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Milestones

The Oral Contraceptive Pill : The early days of a 50 year-old legend

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There is no such thing as the Car or the Shoe or the Laundry Soap. But everyone knows the Pill. It has been 50 years since the oral contraceptive pill was marketed and sex, reproduction and human relations have never been the same ever since.[1] The story of the Pill is one of contradictions: It was the first medicine ever designed to be taken regularly by people who were not sick. The doctor who tested it first was a conservative Catholic looking for a cure for infertility. Its supporters claimed that it would ease the strain of a marriage weighed down by unwanted children, while opponents argued that it lead to promiscuity. Some called it revolutionary while others found it overrated. The medical profession and the media have alternately claimed it to be a breakthrough in women's health or a potentially avoidable health risk. It is the nature of icons to be worshipped and stoned, laden with symbolic value beyond their proportions.

Since time immemorial, human beings have attempted

Fig 1. Margaret Sanger

Fig 2. Katherine MeCormick

Fig 3. Gregory Pincus (at the microscope) and John Rock (standing behind him)

to invent and use contraceptives. Ayurvedic, Egyptian, Arab and Western literature over the ages have mentioned various ways in which pregnancy could be avoided. Oral contraception was practiced with herbs, roots, minerals and oils. However, a reliable method did not exist. It was the passion of Margaret Sanger, the capital of Katherine McCormic, the pharmacological genius of Gregory Pincus and the clinical responsibility of John Rock that saw the birth of the Pill.

Margaret Sanger (Fig 1) was born in the year 1879 to a Catholic mother and a father who carved angels and saints out of marble for New York churches. Margaret Sanger watched her mother die at an early age, which was partly due to the stress of bearing eleven children from eighteen pregnancies. After her mother's death she worked as a nurse in New York City and saw many women die from childbirth and self-induced abortion. The horrors that she witnessed there caused her to devote much of her time to promoting birth control for women. She set up the first clinic in 1916 and founded the American Birth Control League in 1921.[2]

Katherine McCormick (Figure 2) was born in 1875 to a wealthy Chicago family. Unlike many women of her time, she was granted the opportunity of attending college, but despite her education she married Stanley McCormick in 1904. However, two years after their marriage he developed schizophrenia and her life was greatly altered. She soon turned her focus to promoting the cause of women's suffrage. In 1917, McCormick met Margaret Sanger in Boston and they frequently kept in touch. During this time McCormick was devoted to researching schizophrenia while Margaret Sanger was adamant about pursuing the area of birth control. In 1947, McCormick's husband died and she was the heir to his $15 million fortune. She now decided to turn her attention to the birth control movement and joined forces with Sanger. With her astounding wealth, McCormick financed the majority of research and development of The Pill.

Sanger and McCormick turned to Gregory Pincus in their quest for the Pill. Born in 1903 to Russian Jewish immigrants in Woodbine, New Jersey, Pincus won a scholarship to Cornell University, where he excelled in biology. He went on to land an appointment at Harvard as an assistant professor and was widely considered a rising star. In 1934, at age 31, Pincus made national headlines by achieving in-vitro fertilization of rabbits. Pincus was decades ahead of his time. But instead of fame, the accomplishment brought notoriety. Harvard denied him tenure and refused his reappointment. Pincus's career floundered. Pincus was desperate to find a way to support his wife and two small children. An old friend from Harvard, Hudson Hoagland, invited Pincus to work out of his biology department at Clark University in Worcester, where they established the Worcester Foundation for Experimental Biology. The foundation soon found a niche doing applied research, especially in the burgeoning area of steroids, but it was still a struggle to stay solvent. To save money, Pincus did double duty as the lab's janitor.

When Sanger and McCormick approached Pincus, he was aware of a study showing that progesterone could work as an effective anti-ovulent, and he had a hunch it would prove to be a good contraceptive drug. With funding from McCormick, in a matter of months Pincus and his colleague Min-Chueh Chang proved that repeated injections of progesterone stopped ovulation in animals. Pincus's real challenge, however, would be to invent an inexpensive pill form of the drug. In a stroke of good timing, chemists working for two separate drug companies had recently created orally effective forms of synthetic progesterone. Although both pharmaceutical companies were wary of using their new com-

pounds for contraceptive purposes, both Syntex (founded by Carl Djerassi in Mexico) and Searle (represented by Frank Colton in New York) allowed Pincus to use the formulations in his preliminary human studies.[3]

With the pills in hand, Pincus was ready to collaborate with a clinician who would be able to initiate human trials. Pincus met Dr John Rock (Fig. 3) in 1955 through Margaret Sanger's introduction at a scientific meeting in Canada. Dr John Rock was born in 1890 and was considering a career in business before he turned his attention to medicine. After graduating from Harvard, he set up a successful practice in Boston and was well known as a fertility specialist. He postulated that suppressing ovulation for a period of time would allow the ovaries to rest and the rebound would improve pregnancy chances in women who did not conceive. The idea of an agent that would suppress ovulation consistently interested him. After comparing the data from both the formulations, Rock and Pincus picked the formulation from Searle. The first human study of the Pill consisted of 30 women in Boston under the guise of a fertility cure. Due to the US laws, it was not possible to conduct larger studies on the Pill as a contraceptive. Rock and Pincus launched large-scale human trials for the Pill in Puerto Rico in 1956 and reported that the Pill was 100% effective in preventing pregnancies.[3]

The first Pill was thought to be a progestin only formulation but inadvertently it was a combined oral contraceptive. Norethynodrel was subsequently discovered to be contaminated with a small percentage of the estrogen, mestranol, an intermediate in the process of synthesis and purification. The Pill contained 4 – 7% of mestranol. An attempt to purify the Pill resulted in the mestranol content being lower than 1%. But this formulation lead to breakthrough bleeding. It was decided to intentionally incorporate 2.2% mestranol, a percentage that was not associated with breakthrough bleeding, in the first contraceptive trials in women in 1956. The norethynodrel and mestranol combination was given the proprietary name Enovid.[4] The USFDA approved the product for gynecological use in 1957 and as a contraceptive in 1960. There was no looking back ever since. Through umpteen trials, tribulations and "pill scares", the popularity of the Pill only grew. Today more than 100 million women use the Pill.

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