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SECTION: ANNALS OF MEDICINE; Pg. 52**LENGTH:** 7194 words**HEADLINE:** JOHN ROCK'S ERROR WHAT THE CO-INVENTOR OF THE PILL DIDN'T KNOW: MENSTRUATION CAN ENDANGER WOMEN'S HEALTH.;
BY MALCOLM GLADWELL**BODY:**

John Rock was christened in 1890 at the Church of the Immaculate Conception in Marlborough, Massachusetts, and married by Cardinal William O'Connell, of Boston. He had five children and nineteen grandchildren. A crucifix hung above his desk, and nearly every day of his adult life he attended the 7 a.m. Mass at St. Mary's in Brookline. Rock, his friends would say, was in love with his church. He was also one of the inventors of the birth-control pill, and it was his conviction that his faith and his vocation were perfectly compatible. To anyone who disagreed he would simply repeat the words spoken to him as a child by his home-town priest: "John, always stick to your conscience. Never let anyone else keep it for you. And I mean anyone else." Even when Monsignor Francis W. Carney, of Cleveland, called him a "moral rapist," and when Frederick Good, the longtime head of obstetrics at Boston City Hospital, went to Boston's Cardinal Richard Cushing to have Rock excommunicated, Rock was unmoved. "You should be afraid to meet your Maker," one angry woman wrote to him, soon after the Pill was approved. "My dear madam," Rock wrote back, "in my faith, we are taught that the Lord is with us always. When my time comes, there will be no need for introductions."

In the years immediately after the Pill was approved by the F.D.A., in 1960, Rock was everywhere. He appeared in interviews and documentaries on CBS and NBC, in *Time*, *Newsweek*, *Life*, *The Saturday Evening Post*. He toured the country tirelessly. He wrote a widely discussed book, "The Time Has Come: A Catholic Doctor's Proposals to End the Battle Over Birth Control," which was translated into French, German, and Dutch. Rock was six feet three and rail-thin, with impeccable manners; he held doors open for his patients and addressed them as "Mrs." or "Miss." His mere association with the Pill helped make it seem respectable. "He was a man of great dignity," Dr. Sheldon J. Segal, of the Population Council, recalls. "Even if the occasion called for an open collar, you'd never find him without an ascot. He had the shock of white hair to go along with that. And posture, straight as an arrow, even to his last year." At Harvard Medical School, he was a giant, teaching obstetrics for more than three decades. He was a pioneer in in-vitro fertilization and the freezing of sperm cells, and was the first to extract an intact fertilized egg. The Pill was his crowning achievement. His two collaborators, Gregory Pincus and Min-Cheuh Chang, worked out the mechanism. He shepherded the drug through its clinical trials. "It was his name and his reputation that gave ultimate validity to the claims that the pill would protect women against unwanted pregnancy," Loretta McLaughlin writes in her marvellous 1982 biography of Rock. Not long before the Pill's approval, Rock travelled to Washington to testify before the F.D.A. about the drug's safety. The agency examiner, Pasquale DeFelice, was a Catholic obstetrician from Georgetown University, and at one point, the story goes, DeFelice suggested the unthinkable—that the Catholic Church would never approve of the birth-control pill. "I can still see Rock standing there, his face composed, his eyes riveted on DeFelice," a colleague recalled years later, "and then, in a voice that would congeal your soul, he said, 'Young man, don't you sell my church short.'"

In the end, of course, John Rock's church disappointed him. In 1968, in the encyclical "Humanae Vitae," Pope Paul VI outlawed oral contraceptives and all other "artificial" methods of birth control. The passion and urgency that ani-

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mated the birth-control debates of the sixties are now a memory. John Rock still matters, though, for the simple reason that in the course of reconciling his church and his work he made an error. It was not a deliberate error. It became manifest only after his death, and through scientific advances he could not have anticipated. But because that mistake shaped the way he thought about the Pill-about what it was, and how it worked, and most of all what it meant-and because John Rock was one of those responsible for the way the Pill came into the world, his error has colored the way people have thought about contraception ever since.

