Endocrine Function and Emergency Contraception: Physiology and Society

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Relating emergency contraception, commonly referred to as "the morning-after pill," to the menstrual cycle can be used both to teach endocrine function and to show how physiology relates to the world outside the undergraduate classroom. The menstrual cycle is an excellent topic for teaching many features of the physiology of the human endocrine system. Relating emergency contraception to the menstrual cycle makes this topic relevant to both male and female students, provides opportunities for discussions that require the students' understanding of endocrine functions, and illustrates how physiology is connected to social, economic, and political issues. The overview of emergency contraception and literature survey provided here are meant to be adapted for use in a variety of teaching contexts. The depth of coverage and the extent of consideration of issues beyond physiology would depend on many factors including the level of the course and the size of enrollment.

Key words: menstrual cycle; "morning-after pill"; emergency postcoital contraception

Einstein once said, "Politics is more difficult than physics."1 That assertion puts into a nutshell the challenges faced by those of us who teach undergraduate physiology. Although most of us aren't deeply involved in politics, many of our students are likely to become policy makers, whether as politicians, teachers, health care professionals, or other participants in society—a society ever more steeped in science and technology. As teachers of undergraduate physiology, our assignment doesn't stop at conveying content and helping our students learn to think analytically and critically. We have to be aware that they will be in positions in which they will be expected to articulate complex, often subtle ideas about science to people with less experience. To be effective, they will need both solid grounding in physiology and a sense of the link between it and social, economic, and political issues.

In this paper, I present the use of emergency contraception (the "morning-after pill" or "emergency postcoital contraception") as a vehicle for stimulating students' interest in the endocrine system and inviting them also to think about matters of public policy. To consider emergency contraception, one has to understand the menstrual cycle, an excellent system for mastering many fundamentals of endocrine function. Emergency contraception makes the menstrual cycle relevant to both male and female students, and it poses complex issues about which reasonable people can disagree. Seeing how emergency contraception relates to their own lives, students realize that master-

1 In a letter to the editor of the New York Times, Grenville Clark described an exchange between Einstein and another conferee at a meeting on the United Nations Charter held in 1946 in Princeton, NJ. In conversation between sessions, the conferee asked him why we could know so much about the atom but so little about controlling its use. Professor Einstein responded, "That is simple, my friend. It is because politics is more difficult than physics." New York Times, Apr. 22, 1955, p. 24.
ing the physiological foundations of its use gives them much more power in expressing their opinions about a variety of social questions.

The following narrative provides a literature survey and an overview of emergency contraception. Because physiology is taught at many levels of content, from diverse approaches, and to classes of different sizes, the material could, and should, be used in a variety of ways. For example, understanding the timing of ovulation, possible fertilization, and implantation could lead to a discussion of why the term “morning-after pill” is a misnomer for emergency contraception. Or, discussing the way hormonal emergency contraception works could serve as an indicator of the students’ knowledge of the hormones that control ovulation and the thickening and secretory activity of the endometrium, as well as the role of the corpus luteum. For both of these considerations, the level of understanding would depend on the depth of coverage of the menstrual cycle.

The treatment of social issues would also be governed by content, time constraints, the students’ experience and interests, and individual teaching styles. Many questions could be addressed, ranging from those directly related to physiology to much more controversial ones: Does everyone agree with the medical definition of the beginning of pregnancy? Why don’t pharmaceutical companies advertise oral contraceptives as suitable for emergency contraception? Would more use of emergency contraception reduce the number of surgical abortions done in this country? An important goal of drawing the students’ attention to social issues is to emphasize that physiology has a connection to the “real world.” The point of such discussions is not to set moral or ethical guidelines but to illustrate how a sound biological context allows individuals to wrestle with complex issues and to develop their own perspectives.

