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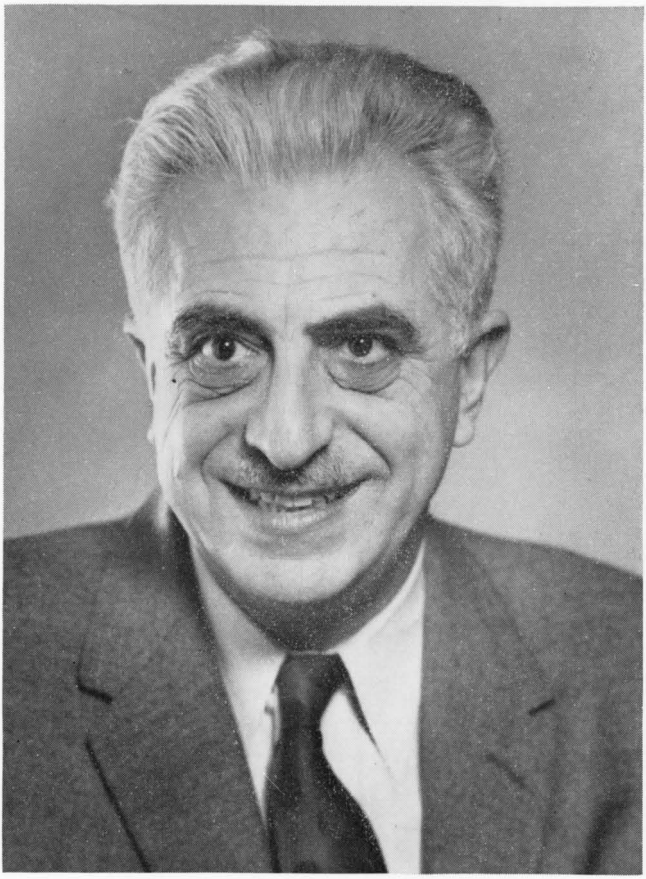
GREGORY GOODWIN PINCUS

1903—1967

A Biographical Memoir by

DWIGHT J. INGLE

Biographical Memoir



Gregory Pincus

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April 9, 1903–August 22, 1967

BY DWIGHT J. INGLE

GREGORY PINCUS achieved important aims in life and had a salubrious influence upon the lives of many others and he died while fully active as a scientist-statesman of the world. Gregory Pincus was an ambitious man who sought, gained, and enjoyed power in certain fields of biology which relate to medicine. He did not achieve power and fame by great discovery, luck, privilege, or favoritism but by devotion to noble goals in which he wholeheartedly believed. He could have used his knowledge and influence to gain wealth but did not. Among a host of individual achievements, three especially brought the power that he quietly cherished. These were the organization and direction of the Laurentian Hormone Conference, the organization and direction, with his friend Hudson Hoagland, of the Worcester Foundation for Experimental Biology, and the development of the antifertility pill.

He was interested in the processes of reproduction and aging, and in several of the great diseases, such as arthritis, cancer, and psychoses. He was interested in the functions of the adrenal cortex and its response to stress. He took the chair at many conferences. He served as chairman of the Endocrinology Study Section of the United States Public Health Service and as chairman of the Endocrinology Panel, Cancer Chemotherapy National Service Center, of the National Institutes of Health. It was

claimed by some that he held too much power over other endocrinologists but I was there and remember him only as a skillful, efficient, impartial chairman. He wrote several books and monographs.

Among the honors received by Gregory Pincus were the Oliver Bird Prize (1957), the Albert D. Lasker Award in Planned Parenthood (1960), the Sixth Annual Julius A. Koch Award (1962), the *Modern Medicine* Award for Distinguished Achievement (1964), the City of Hope National Medical Center Award (1964), and an honorary professorship, San Marcos University, Lima, Peru. He became a Fellow of the American Academy of Arts and Sciences (1939) and a member of the National Academy of Sciences (1965); he was President of the Endocrine Society (1951-1952); he received the Cameron Prize in Practical Therapeutics from the University of Edinburgh (1966) and the Scientific Achievement Award of the American Medical Association (1967).

He was born in Woodbine, New Jersey, the eldest son of Joseph W. and Elizabeth F. Pincus. The father was a graduate of Storrs Agricultural College in Connecticut, taught at a school of agriculture, and edited a farm journal. The mother came of a family which was distinguished in the agricultural sciences. Gregory Pincus was born into an environment which stimulated interest in books, culture, and science.