John Rock believed that the Pill was a "natural" method of birth control. By that he didn't mean that it felt natural, because it obviously didn't for many women, particularly not in its earliest days, when the doses of hormone were many times as high as they are today. He meant that it worked by natural means. Women can get pregnant only during a certain interval each month, because after ovulation their bodies produce a surge of the hormone progesterone. Progesterone-one of a class of hormones known as progestin-prepares the uterus for implantation and stops the ovaries from releasing new eggs; it favors gestation. "It is progesterone, in the healthy woman, that prevents ovulation and establishes the pre- and post-menstrual 'safe' period," Rock wrote. When a woman is pregnant, her body produces a stream of progestin in part for the same reason, so that another egg can't be released and threaten the pregnancy already under way. Progestin, in other words, is nature's contraceptive. And what was the Pill? Progestin in tablet form. When a woman was on the Pill, of course, these hormones weren't coming in a sudden surge after ovulation and weren't limited to certain times in her cycle. They were being given in a steady dose, so that ovulation was permanently shut down. They were also being given with an additional dose of estrogen, which holds the endometrium together and-as we've come to learn-helps maintain other tissues as well. But to Rock, the timing and combination of hormones wasn't the issue. The key fact was that the Pill's ingredients duplicated what could be found in the body naturally. And in that naturalness he saw enormous theological significance.

In 1951, for example, Pope Pius XII had sanctioned the rhythm method for Catholics because he deemed it a "natural" method of regulating procreation: it didn't kill the sperm, like a spermicide, or frustrate the normal process of procreation, like a diaphragm, or mutilate the organs, like sterilization. Rock knew all about the rhythm method. In the nineteen-thirties, at the Free Hospital for Women, in Brookline, he had started the country's first rhythm clinic for educating Catholic couples in natural contraception. But how did the rhythm method work? It worked by limiting sex to the safe period that progestin created. And how did the Pill work? It worked by using progestin to extend the safe period to the entire month. It didn't mutilate the reproductive organs, or damage any natural process. "Indeed," Rock wrote, oral contraceptives "may be characterized as a 'pill-established safe period,' and would seem to carry the same moral implications" as the rhythm method. The Pill was, to Rock, no more than "an adjunct to nature."

In 1958, Pope Pius XII approved the Pill for Catholics, so long as its contraceptive effects were "indirect"-that is, so long as it was intended only as a remedy for conditions like painful menses or "a disease of the uterus." That ruling emboldened Rock still further. Short-term use of the Pill, he knew, could regulate the cycle of women whose periods had previously been unpredictable. Since a regular menstrual cycle was necessary for the successful use of the rhythm method-and since the rhythm method was sanctioned by the Church-shouldn't it be permissible for women with an irregular menstrual cycle to use the Pill in order to facilitate the use of rhythm? And if that was true why not take the logic one step further? As the federal judge John T. Noonan writes in "Contraception," his history of the Catholic position on birth control:

These arguments, as arcane as they may seem, were central to the development of oral contraception. It was John Rock and Gregory Pincus who decided that the Pill ought to be taken over a four-week cycle-a woman would spend three weeks on the Pill and the fourth week off the drug (or on a placebo), to allow for menstruation. There was and is no medical reason for this. A typical woman of childbearing age has a menstrual cycle of around twenty-eight days, determined by the cascades of hormones released by her ovaries. As first estrogen and then a combination of estrogen and progestin flood the uterus, its lining becomes thick and swollen, preparing for the implantation of a fertilized egg. If the egg is not fertilized, hormone levels plunge and cause the lining-the endometrium-to be sloughed off in a menstrual bleed. When a woman is on the Pill, however, no egg is released, because the Pill suppresses ovulation. The fluxes of estrogen and progestin that cause the lining of the uterus to grow are dramatically reduced, because the Pill slows down the ovaries. Pincus and Rock knew that the effect of the Pill's hormones on the endometrium was so modest that women could conceivably go for months without having to menstruate. "In view of the ability of this compound to prevent menstrual bleeding as long as it is taken," Pincus acknowledged in 1958, "a cycle of any desired length could presumably be produced." But he and Rock decided to cut the hormones off after three weeks and trigger a menstrual period because they believed that women would find the continuation of their monthly bleeding reassuring. More to the point,

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if Rock wanted to demonstrate that the Pill was no more than a natural variant of the rhythm method, he couldn't very well do away with the monthly menses. Rhythm required "regularity," and so the Pill had to produce regularity as well.

It has often been said of the Pill that no other drug has ever been so instantly recognizable by its packaging: that small, round plastic dial pack. But what was the dial pack if not the physical embodiment of the twenty-eight-day cycle? It was, in the words of its inventor, meant to fit into a case "indistinguishable" from a woman's cosmetics compact, so that it might be carried "without giving a visual clue as to matters which are of no concern to others." Today, the Pill is still often sold in dial packs and taken in twenty-eight-day cycles. It remains, in other words, a drug shaped by the dictates of the Catholic Church-by John Rock's desire to make this new method of birth control seem as natural as possible. This was John Rock's error. He was consumed by the idea of the natural. But what he thought was natural wasn't so natural after all, and the Pill he ushered into the world turned out to be something other than what he thought it was. In John Rock's mind the dictates of religion and the principles of science got mixed up, and only now are we beginning to untangle them.

