

of the study and to run the subsequent clinical trials. That was John Rock, MD, the last major person to become involved in the development of the birth control pill. Rock was a Harvard professor of obstetrics and gynecology, one of the world's leading experts in the treatment of infertility, and intensely interested in women being able to control their own reproduction. Rock had a sterling reputation and became the ethical standard bearer for the study. Before his participation, and even after he became involved, parts of the trial had ethical lapses that would be unlikely to be tolerated today. In one case, female Puerto Rican medical students were told in one class that they had to be subjects in an early study evaluating the safety of the drug, and that their grades would partly depend on their participation. While Pincus knew and approved of this attempt to force participation, Rock did not.

Even as the date approached on which the group had hoped to have the pill on the market, Pincus had not decided which progestin he would use. He finally settled on a 10 mg dose of norethynodrel, a G.D. Searle patented progestin. The drug choice may have been influenced by Searle's willingness to provide the progestin and manufacture and market the drug, although the cost to the company was very low. The dose was chosen since Pincus knew that it would provide near 100 percent efficacy in preventing pregnancy; the side effects could be reduced later if necessary by reducing the dose.\* One batch of the drug provided to Pincus was inadvertently contaminated by estrogen—when Pincus learned of this, he realized from the test data that the

\*In a study of eighty patients, only five had no side effects. Common side effects were nipple swelling or discoloration, soreness of the breast, nausea or vomiting, vaginal discharge, changes in libido (usually an increase), and occasional subjects experienced lactation. In other studies there was breakthrough bleeding. Thrombophlebitis was later noted as a side effect.

addition of estrogen had reduced the side effects, leading him to incorporate low-dose estrogen in the pill.

Application to the Federal Drug Administration (FDA) faced the problem that no criteria existed for approving a drug to be taken by healthy women for contraception, given the existence of non-drug options, as well as opposition by the Catholic Church. It was decided to apply for permission to market the drug for menstrual disorders (too much bleeding or painful periods), for which there was adequate experimental evidence that the pill had value when taken for several cycles. The FDA at the time was seriously understaffed and overworked, and sought outside advice. The drug was finally approved in 1957; there is no evidence that it could have been approved as a contraceptive. Pincus touted Enovid's use as a contraceptive at conferences, noting that physicians could prescribe it off-label for that purpose. This was reported widely in the news media, leading to the drug being regularly prescribed for contraception. Enovid was approved for contraception in 1960 as an amendment to the original approval.

It would be difficult to think of another drug that has had a greater effect on human behavior than Enovid, initially marketed at about fifty cents a pill. And it is remarkable that only four people were primarily responsible for its development: Sanger with her dream and drive to make it happen, Pincus with his scientific knowledge and skill to develop the drug, McCormick with the funds and commitment to pay the majority of the costs, and Rock with his clinical skills and reputation that made the drug successful.

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## Letter to the editor

### Re "How postoperative respiratory distress conspired with friendly fire to kill 'Stonewall' Jackson"

Kudos to DuBose et al. for their paper in the Autumn 2014 edition of *The Pharos* (pp. 18–24). I was raised in a house devoid of racism but built on a confederate fort (Fort Pemberton) in Charleston, South Carolina. You could say that disparity is an adequate description of my take on general Thomas Jonathan Jackson and the War between the States.

Having studied the Civil War, I must admit that Jackson was the most amazing commander of our "civil" tragedy. He was a leader of men, a genius in both strategy and tactics. In war time this defines a general who will conquer and, by design, kill. His fanatical sense of duty was praised and envied by both sides and highlighted by commanding general Robert E. Lee's dependence upon this rebel general. After hearing the news of the incident and amputation, Lee commented, "He has lost his left arm, but I my right."<sup>1</sup>

The only part lacking from the above paper was one quote, a few simple words whispered from the frail lips of a dying man who had found his purpose. After all of the generalship, after all of the killing, Jackson left to history these last words, "Let us cross over the river and rest under the shade of the trees."<sup>2</sup>

Can one's last words make a warrior poet?

#### References

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2. McGuire H. Death of Stonewall Jackson. Southern Historical Soc Papers 1886; 14: 162–63.

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