



photo credit P.Masson

The message from Palmer Taylor

“Bhupendra P. Doctor, known as “Doc” and sometimes “BP” to others, was head of the Division of Biochemistry at Walter Reed Army Institute of Research in Washington, D.C. (now Silver Spring, MD). Prior to his entry into the cholinesterase era, Doc and his close colleague, Carl Alving, had worked on various aspects of global diseases and chemical threats. The stability and efficacy of antidotes to toxins and toxicants, including the oximes for cholinesterases, became an early consideration. Doc’s interests in tissue targets and scavenging led to the development of monoclonal antibodies to the acetylcholinesterases through a sabbatical visit to Palmer Taylor’s laboratory at UC, San Diego in 1982. B.P. Doctor, Mary Kay Gentry and Robert Ogert at Walter Reed and Shelley Camp at UCSD then began studies on the epitopes and selectivity of the various antibody clones. This led to the consideration of other avenues for scavenging of organophosphates. Accordingly, a large project was spearheaded by Doc to purify, characterize and sequence directly acetylcholinesterase from fetal bovine serum, a source of comparative abundance.

Doc then began collaborations in a wider framework in other Department of Defense laboratories, such as the Institute for Chemical Defense in Edgewood, Maryland. With new sequences of the cholinesterases emerging, emphasis began to shift to butyrylcholinesterase as a stoichiometric scavenger, its comparative efficacy and to develop methods to prolong its lifetime in the body and minimize antigenicity. These efforts were a collaboration of several federal and academic laboratories, involving Ashima Saxena, Richard Gordon, Chunyuan Luo and Madhusodana Nambiar at Walter Reed; Donald Maxwell, David Lenz, Irv Koplovitz, Douglas Cerasoli at the Institute for Chemical Defense and other agencies within the Department of

Defense. The initial successes enabled expansion of the effort to other esterases, such as paraoxonase. These studies involved collaborators throughout the world to include Israel Silman and Joel Sussman at the Weizmann Institute in Israel; Yacov Ashani and Gabriel Amitai at the Israel Institute for Biological Research, Oksana Lockridge, Patrick Masson and Ellen Duysen at the University of Nebraska, and Patrick Masson in Grenoble, France.

It became immediate apparent to Doc that irreversible inhibition of the cholinesterases at both a molecular and systems level became a far easier task than developing antidotes and scavenging agents. Undaunted, he and his colleagues at Walter Reed engaged with the laboratories of Patrick Masson, Oksana Lockridge, Dan Quinn, Terry Rosenberry, Israel Silman, Gabi Amitai, Yacov Ashani, Joel Sussman, Martin Weik and Zoran Radic' to investigate mechanisms of cholinesterase catalysis, alkylphosphate inhibition and nucleophilic reactivation mechanisms. They identified phospho-oxime intermediates and differences in the deconstructed steps of substrate catalysis and oxime reactivation. Indeed, these collaborations involved far more than exchange of materials and cyberspace communications, but rather travel to other investigator's laboratories or to core resource laboratories and continuing investigations at the bench.

Extending beyond the specifics of scientific endeavor, Doc recognized that understanding the cholinesterases and their associated therapeutic and toxicologic manifestations can best emerge through global communication and collaboration. His efforts in convincing administrative colleagues of the importance meetings being international and addressing basic mechanism as well as practical applications have been an essential factor for the cholinesterase field is now planning for its thirteen meeting extending from the original one in 1975 in Split and spinning off two separate meetings in Cholinergic Mechanisms and in Related Esterases Modifying Organophosphates. At a previous planning meeting, Doc was adamant about having the 1994 Cholinesterase meeting in his home country of India in the interests of promoting geographic diversity and demonstrating that such meetings should not be constrained by international borders. While some on the planning committee were not sanguine about the idea and thought it may pose some financial risk to the sustainability of these meetings, Doc prevailed. Indeed, that meeting has been one of the most successful and inclusive of the eleven Cholinesterase meetings. Although beleaguered a bit with the infirmities of age, but not spirit or intellectual prowess, Doc, with his wife Ellen shepherding him between locations and the negotiating the travails of travel to Russia, was offering invaluable comments at the XI Cholinesterase meeting in Kazan. It has been these commitments that have sustained these meetings and enable the planning of the XII International Meeting in Spain next year, and the separate meetings on Cholinergic Mechanisms and Hydrolases Catalyzing Organophosphates as valuable products of the first cholinesterase meeting in 1975."

Development of a fund for travel of young investigators attending International Meetings of the Cholinesterases

After consultation with Ellen Doctor and past associates of B. P. Doctor at Walter Reed Army Institute of Research and elsewhere, we feel that an appropriate memorial in his name would be the development of a fund for travel of young investigators attending International Meetings of the Cholinesterases. Priority would be accorded to students, fellows and beginning faculty lacking grant funds or other means for travel to scientific meetings. Those awarded travel

funds would be expected to present at either poster sessions or workshops scheduled for the meeting. B.P. Doctor had an abiding interest in international meetings, and believed that research on the cholinesterases and related targets required global perspectives and cooperation. He felt that research in cholinesterases should meet the needs of third world countries where misuse and accessibility to pesticides are high, as well as in built environment locations with controlled ventilation systems where substantial populations of individuals could be exposed through terrorist activities.

Those colleagues wishing to contribute should send checks to:

Pharmacology Education and Research Foundation
P.O. Box 144
9700 Gilman Drive
La Jolla, CA 92093-5010

Individual checks and accompanying letters should be labeled as the B. P. Doctor Memorial Travel Award Fund. The Pharmacology Education and Research Foundation has been categorized as a foundation by the United States Internal Revenue Service. All donations will be acknowledged as support for a tax-free foundation. The Organizing Committees of the respective International Cholinesterase Meetings shall award funds to the applicants in relation to the funds available. The Doctor family will be apprised of the fund donors, the fund financial base, and the awardees.

Palmer Taylor December 2014

In Memoriam: Bhupendra P. Doctor

Dear Members of the Scientific Advisory Board of the ISCM

Our friend and colleague, Bhupendra P Doctor, known to all of us as 'Doc', who was, until recently, a member of the board, passed away at the end of november after undergoing cardiac surgery.

We do not wish to describe at length Doc's scientific and professional status and achievements, which are well documented and recognized by numerous awards and citations. He will be remembered as an energetic investigator, charged with curiosity and full of initiatives, who never left a stone unturned. Doc was Head of the Biochemistry Division at WRAIR for 40 years, in itself an unusual phenomenon, because division heads at WRAIR were usually colonels, and were replaced within a few years. He was a natural leader, who assumed responsibility, demanded and received the funding, and created the facilities and equipment needed to solve the important scientific and technical questions that he was addressing. Although often this meant overcoming formidable bureaucratic obstacles, he never gave up. When he felt that there was a need to collaborate with others, he did it very graciously. He was very open and fair, readily sharing his knowledge with others, and was very generous in crediting his colleagues.

The major theme to which Doc devoted his scientific talents and administrative skills was to advance the concept of bio-scavengers by turning human butyrylcholinesterase into the first realistic candidate from a biological source that could serve as an antidote against nerve agents and pesticide intoxications. When he commenced this effort, some 30 years ago, many considered it far fetched. But time has proved how perceptive Doc was; butyrylcholinesterase itself, and newer candidates, are at various levels of development.

When Doc approached retirement he was asked about his future plans. Who, me? He responded immediately – I'll never quit science! And so it was. It sounds strange and sad to use the past tense in talking about Doc - a delightful and determined person, with a great sense of humor, who had unlimited patience in listening to others, and in seeing the other person's point of view.

Hermona Soreq and Israel Silman