

Oral Contraceptives and Their Social Consequences and their Social Consequences

ABSTRACT

In 1938, Russell Marker developed the first cost-efficient chemical process that made synthetic progesterone available for medical use. As a result, progestins have been used for decades as birth control pills and to treat various female reproductive disorders. In 2006, high doses of progestins that have an emergency contraceptive effect have been approved for over-the-counter access for persons eighteen years or older. Increased access to emergency contraception has sparked debate between Pro-Life and Pro-Choice groups. Debate over the morality of emergency contraception may produce compromises in healthcare.

INTRODUCTION

During the 1930s, referred to by steroid chemists as the “Decade of Sex Hormones,” scientists realized the medical potential of sex steroid hormones such as testosterone, estrogen, and progesterone. Although progesterone was known for both its unique chemical property as a precursor to glucocorticoids (a class of hormones, including cortisol that regulates many life processes) and its medicinal value to treat menstrual disorders and prevent miscarriages. However, the chemistry of progesterone was not well studied due to its high cost. In the 1930s, progesterone was inefficiently derived from the byproducts of cholesterol oxidation, yielding a product worth \$80 per gram.^{1,2}

¹ The Journal of Young Investigators, “Yams of Fortune: The (Uncontrolled) Birth of Oral Contraceptives,” 2005, <<http://www.jyi.org/features/ft.php?id=540>> (18 April 2007)

² American Chemical Society, “The Decade of the Sex Hormones,” *The “Marker Degradation,”* n.d., <<http://acswebcontent.acs.org/landmarks/marker/decade.html>> (18 April 2007)

MARKER DEGRADATION

In 1938, Russell Marker, a chemistry professor at Pennsylvania State University, presented a hypothesis, known as the Marker degradation, to synthesize progesterone by modifying the side chain of sarsasapogenin which was previously believed to be unreactive. Marker's original hypothesis was not economical due to the high cost of sarsasapogenin and the chemical reactions to modify it. Marker then considered synthesizing progesterone from diosgenin (a chemical more similar to progesterone than sarsasapogenin) which was previously studied by Japanese scientists. Although diosgenin did successfully produce progesterone, Marker's progesterone synthesis was still not cost-effective because it was expensive to produce.³

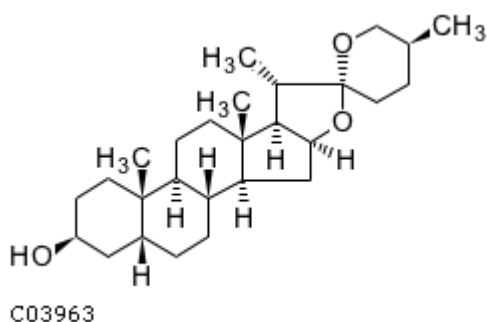


FIGURE 1. Sarsasapogenin⁴

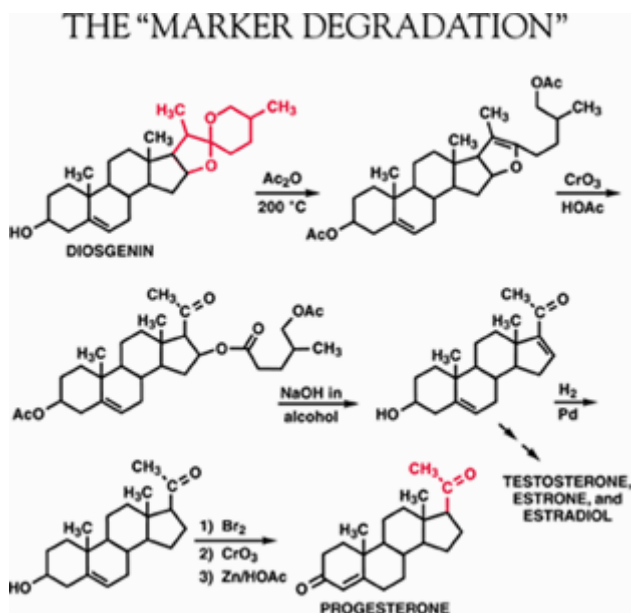


FIGURE 2. Marker Degradation of Diosgenin⁵

³ *Ibid.*

⁴ GenomeNet, "Compound: C03963," n.d., <http://www.genome.ad.jp/dbget-bin/www_bget?compound+C03963> (18 April 2007)

