

**THE SIXTEENTH CARL G. HARTMAN AWARD  
HENRY A. LARDY**

The Carl G. Hartman Award is given in recognition of a career of research and scholarly contributions in the field of reproductive biology. Since its inception, the award has been generously funded by Ortho Pharmaceutical Corporation.

The 1984 award is presented to Professor Henry A. Lardy for outstanding contributions to research, teaching, and leadership in reproductive biology. He is a man for all seasons and subjects.



He was born in 1917 in Roslyn, South Dakota where he grew up on the family farm. In this setting of the traditional midwestern values, steadfastness, diligence, common sense, rigorous honesty, and concern for his fellow human beings became deeply ingrained in his character. He developed abiding interests in biology, domestic animals, agriculture and conservation. His experiences on a farm during the years of the Great Depression may have developed a compelling need to contribute through science and humanitarian actions. In 1939 Henry Lardy received the B.S. degree, with a major in chemistry, from South Dakota University. He then moved to Madison, Wisconsin which has been home ever since. After receiving the M.S. and Ph.D. degrees in biochemistry from Wisconsin, he did post-graduate work at the Banting Institute. He joined the faculty at Wisconsin in 1945 and at the age of 33 became Professor of Chemistry in 1950.

In 1939 it was known that bull sperm could be used to inseminate cows artificially. However, this was not a matter of practicality because sperm could not be preserved for a sufficient period of time, despite the efforts of many investigators. In 1940 Lardy, at the age of 23, published with Phillips a trail-blazing investigation which demonstrated that an egg yolk-buffer medium would preserve the fertility of bull sperm for prolonged periods. Semen could now be shipped to various parts of the United States and Canada. This technical advance fostered the development

of artificial insemination as an industry, and steadily lead to the improvement of dairy herds throughout North America. Between 1940 and 1945 Lardy and Phillips published 11 papers on the metabolism of sperm that stand as classics. The principal findings were: 1) the phospholipid fraction of egg yolk is responsible for prolonged motility of sperm, 2) an interrelationship exists between the oxidative and glycolytic pathways, 3) motility depends on energy sources as demonstrated by metabolic inhibitors and uncouplers of oxidative phosphorylation, and 4) oxidation of sperm lipid resulted in the production of ATP. These contributions marked the beginning of sperm metabolism as a field of biologic investigation.

These findings about spermatozoa had broad implications for general cellular metabolism in other tissues. They indicated, for the first time, that acetate and fats were oxidized through the citric acid cycle. Quite appropriately Lardy expanded his investigations to include muscle and visceral tissues such as liver and kidney. His fundamental contributions in general cellular metabolism are legion. Only a few of his fundamental contributions to mammalian cell physiology and metabolism are indicated here: 1) the role of inorganic phosphate and ADP in the control of the respiratory rate; 2) the carboxylation of propionate to form succinate; 3) solubilization of the fatty acid-oxidizing system of mitochondria; 4) systematic use of toxic antibodies, including oligomycin and other inhibitors, to study oxidative phosphorylation and other metabolic events; 5) the critical roles of oxaloacetate, malate and aspartate in the gluconeogenic pathway from pyruvate; and 6) the regulation of gluconeogenesis by epinephrine and the a-adrenergic system.

Throughout these basic discoveries, Lardy and his co-workers regularly returned to the study of spermatozoa. They defined the differences in the metabolism of ejaculated and epididymal spermatozoa. The reactions of oxidative phosphorylation in spermatozoa were described. The stimulatory effects of methylxanthines and cyclic AMP on sperm motility were reported. Sperm cyclic AMP-dependent protein kinase activity was demonstrated. The role of pyruvate in the formation of acetyl carnitine, an energy source for motility, was elucidated. Through the use of a

calcium ionophore, which he had previously developed, Lardy and his colleagues demonstrated that sperm accumulate  $\text{Ca}^{2+}$  during capacitation and that the influx of  $\text{Ca}^{2+}$  stimulates motility. Most recently a bovine seminal plasma calcium transport inhibitor protein was isolated and characterized. As colleagues in these endeavors he has had many graduate students, postdoctoral fellows, and collaborators among his peers.