In 1986, a young scientist named Beverly Strassmann travelled to Africa to live with the Dogon tribe of Mali. Her research site was the village of Sangui in the Sahel, about a hundred and twenty miles south of Timbuktu. The Sahel is thorn savannah, green in the rainy season and semi-arid the rest of the year. The Dogon grow millet, sorghum, and onions, raise livestock, and live in adobe houses on the Bandiagara escarpment. They use no contraception. Many of them have held on to their ancestral customs and religious beliefs. Dogon farmers, in many respects, live much as people of that region have lived since antiquity. Strassmann wanted to construct a precise reproductive profile of the women in the tribe, in order to understand what female biology might have been like in the millennia that preceded the modern age. In a way, Strassmann was trying to answer the same question about female biology that John Rock and the Catholic Church had struggled with in the early sixties: what is natural? Only, her sense of "natural" was not theological but evolutionary. In the era during which natural selection established the basic patterns of human biology-the natural history of our species-how often did women have children? How often did they menstruate? When did they reach puberty and menopause? What impact did breast-feeding have on ovulation? These questions had been studied before, but never so thoroughly that anthropologists felt they knew the answers with any certainty.

Strassmann, who teaches at the University of Michigan at Ann Arbor, is a slender, soft-spoken woman with red hair, and she recalls her time in Mali with a certain wry humor. The house she stayed in while in Sangui had been used as a shelter for sheep before she came and was turned into a pigsty after she left. A small brown snake lived in her latrine, and would curl up in a camouflaged coil on the seat she sat on while bathing. The villagers, she says, were of two minds: was it a deadly snake-Kere me jongolo, literally, "My bite cannot be healed"-or a harmless mouse snake? (It turned out to be the latter.) Once, one of her neighbors and best friends in the tribe roasted her a rat as a special treat. "I told him that white people aren't allowed to eat rat because rat is our totem," Strassmann says. "I can still see it. Bloated and charred. Stretched by its paws. Whiskers singed. To say nothing of the tail." Strassmann meant to live in Sangui for eighteen months, but her experiences there were so profound and exhilarating that she stayed for two and a half years. "I felt incredibly privileged," she says. "I just couldn't tear myself away."

Part of Strassmann's work focussed on the Dogon's practice of segregating menstruating women in special huts on the fringes of the village. In Sangui, there were two menstrual huts-dark, cramped, one-room adobe structures, with boards for beds. Each accommodated three women, and when the rooms were full, latecomers were forced to stay outside on the rocks. "It's not a place where people kick back and enjoy themselves," Strassmann says. "It's simply a nighttime hangout. They get there at dusk, and get up early in the morning and draw their water." Strassmann took urine samples from the women using the hut, to confirm that they were menstruating. Then she made a list of all the women in the village, and for her entire time in Mali-seven hundred and thirty-six consecutive nights-she kept track of everyone who visited the hut. Among the Dogon, she found, a woman, on average, has her first period at the age of sixteen and gives birth eight or nine times. From menarche, the onset of menstruation, to the age of twenty, she averages seven periods a year. Over the next decade and a half, from the age of twenty to the age of thirty-four, she spends so much time either pregnant or breast-feeding (which, among the Dogon, suppresses ovulation for an average of twenty months) that she averages only slightly more than one period per year. Then, from the age of thirty-five until menopause, at around fifty, as her fertility rapidly declines, she averages four menses a year. All told, Dogon women menstruate about a hundred times in their lives. (Those who survive early childhood typically live into their seventh or eighth decade.) By contrast, the average for contemporary Western women is somewhere between three hundred and fifty and four hundred times.