HISTORY

Three recent review articles (3, 7, 25) describe the history of emergency contraception. For centuries, women have used postcoital douches of various substances, including Coca-Cola, in attempts to avoid getting pregnant. Such douches are completely ineffective, however, because sperm cells are known to make their way into the oviducts within a few minutes of sexual intercourse. Emergency methods that actually work came into use in the 1960s when women were treated with high doses of estrogens. These techniques were developed from animal studies done decades earlier and were first used by veterinarians to prevent possible pregnancies from unwanted matings of pets and livestock. In 1974, Albert Yuzpe and his colleagues published the first of several studies using estrogen combined with progestin. The “Yuzpe method,” which employs combination birth control pills containing estrogen and progestin, is still used today (29). It is administered in the following way. Within 72 h of unprotected sexual intercourse, a woman takes an initial dose of 0.1 mg of the estrogen ethinyl estradiol and 1.0 mg of the progestin norgestimate. The number of pills that contain these amounts of the hormones varies depending on the brand of oral contraceptive used. The same dose is then repeated 12 h later (23).

Hormonal treatments that included only progestins were also tested beginning in the early 1970s with the idea that they could be used regularly after intercourse as postcoital contraceptives, but they were found to cause unacceptable levels of “cycle disturbances” (25). Today, progestin-only birth control pills known as minipills are prescribed for emergency contraception when a woman is not able to tolerate the estrogen in the combination birth control pills.

The first report of an intrauterine device (IUD) used for emergency contraception was published in 1976. The Copper-T, a T-shaped plastic device ~1.5 in. in length that is impregnated with copper, is the one most commonly used now for that purpose (5). Unlike hormonal emergency contraceptive treatments, which are short-lived in their effects, the IUD provides continuous, long-term contraception.

CURRENT EVENTS IN THE UNITED STATES

Although emergency contraception is widely used in the United Kingdom and the Netherlands (12), it is not well known as an option for family planning among women in the US. A 1994 telephone survey of 2,002 adults (18) found that about one-half were aware of emergency contraception or the “morning-after pill,” but most of those (69%) thought it was effective only 24 h after unprotected intercourse. Only 9% knew it was possible to seek emergency contraception up to 3
days afterward. Many proponents of emergency contraception contend that one reason women are not informed about it, and doctors do not frequently prescribe it, is that drug companies do not label birth control pills as suitable for emergency contraception.

For this reason, in November of 1994, the New York-based Center for Reproductive Law and Policy filed a petition with the Food and Drug Administration (FDA) on behalf of several clients, including Planned Parenthood of New York, the American Public Health Association, and the American Medical Women’s Association. The petition held that the FDA should require drug companies to include information about emergency contraception in packets of oral contraceptives. Subsequently, the FDA convened an advisory committee and held hearings on this matter. At the conclusion of the hearings on July 1, 1996, Mary Pendergast, the Deputy Commissioner of the FDA, announced that the advisory committee unanimously agreed that oral contraceptives could be used safely and effectively for emergency contraception up to 72 h after unprotected intercourse. She said that the FDA would not require drug companies to label their products for emergency contraception, but that the agency hoped companies would come forward with proposals to do so. Following up on this conclusion, the FDA officially stated in the February 25, 1997 Federal Register (10) that it would accept applications from pharmaceutical companies to include information about emergency contraception in packets of birth control pills. Two articles in the New York Times provide a good overview of these events (2, 19). The Federal Register (10) lists specific regimens for emergency contraception, addresses safety and effectiveness, and provides references.

More recently, doctors have begun to take action. At their meeting in late April 1997, the American College of Obstetricians and Gynecologists (ACOG) announced that they believe it essential that both doctors and women become more aware of emergency contraception. To accomplish this goal, they plan to distribute 50,000 informational packets containing manuals and brochures to their members (21).

**PRACTICAL INFORMATION**

A 24-h toll-free Emergency Contraception Hotline (1-800-584-9911) was established in February 1996 by the Office of Population Research at Princeton University. It offers prerecorded information in both English and Spanish and identifies providers of emergency contraception located near the caller. The Office of Population Research also maintains a World Wide Web site that provides information, advice, and an up-to-date directory of clinics and doctors (8).

The book *Emergency Contraception: The Nation’s Best Kept Secret*, written by Robert A. Hatcher and others, was published in 1995 and is available from Bridging the Gap Communications (1-800-721-6990).

