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OBITUARY

The community of scientists interested in Free Radicals has lost two of its great figures recently. Trevor F. Slater and Richard O. Recknagel were pioneers in the identification of Free Radicals and their involvement in cell damage and toxicity. Both these scientists, furthermore, were strong personalities who gathered friends and colleagues from all over the world around their field of scientific enthusiasm.

There is a noticeable void and an irreplaceable loss.

Both of us have had many interactions with these great scientists and friends, and Trevor Slater also was a colleague on the Editorial Board of this Journal. Not only ourselves, but innumerable scientists around the world are thankful to these great persons.

We have asked Professors Dianzani and Comporti, probably among the closest friends, for a few lines in remembrance, which are printed on the following pages.

BARRY HALLIWELL AND HELMUT SIES

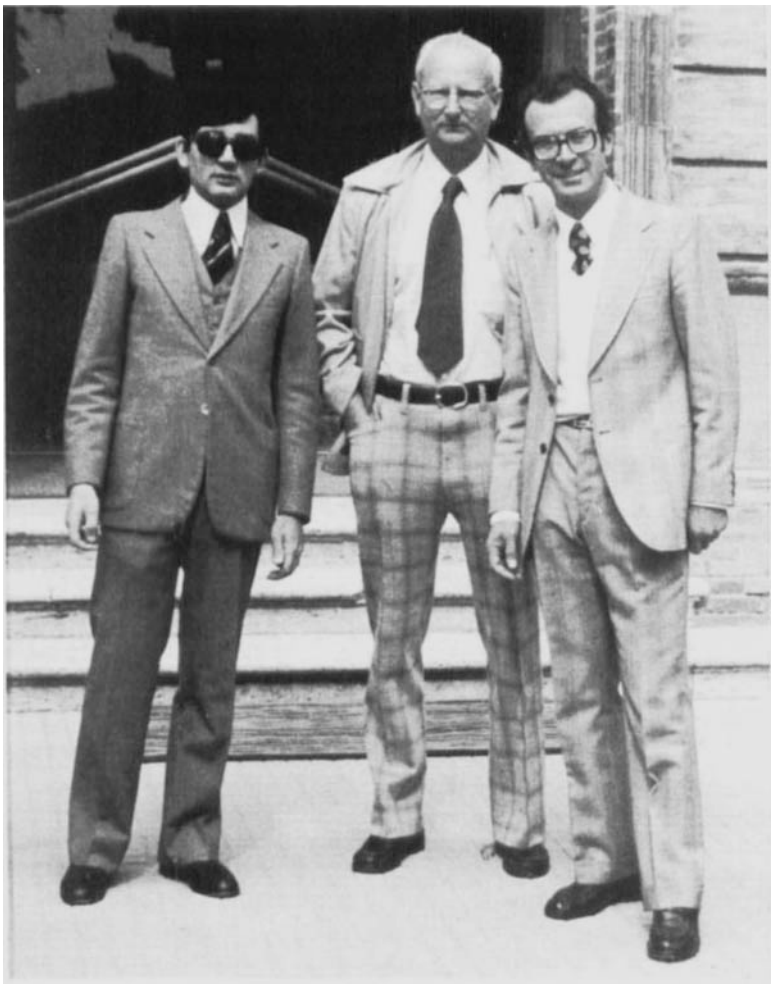
RICHARD O. RECKNAGEL

On December 2, 1991, we lost Richard O. Recknagel, Professor Emeritus of Physiology and former Chairman of the Departent of Physiology, School of Medicine, Case Western Reserve University (Cleveland).

Professor Recknagel was a pioneer in the field of experimentally induced liver injury and an internationally recognized leader in cellular pathophysiology. His work greatly expanded the understanding of the mechanisms of cellular alterations at subcellular and molecular levels. Much of his work was accomplished with the model of carbon tetrachloride induced liver injury, and it is impressive to recognize the wealth of information that stemmed from this model, not only in the field of basic pathology, but also in cellular physiology. In this sense he was one of the most genuine heirs of the lesson, clearly formulated by Claude Bernard, that besides other uses, a poison can be used as "an instrument which dissociates and analyzes the most delicate phenomena of the living machine", and can help to understand the physiological mechanisms of life.

