

ANNUAL REVIEW OF BIOCHEMISTRY

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ANNUAL REVIEW OF BIOCHEMISTRY

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PREFACE

In its 52-year history as one of the most influential publications in biomedical science, the *Annual Review of Biochemistry* has had only three editors, J. Murray Luck, Paul D. Boyer (now serving as associate editor), and Esmond E. Snell. Fortunately, all three men are still vital members of the editorial committee that guides the series.

However, the present volume is the final one to be published during the editorship of Dr. Snell [although because of the *Review's* two-year planning cycle, Volume 54 (1985) will be the last planned under his chairmanship of the editorial committee]. During Dr. Snell's 15-year term as editor (he also served as acting editor in 1963–1964), the volume—and *Annual Reviews Inc.* itself—joyously celebrated its 50th anniversary in 1981. Also during this period, several new *Annual Review* series were sired to fill the needs of those subdisciplines of biochemistry that had grown into clearly defined fields of their own—namely the *Annual Reviews of Biophysics and Bioengineering, Neuroscience, and Nutrition*. The first volume of the most recent addition, the *Annual Review of Immunology*, was published earlier this year. None of these offspring has undermined the preeminent position of the *Annual Review of Biochemistry*; highly qualified authors continue generously to contribute to the *Review*. As Associate Editor Boyer commented in the preface to Volume 50, those who contributed to the first volume back in 1932 could have had little idea how enormous the field of biochemical research would become in the ensuing half century. This exponential growth will surely continue, and further subdisciplines of biochemistry will gain their own *Annual Review* volumes.

Happily for *Annual Reviews Inc.* as a whole, however, this year does not signal a farewell to Dr. Snell, who will continue to serve on the Board of Directors (which he chaired while serving as President of *Annual Reviews Inc.* in 1973–1975). In this way, he will be able to keep a close watch over the progress of the series he has served so devotedly and with such editorial acumen. We thank him heartily for his lasting contribution to the *Annual Review of Biochemistry*. Dr. Snell can leave the editorial chair with the assurance that this prestigious series has earned increased international respect under his guidance.

Regular readers will notice that the present volume lacks the customary author index. Typesetting problems encountered in mid-production re-

quired that we engage the services of Aberdeen University Press of Glasgow, Scotland, who are to be thanked for completing the book at extremely short notice. Unfortunately, the computer program needed to generate the author index was not transferable to our new typesetter. An attempt to develop the author index computer program or to index by hand would have greatly delayed the publication of this volume. We thus postponed the author index in order to maintain our July publication date. It will appear next year in Volume 53 (1984).

ALISTER BRASS
EDITOR-IN-CHIEF
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SOME RELATED ARTICLES IN OTHER ANNUAL REVIEWS

From the *Annual Review of Biophysics and Bioengineering*, Volume 12 (1983)

Interactions of Water With Nonpolar Solutes, A. Hvidt

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Intracellular Measurements of Ion Activities, R. Y. Tsien

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From the *Annual Review of Immunology*, Volume 1 (1983)

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From the *Annual Review of Microbiology*, Volume 37 (1983)

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Structure, Assembly, and Function of Cell Walls of Gram-Positive Bacteria, G. D. Shockman and J. F. Barrett

Role of Proton Motive Force in Sensory Transduction in Bacteria, B. L. Taylor

From the *Annual Review of Neuroscience*, Volume 6 (1983)

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From the *Annual Review of Pharmacology and Toxicology*, Volume 23 (1983)

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From the *Annual Review of Physical Chemistry*, Volume 34 (1983)

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From the *Annual Review of Physiology*, Volume 45 (1983)

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Bile Acid Synthesis, G. Salen, S. Shefer

Special Announcement : New From Annual Reviews

Volume 1 of the *Annual Review of Immunology* (Editors: William E. Paul, C. Garrison Fathman, and Henry Metzger). Published April, 1983. 666 pp.; \$27.00 USA/\$30.00 elsewhere, postpaid per copy.

Some Historical and Modern Aspects of Amino Acids, Fermentations and Nucleic Acids, Proceedings of a Symposium held in St. Louis, Missouri, June 3, 1981, edited by Esmond E. Snell. Published October, 1982. 141 pp.; softcover; \$10.00 USA/\$12.00 elsewhere, postpaid per copy.

ERRATA

ANNUAL REVIEW OF BIOCHEMISTRY, Volume 50 (1981)

In *In Vivo Chemical Modification of Proteins (Post-Translational Modification)*, by Finn Wold:

On page 811, Ref. 62 should read, "Lederer, F..." (not Lederer, P.). On page 1117, in the Author Index, that reference (cited on page 792) should be listed with the other references to Lederer, F.

ANNUAL REVIEW OF BIOCHEMISTRY, Volume 51 (1982)

In *Enzymes of the Renin-Angiotensin System and Their Inhibitors*, by M. A. Ondetti and D. W. Cushman:

On page 286, paragraph two, the statement in which the definition of the International Unit of renin is equated with that of the Goldblatt Unit is incorrect. The Goldblatt Unit is an "animal unit" depending on the (variable) response in a dog. The International Unit of human renin is defined by the International Reference Preparation of Renin, human, for Bioassay, established by the World Health Organization in 1974.¹ Ampoules of this International Reference Preparation, each containing 0.1 IU of human renin, are available on request from the National Institute for Biological Standards and Control, Hampstead, London NW3 6RB, England.