⁵ American Chemical Society, "The Decade of the Sex Hormones," *The "Marker Degradation,"* n.d., <<http://acswebcontent.acs.org/landmarks/marker/decade.html>> (18 April 2007)

Marker headed to Mexico in search for an economical source of a chemical similar to sarsasapogenin. In November 1941 in Orizaba, Veracruz, Marker found the wild yam *Dioscorea* (a.k.a.: *cabeza de negro*) that yielded diosgenin. Despite not having a plant-collecting permit, Marker was able to smuggle the yams into the United States by bribing a local policeman. Marker then took his research to Parke-Davis's laboratories in Detroit because Parke Davis was funding his research. Although Marker confirmed that his degradation could efficiently synthesize progesterone from diosgenin, Parke-Davis refused to commercialize Marker's success since Parke-Davis' president did not believe successful chemical processes could be performed in Mexico.⁶ Afterwards, other American pharmaceutical companies also refused to commercialize Marker's process.⁷

Marker returned to Veracruz, Mexico, where he collected ten tons of *cabeza de negro* and extracted syrup from the roots. Marker then proceeded to synthesize a large quantity of progesterone worth \$240,000 in 1943. In 1944, Marker created a company named Syntex, S.A. with Emeric Somlo, a Hungarian immigrant to Mexico, and Dr. Frederic Lehmann, a German-trained scientist. Although Syntex successfully sold progesterone, the company fell apart due to a disagreement concerning profit distribution.

In July 1945, Marker began making progesterone with his new company, Botanica-mex, later renamed Hormonosynth. In 1946, progesterone was synthesized from the yam *barbasco*, which yielded five times more diosgenin than *cabeza de negro*. Hormonosynth was later reorganized as Diosynth after Marker's retirement.⁸

⁶ *Ibid.*

⁷ The Journal of Young Investigators, "Yams of Fortune: The (Uncontrolled) Birth of Oral Contraceptives," 2005, <<http://www.jyi.org/features/ft.php?id=540>> (18 April 2007)

⁸ American Chemical Society, "A Steroid Industry in Mexico," *The "Marker Degradation,"* n.d., <<http://acswebcontent.acs.org/landmarks/marker/mexico.html>> (18 April 2007)

PROGESTERONE

Progesterone is a key hormone in facilitating female reproduction. Progestagens is the group of all hormones with effects similar to those of progesterone. Progesterone is the only progestagen that is made in the body. Synthetic progestagens are called progestins. However, since the Marker Degradation yields a compound chemically identical to progesterone, it is common to regard synthetic progestogens as 'natural' progesterone even though it is not made in the body because they are chemically identical to natural progesterone. Using newer methods, today's progestogens are many times more potent than natural progesterone.^{9,10}

The Marker degradation paved the way for female reproductive freedom. The most renowned use of progesterone synthesized via Marker degradation is to produce oral contraceptive pills (birth-control pills.) Today, progestins, rather than progesterone, are used in birth control; these progestins include desogestrel, ethynodiol diacetate, norethindrone, norgestrel, and levonogestrel.¹¹ Progestins are found in oral contraceptive pills that may be taken daily. Oral contraceptive pills come in estrogen-progestin combination pills and progestin-only pills, combination pills function by preventing ovulation and thickening cervical mucus whereas progestin-only pills and act by only thicken the cervical mucus.¹² Progestins such as levonorgestrel are also used in emergency contraception pills, known as Barr pharmaceutical's

⁹ American Chemical Society, "The Decade of the Sex Hormones," *The "Marker Degradation,"* n.d., <<http://acswebcontent.acs.org/landmarks/marker/decade.html>> (18 April 2007)

¹⁰ Pete Hueseman, Synthetic Progestins and Natural Progesterone, A Pharmacist Explores the Differences, 1997, <<http://www.project-aware.org/Resource/articlearchives/differences.shtml>> (18 April 2007)

