THE FACULTY OF MEDICINE
Harvard University

Roy Orval Greep

Roy Orval Greep was born in 1905 on a farm near Longford, Kansas where his grandfather, David, had homesteaded. His education began in a one-room elementary school. He continued in the two-room high school but after six weeks he withdrew for "more soul-satisfying interests such as herding cattle, hunting coyotes, trapping etc." After three years, a life-changing experience occurred on a sweltering September afternoon: from farmer to entering the road to becoming one of the truly great endocrinologists of his day. Roy was shucking heavy sheaves of sorghum left to dry by a horse-drawn binder. He was approached by a well-dressed man, "a city dude", who he presumed was an insurance salesman but proved to be the new high school principal, seeking Roy's return to high school. With the burdensome workload and disappointing financial returns on the farm, Roy accepted the principal's challenge. This time he was captivated by the excitement of learning and graduated from high school in 1926.

Roy went to Kansas State Agricultural College where his freshman performance in zoology, earned him an assistantship at $9.00/month. His first research experience was collecting cow's urine, to be processed in an unsuccessful search for a female sex hormone recently reported in urine of pregnant women. After graduation in 1930, Roy enrolled in the University of Wisconsin and earned the Master's and Doctor's degrees (1934) in Zoology working with highly motivated graduate students and postdoctoral fellows in the laboratory of F.L. Hisaw (also a Kansas stater) who was becoming well known for research on the reproductive hormones of the anterior pituitary gland and the gonads. Recent Ph.D.'s in the Great Depression received few job offers; Roy stayed at Wisconsin as a postdoctoral Fellow with the meager stipend of $62.50/month. The ability to remove the pituitary gland from juvenile rats was urgent and had proved elusive to numerous investigators. Roy, with his wife, Eunice (married in 1931), worked late at night for weeks and perfected the parapharyngeal approach. Finally, he could cut through the palate of

a weanling rat with a tiny trephine, expose the glistening pink pituitary gland, remove it by suction without hemorrhage and suture the wound, producing a viable hypophysectomized rat for research - all within a few minutes. The availability at will of hypophysectomized rats made possible the design of assays for the characterization of two pituitary gonadotrophic hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH). A bioassay for luteinizing hormone devised by Janet McArthur, using a Greep-identified prostate weight parameter, revealed that luteinizing hormone is present in adult women at all times and is a key component of the mid-cycle gonadotropic surge that triggers ovulation.

In 1935 Hisaw was invited to become a Professor at the Harvard Biological Laboratories and took with him Roy and another Fellow, H.L. Fevold, to establish an endocrine research program. Roy remained at Harvard for three years where he had numerous opportunities for independent and collaborative research which he extended to the control of spermatogenesis and androgenic functions of the testes in hypophysectomized immature and adult rats, rabbits and monkeys. In seminal observations, he demonstrated that sexual dimorphism and sexual maturity were not imparted by the pituitary gland, as believed at the time, but by higher centers. This observation anticipated the revolution in endocrinology and a beginning emphasis on neuroendocrinology.

In 1938, Roy joined the new Squibb Institute for Medical Research for three years with complete freedom in research and unlimited financial support. With van Dyke and Chow he set out to purify and characterize, chemically and biologically, the pituitary gonadotrophic hormones, FSH and LH. Numerous of these fundamental studies of reproductive physiology had practical medical applications, such as an assay for LH in urine based on his demonstration that androgen secretion can be induced by LH stimulation of the Leydig cells of the testes of the hypophysectomized immature rat. His research on the basic physiology of pituitary gonadotrophic hormones contributed in a major way much later to the development of birth control pills.

Still proficient at performing hypophysectomies, Roy one day was unable to fasten a young rat to the operating board with an elastic band hooked over the maxillary incisors. Examination showed that its incisors were missing. Instead of discarding it (“Chance favors the prepared mind” – Pasteur), the rat was set aside to breed using a ground diet to enable it to ingest adequate calories. Later he found that the diet could be made still more suitable by increasing its caloric concentration by adding fat. (He found that the same was true for hypophysectomized rats.) This was the beginning of the “ia” (incisor absent) strain - a simple homozygous recessive. Dissection indicated that the incisors and molars had formed embryologically but were unable to erupt because no openings in the alveolar bone had been created by selective resorption. These rats were found to have an abnormality of parathyroid hormone function. This observation attracted the attention of Dr. A. LeRoy Johnson and others at the newly reorganized Harvard School of Dental Medicine. They were seeking scientists to conduct research within the School to increase knowledge in the biological sciences underlying the specialty of dental medicine and to foster the spirit of inquiry among students and faculty. In the fall of 1944 Roy returned to Harvard with a joint appointment in Anatomy in the Harvard Medical School and in Dental Science in the

Harvard School of Dental Medicine. His ability to provoke and stimulate inquiry was illustrated by his excitement years later, when a young postdoctoral fellow (Paul Goldhaber) called him to his laboratory to see the positive influence of parathyroid hormone on resorption of bone in culture from an "ia" rat.

