Aging Pathobiology and Therapeutics 2024; 6(3): 136-137 **136**
DOI: 10.31491/APT.2024.09.154

A natural way for a healthier lifestyle—an interview with Prof. Stephen C. Bondy

Alessandro Bitto[a,*]

[a] *Department of Laboratory Medicine and Pathology, University of Washington, Seattle, WA, 98195-7470, USA.*

Abstract

The article is an interview with Prof. Stephen C. Bondy, Department of Environmental & Occupational Health and Department of Medicine, University of California, USA, conducted by Alessandro Bitto of the Department of Laboratory Medicine and Pathology, University of Washington, Seattle, WA, 98195-7470, USA, on behalf of *Aging Pathobiology and Therapeutics*.

Stephen C. Bondy, PhD

Stephen Bondy is Professor of Neuroscience at the Center for Occupational and Environmental Health at the University of California, Irvine. He obtain an M.A. from the University of Cambridge in 1962 and a Ph.D. in biochemistry from the University of Birmingham. He has held positions at Columbia University, UCLA, University of Colorado, and the National Institute for Environmental Health Sciences where he was Head of the Neurochemistry Section. The focus of his research concerns the mechanistic processes underlying the effect of environmental or nutritional agents in altering the rate of brain aging, with an emphasis on the contribution of inflammatory events to neural aging, and the potential slowing of brain aging by antioxidants and anti-inflammatory agents such as melatonin. Prof. Stephen Bundy has published more than 400 articles in the field. (https://www.faculty.uci.edu/profile/?facultyId=2283)

Alessandro Bitto: Can you give a general introduction to your research direction?
Stephen C. Bondy: I am interested in the fact that most disease states involve misguided enthusiasm by the immune system, leading to a non-productive and extended inflammatory state. In view of our rapidly aging population and the fact that age is associated with such a chronic inflammatory condition, the question as to what forms the basis of this unhelpful response and what can be done to alleviate it need to be addressed.

Alessandro Bitto: Can you tell us about your career path so far? What has been the most interesting stage of your scientific career?
Stephen C. Bondy: My career has been rather long and in consequence has several facets but it has always been focused on the central nervous system. As a graduate student I was assigned the job of characterizing brain proteins. The methodology was rather primitive in those days.
Later my laboratory developed a method of determining levels of free ionic intracellular calcium within cells using a fluorescent probe. This is usually very low but many toxic agents elevated this to harmful concentrations. We also pioneered the use of a fluorescent probe (DCFH-DA) that measures reactive oxygen species in tissues. This turns out to be our most widely cited paper. We then exploited these two methods by applying them to a range of neurotoxic materials. This was subsequently widely adopted by other laboratories.
When molecular biology arrived, naturally I was inter-

* Corresponding author: Alessandro Bitto, MD.
Mailing address: Department of Laboratory Medicine and Pathology, University of Washington, Seattle, WA, 98195-7470, USA.
Email: ab62@uw.edu
Received: 06 August 2024 / Accepted: 8 August 2024
Published: 30 September 2024

ested. One of my graduate students was the first to quantitate cerebral mRNA. We later demonstrated that the genetic profile of the brain during aging shows increasing expression of inflammatory genes even in the absence of a provocative immune stimulus. This altered expression of genes with senescence could be blocked in the brain by dietary melatonin which largely restored the pattern of gene expression to a more youthful configuration.

Unexpected findings that are not based on your hypotheses are always exciting. An example: my assistant carefully retained the bodies of our experimental animals although I was only interested in cerebral effects of melatonin. did. Because of her diligence, we found that the dietary use of melatonin dramatically reduced the overall rate of tumor development in aged mice. This unanticipated departure from our predictable hypothesis-based work was exhilarating. The implications of this work which utilizes an inexpensive and very non-toxic chemical are not trivial.

Alessandro Bitto: What do you see as the most promising way forward to increase lifespan/healthspan in the human population? Drugs, dietary interventions, lifestyle interventions, others?

Stephen C. Bondy: The way forward to a good health span probably needs to be addressed in a variety of ways. I would give regular exercise and dietary considerations a priority in this respect. Naturally I believe that the regulation on inflammatory conditions need to be controlled. Pharmacological anti-inflammatory drugs do not seem to be subtle enough to bring this about without significant side effects. However, a range of chemical of plant origin have be shown to successfully modulated the inflammatory response without eliminating the beneficial properties of immune function. They can be considered as modulating rather then merely inhibiting the immune system. Many of these micronutrients are not very specific and may cause several additional positive changes such as promoting autophagy, essential for the clearance of non-functioning organelles, which accumulate especially with senescence.

Alessandro Bitto: Failed interventions and less than rigorous research in the field of aging have been hyped in the past by unscrupulous actors. How do you suggest the field protects itself from these events which cast a shadow on legitimate aging research?

Stephen C. Bondy: Science tends to be self-correcting in the long run. If an interesting claim is made, others will soon check it with a desire to further the work. Only findings that are of no interest to anyone can survive unchallenged for a longer period.

Alessandro Bitto: What do you think of the hallmarks of aging? Is it a good framing to understand aging biology or a needless categorization? Which one is your favorite?

Stephen C. Bondy: Overall, aging seems to involve diminished efficiency. An increasing poorly targeted penumbra grows around a diminishing umbra of effectiveness. Features that should be useful like pro-oxidant defenses and the immune system do not merely become less operative but actually transform into an actively harmful configuration.

It is worth bearing in mind that aging is an essential substrate for several common neurodegenerative diseases. If aging were delayed, this would have a major effect on the incidence of these diseases despite the specific features of an age-related neurological disorder not being considered.

Alessandro Bitto: What should researchers in the basic biology of aging pay attention to in designing their experiments?

Stephen C. Bondy: Try and limit the number of variables to one at a time. Be modest in what you think is possible in a single experiment. Repeat the experiment at a different time not just as a series of replications all run on he same day. Remember that the significance of findings tends to decline with replication.

Alessandro Bitto: Which area of biology do you see as the next frontier in aging research?

Stephen C. Bondy: Focusing on the health span rather than trying to extend the lifespan. Living many years in an aged condition is not as desirable as having a healthy life terminated by a rapid decline. Much more effective communication about what is already known about maintaining a long and healthy life is needed. I would emphasize better understanding of how phytochemicals and zoochemicals such as melatonin, curcumin and spermidine, act at a molecular level. The interactions seen between oxidative stress, inflammation, autophagy, and epigenetic changes need to be untangled.

Alessandro Bitto: Prof. Stephen C. Bondy, how do you manage your multiple roles as researcher, author, editor, and mentor? Could you share some of your experiences with us? How do you balance work and life?

Siyan Chen: Some people can multi-task, I know that I cannot. Whatever time I set aside for one of these tasks has to be exclusive. This allows descent into a trance-like focused state where time flies and all else is shelved.

Alessandro Bitto: What advice, on elements inside or outside the lab, would you give to scientists developing their careers?

Stephen C. Bondy: Try not to compromise more than absolutely necessary. Do not hesitate to build upon and extend the ideas and findings of others. Keep an eye open for unexpected rather than predictable findings. It's easy to despair when trying to find a suitable position. However, one has to persist and eventually things will work out.

Alessandro Bitto: Yes! Your opinion is very enlightening to me! Thank you very much for sharing your valuable time and experience.