Dr. Lardy is a member of the National Academy of Sciences and has served as President of the American Society of Biological Chemists. He has participated in numerous editorial boards and advisory committees and received prizes and distinguished lectureships.

The SSR recognizes Henry A. Lardy as a pioneering reproductive biologist of impressive breadth and depth who introduced and developed the field of sperm metabolism while establishing many of the ABCs of general biochemistry.

*Helen A. Padykula, Chairperson*

SSR Awards Committee

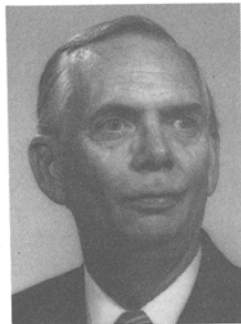
University of Massachusetts Medical School

Department of Anatomy

Boston, Massachusetts 01605

**THE SEVENTH SSR RESEARCH AWARD  
CHARLES BARRACLOUGH**

The SSR Research Award is given to an active regular member of the Society for outstanding research published over the past 6 years, regardless of the age of the recipient. The 1984 award is presented to Professor Charles A. Barraclough of the University of Maryland for outstanding contributions to current understanding of the neuroendocrine mechanisms that control the release of pituitary gonadotropins.



Charles Barraclough was born in New Jersey in 1926. He received a B.S. degree from St. Joseph's College, Philadelphia, and then from Rutgers University the M.S. degree and Ph.D. in physiology. His predoctoral studies under the guidance of Dr. James Leatham were conducted in a laboratory located over a garage in New

Brunswick. The animals were housed in cages fabricated from bread boxes; woodshavings were obtained by weekly trips to the local sawmill. This was truly "hands-on" research.

Infertility produced in neonatal female rodents by a single injection of testosterone was the topic under study. It marked the origin of a lifelong interest in neuroendocrinology. As well as being the first of many models Barraclough would develop, this animal model was to be used repeatedly to obtain answers to the questions posed. At this time Barraclough stood at a crossroads: a career in biologic research or a career as a piano player in well-known bands? Fortunately for us he went up the hard road of basic biomedical research, but according to admirers the world of popular entertainment lost out greatly.

Barraclough proceeded into fruitful postdoctoral years at UCLA under the guidance of the remarkable Dr. Charles Sawyer. From then on, Barraclough's research program has been a closely interwoven series of physiologic experiments directed at unraveling the complex interactions that occur along the hypothalamic-pituitary-gonadal axis. The internal coherence of these numerous experiments creates the exceptional strength and validity of his overall scientific contribution.

His unusual persistence in attacking this important and complex problem has produced an abundance of new information and creative interpretations. His remarkable staying power is reflected in an unrelenting continuity of thought and effort which pervades his publications in relation to experimental design, development of animal models, and careful evaluation of existing literature. His motto in research appears to be "in vivo veritas," since his work emphasizes the basic importance of defining hormone action under physiologic conditions.

It is generally agreed that during the past 6 years Barraclough and his associates have provided us with a brilliant series of experiments on the role of catecholamines in the regulation of gonadotropin secretion. This remarkable achievement is a synthesis which rests on a long preamble of experimentation in Barraclough's laboratory. We now have better comprehension of the natural process that activates the neural component involved in ovulation. The high quality of these experiments led in 1983 to a return

engagement to speak at the Laurentian Hormone Conference. Here only some of the highlights of these investigations can be mentioned.