¹¹ The New England Journal of Medicine, "Types of Progestins in Combination Estrogen-Progesterone Oral Contraceptives Marketed in the United States or Mentioned in Studies of Types of Progestin and Cardiovascular Disease," 9 October 2003, <<http://content.nejm.org/cgi/content/full/349/15/1443/T1>> (18 April 2007)

¹² Planned Parenthood, "The Pill," 1 March 2006, <<http://www.plannedparenthood.org/birth-control-pregnancy/birth-control/the-pill.htm>> (18 April 2007)

“Plan B pill,” that are the equivalent to twenty times the dose of one progestin-only-pill and about five times the dose of one combination pill.¹³

Progestins prevent pregnancy in one of three ways: suppressing ovulation, preventing physical union of egg and sperm, and preventing implantation of the fertilized egg into the uterine lining. The first mechanism is common to normal birth-control pills. High progesterone and estrogen levels trick the woman’s body into believing that she is pregnant by inhibiting luteinizing hormone, which is necessary for ovulation. In the second mechanism, used in emergency contraception, progesterone can prevent physical union of sperm and egg by causing the woman’s cervical mucus to thicken and/or interfere with sperm maturation. Many suspect emergency contraception worked through a third mechanism of preventing implantation of a fertilized egg into the uterine lining; however, studies measuring the pregnancy rate of after mating (whose eggs are probably fertilized) and given either levonorgestrel or placebo treatment revealed identical pregnancy rates, inferring implantation is not affected by emergency contraception.¹⁴ However, since no method exists to *directly* determine the mechanism of implantation of the fertilized egg, the possibility of the third mechanism persists. The mechanism of contraceptive action depends on the timing of sexual intercourse relative to the woman’s menstrual cycle.¹⁵

¹³ Planned Parenthood, “How to Take [Emergency Contraception],” n. d., <<http://www.plannedparenthood.org/birth-control-pregnancy/emergency-contraception/procedure-4366.htm>> (18 April 2007)

¹⁴ Population Council, “Emergency Contraception Prevents Fertilization, Not Implantation, Studies Show,” 2 March 2005, <<http://www.popcouncil.org/mediacenter/newsreleases/ecdisruptsovulation.html>> (27 April 2007)

¹⁵ Rachel Benson Gold, “Implications of Defining When a Woman Is Pregnant,” *The Guttmacher Report on Public Policy*, Vol. 8, No. 2. (May 2005), pp. 10.

FDA POLICY

In August, 2006, the FDA approved over-the-counter access to Plan B pills for women 18 and older; women 17 and younger require a prescription. The age limit for access to plan B was established for two reasons. First, Barr pharmaceuticals had less clinical data on Plan B use in women under 18. Second, it is easy to categorize the Plan B pill into well-established state and private-sector infrastructures that set the age limit of 18 to restrict sales of certain products such as cigarettes, non-prescription nicotine therapy products, and non-prescription cough-cold products such as pseudoephedrine.¹⁶

BEGINNING OF PREGNANCY CONTROVERSY

The controversy over contraception is rooted in arguments concerning the beginning of life. The third mechanism for preventing pregnancy (mentioned above) prevents the already fertilized egg from implantation. Some groups believe that life begins before the implantation of a fertilized egg into the uterus; others believe life begins after implantation. If life begins upon fertilization (before implantation), the third mechanism of emergency contraception is equivalent to abortion.^{17, 18}

The medical community maintains that “pregnancy is established when a fertilized egg has been implanted in the wall of a woman’s uterus.” The Department of Health and Human Services (under both the Clinton and Bush administrations) has maintained this definition; the Bush administration explicitly says that pregnancy “encompasses the period of time from implantation until delivery.”

¹⁶ Andrew C. Von Eschenbach, “Memorandum: Appropriate age restriction for Plan B®,” 23 August 2006. <<http://www.fda.gov/cder/drug/infopage/planB/avememo.pdf> > (19 April 2007)

¹⁷ J.T. Finn, “‘Birth Control’ Pills Cause Early Abortions” *Pro-Life America – Facts on Abortion*, 23 April 2005, <<http://www.prolife.com/BIRTHCNT.html>> (9 March 2007)

¹⁸ Rachel Benson Gold, “Implications of Defining When a Woman Is Pregnant,” *The Guttmacher Report on Public Policy*, Vol. 8, No. 2. (May 2005), pp. 7-10.