He attended elementary and secondary public schools in New York City and became an honor student at Morris High School, from which he graduated. He was president of high school literary and debating societies. He earned money doing odd jobs outside of school and doing farm work during summers.

In 1924 he received a B.S. degree from Cornell University. While there as an undergraduate he founded and edited the *Cornell Literary Review*. He entered graduate school at Harvard, majoring in genetics and minoring in physiology. He received the M.S. and Sc.D. degrees in 1927. Following this, he became

a National Research Council Fellow for three years and studied at the Kaiser Wilhelm Institute and at Cambridge University. He returned to Harvard as an instructor in biology in 1930 and became an assistant professor in 1931, holding this appointment until 1938. He spent 1937-1938 as a visiting investigator at Cambridge University.

His early training and research represented an interest in the inheritance of physiological traits. His first scientific paper, published in 1926 with Horace W. Feldman as co-author, was "On the Inheritance of Albinism and Brown Pigmentation in Mice." Other studies on genetics were done later. A series of studies of geotropisms in rats and other mammals in which the mode of transmission of proprioceptive function was analyzed were reported by Gregory Pincus and Professor W. J. Crozier of the Biological Laboratories of Harvard. There were related studies of the transmission of reaction mechanisms governing respiratory movements and heartbeat in inbred mouse strains. He was influenced by Crozier and by W. E. Castle to turn to reproductive physiology and he published a paper on the living eggs of the rabbit in 1930. During the early part of the 1930s his interest in reproductive physiology, including the sex hormones and the gonadotrophic hormones, was represented by research reports in this field, but he also did collaborative studies on the inheritance of diabetes mellitus with members of the staff of the famed Joslin Clinic in Boston, especially with Priscilla White. With R. Shapiro, he developed the first successful method of extensive partial pancreatectomy in the rat, a procedure that has been widely used.

In 1932, with O. S. Baum as co-author, Gregory Pincus published his first paper on ovarian hormones and the gonadotrophic principles of pregnancy urine, and for the rest of his life much of his research was focused on the hormones associated with reproductive processes. He studied living ova *in vivo* and *in vitro* and the processes of fertilization. During these

years at Harvard, he pioneered in producing multiple ovulation in animals and in transplanting animal ova from one female into another which then carried growing embryos to term. He found that certain phases of ovum development *in vivo* were regulated by ovarian hormones and launched a series of studies on ovarian hormone biogenesis and metabolism along with studies of their effects on ovum travel, uterine function, and blastocyst and embryo maintenance. Studies on the actions, metabolism, and biochemical determination of ovarian hormones grew apace during these years. Toward the end of the 1930s he published reports on the production of fatherless rabbits produced by the artificial activation of ova.

Suddenly, Gregory Pincus became widely known, for the news appealed to the lay press and the public. His friends began to refer to the process as "Pincogenesis." The achievement has never been shown to be independently reproducible upon demand, a requirement for proof of a claim in science. His detractors, of whom there have been a significant number, have never forgotten the matter; his friends and admirers, not all free of uncertainty about the validity of the claim, believe that he was always an honest scientist who did not knowingly go beyond his facts.

In 1938 Gregory Pincus moved from Harvard to Clark University where he became a visiting professor of experimental zoology until 1945 and held a Guggenheim fellowship from 1939 to 1941. He also held a titular professorship in physiology at Tufts Medical School from 1946 to 1950, which was followed by a similar professorship in biology at Boston University Graduate School.

During the spring of 1943, a conference on hormones, sponsored by the American Association for the Advancement of Science, was held at Gibson Island near Baltimore. It was a significant event in the lives of some thirty participants, especially for Gregory Pincus, and the consequences had an en-

during impact throughout the world of endocrinology. The conference was organized by Hans Jensen, then of the Upjohn Company, and by Fred Koch of the University of Chicago. The conference was a great success but for many reasons Gibson Island, a private club, was an unpleasant place to meet. For example, a distinguished Negro scientist, Dr. Percy Julian, had been invited to the conference. He was not permitted to enter the club until after three days of protesting by members of the conference. Significantly, it was Gregory Pincus who led the belatedly successful appeal to the management of the club to permit Dr. Julian to join us. The group wanted to meet again but not at Gibson Island. Gregory Pincus, Robert W. Bates, and Samuel Gurin were selected to arrange the next conference. The Montreal Physiological Society invited the group to come to Canada and hold the conference at Mont Tremblant. And so the Laurentian Hormone Conference was born with Gregory Pincus as the permanent chairman.