Essential components of the neuroendocrine control system and their interrelationships have been defined. Studies with Scott Chappell demonstrated that selective release of FSH occurs from activation of only a portion of GnRH system. The strength and duration of the GnRH stimulus delivered to the pituitary cells determines whether FSH or LH or both hormones are released. Also, an inhibin-like ovarian factor was identified as a potential control mechanism for blocking preovulatory FSH selectively. The positive feedback effects of estradiol and progesterone on induction of ovulatory LH and FSH secretion were examined. Recent work demonstrates that progesterone amplification of LH secretion depends on the amount of estrogen receptors produced by estradiol in the hypothalamus. The turnover rates of norepinephrine and dopamine were measured in microdissected hypothalamic nuclei. Norepinephrine initiates the preovulatory gonadotropic surge by releasing newly synthesized GnRH from axon terminals. The relationship between catecholamine turnover rates and plasma concentrations of estradiol and progesterone were determined. From the interrelationships of these physiologic phenomena, a detailed timetable for the intrahypothalamic events has been constructed for proestrous rats. The preovulatory secretion of gonadotropins is preceded by sequential changes in norepinephrine, dopamine, and GnRH content.

The expression of the entire sequence of neuroendocrine events depends on the maturation of the ovarian follicles under basal FSH and LH. As serum estradiol rises, there is increased hypothalamic release of norepinephrine and increased hypothalamic synthesis of GnRH. Estrogen present in "adequate concentration and duration" is the zeitgeber of events that precede ovulation. The neurohypophyseal-ovarian circle appears to have been completed.

Charles Barraclough has been accompanied in this great, continuing adventure by many predoctoral and postdoctoral students. His leadership in research has been recognized by the national scientific community through continuous NIH funding for over two decades, his membership and chairmanship of NIH

Reproductive Biology Study Section, and as a member of several editorial boards.

Dr. Charles Barraclough is an astute experimentalist of impressive originality and of high productivity in reproductive biology. His investigations of neurohypophyseal-ovarian interrelationships have paved the way toward greater understanding of the physiologic control of ovulation.

*Helen A. Padykula, Chairperson*

SSR Awards Committee

University of Massachusetts Medical School

Department of Anatomy

Boston, Massachusetts 01605

#### NEW INVESTIGATOR AWARD

Kristen A. Ivani of the University of Idaho won first place in the New Investigator Award. A native of San Francisco, she received a B.S. in Animal Science from the University of California at Davis in 1982 and a M.S. in Animal Science from the University of Idaho in 1984. The topic of her prize-winning Master's degree research, "Diagnosis of pregnancy by RIA of a pregnancy-specific protein in serum of the cow," was performed in the laboratory of Dr. R. G. Sasser and C. A. Ruder at the University of Idaho. This investigation proceeded from molecule to meadow. A pregnancy-specific protein was isolated and characterized. A pregnancy test was developed and tested on a herd of 100 beef cows. The test has high accuracy and considerable potential for wide application. Ivani is currently a predoctoral student at Colorado State University.

Dr. K.Y.F. Pau of the Oregon Regional Primate Research Center won the second place award. A native of Hong Kong, he received the B. S. (1971) and M. S. (1974) degrees in Zoology from the National Taiwan University. His Ph.D. study in Veterinary Biosciences (1983) was performed in the laboratory of Dr. Gary Jackson at the University of Illinois. The topic of his prize-winning postdoctoral research, "Release of GnRH and gonadotropins in the rabbit: intrahypothalamic perfusion of norepinephrine stimulates GnRH release," was pursued in the laboratory of Dr. Harold Spies at the Oregon Regional Primate Research Center. This well-designed project provided clear-cut new observations on the interrelationships of the

hypothalamic-pituitary-gonadal circuit in the rabbit. By use of the technique of push-pull perfusion, Dr. Pau made direct measurements of GnRH secretion by the hypothalamus. A local stimulatory effect of norepinephrine on neuronal release of GnRH was identified. He demonstrated that GnRH is released in a pulsatile manner that coincides with pulsatile release of FSH from the pituitary. The tight coupling of pulsatile GnRH and LH secretion was documented, along with negative feedback of physiologic levels of estrogen on GnRH.