Strassmann's office is in the basement of a converted stable next to the Natural History Museum on the University of Michigan campus. Behind her desk is a row of battered filing cabinets, and as she was talking she turned and pulled

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out a series of yellowed charts. Each page listed, on the left, the first names and identification numbers of the Sanguini women. Across the top was a time line, broken into thirty-day blocks. Every menses of every woman was marked with an X. In the village, Strassmann explained, there were two women who were sterile, and, because they couldn't get pregnant, they were regulars at the menstrual hut. She flipped through the pages until she found them. "Look, she had twenty-nine menses over two years, and the other had twenty-three." Next to each of their names was a solid line of x's. "Here's a woman approaching menopause," Strassmann went on, running her finger down the page. "She's cycling but is a little bit erratic. Here's another woman of prime childbearing age. Two periods. Then pregnant. I never saw her again at the menstrual hut. This woman here didn't go to the menstrual hut for twenty months after giving birth, because she was breast-feeding. Two periods. Got pregnant. Then she miscarried, had a few periods, then got pregnant again. This woman had three menses in the study period." There weren't a lot of x's on Strassmann's sheets. Most of the boxes were blank. She flipped back through her sheets to the two anomalous women who were menstruating every month. "If this were a menstrual chart of undergraduates here at the University of Michigan, all the rows would be like this."

Strassmann does not claim that her statistics apply to every preindustrial society. But she believes-and other anthropological work backs her up-that the number of lifetime menses isn't greatly affected by differences in diet or climate or method of subsistence (foraging versus agriculture, say). The more significant factors, Strassmann says, are things like the prevalence of wet-nursing or sterility. But over all she believes that the basic pattern of late menarche, many pregnancies, and long menstrual-free stretches caused by intensive breast-feeding was virtually universal up until the "demographic transition" of a hundred years ago from high to low fertility. In other words, what we think of as normal-frequent menses-is in evolutionary terms abnormal. "It's a pity that gynecologists think that women have to menstruate every month," Strassmann went on. "They just don't understand the real biology of menstruation."

To Strassmann and others in the field of evolutionary medicine, this shift from a hundred to four hundred lifetime menses is enormously significant. It means that women's bodies are being subjected to changes and stresses that they were not necessarily designed by evolution to handle. In a brilliant and provocative book, "Is Menstruation Obsolete?," Drs. Elsimar Coutinho and Sheldon S. Segal, two of the world's most prominent contraceptive researchers, argue that this recent move to what they call "incessant ovulation" has become a serious problem for women's health. It doesn't mean that women are always better off the less they menstruate. There are times-particularly in the context of certain medical conditions-when women ought to be concerned if they aren't menstruating: In obese women, a failure to menstruate can signal an increased risk of uterine cancer. In female athletes, a failure to menstruate can signal an increased risk of osteoporosis. But for most women, Coutinho and Segal say, incessant ovulation serves no purpose except to increase the occurrence of abdominal pain, mood shifts, migraines, endometriosis, fibroids, and anemia-the last of which, they point out, is "one of the most serious health problems in the world."

Most serious of all is the greatly increased risk of some cancers. Cancer, after all, occurs because as cells divide and reproduce they sometimes make mistakes that cripple the cells' defenses against runaway growth. That's one of the reasons that our risk of cancer generally increases as we age: our cells have more time to make mistakes. But this also means that any change promoting cell division has the potential to increase cancer risk, and ovulation appears to be one of those changes. Whenever a woman ovulates, an egg literally bursts through the walls of her ovaries. To heal that puncture, the cells of the ovary wall have to divide and reproduce. Every time a woman gets pregnant and bears a child, her lifetime risk of ovarian cancer drops ten per cent. Why? Possibly because, between nine months of pregnancy and the suppression of ovulation associated with breast-feeding, she stops ovulating for twelve months-and saves her ovarian walls from twelve bouts of cell division. The argument is similar for endometrial cancer. When a woman is menstruating, the estrogen that flows through her uterus stimulates the growth of the uterine lining, causing a flurry of potentially dangerous cell division. Women who do not menstruate frequently spare the endometrium that risk. Ovarian and endometrial cancer are characteristically modern diseases, consequences, in part, of a century in which women have come to menstruate four hundred times in a lifetime.

In this sense, the Pill really does have a "natural" effect. By blocking the release of new eggs, the progestin in oral contraceptives reduces the rounds of ovarian cell division. Progestin also counters the surges of estrogen in the endometrium, restraining cell division there. A woman who takes the Pill for ten years cuts her ovarian-cancer risk by around seventy per cent and her endometrial-cancer risk by around sixty per cent. But here "natural" means something different from what Rock meant. He assumed that the Pill was natural because it was an unobtrusive variant of the body's own processes. In fact, as more recent research suggests, the Pill is really only natural in so far as it's radical-rescuing the ovaries and endometrium from modernity. That Rock insisted on a twenty-eight-day cycle for his pill is evidence of just how deep his misunderstanding was: the real promise of the Pill was not that it could preserve the menstrual rhythms of the twentieth century but that it could disrupt them.

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