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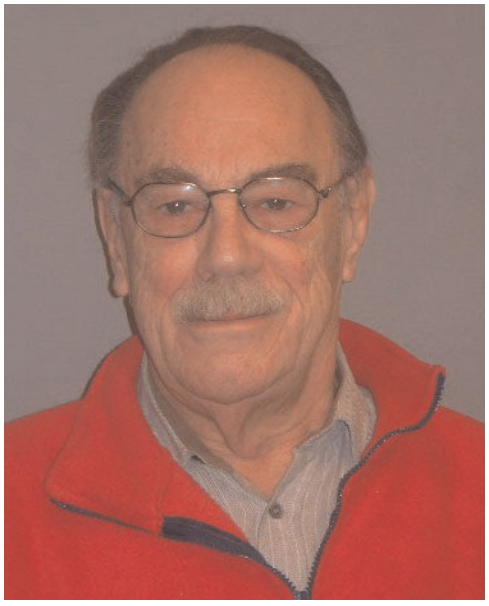
OBITUARY

Lars Ehrenberg (1921–2005)



Lars Ehrenberg, professor emeritus at Stockholm University, passed away in June 2005, a short time after his 84th birthday. Ehrenberg's main research fields were radiobiology and chemical carcinogenesis, where he was a pioneer and made numerous contributions of vast significance. His research was characterized by quantitative and interdisciplinary approaches at a fundamental level for understanding problems, e.g. with regard to cancer risk assessment of chemicals. The research in this area has rightly received international recognition. Ehrenberg's research work has inspired many colleagues and has led to many new developments. He was a scientist with an unusually broad, yet deep knowledge.

He grew up in Falun in Dalecarlia in Sweden where his father was a physician. From 1941 he studied at Lund University in the south of Sweden, while simultaneously, due to the ongoing war in Europe, he was drafted into military service in the north of Sweden. Although he could only spend little time in Lund he completed a B. Sci. in genetics, botany and mathematics in 1943. He then continued with studies in chemistry at Stockholm University, where he completed a Ph. Lic. in 1948, and in 1955 he presented his Dr Sci. thesis. In 1962, Stockholm University installed a special Chair of Radiobiology for him.

Lars Ehrenberg's broad scientific approach was founded in his early studies within cytology and botany, followed by studies in biochemistry. Among the works from the outset of his academic career are investigations of the hydrogen bond, and other phenomena concerned with chemical specificity, mechanisms of action and potency of local anaesthetics (1). Lars had a gift for telling stories, and many of the most colourful stories about his life as a scientist originated from the period he spent with the team of Nils Löfgren studying local anaesthetics at the Institute of Biochemistry and Organic Chemistry in Stockholm.

During his time in Lund, Lars Ehrenberg came in contact with the plant breeding group around Åke Gustafsson. Together with the plant breeders he introduced ionizing radiation as a means of increasing genetic variability for selective plant breeding. The work included comparison of different types of radiation with regard to mutagenic effectiveness and studies of action mechanisms. The work was carried out quantitatively, which, for instance, required that dosimetric methods were developed. In a research project with his brother, Anders Ehrenberg, and K. G. Zimmer, he demonstrated experimentally that free radicals are intermediates in the induction of biological radiation effects. At the stage when he had published nearly 50 scientific papers, most of them within radiobiology, he presented his doctoral thesis concerning the mechanism of action of ionizing radiation in plant seeds.

In 1954 chemical mutagens were introduced in the plant mutation studies and compared with ionizing radiation, e.g. with regard to mutation spectra (2). Some alkylating agents were found to be far more efficient mutagens than ionizing radiation. This finding led Ehrenberg to present in 1959 a warning to the Swedish National Board of Health about mutagens and carcinogens in the environment. This was probably one of the first warnings of this kind. He now felt a responsibility to include the problem of risk assessment of environmental genotoxic agents in his research.