The Laurentian Hormone Conference was a success from the beginning but determination and skill in human relations were necessary to carry it past threatening problems. The personal qualities of Gregory Pincus became known and appreciated by his fellow conferees. He was not a modest man but neither was he haughty nor was he intolerant of the limitations and foibles of others. It was not possible to publish the papers presented at the first hormone conference as planned but an annual volume called *Recent Progress in Hormone Research* was published each subsequent year and the publication lag was reduced to a reasonable period. Early financial problems were solved in part by contributions from pharmaceutical houses. During the second annual meeting at Tremblant, the anti-semitism of the owner of the club became overt and arrangements were made to meet elsewhere. The Laurentian Hormone Conference did not return to Tremblant until the owner of the club died and it came under new management.

Membership in the conference required application and it was not possible to accommodate all applicants. For a time, many who were not invited to the conference became critical of what they claimed were arbitrary decisions by Gregory Pincus to invite only his personal friends. These criticisms were not deserved. Gregory was never overtly distressed by criticism or hostility but those close to him knew that he was hurt by accusations of partiality. He established an anonymous committee which processed applications for membership and assigned priority ratings favoring qualified endocrinologists who had not been accommodated the first or second year of application. He appointed committees on arrangements and on programs as well as a senior advisory committee of some of us who were "old guard." Criticisms of the management of the conference by Gregory Pincus gradually abated, and his skills as an organizer became widely appreciated. When the business affairs of the conference grew, a corporation was formed to handle its funds and business transactions. After the conference began to earn its way, it became possible to pay the traveling expenses of invited speakers from abroad. It was characteristic of Gregory Pincus to be unobtrusive; he spoke briefly to open each conference and to set the tone of informality and good humor. Thereafter he made necessary announcements, but generally kept in the background.

This, in brief, is how Gregory Pincus came to create a ferment in the field of endocrinology, to facilitate the exchange of ideas and the excitement of discovery, and to winnow out much of the dogma which was once taught about the ductless glands. The Laurentian Hormone Conference set new standards in a field previously dominated by physicians who were strangers to the laboratory by bringing together from all over the world outstanding medical and nonmedical scientists from universities, institutes, research hospitals, and from industry.

Although Gregory Pincus did not achieve success by falling heir to a kingdom, there were several friends and admirers who

helped him create domains, and to them he was deeply grateful. The most important was his friend Hudson Hoagland, with whom he joined in 1944 in founding the Worcester Foundation for Experimental Biology (WFEB). This was a bootstrap operation representing scientific free enterprise, and under the co-directorship of the two men it grew and attracted to it some of the world's most gifted young endocrinologists. Pincus now assumed the role of a research director. Although active in the planning of research, he did less and less of it with his own hands. He was now creating a role for himself as an organizer and director and was to develop into a scientist-statesman.

One of the most remarkable and fruitful accomplishments at the WFEB was the perfusion of beef adrenal glands so that large amounts of corticosteroids were produced. Gregory Pincus believed the procedure had commercial possibilities. He assigned Oscar Hechter to the problem. Five years passed before beginning success was achieved, much of the credit for which belongs to Hechter. By then the chemical synthesis of the corticosteroids had become successful and microbiological methods were soon to come. Hechter was among the first to predict the usefulness of the latter. He and his team of collaborators, whose selection and organization were guided by Pincus, then exploited this biological system to elucidate the steps of biosynthesis of the corticosteroids and the site of action of the adrenocorticotrophic hormone of the anterior pituitary.

The WFEB became an important center for research on the steroid hormones and for training young investigators in the methods of steroid biochemistry. It represented many other research activities as well. Hoagland and Pincus invited to it many gifted young scientists who were in need of opportunity. The two men, Hoagland, the Executive Director, and Pincus, the Scientific Director, so different in many traits of personality, were alike in exhibiting a generous spirit.

His titular professorships, first at Tufts and later at Boston

University Graduate School, were for the purpose of allowing graduate students to work for the Ph.D. at the WFEB. Although Gregory Pincus was a gifted lecturer, he devoted relatively little time to formal teaching. Most of the young scientists whose advancement was enhanced by him were postdoctorates and were already zealous achievers by the time they came to him.

