

JOHN ROCK'S ERROR

BY MALCOLM GLADWELL

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 animated 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

The Pill's designers assumed that monthly menses were part of the natural order, and took pains that they would be preserved

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:

If it was lawful to suppress ovulation to achieve a regularity necessary for successfully sterile intercourse, why was it not lawful to suppress ovulation without appeal to rhythm? If pregnancy could be prevented by pill plus rhythm, why not by pill alone? In each case suppression of ovulation was used as a means. How was a moral difference made by the addition of rhythm?

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 con-

ceivably 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, 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 out a series of yellowed charts. Each page listed, on the left, the first names and identification numbers of the Sangui 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.

Today, a growing movement of reproductive specialists has begun to campaign loudly against the standard twenty-eight-day Pill regimen. The drug company Organon has come out with a new oral contraceptive, called Mircette, that cuts the seven-day placebo interval to two days. Patricia Sulak, a medical researcher at Texas A. & M. University, has shown that most women can probably stay on the Pill, straight through, for six to twelve weeks before they experience breakthrough bleeding or spotting. More recently, Sulak has documented precisely what the cost of the Pill's monthly "off" week is. In a paper in the February issue of the journal *Obstetrics and Gynecology* she and her colleagues documented something that will come as no surprise to most women on the Pill: during the placebo week, the number of users experiencing pelvic pain, bloating, and swelling more than triples, breast tenderness more than doubles, and headaches increase by almost fifty per cent. In other words, some women on the Pill continue to experience the kinds of side effects associated with normal menstruation. Sulak's paper is a short, dry, academic work, of the sort intended for a narrow professional audience. But it is impossible to read it without being struck by the consequences of John Rock's desire to please his church. In the past forty years, millions of women around the world have been given the Pill in such a way as to



maximize their pain and suffering. And to what end? To pretend that the Pill was no more than a pharmaceutical version of the rhythm method?

In 1980 and 1981, Malcolm Pike, a medical statistician at the University of Southern California, travelled to Japan for six months to study at the Atomic Bomb Casualties Commission. Pike wasn't interested in the effects of the bomb. He wanted to examine the medical records that the commission had been painstakingly assembling on the survivors of Hiroshima and Nagasaki. He was investigating a question that would ultimately do as much to complicate our understanding of the Pill as Strassmann's research would a decade later: why did Japanese women have breast-cancer rates six times lower than American women?

In the late forties, the World Health organization began to collect and publish comparative health statistics from around the world, and the breast-cancer disparity between Japan and America had come to obsess cancer specialists. The obvious answer—that Japanese women were somehow genetically protected against breast cancer—didn't make sense, because once Japanese women moved to the United States they began to get breast cancer almost as often as American women did. As a result, many experts at the time assumed that the culprit had to be some unknown toxic chemical or virus unique to the West. Brian Henderson, a colleague of Pike's at U.S.C. and his regular collaborator, says that when he entered the field, in 1970, "the whole viral- and chemical-carcinogenesis idea was huge—it dominated the literature." As he recalls, "Breast cancer fell into this large, unknown box that said it was something to do with the environment—and that word 'environment' meant a lot of different things to a lot of different people. They might be talking about diet or smoking or pesticides."

Henderson and Pike, however, became fascinated by a number of statistical peculiarities. For one thing, the rate of increase in breast-cancer risk rises sharply throughout women's thirties and forties and then, at menopause, it starts to slow down. If a cancer is caused by some toxic outside agent, you'd expect

that rate to rise steadily with each advancing year, as the number of mutations and genetic mistakes steadily accumulates. Breast cancer, by contrast, looked as if it were being driven by something specific to a woman's reproductive years. What was more, younger women who had had their ovaries removed had a markedly lower risk of breast cancer; when their bodies weren't producing estrogen and progesterin every month, they got far fewer tumors. Pike and Henderson became convinced that breast cancer was linked to a process of cell division similar to that of ovarian and endometrial cancer. The female breast, after all, is just as sensitive to the level of hormones in a woman's body as the reproductive system. When the breast is exposed to estrogen, the cells of the terminal-duct lobular unit—where most breast cancer arises—undergo a flurry of division. And during the mid-to-late stage of the menstrual cycle, when the ovaries start producing large amounts of progesterin, the pace of cell division in that region doubles.

