



Obituary

In Memoriam: Professor James Shepherd FRSE

(1944-2022)

Visionary scientist and communicator



Many have expressed their admiration for the life and work of Professor James Shepherd, and it is fitting that these messages came from around the world for Jim was a scientist with global vision. A medal-winning graduate from the School of Medicine at Glasgow University, Professor Shepherd pursued a career in clinical research that spanned four decades, made seminal discoveries, and it is not an exaggeration to say that his endeavours changed the practice of medicine.

It was in the mid-1970s that he developed an interest in lipoproteins and their association with cardiovascular disease. Those were the days when popular debate in scientific (and lay) circles centred on whether cholesterol had any role to play in causing atherosclerosis. Early research conducted in Glasgow (after Jim secured an academic position in the Department of Clinical Biochemistry) focussed on the metabolism of low-density lipoprotein (LDL) and how it was affected by diet and drugs. In these pioneering days, kinetic studies used radioactively labelled lipoproteins and investigations in patients with hypercholesterolaemia and animal models began to reveal how LDL levels in the circulation were regulated. Seminal studies using the novel technology of injecting normal and modified LDL revealed for the first time that the LDL receptor - newly discovered in cultured fibroblasts - played an important role in the metabolism of LDL in humans. The consequent demonstration that cholestyramine increased receptor-mediated LDL clearance established the conceptual framework for how many LDL-lowering drugs, including statins, worked. In further kinetic studies Jim, with the expanding research group in Glasgow and a wide network of international collaborators, went on to explore the intricacies of HDL and VLDL metabolism.

It was during a sabbatical in Houston, Texas in the laboratory of Dr Tony Gotto, that Jim was exposed to the world of large-scale clinical outcome trials by acting as a local investigator in the Lipid Research Clinics Primary Prevention Trial. Returning to Glasgow, it was 10 years

later when representatives from Bristol-Myers Squibb were passing through town that he used his powers of persuasion to convince them that a primary prevention study with their new agent, pravastatin, was warranted. After a frantic two weeks of figuring how such trials were organised and gathering a group of experts in cardiology (Stuart Cobbe), statistics (Ian Ford) and laboratory medicine (Chris Packard), the proposal landed on the desk of the president of the company and the landmark West of Scotland Coronary Prevention Study was born. The rest as they say is history. WOSCOPS exceeded expectations in terms of the benefit seen from statin therapy, and its first presentation at the American Heart Association meeting in November 1995 had an immediate and worldwide impact, as reported in the New York Times, Sydney Morning Herald, and even the Glasgow Herald! Due to the unique (at the time) electronic records system in Scotland it was possible to undertake a 15- and then 20-year follow up of the trial which helped established the long-term efficacy and safety of statins.

After allowing a few years to pass to recover from the rigours of conducting WOSCOPS, Jim alongside senior colleagues in Scotland, Ireland and the Netherlands conceived and launched a trial of statin treatment in older people. PROSPER (the Prospective Study of Pravastatin the Elderly at Risk) addressed the lack of evidence for LDL-lowering over the age of 70 years, and showed that statin therapy was effective in preventing cardiovascular disease even in the later stages of life.

Professor Shepherd served as head of the Department of Vascular Biochemistry at Glasgow University and then also took on the lead consultant position at the NHS Greater Glasgow Dept. of Clinical Chemistry, steering it through challenging times of reorganisation and expansion. Jim's gift for diplomacy and his talent for 'herding cats' was the stuff of legend. He embarked on a number of international initiatives serving as president of the European Atherosclerosis Society from 1993 to 6, and chairing EAS Congresses in Glasgow in 1994 and 2001. Many will remember with pleasure (and nostalgia for a bygone age) the rather elegant series of symposia organised by him at Gleneagles Hotel in Scotland. Professor Shepherd was 'at home' wherever he went in the world. The Asia-Pacific region held great attraction and he visited often to inform, educate, and establish long term friendships and collaborations. It was in hearing him lecture or attending one of the many educational activities that he ran across the world that many will have personally interacted with Jim. His infectious enthusiasm for the topic and ability to connect with people helped promote the cause of cardiovascular disease prevention worldwide.

In terms of publications, Professor Shepherd authored over 600 scientific articles, frequently appearing in leading medical journals. He served as editor-in-chief of *Atherosclerosis* and oversaw an increase in the impact and reach of the journal. However, the main activity most people

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will remember is his (possibly unique) engaging and enthusiastic communication style. Presentations, he felt, should contain not only the appropriate high-level science but should also ‘tell a story’. Professor Shepherd was at heart a clinician whose driving ambition was to improve patient’s lives. When asked why he then chose to take on the role of clinician scientist, his response was that by ‘standing back’ he could help more people.

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