In 1952, Roy was invited to become Dean of the Harvard School of Dental Medicine. He accepted - the first Dean of an American dental school who was not a dentist. As Dean he maintained a highly active research program. That same year he also became the Managing Editor of *Endocrinology*, a responsibility held for seven years. The editorial office was in their home and Eunice was his enthusiastic and untiring assistant and secretary. They did much of the editorial work after they had had family dinner with their three daughters, Ann Louise, Marjorie and Nancy. That year he took over as editor of the Department of Anatomy's Textbook of Histology for which he wrote seven chapters. Greep's *Histology* was first published in 1953, with successive editions in 1968, and in '73 and '77 joined by Leon Weiss as co-editor, with translations into Spanish, Italian and Portuguese. Roy was chosen for other major editorial responsibilities over the years, such as co-editor of the *Handbook of Physiology*, section on Endocrinology, and Volume Editor of a series of books on reproductive physiology. He was a founder of the Laurentian Hormone Conference; for 13 years he was the editor of the conference proceedings, "Recent Progress in Hormone Research". During these years, he continued to push the frontiers of endocrinology beyond the conventional and produced a cornucopia of important findings. Two major examples include his fostering of the studies of Ernst Knobil on the species specificity of growth hormone, and the development with Paul Munson of a rapid effective method (by cautery) for parathyroidectomizing young rats. The former endeavor led to the successful use of primate growth hormone in the treatment of pituitary dwarfism in children. The latter led to the bioassay method that enabled isolation of pure parathyroid hormone and indirectly to the discovery of the hormone, calcitonin (Paul Munson and Phil Hirsch) which lowers blood calcium and is used in the treatment of certain bone diseases.

The ability to carry numerous major responsibilities simultaneously resulted in part from Roy's ability to understand needs, to select dependable, imaginative colleagues, to challenge them with tasks and entrust them to carry through. When he became Dean, only a few lectures in the predoctoral program were devoted to Orthodontics, even though there was a strong postdoctoral program, located at the affiliated Forsyth Dental Infirmary for Children (now the Forsyth Institute). When the dental faculty decided that predoctoral students should receive clinical instruction in Orthodontics, Roy appointed the head of the latter program, C.F.A. Moorrees, to plan a predoctoral program. The objective was to show dental students the spectrum of orthodontic needs and care. Postdoctoral Fellows in Orthodontics became primary instructors explaining diagnosis, development of a treatment plan and the objectives of this plan. Predoctoral students participated in the actual treatment. This program soon was considered revolutionary at national meetings and was adopted at other schools.

Dental students were often perplexed that their Dean did not have the degree that they were aspiring to achieve. Nonetheless, Roy and Eunice, a tall handsome couple, were very popular in every situation,

entertaining students and colleagues frequently. Roy had a great knack for delivering short, humorous addresses to varied audiences. An example is the frequency with which students invited him to speak on Class Day in the Medical Area Quadrangle to the graduating medical and dental seniors and their families. (It was often suspected that Eunice was partly responsible for the humor and aptness of his comments.)

In 1967, Roy resigned as Dean to become the John Rock Professor of Population Studies and first Director of the newly created Laboratory of Human Reproduction and Reproductive Biology in the Harvard Medical Area. Following his retirement from Harvard in 1971, he was involved full time with the Ford Foundation as Project Director for the massive Review of Reproductive Sciences and Contraceptive Development. He was a member of the World Health Organization Expert Advisory Panel on Human Reproduction from 1963 to 1979.

Roy served many scientific organizations in numerous capacities. He was honored with their highest awards. From the Endocrine Society he received the Fred Conrad Koch medal in 1971 and the Distinguished Leadership Award in 1978. The British Society of Endocrinology presented him the Henry Dale Medal; the British Society for the Study of Reproduction with the Carl Hartman Award, and the British Society for the Study of Fertility with the F.H.A. Marshall Medal - truly a quintuple crown for a man who in the face of many honors remained genuinely modest and self-effacing. This outward demeanor belied his remarkable erudition, the breadth and depth of his scholarship and the large number of young investigators attracted to him who he selflessly guided in their careers.

Roy's many accomplishments were attained in the midst of wholehearted commitment to family and great enjoyment of life. His devotion for Eunice and their three daughters had top priority to be certain that their lives were enhanced to their full potential in enjoyable ways. Eunice died a few months before him after 66 years of marriage. He was committed tirelessly to hard work, clearly an example to family, friends and colleagues. His contagious joy in life with that infectious, irrepressible chuckle, encompassed his work, his relationships to people, as well as his travels, and delight in being exposed to the new and challenging. At 90 he purchased and learned to use a Macintosh computer above which he had a quote: "Yesterday is gone, tomorrow is a mystery, today is a gift." In his memoir he states "As an anatomist my interest was not in form per se – but in the functional interpretation of form." "What does it do and how?" That Roy Orval Greep endeavored to do with gusto throughout his long life and to the enjoyment of all around him.

Respectfully submitted,

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