It made intuitive sense, then, that a woman's risk of breast cancer would be linked to the amount of estrogen and progesterin her breasts have been exposed to during her lifetime. How old a woman is at menarche should make a big difference, because the beginning of puberty results in a hormonal surge through a woman's body, and the breast cells of an adolescent appear to be highly susceptible to the errors that result in cancer. (For more complicated reasons, bearing children turns out to be protective against breast cancer, perhaps because in the last two trimesters of pregnancy the cells of the breast mature and become much more resistant to mutations.) How old a woman is at menopause should matter, and so should how much estrogen and progesterin her ovaries actually produce, and even how much she weighs after menopause, because fat cells turn other hormones into estrogen.

Pike went to Hiroshima to test the cell-division theory. With other researchers at the medical archive, he looked first at the age when Japanese women got their period. A Japanese woman born at the turn of the century had her first period at sixteen and a half American women born at the same time

had their first period at fourteen. That difference alone, by their calculation, was sufficient to explain forty per cent of the gap between American and Japanese breast-cancer rates. "They had collected amazing records from the women of that area," Pike said. "You could follow precisely the change in age of menarche over the century. You could even see the effects of the Second World War. The age of menarche of Japanese girls went up right at that point because of poor nutrition and other hardships. And then it started to go back down after the war. That's what convinced me that the data were wonderful."

Pike, Henderson, and their colleagues then folded in the other risk factors. Age at menopause, age at first pregnancy, and number of children weren't sufficiently different between the two countries to matter. But weight was. The average post-menopausal Japanese woman weighed a hundred pounds; the average American woman weighed a hundred and forty-five pounds. That fact explained another twenty-five per cent of the difference. Finally, the researchers analyzed blood samples from women in rural Japan and China, and found that their ovaries—possibly because of their extremely low-fat diet—were producing about seventy-five per cent the amount of estrogen that American women were producing. Those three factors, added together, seemed to explain the breast-cancer gap. They also appeared to explain why the rates of breast cancer among Asian women began to increase when they came to America: on an American diet, they started to menstruate earlier, gained more weight, and produced more estrogen. The talk of chemicals and toxins and power lines and smog was set aside. "When people say that what we understand about breast cancer explains only a small amount of the problem, that it is somehow a mystery—it's absolute nonsense," Pike says flatly. He is a South African in his sixties, with graying hair and a salt-and-pepper beard. Along with Henderson, he is an eminent figure in cancer research, but no one would ever accuse him of being tentative in his pronouncements. "We understand breast cancer extraordinarily well. We understand it as well as we understand cigarettes and lung cancer."

What Pike discovered in Japan led him to think about the Pill, because a tablet that suppressed ovulation—and the monthly tides of estrogen and progesterin that come with it—obviously had the potential to be a powerful anti-breast-cancer drug. But the breast was a little different from the reproductive organs. Progesterin prevented ovarian cancer because it suppressed ovulation. It was good for preventing endometrial cancer because it countered the stimulating effects of estrogen. But in breast cells, Pike believed, progesterin wasn't the solution; it was one of the hormones that *caused* cell division. This is one explanation for why, after years of studying the Pill, researchers have concluded that it has no effect one way or the other on breast cancer: whatever beneficial effect results from what the Pill does is cancelled out by how it does it. John Rock touted the fact that the Pill used progesterin, because progesterin was the body's own contraceptive. But Pike saw nothing "natural" about subjecting the breast to that heavy a dose of progesterin. In his view, the amount of progesterin and estrogen needed to make an effective contraceptive was much greater than the amount needed to keep the reproductive system healthy—and that excess was unnecessarily raising the risk of breast cancer. A truly natural Pill might be one that found a way to suppress ovulation *without* using progesterin. Throughout the nineteen-eighties, Pike recalls, this was his obsession. "We were all trying to work out how the hell we could fix the Pill. We thought about it day and night."

Pike's proposed solution is a class of drugs known as GnRHAs, which has been around for many years. GnRHAs disrupt the signals that the pituitary gland sends when it is attempting to order the manufacture of sex hormones. It's a circuit breaker. "We've got substantial experience with this drug," Pike says. Men suffering from prostate cancer are sometimes given a GnRHA to temporarily halt the production of testosterone, which can exacerbate their tumors. Girls suffering from what's called precocious puberty—puberty at seven or eight, or even younger—are sometimes given the drug to forestall sexual maturity. If you give GnRHAs to

women of childbearing age, it stops their ovaries from producing estrogen and progesterin. If the conventional Pill works by convincing the body that it is, well, a little bit pregnant, Pike's pill would work by convincing the body that it was menopausal.

