82 GREGORY PINCUS

1903-1967

Gregory Pincus was the American biologist who played the principal role in the development of the oral contraceptive pill. Although he was never particularly well known, he had far more actual influence on the world than many people who are world-famous.

The pill has a twofold importance. In a world that is increasingly concerned with the dangers of overpopulation, the significance of the pill as an agent for population control is obvious. Less direct perhaps, but equally revolutionary, is the effect the pill has had in changing sexual mores. It is widely recognized that over the last thirty years there has been a revolution in sexual attitudes in the United States. Doubtless, there are many other political, economic, and sociological factors that have

influenced that revolution; but the largest single factor has clearly been the advent of the pill. Previously, the fear of unwanted pregnancy was a major factor in inhibiting many women from engaging in pre-marital, or even marital, sex. Suddenly, women have been presented with the opportunity to engage in sexual relations without fear of pregnancy, and the change in circumstances has frequently produced a change in both attitude and behavior.

It might be objected that the development of *Enovid* (the first birth control pill) was not really all that important, since safe and reasonably reliable contraceptive methods had been known previously. Such an argument ignores the distinction between a method of contraception that is technically effective and one that is psychologically acceptable. Before the development of the pill, the contraceptive most recommended by "experts" was the diaphragm. Diaphragms are indeed safe and reasonably reliable, but in practice the great majority of women were, and still are, reluctant to use them. It is noteworthy that when the pill was first being tested, many hundreds of women preferred to take a chance with an untried (and perhaps dangerous) method of birth control, rather than use the safe and time-tested diaphragm.

It might also be objected that the development of *Enovid* was not really such a great triumph, since there are some risks to health involved in its use, and since it may eventually be superseded—perhaps even in the near future—by newer and safer drugs or devices. But in the nature of things, future methods of contraception can represent only a comparatively slight improvement, since the pill is already widely accepted and is generally satisfactory. (It is worth noting that over the past thirty years—a period during which many millions of American women began using the pill regularly—life expectancy among American women has *increased* significantly. That fact alone should make it obvious that the pill is not a *major* health hazard.) History will, or at least should, consider the development of *Enovid* in the 1950s as the crucial breakthrough in birth control methods.

Many persons contributed to the development of the oral contraceptive pill. Indeed, the idea had been talked about for a long time; the trouble was that nobody knew just what chemicals should go inside such a pill. Curiously, the key discovery had been made as far back as 1937. In that year, A. W. Makepeace, G. L. Weinstein, and M. H. Friedman had demonstrated that injections of progesterone (one of the female sex hormones) would inhibit ovulation in laboratory animals. However—perhaps because hypodermic injections did not sound like an attractive method of birth control, or perhaps because progesterone was at that time an extremely expensive chemical—that discovery had not aroused the interest of birth control advocates.

The main development of the pill did not start until about 1950, when the American biologist Gregory Pincus began to work on the problem. Apparently it was Margaret Sanger, the long-time advocate of family planning, who persuaded him to work on the project. She could hardly have chosen a better man, for Pincus was an expert in steroid metabolism and in the physiology of reproduction in mammals, as well as being director of laboratories at the Worcester Foundation for Experimental Biology, in Shrewsbury, Massachusetts.

Apparently Pincus, with his superb combination of technical knowledge and scientific intuition, hit upon the general nature of the solution almost immediately. Soon he had Dr. Min-Chueh Chang, a researcher at the Worcester Foundation, testing progesterone on laboratory animals, to see if it would suppress ovulation even when taken orally. Chang's experiments were successful. This was certainly a promising beginning, particularly in view of the fact that a few years earlier a chemist named Russell Marker had invented a way to synthesize progesterone cheaply.

Another important contributor was Dr. John Rock, a gynecologist who, at Pincus's suggestion, conducted tests which showed that progesterone, taken orally, would inhibit ovulation in human females. However, Rock's research also disclosed two serious difficulties with using progesterone as an oral contracep-

tive. In the first place, it only suppressed ovulation about 85 percent of the time. In the second place, unreasonably large doses were needed to accomplish even that.

But Pincus, who was convinced that he was on the right track, was not ready to give up. He realized that there might be another compound chemically similar to progesterone, but without its disadvantages. In September 1953, he asked various chemical companies to send him samples of any synthetic steroids they had manufactured that were chemically related to progesterone. Pincus tested the chemicals that he received, and one of them, norethynodrel (manufactured by G. D. Searle and Company), seemed particularly effective.

This was a lucky break for Pincus, since when he had begun his research, back in 1950, norethynodrel had not even existed! It had been synthesized in 1952 by Dr. Frank B. Colton, a biochemist working in the Searle laboratories, and was later patented in his name. However, neither Colton nor any of his supervisors at G. D. Searle had been deliberately trying to create an oral contraceptive—nor at the time did they realize they had created one.

Further tests performed by the research group that had been assembled by Pincus indicated that norethynodrel would be still more effective if supplemented by a small admixture of another chemical, mestranol. It was this combination of drugs which was eventually marketed by G. D. Searle and Company as *Enovid.*

By 1955, Pincus could see that the time was ripe for a large-scale field test of the pill. The tests were begun in April 1956, in a suburb of San Juan, Puerto Rico, under the supervision of Dr. Edris Rice-Wray. Within about nine months, her tests indicated how strikingly effective the oral contraceptive pill was. Nevertheless, testing was continued for three more years before the Food and Drug Administration approved the marketing of *Enovid* in May 1960.

From the foregoing, it is obvious that Gregory Pincus did not develop the contraceptive pill by himself. It was Frank Colton who actually created norethynodrel; clearly, Colton and the

various chemists who paved the way for his achievement are entitled to a considerable part of the credit. Similarly, various other men who worked with the Pincus group, including John Rock, Min-Chueh Chang, and Dr. Celso-Ramon Garcia made important contributions. For that matter, Dr. Rice-Wray, Margaret Sanger, and various others whom I have not mentioned each played a role in the overall accomplishment. Nevertheless, there seems no doubt that Gregory Pincus was the principal figure and the driving force behind the entire project. He was the scientist who decided to devote his time and effort to an active search for an oral contraceptive; he was the one who had the scientific and organizational ability to carry the project through successfully; he thought of the basic idea, obtained financing for the research, and got other talented men to work on the project. He had the vision and determination to push the project through to successful completion, and he is the one who has received, and who deserves, the principal credit for the accomplishment.

Gregory Pincus was born in 1903, in Woodbine, New Jersey, the son of Russian-Jewish parents. He graduated from Cornell in 1924, and received a doctorate from Harvard in 1927. Afterward, he did research in several institutions, including Harvard and Cambridge, and was a professor at Clark for several years. In 1944, he helped found the Worcester Foundation for Experimental Biology, and for a long time afterwards was director of laboratories there. He was the author of over 250 scientific papers, as well as a book, *The Conquest of Fertility*, published in 1965.

During his lifetime, Pincus received many scientific honors; however, neither he nor any of the men involved in the development of the pill received a Nobel Prize. When Pincus died in Boston, in 1967, his death went almost unnoticed by the general public, and for that matter, by most scientists. Today, few encyclopedias even mention his name. Nevertheless, he was the principal architect of one of the most significant developments in human history.