It is important to mention Min Chueh Chang, one of the first members of the Institute, who became a foremost authority on mammalian reproduction. Studies done in the early 1930s had demonstrated that the overdosing of laboratory animals with ovarian hormones would interfere with the reproductive cycle and cause sterility. In 1936, Pincus and Kirsch published on sterility in rabbits caused by injections of oestrone and related compounds. Subsequent studies demonstrated the possibility of achieving physiologic control over fertility rather than pathologic interference with reproduction. M. C. Chang began to search among the steroids for antifertility agents and found a number which were orally active in rats and rabbits. Gregory Pincus, influenced by his friend Margaret Sanger, knew the need of the world for effective social control of human fertility and had the knowledge and the courage to aim for this goal.

Funds for research on fertility-controlling agents could not be obtained fifteen years ago from the large foundations or from the federal government. However, the late Mrs. Stanley McCormack generously contributed a sizable annual budget to support this work and did so continually until her death in January 1968. Without her aid, this program of research would have been greatly handicapped. Later, the Josiah Macy, Jr. Foundation and the G. D. Searle Company, and still later the Ford Foundation, through the Population Council and the National Institutes of Health, contributed to this work.

When the clinical testing of antifertility agents by Dr. Celso Garcia and Dr. John Rock confirmed the results on ex-

perimental animals, Gregory Pincus set up clinical field tests in Puerto Rico and Haiti. He now became an entrepreneur and a missionary who traveled all over the world studying the problems of human numbers, teaching means of control, and recruiting disciples. Always a voracious reader, he kept in touch with the scientific literature and with the details of research in his Institute.

Gregory Pincus was sensitive to the medical, ethical, political, and religious problems relating to population control and he responded to them as a wise scientist. At least twice in his life he had authored research reports in which the conclusions were not documented by well-controlled experiments. He knew that he had been criticized and was now determined that each step forward should be supported by unassailable evidence. The long-term effects of antifertility agents are not yet known with certainty and now and then there are sobering claims for pathogenesis in a small number of patients, but in general, the laboratory and clinical testing of these agents was done in the best possible way.

The activities described above, plus love and selflessness to family, would have drained the energies of any man not well endowed with physical strength and emotional reserve, but Gregory Pincus attended to these and many other interests and responsibilities, and for most of his life seemed as fresh and relaxed as he was urbane. When confronted by emotional flare-ups, he remained calm. He knew how to relax. I am reminded again of the first hormone conference held at Gibson Island. A number of conferees were crowded into an untidy, too warm, poorly ventilated dormitory where the odds against restful sleep were higher than wanted. It was Gregory Pincus who slept soundly and soundfully throughout the night and awakened in the morning to remark to his less fortunate companions, "Isn't it amazing that this number slept in one room and nobody snored?"

I do not know when Gregory Pincus became ill, but during the last three years of his life there were times that he looked unwell and there were rumors that this was so. He either did not then know that his illness was serious or, if he recognized the fact within the quiet of his mind, he did not want it known to others. I quote from a letter written by him to me March 28, 1966: "Oscar Hechter tells me that you have been informed that I am a seriously ill man. This is entirely untrue, and I wish you would do your utmost to scotch this rumor. At the moment I am healthier than I have been in many years. As nearly as I can make out, a minor setback which occurred about a year ago has been the source of the unfounded rumor." Shortly thereafter, a physician friend told me the nature of Gregory's illness, a correct deduction which was made from his appearance and a knowledge of the symptoms rather than a personal medical examination. In any case, Gregory Pincus would not play the role of an invalid. When it became known that he had myeloid metaplasia, he assured his friends that modern therapeutic measures would allow him to live into retirement years. He continued to work and travel. I received a letter from him written a week before he died, asking me to chair a session at the 1967 Laurentian Hormone Conference. I was traveling on the day of his death and did not learn of it until we arrived at Tremblant. His secretary said that in lucid moments prior to death he asked that the hormone conference be held as planned. I remembered that many years earlier Gregory Pincus had opened a conference with the announcement of the first deaths among members of the old guard and had commented that the future of the hormone conference was uncertain, that man is mortal, and that the conference might not endure beyond the lives of those who presently organized and enjoyed it. But when Gregory Pincus died, the Laurentian Hormone Conference had long since become a viable, healthy institution, with an organization and gist that would serve the future as a living me-

morial to the man who guided it for more than two decades.