**HOW EMERGENCY CONTRACEPTION WORKS**

During the first half of the menstrual cycle, the lining of the uterus, the endometrium, thickens in response to estrogen produced by developing follicles in the ovary. During ovulation, at the middle of the cycle, the ovum and a few attached cells leave the mature follicle(s). The remaining cells of the follicle collapse back into the ovary and reorganize into a new hormone-secreting structure, the corpus luteum, which secretes both estrogen and progesterone. During the second half of the cycle, these two hormones stimulate the thickened endometrium to secrete nutritive substances that provide a lush habitat for the newly formed embryo to burrow into, if fertilization has occurred. When the ovum leaves the ovary at ovulation, it begins a 4-day journey down the oviduct to the uterus. Because the ovum is fertile no more than 24 h (11), fertilization occurs within the oviduct. The time between events leading to ovulation and arrival of the embryo at the uterus is the window of opportunity for emergency contraception to work.

If the woman had not ovulated before receiving treatment with the Yuzpe method, the combined hormones would prevent ovulation (which is what they do when taken for ordinary contraception) or delay it (4, 11). Indeed, Glasier (11) asserts that the main mode of action of the Yuzpe emergency contraceptive method is to interfere with ovulation. Other reports suggest that the Yuzpe method also disrupts the functions of both the corpus luteum and the endometrium (4) so that the endometrium is not able to sustain an embryo at the time it arrives in the uterus (28). Similarly, minipills, which contain only progestin, are thought to interfere with implantation by...
acting at both the corpus luteum and endometrium (4).

The copper IUD, when used for ordinary contraception, prevents fertilization by making sperm less mobile and the egg less able to be fertilized (4). In emergency situations, it is thought to prevent implantation by causing local inflammation of the endometrium, by the copper exerting a toxic effect on the embryo, or by both of these effects (4, 7, 11).

**SIDE EFFECTS OF HORMONAL EMERGENCY CONTRACEPTION**

About one-half of the women who take emergency contraceptive pills containing both estrogen and progesterin experience nausea, and about 20% vomit (4, 7). Many physicians recommend taking antinausea medication. Some provide a woman with extra pills in case she vomits before the hormones are absorbed into her system. Less frequently, women report headaches, breast tenderness, abdominal pain, and dizziness. Women who take minipills experience less nausea. The effects of both types of hormone treatment dissipate quickly. If a woman does not become pregnant, she will menstruate, although her menstrual period may be a few days earlier or later than expected.

Although the treatment causes many women temporary distress, several studies of more than 6,600 women treated with the Yuzpe method report no long-term or serious side effects (4). Nevertheless, some physicians have believed that women with blood clotting disorders, for whom estrogen-containing birth control pills are not prescribed for ordinary contraception, should not take these pills for emergency contraception. Researchers now believe that such a concern is unwarranted because the hormones are given over a short period of time and exert only temporary effects (7, 27).

If a woman is already pregnant, emergency contraception will have no effect. Some physicians have voiced concern that the treatment could cause birth defects. No studies have been done to address this issue directly; however, information is available about women who continued to take birth control pills after they became pregnant. Analysis of data from 12 different studies showed that taking oral contraceptives in early pregnancy did not cause birth defects (7).

**EFFECTIVENESS OF HORMONAL EMERGENCY CONTRACEPTION**

When a woman seeks out emergency contraception, she doesn’t know if she will become pregnant if she does nothing at all. It is estimated that of 100 women who have unprotected sexual intercourse once in the middle of their menstrual cycle, 7 would become pregnant (6). Both the Yuzpe method and minipills are estimated to be 75% effective (23). Therefore, treating all 100 women would result in 25% of 7 (instead of 7) pregnancies. For the Yuzpe method, this 75% effectiveness remains constant whether the emergency contraceptive regimen was begun on the first, second, or third day after unprotected intercourse (22).

**SAFETY AND EFFECTIVENESS OF THE IUD**

The IUD is estimated to be 99% effective in preventing pregnancy, and it is a reasonable option for a woman interested in long-term contraception—the copper IUD can remain in place for as long as 10 years (5).

However, the IUD cannot be used by women at risk for sexually transmitted diseases (STDs) (5). IUDs increase the likelihood that an STD will lead to pelvic inflammatory disease (PID). This infection within the uterus and oviducts can cause chronic pelvic pain, ectopic pregnancies, and infertility. Women who have experienced sexual assault, have more than one sexual partner, or have a partner who has more than one sexual partner, are all at risk. And this is no small risk, given that 12 million new STD cases are diagnosed each year (9).