His work substantially clarified the pathogenesis of CCl_4 induced fatty liver, as a result of a blockade of liver triglyceride secretion. In searching the molecular mechanism of such alteration, he directed his attention to the endoplasmic reticulum, and was one of the first to recognize that CCl_4 promotes lipid peroxidation through the haloalkane free radicals originating from its metabolism. He then studied lipid peroxidation in cellular membranes and actively contributed to the demonstration that cytotoxic products are produced from lipid peroxidation. Many other studies, such as those attempting to demonstrate the implication of Ca^{2+} as a second toxicological messenger, would deserve being recalled here.

What was impressive in him as scientist, was the creativeness, the sharpness and the logic connection of thought, the lucidity in the experimental design, the very



Professor Recknagel (center), together with Professor Comporti (right) and Professor Benedetti (left) during one of his visits to Siena.

profound critical sense, the scientific rigour. He was also endowed with an impressive clearness in expressing results and hypotheses.

These qualities made up his outstanding scientific personality and his lesson remains engraved not only in those who attended his laboratory, but also in those who indirectly came in contact with him through meetings and even through his articles. I believe that Richard has been an unique example of how a scientific problem is to be approached, of how scientific research is to be done.

I remember him with the highest consideration and the warmest affection. Over many years he would come and spend a few days in my Institute in Siena, and on those occasions we would discuss results just obtained and future plans. Those were days of great interest, of renewed enthusiasm and desire to proceed along the hard path of scientific research.

We miss Richard greatly and we shall for a long time. His lesson will stand firm in front of us and he will survive in so far as "Death begins where remembrance be lost".

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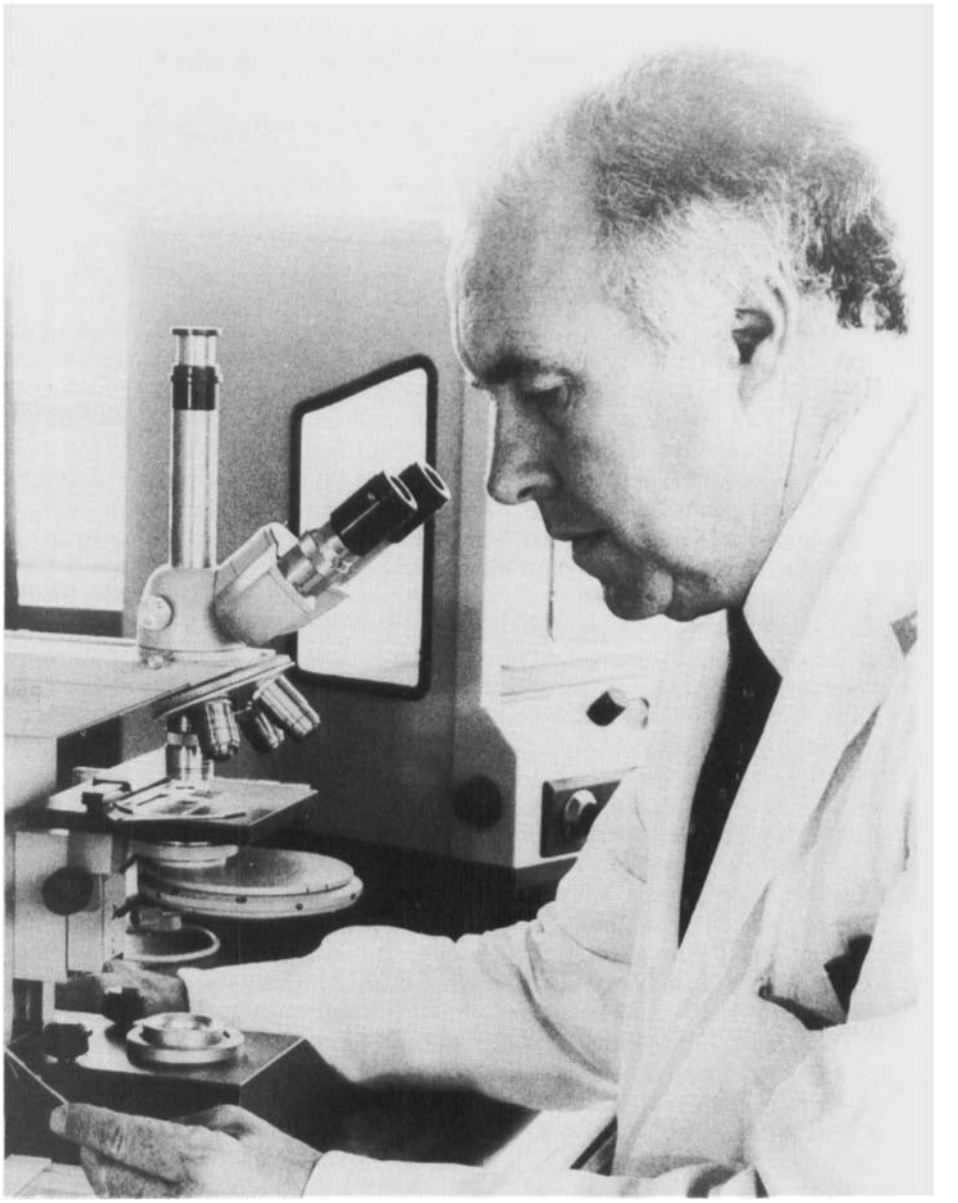
TREVOR F. SLATER

