professors to his department."

In a paper published last year, when he was 92 years old, chronicling his work and his life,<sup>10</sup> Larner wrote: "I am blessed to have had such superlative scientific mentors, a productive group of students and postdoctoral fellows, a loving wife of 65 years, three remarkable sons, and eight wonderful grandchildren. I am (still) working full time on insulin, which has entranced me for a long time."

Larner continued working full time in his laboratory until just a month before his death. He died at home in the company of his wife, Frances, and their three sons.

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References are in the version on bmj.com.

Cite this as: *BMJ* 2014;348:g1909

**Solomon Leonard Barron**



**Former consultant obstetrician and gynaecologist Royal Victoria Infirmary and Associated Hospitals NHS Trust, Newcastle upon Tyne (b 1926; q St Thomas' Hospital, London, 1949; FRCS, FRCOG), died from cancer of the prostate on 17 December 2013.**

Solomon Leonard Barron moved to Newcastle as consultant in 1967. Well schooled in research methods for the epidemiology of human reproduction and sociology, he undertook overseas advisory work for the World Health Organization and the International Federation of Gynecology and Obstetrics. A superb clinician and an excellent teacher, he was also the consummate politician and a skilful "committee man." After retiring in 1991 he became chairman of Gateshead area health authority, then chairman of the Freeman Group of Hospitals NHS Trust from 1993 for nearly five years, paving the way for the merger of major hospitals in Newcastle into one trust as well as becoming one of the first to have worked in the NHS for 50 years. Leonard leaves his wife, Eleanor; two children; and two grandsons.

**David Barron, John Davison**  
Cite this as: *BMJ* 2014;348:g3106

**Basil Frank Clarke**

**Former consultant physician and senior lecturer in medicine Royal Infirmary, Edinburgh (b 1928; q Otago, New Zealand, 1955; FRCP Ed), died from metastatic carcinoma on 13 July 2013.**



After junior medical and general practice jobs in New Zealand, Basil Frank Clarke came to Edinburgh to study for the MRCP. He obtained a medical post in the Royal Infirmary of Edinburgh and stayed there for the rest of his career. After training as a physician in general medicine and diabetes, he became a consultant in the diabetes department, which became a unit of international repute. An excellent teacher and mentor, his research contribution included long term clinical trials with metformin and studies of cardiovascular reflexes in diabetic autonomic neuropathy. After retiring in 1993 he returned to his native New Zealand, where he leaves a brother and two nieces.

**Ian W Campbell, Brian M Frier**  
Cite this as: *BMJ* 2014;348:g3105

**David John Christopher Felton**

**Consultant obstetrician and gynaecologist Peterborough and Stamford Hospitals (b 1929; q Bristol 1955; FRCOG), died from a coronary on 6 February 2014.**

David John Christopher Felton was appointed as consultant in January 1969 and spent most of his working life at Peterborough District Hospital and Stamford Hospitals. The first 18 years of his life had been spent in India, and he would later often surprise some of his Indian patients by addressing them in their native tongue. After a period of general practice he decided that obstetrics and gynaecology were his real interests, but his talents were not confined to his purely medical abilities: his competence at administration resulted in his being called on to act as chairman on various committees. David was reluctant to retire and continued doing locums for the NHS and was also involved with the local authority assessing disablement cases. He leaves his wife, Jane; two sons; and a daughter.

**Alan Lyne**  
Cite this as: *BMJ* 2014;348:g3103

**Nicola Jane Gilbertson**

**Paediatrician Royal Cornwall Hospital Trust (b 1958; q Liverpool 1981; MRCP(UK), FRCPCH, FRSA), died from a cerebral tumour on 9 December 2013.**



On her arrival at Royal Cornwall (Treliske) Hospital, Nicola Jane Gilbertson ("Nicki") took on a role within the oncology team. Soon afterwards she was asked to assume the lead for this service, a move that was to shape her career. She soon took on the role of clinical director and led the child health service through several important transformations, which have found their way into national policy and frameworks. In addition, Nicki found time to lead paediatric involvement in the critical care group and was a trustee for the Cornwall Music Therapy trust. A service of celebration of her life was organised by her colleagues on 1 March 2014 in Truro Cathedral, which was so full of colleagues, families, patients, and parents that extra chairs had to be provided in the aisles.

**Matt Thorpe, Tony Gilbertson**  
Cite this as: *BMJ* 2014;348:g3109

**James Francis Hanratty**



**Former general practitioner and clinical director St Joseph's Hospice, London (b 1919; q University of Leeds 1943; OBE, KSG), d 27 December 2013.**

As surgeon lieutenant in the Royal Naval Volunteer Reserve, James Francis Hanratty served as the only doctor for six ships escorting convoys between Liverpool and the north Atlantic. In 1946 he went into general practice in Derbyshire and worked with the mining industry. But it was his father's death with stomach cancer, and his poorly managed pain control, that led James to take an interest in hospice care. He became St Joseph's Hospice's first medical director in 1979, ensuring it was among the early hospices to use and train others in providing analgesia

by continuous subcutaneous infusion via a syringe driver. James co-founded Help the Hospices, the leading charity supporting hospice care throughout the UK. Predeceased by Irene, his wife of 68 years, he leaves four sons and a daughter.

**Irene J Higginson**  
Cite this as: *BMJ* 2014;348:g2538

**Maurice George Philpott**



**Former consultant paediatrician Kingston upon Hull (b 1919; q St Bartholomew's Hospital 1943; DCH; MD, MRCP), d 7 February 2014.**

Maurice George Philpott did his national service in the Royal Army Medical Corps, on the hospital ship *Oxfordshire*. He extended his paediatric training at Great Ormond Street in the late 1940s and was then appointed tutor in child health at Sheffield University. In 1953 he was offered a paediatric consultantship in Hull. With his colleagues Maurice developed child care services from a basic level. He was secretary of Hull Medical Society for several years and served on hospital committees. In the mid-1960s he led the team planning paediatric services at the new Hull Royal Infirmary, which was then under construction. He ceased practising on his 65th birthday in 1984. Predeceased by his wife, Connie, he leaves three children, six grandchildren, and four great grandchildren.

**Nicholas Philpott**  
Cite this as: *BMJ* 2014;348:g2526

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