Anti-abortion activists stand at the opposite end of the spectrum – many groups maintain that a fertilized egg is the beginning of both a pregnancy and a “brand new life.” These groups include Concerned Women for America and the Secretariat for Pro-Life Activities of the U.S. Conference of the Catholic Bishops, and the American Life League. Notably, some anti-abortion groups, e.g. the Right to Life Committee, avoid the beginning-of-pregnancy controversy and do not maintain a position on contraception.

Unfortunately, state legislators are ambiguous. State policy usually defines the beginning of pregnancy to regulate abortion and establish consequences for “assaulting” pregnant women. State laws sometimes use the word “fertilization” or “implantation”, sometimes both. Some state laws use the word “conception”, which is often used interchangeably with fertilization, but is medically defined as implantation.¹⁹

OTHER OBJECTIONS TO EMERGENCY CONTRACEPTION

Some activist groups are concerned that the availability of emergency contraception will affect sexual and contraceptive behavior; Concerned Women for America is alarmed that increased access to Plan B may reduce alertness to transmission of sexually transmitted diseases (STD) by creating a false sense of security.²⁰ The condom, a less effective contraceptive implement, is the most popular protection against STD’s; progestin contraception does not offer protection against STD’s.

A study published in the Journal of the American Medical Association investigated the influence of access to emergency contraception on sexual behavior. Women were assigned into one of three groups: the first group was able to obtain emergency contraception directly from

¹⁹ *Ibid.*

²⁰ Wendy Wright and Jody Porowski, “Uncovering Lies – What Pro-Abortionists Don’t Want You to Know About the Morning-After Pill,” *Concerned Women For America*, 25 August 2006. <<http://www.cwfa.org/articles/11112/CWA/life/index.htm>> (19 April 2007)

pharmacists without a prescription; the second group was provided three doses of emergency contraception in advance; the third group was assigned to procure the drug through a family-planning clinic (the control group.) Results showed that women who were able to obtain emergency contraception from the pharmacy were no more likely to use emergency contraception than women who obtained emergency contraception through a family-planning clinic. Women who possessed emergency contraception in advance were twice more likely to use it than women in other groups. The three groups maintained similarities aside from emergency contraception use: 8% of the women in each group became pregnant, and 12% in each group contracted a sexually transmitted infection (STI). Results suggest that sexual behavior is not affected by availability of emergency contraception and that women are not taking advantage of easier access to emergency contraception.²¹

PATIENT BILL OF RIGHTS

Regardless of whether or not it is a woman's right to obtain emergency contraception without a prescription, obtaining the drug also depends on the moral or religious position of the pharmacist dispensing the drug. National and international codes of bioethics exist to guide healthcare professionals; however, interpretations of bioethics are variable. Professional standards usually endorse a provider's right to refuse or "withdraw" from providing healthcare that conflicts with the provider's moral or religious values; these rights are often stipulated in "conscience clauses."^{22,23}

²¹ Science Daily, "Sexual Behavior Not Influenced By Increasing Young Women's Access To 'Morning After Pill,' UCSF Study Finds," 22 January 2005. <<http://www.sciencedaily.com/releases/2005/01/050121110428.htm>> (19 April 2007)

²² Paul Rosenzweig, "Balancing Conscience and the Law," *The Heritage Foundation*, 26 April 2004. <<http://www.heritage.org/Press/Commentary/ed042604c.cfm>> (19 April 2007)

²³ Allison Grady, "Legal Protection for Conscientious Objections by Health Professionals," *American Medical Association*, 2006. <<http://www.ama-assn.org/ama/pub/category/16187.html>> (19 April 2007)