The scientific world had an important loss last year. During the month of April, 1992. Thursday before Easter, Professor Trevor Slater died in London.

Trevor Slater has been one of the leaders in the field of free radical biochemistry and of its application to pathology. His death was very premature (he was 61), but occurred when the theories he developed during some 30 years of scientific activity had assumed a great expansion. For this reason he must be considered much more than a pioneer in the field, where he was an eminent leader.

I met Trevor Slater for the first time on the occasion of the Ciba Foundation Meeting on Lysosomes, organized by Christian de Duve in February 1961. At that time Trevor was 30 years old and had been collaborating for a few years with Professor Claude Rimington, working especially on porphyrins and their pathology. But the reason Trevor had been invited to the Meeting was his work on the importance of lysosomal damage in CCl_4-induced liver injury and in post-lactation atrophy of the mammary gland in rats. I had shown lysosomal damage after CCl_4 in 1954 and I was especially anxious to meet another at that time unknown person who was working on the same subject. Our results fitted very well together and I found the man extremely open and sympathetic. This started a long friendship and collaboration. At that time I was Professor in Cagliari, where I had found, together with my collaborator Luigi Congiu, that CCl_4 exerted a prooxidant effect on liver proteins. The discussion with Albert Tappel and Trevor originated my moving to investigate lipid peroxidation. In the meantime I became Professor in Siena, where I met as a young collaborator Mario Comporti. We published the discovery of the increase of lipid peroxidation after CCl_4 in 1954. Trevor repeated the experiments *in vitro* with isolated microsomes and was the first scientist to hypothesize that this was the consequence of CCl_4 metabolism involving the production in the smooth endoplasmic reticulum of liver cells of the trichloromethyl free radical.