Oscar Hechter has written a homage* to Gregory Pincus in which he says, "I feel that Gregory Goodwin Pincus—Goody to his friends—is too big a man to treat in a ritualistic fashion. Pincus for me represents the prototype of a *new* scientist, whose life and achievements merit critical examination and analysis. On a planet rapidly being irreversibly transformed by science and technology in ways not clearly foreseen, we desperately need information about the mechanisms by which individual scientists change the world. Pincus and his life merit a critical case history, because if new Pincuses arise in the future, they will have a powerful impact upon the world."

Hechter examines the life of Gregory Pincus candidly and concludes that he was a great man because he was a person of action who showed the world that the population crisis is not an impossible problem. Few scientists have had so great an impact upon the lives of others as did Gregory Pincus by promoting the antifertility properties of certain steroids, now known as The Pill. The Pill may not remain the antifertility agent of choice, but its development created a climate of interest and opinion needed for extensive research on antifertility and the aim to apply this knowledge to save mankind.

To oversimplify, some scientists become great by making important contributions to knowledge—discovery in the laboratory—and others become great as organizers and by making important applications of knowledge. Gregory Pincus, a scientist-statesman, was one of the latter.

* Oscar Hechter, "Homage to Gregory Pincus," *Perspectives in Biology and Medicine,* Spring 1968 (an *In Memoriam* issue to Gregory Pincus).

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KEY TO ABBREVIATIONS

Acta Endocrinol. = Acta Endocrinologica
Acta Endocrinol., Suppl. = Acta Endocrinologica, Supplementum
Am. J. Med. Sci. = American Journal of Medical Sciences
Am. J. Obstet. Gynecol. = American Journal of Obstetrics and Gynecology
Am. J. Physiol. = American Journal of Physiology
Am. J. Psychiat. = American Journal of Psychiatry
Am. Naturalist = American Naturalist
Am. Zool. = American Zoologist
Anat. Record = Anatomical Record
Anat. Record Suppl. = Anatomical Record Supplement
Ann. N.Y. Acad. Sci. = Annals of the New York Academy of Sciences
Arch. Biochem. = Archives of Biochemistry
Arch. Biochem. Biophys. = Archives of Biochemistry and Biophysics
Biochem. Pharmacol. = Biochemical Pharmacology
Bull. Post Grad. Comm. Med. Univ. Sydney = Bulletin of the Postgraduate Committee in Medicine, University of Sydney
Cancer Res. = Cancer Research
Ciba Found. Colloq. Aging = Ciba Foundation Colloquia on Aging
Ciba Found. Colloq. Endocrinol. = Ciba Foundation Colloquia on Endocrinology
Current Med. Dig. = Current Medical Digest
Federation Proc. = Federation Proceedings
Gen. Comp. Endocrinol. = General and Comparative Endocrinology
J. Am. Chem. Soc. = Journal of the American Chemical Society
J. Am. Med. Assoc. = Journal of the American Medical Association
J. Aviation Med. = Journal of Aviation Medicine
J. Biol. Chem. = Journal of Biological Chemistry
J. Clin. Endocrinol. = Journal of Clinical Endocrinology (later, J. Clin. Endocrinol. Metab.)
J. Clin. Endocrinol. Metab. = Journal of Clinical Endocrinology and Metabolism
J. Clin. Invest. = Journal of Clinical Investigation
J. Embryol. Exp. Morphol. = Journal of Embryology and Experimental Morphology
J. Exp. Med. = Journal of Experimental Medicine
J. Exp. Zool. = Journal of Experimental Zoology
J. Gen. Physiol. = Journal of General Physiology
J. Gerontol. = Journal of Gerontology
Physiol. Rev. = Physiological Reviews
Proc. ——— Internat. Conf. Planned Parenthood = Proceedings of the —— International Conference on Planned Parenthood.
Proc. ——— Internat. Congr. Hormonal Steroids = Proceedings of the —— International Congress on Hormonal Steroids

Proc. ——— Internat. Physiol. Congr. = Proceedings of the ——— International Physiological Congress
Proc. Nat. Acad. Sci. = Proceedings of the National Academy of Sciences
Proc. 6th Pan-Am. Congr. Endocrinol. = Proceedings of the 6th Pan-American Congress of Endocrinology
Proc. Roy. Soc. London = Proceedings of the Royal Society of London (Ser. A = Mathematical Sciences; Ser. B = Biological Sciences)
Proc. Soc. Exp. Biol. Med. = Proceedings of the Society for Experimental Biology and Medicine
Psychosomat. Med. = Psychosomatic Medicine
Recent Progr. Hormone Res. = Recent Progress in Hormone Research

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