The studies of biological effects of radiation and chemicals were carried out quantitatively, with definitions of concepts such as 'mutagenic efficiency' and 'mutagenic effectiveness', as well as a dose concept of genotoxic chemicals, which formed a basis for further work (3,4). The question about the true shape of the dose-response curves for mutation at very low doses was studied in sensitive plant systems (5). In studies aiming to find the properties that render an alkylating agent to be an efficient mutagen, alkylating agents were investigated with regard to reaction-kinetics (6). It was shown that the mutagenic potency could be described to a large extent by the reactivity towards nucleophilic centres with low nucleophilic strength, commensurate with the oxygens in DNA bases.

By now, the research had progressed to the stage where the problems involved in risk assessment of mutagens/carcinogens could be identified (3). Lars Ehrenberg's continuing work focussed mainly on improved methods and models for risk assessment of carcinogens. The development of methods was based on the experience from radiation biology and radiation protection philosophy. He suggested expressing the dose of mutagenic chemicals as radiation-dose equivalents, in order to obtain a unit useful for application in models for cancer risk estimation (3). This could be derived from the determination of the relative genotoxic potency, with ionizing radiation as a standard, in *in vitro* mutation tests (7).

Another development, based on the identified needs for improved methods, was to measure *in vivo* doses of reactive

chemicals/metabolites as their stable adducts to blood proteins, particularly haemoglobin. Along with the development of analytical methods, this approach has become an efficient tool in work aiming at cancer risk estimation. The usefulness of the method was shown already in 1978 in studies of *in vivo* doses in ethylene oxide-exposed workers.

During the 1990s, the collective experience and developments from Lars Ehrenberg's 50 years of scientific work resulted in the evaluation of risk models for chemical carcinogens (8). This work demonstrated that the relative cancer risk model used for ionizing radiation could be applied to animal cancer test data for chemical carcinogens (models: ethylene oxide, acrylamide and butadiene). This research, which is still ongoing, deeply engaged Ehrenberg, even when his younger colleagues and former students had taken over the responsibility.

The developed methods and quantitative procedures introduced by Lars Ehrenberg have also led to a system that permits the detection of previously unknown exposure to carcinogens through measurement of haemoglobin adducts. This was, for instance, demonstrated in the case of the detection of a generally occurring, and relatively high, exposure to acrylamide, shown to originate from heated foods. In Lars' final work as a co-author the circle was closed: in studies aiming at improved cancer risk estimation of the identified background exposure to acrylamide, the reaction-kinetics and relative genotoxic potency of glycidamide, the metabolite of acrylamide, were studied (9).

This summary of Lars Ehrenberg's work is far from complete. His unusually broad scientific interests and originality were reflected in about 400 publications, which, in addition to the main research lines summarized above, included mathematical–statistical and epidemiological papers, and others concerning, for example, mechanisms of action of radioprotective agents. Furthermore, he was engaged as an expert by OECD, FN, FAO/WHO and worked as an advisor in Yugoslavia, India and Bangladesh. He was honoured by several Swedish and international awards, including a medal from the International Agency for Research on Cancer, as well as awards from the European Environmental Mutagenic Society and from the Collegium Ramazzini. He was *inter alia* a member of The Royal Academy of Sciences, Stockholm and Collegium Ramazzini.

Lars Ehrenberg was inspiring to colleagues and students, freely sharing ideas and always showing interest in the work of junior scientists and students. As long as his health permitted, until the summer of 2004, he was at the laboratory 7 days a week, where he was appreciated for taking time for discussions with the students and as an unfailing source of knowledge, or just for telling some of his stories. Scientific discussion in small groups was what he enjoyed the most, much more than the larger and public arena. The scientific problems were always the first priority for him and political correctness was of little importance, which made him controversial now and then.

Throughout the years Lars maintained a keen interest in botany, and for colleagues who accompanied him for a walk in a garden or forest, it became an exciting botanical excursion. Lars also had a great talent for languages—his English was masterly; he had a good knowledge and appreciation for classical music, literature and art. As someone once said, he was a renaissance person.

He will be remembered as a charismatic scientist and person, and most fondly by the colleagues and students who experienced his generosity and good humour as a friend or mentor. His memory will live on in the minds of his wife Maria, his son Måns and daughter Zorica, and Maria's son Felix, and all of us.

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