His efforts to prove the real production of this free radical started from the use of pulse radiolysis methods, that were applied to this topic in the Department of Biochemistry of Brunel University, where Trevor had become Professor and head of department in 1970. Trevor, in collaboration with Robin Willson, was able to bring evidence on the formation of $CCl_3^{\cdot}$ free radical by irradiation of CCl_4 *in vitro*. The free radical was demonstrated by a spin trapping method, using as spin trap phenylbutylnitrone. Further, the group of Trevor moved to the demonstration of $CCl_3^{\cdot}$ in liver systems (especially microsomes) *in vitro* as well as *in vivo* after CCl_4 poisoning in the rat. These demonstrations were done with the collaboration of young Italian scientists (Emanuele Albano from Turin and Aldo Tomasi from Modena) who spent several years in Brunel. After this demonstration, Packer, Willson *et al.* in Trevor's lab showed the possible production of $CCl_3O_2^{\cdot}$ (trichloromethylperoxyl) free radical. The use of promethazine or vitamin E as antioxidants led Trevor's group to



show that the CCl_3 free radical, whose formation is practically not influenced by these antioxidants, is responsible for covalent binding to liver structures, whereas the trichloromethylperoxyl free radical was responsible mainly for the onset of lipid peroxidation. These points were confirmed in Turin by Poli and others *in vivo* and led to the separation in CCl_4 poisoning of damage related to covalent binding from that related to light peroxidation.

Trevor's group expanded his interest to a wide range of other substances, either haloalkanes or haloalkenes, or compounds of different nature, that become toxic after metabolism in the smooth endoplasmic reticulum of liver cells. This research led to the discovery of numerous other free radicals, so expanding enormously the field of free radical toxicology. A further great progress in the field occurred when Trevor showed that vitamin E *in vitro* is able to quench the $CCl_3O_2^{\cdot}$ radical, and that ascorbic acid can restore the non-radical form of vitamin E, being transformed itself into the ascorbyl free radical. The same effect may be displayed also by reduced glutathione. These mechanisms may be relevant in the physiological cell protection from poisons.

During these years, Trevor increased greatly his collaboration at the international level. His collaboration with the Torino group started in 1967. Since that time, more than 20 Turinese scientists frequented, sometimes for long extents of time, the Brunel lab. Trevor came himself to Turin practically every month, sometimes more frequently, so that the collaboration between Torino and Brunel became intense, as if the two labs were really a single lab. The collaboration with Italian labs was extended also to other laboratories strictly connected with Turin from the point of view of scientific derivation and interests. I refer especially to Mario Comporti's lab in Siena and to the lab of Umberto Marinari and Giorgio Nanni in Genoa. In Austria, this rather complex group met the strict collaboration of Hermann Esterbauer, one of the most important chemists and biochemists in the field of lipid peroxidation and derived compounds. Under the support of the National Foundation for Cancer Research, that had Albert Szent Gyorgyi as President and Trevor Slater as Scientific Director, the group was able to discover the production of many toxic carbonyl compounds formed during lipid peroxidation and especially of the 4-hydroxy-2,3-trans-ene series. The most important compound, 4-hydroxynonenal, was first isolated from peroxidizing liver microsomes by Benedetti, Comporti and Esterbauer.

Trevor Slater became very interested even in the problem of the relevance of free radicals in tumours. The fact that most tumours display very low lipid peroxidation attracted his scientific attention. But at the same time he had an interest in human cancer. He said to me that his original interest in the field of cancer of the cervix came from the time he was still in University College London as a young scientist. At that time, he had to give scientific advice to gynaecologists. But his interest became stronger after having read the book by Schauenstein, Esterbauer and Zollner on aldehydes. A young scholar of mine, Chiara Benedetto, who was very interested in the subject, became his most assiduous collaborator in this field.

Trevor was not only a great scientist, but also a great manager and organizer of scientific collaborations. His intelligence, combined with his natural gifts of benign disposition, friendly feeling and love for life helped him so much in his scientific environment. His diplomatic way of handling situations and his smile, were a considerable part of his success. He loved good food, good friends, good wine, the sun and nature. I must add that he loved Italy and Italians, probably more than the Italians do themselves.

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