In the form Pike wants to use it, GnRHA will come in a clear glass bottle the size of a saltshaker, with a white plastic mister on top. It will be inhaled nasally. It breaks down in the body very quickly. A morning dose simply makes a woman menopausal for a while. Menopause, of course, has its risks. Women need estrogen to keep their hearts and bones strong. They also need progesterin to keep the uterus healthy. So Pike intends to add back just enough of each hormone to solve these problems, but much less than women now receive on the Pill. Ideally, Pike says, the estrogen dose would be adjustable: women would try various levels until they found one that suited them. The progesterin would come in four twelve-day stretches a

year. When someone on Pike's regimen stopped the progesterin, she would have one of four annual menses.

Pike and an oncologist named Darcy Spicer have joined forces with another oncologist, John Daniels, in a startup called Balance Pharmaceuticals. The firm operates out of a small white industrial strip mall next to the freeway in Santa Monica. One of the tenants is a paint store, another looks like some sort of export company. Balance's offices are housed in an oversized garage with a big overhead door and concrete floors. There is a tiny reception area, a little coffee table and a couch, and a warren of desks, bookshelves, filing cabinets, and computers. Balance is testing its formulation on a small group of women at high risk for breast cancer, and if the results continue to be encouraging, it will one day file for F.D.A. approval.

"When I met Darcy Spicer a couple of years ago," Pike said recently, as he sat at a conference table deep in the Balance garage, "he said, 'Why don't

we just try it out? By taking mammograms, we should be able to see changes in the breasts of women on this drug, even if we add back a little estrogen to avoid side effects.' So we did a study, and we found that there were huge changes." Pike pulled out a paper he and Spicer had published in the *Journal of the National Cancer Institute* showing breast X-rays of three young women. "These are the mammograms of the women before they start," he said. Amid the grainy black outlines of the breast were large white fibrous clumps-clumps that Pike and Spicer believe are indicators of the kind of relentless cell division that increases breast-cancer risk. Next to those X-rays were three mammograms of the same women taken after a year on the GnRHA regimen. The clumps were almost entirely gone. "This to us represents that we have actually stopped the activity inside the breasts," Pike went on. "White is a proxy for cell proliferation. We're slowing down the breast."

Pike stood up from the table and

turned to a sketch pad on an easel behind him. He quickly wrote a series of numbers on the paper. "Suppose a woman reaches menarche at fifteen and menopause at fifty. That's thirty-five years of stimulating the breast. If you cut that time in half, you will change her risk not by half but by half raised to the power of 4.5." He was working with a statistical model he had developed to calculate breast-cancer risk. "That's one-twenty-third. Your risk of breast cancer will be one-twenty-third of what it would be otherwise. It won't be zero. You can't get to zero. If you use this for ten years, your risk will be cut by at least half. If you use it for five years, your risk will be cut by at least a third. It's as if your breast were to be five years younger, or ten years younger—*forever*." The regimen, he says, should also provide protection against ovarian cancer.

Pike gave the sense that he had made this little speech many times before, to colleagues, to his family and friends—and to investors. He knew by now how

strange and unbelievable what he was saying sounded. Here he was, in a cold, cramped garage in the industrial section of Santa Monica arguing that he knew how to save the lives of hundreds of thousands of women around the world. And he wanted to do that by making young women menopausal through a chemical regimen sniffed every morning out of a bottle. This was, to say the least, a bold idea. Could he strike the right balance between the hormone levels women need to stay healthy and those that ultimately make them sick? Was progesterin really so important in breast cancer? There are cancer specialists who remain skeptical. And, most of all, what would women think? John Rock, at least, had lent the cause of birth control his Old World manners and distinguished white hair and appeals from theology; he took pains to make the Pill seem like the least radical of interventions—nature's contraceptive, something that could be slipped inside a woman's purse and pass without notice.

Pike was going to take the whole forty-year mythology of "natural" and sweep it aside. "Women are going to think, I'm being manipulated here. And it's a perfectly reasonable thing to think." Pike's South African accent gets a little stronger as he becomes more animated. "But the modern way of living represents an extraordinary change in female biology. Women are going out and becoming lawyers, doctors, presidents of countries. They need to understand that what we are trying to do isn't abnormal. It's just as normal as when someone hundreds of years ago had menarche at seventeen and had five babies and had three hundred fewer menstrual cycles than most women have today. The world is not the world it was. And some of the risks that go with the benefits of a woman getting educated and not getting pregnant all the time are breast cancer and ovarian cancer, and we need to deal with it. I have three daughters. The earliest grandchild I had was when one of them was thirty-one. That's the way many women are now. They ovulate from twelve or thirteen until their early thirties. Twenty years of uninterrupted ovulation before their first child! That's a brand-new phenomenon!"