According to Adam Sonfield, writer for The Guttmacher Report, health care providers are required to maintain three values: obligation of the provider to act in the patient's best interest; obligation of the provider to provide nondiscriminatory care and to work for the public good; and to respect the autonomy of the individual patient. Sonfield notes the importance of all three guidelines existing at once. For example, a lack of respect for autonomy could result in the provider's care turning into paternalism.²⁴ Official policy in the United States follows the World Medical Association and the U.S. Patients' Bill of Rights, adopted by the U.S. Advisory Commission on Consumer Protection and Quality in the Health Care Industry in 1988. The International Code of Medical Ethics asserts that the physician shall "respect the rights and preferences of patients, colleagues, and other health professionals," "act in his patients' best interest when providing medical care" and owe "his patients complete loyalty and all the scientific resources available to him/her".²⁵ The Patients' Bill of Rights asserts consumers have the right to accurate and easily understood information to make informed healthcare decisions (Information Disclosure), the right to a choice of health care providers that will provide access to quality healthcare services (Choice of Providers and Plans), and the right to know all treatment options and to participate in decisions about the consumer's care (Participation in Treatment Decisions).²⁶

These codes of bioethics can be interpreted with much variation depending on the provider's perspective on the beginning of pregnancy. When faced with a woman seeking emergency contraception, healthcare professionals who see implantation as the beginning of pregnancy regard the patient in need of medical care – the mother – whereas professionals who

²⁴ Adam Sonfield, "Rights vs. Responsibilities: Professional Standards and Provider Refusals," *The Guttmacher Report on Public Policy* Vol. 8, No. 3 (August 2005), pp. 7-9.

²⁵ *World Medical Association*, "World Medical Association International Code of Medical Ethics," n.d., <<http://www.wma.net/e/policy/c8.htm>> (19 April 2007)

²⁶ *Consumer.gov*, "Patient Rights and Responsibilities," 9 December 1999. <<http://www.consumer.gov/qualityhealth/rights.htm>> (9 March 2007)

see fertilization as the beginning of pregnancy consider two patients – the mother and child – who are in need of medical care. This difference in interpretations blurs the World Medical Association International Code of Ethics: does the pharmacist treat the mother, or both the child and the mother?

In general, professional healthcare associations maintain this policy: if a healthcare provider's moral or religious beliefs conflict with the patient's, the provider, though not required to provide the service him/herself, is required to avoid patient abandonment by referring the patient to another provider who is capable and ready to fulfill the patient's needs.

However, supporters for a provider's more extensive refusal rights maintain that a healthcare provider must "always bear in mind the obligation of preserving human life" as stated in the World Medical Association's International Code of Medical Ethics. Concerning pharmacists who oppose emergency contraception, because they equate that to abortion, the pharmacist who refuses to dispense emergency contraception and refers the patient to another professional who will dispense the drug is just as guilty as if the pharmacist had dispensed the drug himself. Through this interpretation, referral to other pharmacists to provide the emergency contraception pill violates the providers' obligation to preserve human life.^{27,28,29}

CONCLUSION

The Marker Degradation produces synthetic progesterone that has improved female reproductive health and paved the way for women's reproductive freedom. High doses of synthetic progesterone (an established American brand is the Barr pharmaceutical's Plan B® pill) have an emergency contraceptive effect. Easier access to emergency contraception has raised

²⁷ Adam Sonfield, "Rights vs. Responsibilities: Professional Standards and Provider Refusals," *The Guttmacher Report on Public Policy* Vol. 8, No. 3 (August 2005), pp. 7-9.

²⁸ Rachel Benson Gold, "Contraceptive Coverage: Toward Ensuring Access While Respecting Conscience," *The Guttmacher Report on Public Policy* Vol. 1, No. 6, (December 1998), pp. 1-3.

²⁹ Cynthia Dallard, "Beyond the Issue of Pharmacist Refusals: Pharmacies That Won't Sell Emergency Contraception," *The Guttmacher Report on Public Policy* Vol. , No. (August 2005), pp. 10-12.

questions concerning the product's effect on women's sexual behavior. Emergency contraception has also raised questions between pro-life and pro-choice groups; Plan B® can prevent a fertilized egg from implanting into the uterus – a mechanism considered equivalent to abortion by those who regard fertilization as the beginning of pregnancy. Debate about the ethics of Plan B® has raised serious controversy about the future of healthcare policy. We see here how an advance in synthetic chemistry has produced a significant moral and public-policy controversy.