¹ Bangham, D. R., Robertson, I., Robertson, J. I., Robinson, C. J., Tree, M. 1975. *Clin. Sci. Mol. Med.* 48: (Suppl. 2) 135-59

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Luis Hebeij



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FAR AWAY AND LONG AGO

Luis F. Leloir

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WHY RESEARCH	14

Biochemistry and I were born and grew at about the same time. Before the turn of the century some organic chemists and physiologists had laid the bases of Biochemistry. In 1906 two journals dealing with it appeared, the *Biochemische Zeitschrift* and the *Biochemical Journal*. The *Journal of Biological Chemistry* had started publication only one year before. In 1906 Arthur Harden and W. J. Young were able to separate "yeast juice into a residue and filtrate, each of which was itself incapable of setting up the alcoholic fermentation of glucose, whereas, when they were reunited the mixture produced almost as active fermentation as the original juice." This finding occurred only nine years after Edward Buchner had prepared a cell free yeast juice capable of fermentation. This line of work led eventually to the discovery of the multitude of enzymes, coenzymes, and intermediates of cell metabolism. In 1906 Tswett published the first description of chromatography.

Another important event (from my point of view) occurred in 1906. This was my birth in Paris, 81 Avenue Victor Hugo, just a few blocks away from the Arc de Triomphe.

The growth of Biochemistry was rapid; in a few decades most of the vitamins, hormones, enzymes, and coenzymes were discovered but at the

time of writing this essay it is showing signs of dismemberment. Molecular Biology, Cell Biology, Chemical Genetics, etc have risen from it and surely there will be others. I reached the age of 76 thanks to some clever arterial repair work carried out by Michael DeBakey in Houston.

I have borrowed the title of this essay from a delightful book by W. H. Hudson (1) that describes the wild life in the country near Buenos Aires. Hudson describes the same scenery and the same animals, flamingoes, armadillos, caranchos, vizcachas, etc that I saw in my infancy. It seems that both of us were interested in animal life and understanding nature, but while I became convinced that scientific knowledge and technology would be good for mankind, Hudson (2) had some doubts and he expressed them as follows: "Ah yes, we are all seeking after happiness in the wrong way. It was with us once, and ours, but we despised it, for it was only the old common happiness which Nature gives to all her children, and we went away from it in search of another grander kind of happiness, which some dreamer—Bacon or another—assured us we would find. We had only to conquer Nature, but how weary and sad we are getting!! The old joy in life and gaiety of heart have vanished."

B. A. HOUSSAY'S INSTITUTE OF PHYSIOLOGY

When I was two years old my Argentine parents brought me to Buenos Aires, where, after going through the studies and examinations necessary for graduating as an M.D. at the University of Buenos Aires in 1932, I worked at the Hospital of the University (Hospital de Clinicas) for about two years. I was never satisfied with what we did for the patients. Looking back on those times, I realize how profoundly medicine has changed since then. Medical treatment was in those days only slightly better than that exemplified by the French story, in which the doctor ordered, "Today we shall bleed all those on the left side of the ward and give a purgative to all those on the right side."

When I practiced medicine, except for surgery, digitalis, and a few other active remedies, we could do little for our patients. Antibiotics, psychoactive drugs, and all the new therapeutic agents were unknown. It was therefore not strange in 1932 that a young doctor such as I should try to join efforts with those who were trying to advance medical knowledge. The most active research laboratory in town was that directed by Dr. Bernardo A. Houssay, professor of physiology. In his work on the role of the pituitary gland on carbohydrate metabolism, he obtained some very novel findings, for which he, along with Carl and Gerty Cori, was awarded the Nobel Prize in Physiology and Medicine in 1947. Dr. Houssay suggested that I could do my thesis work under his direction and proposed several topics. My choice was the role of the adrenals in carbohydrate metabolism. My first

task was to learn how to measure blood sugar with the method of Hagedorn & Jensen. It was my first experience in a research laboratory. My ignorance in chemistry was unfathomable; for that reason I decided to follow some courses in the Faculty of Sciences.

Houssay helped me a lot. Not only did he do the brain work but he also carried out most of the adrenalectomies on the dogs. Houssay made daily rounds in the Institute and often left messages on minute pieces of paper. It was apparently through him that I learned to be economical. Even now, I usually write manuscripts on half sheets of paper already used on one side. Young people now are spendthrifts and would scandalize Houssay as they do me. The thesis work was awarded the Annual Prize of the Faculty for the best thesis, but it was undoubtedly Houssay's merit, not mine. Our close association lasted until Dr. Houssay's death in 1970. During all those years we saw each other daily and I could appreciate his cyclopean work in favor of Argentine science.

My enthusiasm for research increased gradually and, without noticing the change, I began to put in more hours at the laboratory and less at the hospital. I could do so because I did not have to earn my living with medical work. My great-grandparents came to Argentina, some from France, others from Spain, and bought land when it was cheap but still unsafe from the incursions of the Indians. Later these lands produced the cereal and grains and the cattle that brought riches to the country and to the pioneers who worked on them. These circumstances allowed me to devote myself to research when it was very difficult or impossible to find a full-time position for research.

It was a great privilege to be associated with Houssay. He worked very hard all his life trying to modernize the teaching of medicine, as well as directing his numerous students. His interest in research was very wide. Endocrinology was his main concern but he also ventured into many other aspects of physiology and biochemistry. He made intensive efforts to promote science. He was for many years president of the Argentine Association for the Progress of Science and later president of the Argentine Research Council. At times his efforts were very successful, but at other times the government was against him because of his outspoken manner and his liberal views.

INITIATION IN BIOCHEMISTRY (3)

After I finished my thesis work, Dr. Houssay advised me to work some time abroad. In consultation, with Dr. V. Deulofeu, professor of biochemistry, and Dr. R. de Meio, I decided that a good place would be the Biochemical Laboratory of Cambridge University, directed by Sir Frederick Gowland Hopkins, who had received the Nobel Prize in 1929, together with Eijkman,