John Rock's long battle on behalf of his birth-control pill forced the Church to take notice. In the spring of 1963, just after Rock's book was published, a meeting was held at the Vatican between high officials of the Catholic Church and Donald B. Straus, the chairman of Planned Parenthood. That summit was followed by another, on the campus of the University of Notre Dame. In the summer of 1964, on the eve of the feast of St. John the Baptist, Pope Paul VI announced that he would ask a committee of Church officials to reexamine the Vatican's position on contraception. The group met first at the Collegio San Jose, in Rome, and it was clear that a majority of the committee were in favor of approving the Pill. Committee reports leaked to the *National Catholic Register* confirmed that Rock's case appeared to be winning. Rock was elated. *Newsweek* put him on its cover, and ran a picture of the Pope inside. "Not since the Copernicans suggested in the sixteenth century that the sun was the center of the planetary system has the Roman

Catholic Church found itself on such a perilous collision course with a new body of knowledge," the article concluded. Paul VI, however, was unmoved. He stalled, delaying a verdict for months, and then years. Some said he fell under the sway of conservative elements within the Vatican. In the interim, theologians began exposing the holes in Rock's arguments. The rhythm method 'prevents' conception by abstinence, that is, by the non-performance of the conjugal act during the fertile period," the Catholic journal *America* concluded in a 1964 editorial. "The pill prevents conception by suppressing ovulation and by thus abolishing the fertile period. No amount of word juggling can make abstinence from sexual relations and the suppression of ovulation one and the same thing." On July 29, 1968, in the "Humanae Vitae" encyclical, the Pope broke his silence, declaring all "artificial" methods of contraception to be against the teachings of the Church.

In hindsight, it is possible to see the opportunity that Rock missed. If he had known what we know now and had talked about the Pill not as a contraceptive but as a cancer drug—not as a drug to prevent life but as one that would save life—the Church might well have said yes. Hadn't Pius XII already approved the Pill for therapeutic purposes? Rock would only have had to think of the Pill as Pike thinks of it: as a drug whose contraceptive aspects are merely a means of attracting users, of getting, as Pike put it, "people who are young to take a lot of stuff they wouldn't otherwise take."

But Rock did not live long enough to understand how things might have been. What he witnessed, instead, was the terrible time at the end of the sixties when the Pill suddenly stood accused—wrongly—of causing blood clots, strokes, and heart attacks. Between the mid-seventies and the early eighties, the number of women in the United States using the Pill fell by half. Harvard Medical School, meanwhile, took over Rock's Reproductive Clinic and pushed him out. His Harvard pension paid him only seventy-five dollars a year. He had almost no money in the bank and had to sell his house in Brookline. In 1971, Rock left Boston and retreated to a farmhouse in the hills of New Hampshire. He swam in the stream behind the

house. He listened to John Philip Sousa marches. In the evening, he would sit in the living room with a pitcher of Martini. In 1983, he gave his last public interview, and it was as if the memory of his achievements was now so painful that he had blotted it out.

He was asked what the most gratifying time of his life was. "Right now," the inventor of the Pill answered, incredibly. He was sitting by the fire in a crisp white shirt and tie, reading "The Origin," Irving Stone's fictional account of the life of Darwin. "It frequently occurs to me, gosh, what a lucky guy I am. I have no responsibilities, and I have everything I want. I take a dose of equanimity every twenty minutes. I will not be disturbed about things."

Once, John Rock had gone to seven o'clock Mass every morning and kept a crucifix above his desk. His interviewer, the writer Sara Davidson, moved her chair closer to his and asked him whether he still believed in an afterlife.

"Of course I don't," Rock answered abruptly. Though he didn't explain why, his reasons aren't hard to imagine. The Church could not square the requirements of its faith with the results of his science, and if the Church couldn't reconcile them how could Rock be expected to? John Rock always stuck to his conscience, and in the end his conscience forced him away from the thing he loved most. This was not John Rock's error. Nor was it his church's. It was the fault of the haphazard nature of science, which all too often produces progress in advance of understanding. If the order of events in the discovery of what was natural had been reversed, his world, and our world, too, would have been a different place.

"Heaven and Hell, Rome, all the Church stuff—that's for the solace of the multitude," Rock said. He had only a year to live. "I was an ardent practicing Catholic for a long time, and I really believed it all then, you see." +