Indeed, no form of emergency contraception protects against the transmission of STDs, and some are concerned that if emergency contraception were more widely known, women might use it routinely instead of other methods that protect against STDs. However, others argue that the side effects of nausea and vomiting would prevent women from routinely choosing emergency contraception, that this method is less effective than other forms of contraception, and that it is more expensive (8).
COULD RU-486 BE USED FOR EMERGENCY CONTRACEPTION?

RU-486, “the abortion pill,” known in the United States as mifepristone, is an antiprogestogen. By attaching to the same sites in cells normally bound by progesterone, it blocks the actions of this hormone, which is essential for assuring implantation of the embryo (11, 26).

Outside the US, researchers tested mifepristone for emergency contraception and compared it with the Yuzpe method (13). In these studies the researchers used the same high dose of mifepristone used to induce abortions, but they did not follow it with a prostaglandin as would be done for the abortion procedure. The results showed that none of the 402 women treated with mifepristone became pregnant, whereas 4 of the 398 women treated with the Yuzpe method did. Mifepristone caused fewer side effects, but 42% of the women treated with mifepristone had a delayed menstrual period compared with only 13% treated with the Yuzpe method. Further research has been aimed at finding how much smaller the dose of mifepristone can be for effective emergency contraception (26).

More recently, new progesterone antagonists have been developed, and the National Institute of Child Health and Human Development announced in February 1997 that it was offering the opportunity for licensing or cooperative research on progesterone antagonists with the aim of making them commercially available (20).

REPRODUCTIVE DECISIONS, ECONOMICS, AND SOCIAL ATTITUDES

Medically, pregnancy begins with implantation. Thus, by medical definition, emergency contraception, which exerts its effects before implantation, does not terminate a pregnancy. This is not the view held by all people, however. The Roman Catholic Church and other opponents of abortion state that pregnancy begins when the sperm and egg unite. In their view, if fertilization occurred, then emergency contraception would have caused an abortion. Although proponents of emergency contraception argue that its use would prevent induced abortions at later stages of pregnancy (24), opponents counter that any abortion is morally unacceptable. (However, Catholic hospitals will prescribe emergency contraceptive pills for women who have been raped).

Only a handful of studies have assessed the knowledge and attitudes of Americans toward emergency contraception. In 1994, a survey of 2,002 adults (18) found that many had misconceptions about it. When the interviewers explained more about the method, a majority were favorably disposed toward its use. Two studies of students’ attitudes were conducted at Princeton University, a telephone survey (16) and focus groups (15). The survey (16) found that approval of emergency contraception increased with the students’ knowledge about the method and that religious and political views also influenced attitudes toward emergency contraception. The majority of students participating in the focus groups (15) thought that information should be more freely available, but with the emphasis that emergency contraception should not be considered a routine method. The question of whether emergency contraception was more like abortion than contraception was repeatedly debated.

Clearly, abortion is an issue about which Americans are uneasy. The Alan Guttmacher Institute (1) reports that more than one-half of the pregnancies that occur each year are unplanned, and one-half of those are terminated by abortion. An estimated 1.4 million abortions occurred in 1994. Many of the women who had abortions, in fact, 58%, were using a contraceptive in the month they became pregnant (17). Taking into account facts such as these, proponents of emergency contraception argue that greater use of this method could reduce the number of unplanned pregnancies by at least one-half and therefore also reduce the number of surgical abortions by some hundreds of thousands (24).

However, emergency contraception is ensnared in a web of concerns about liability, economics, and personal codes of morality. Drug manufacturers have little financial incentive to seek approval from the FDA to relabel a drug that is already approved for a very lucrative purpose—oral contraceptives taken by millions of women every month for many years. Nor do they care to incur boycotts by antiabortion forces or
to be targets of liability suits from women who, for example, claim adverse side effects from emergency contraception.

Physicians may also worry about liability. Although a physician is legally permitted to prescribe drugs for unlabeled purposes, a patient may sue her doctor instead of the manufacturer for any adverse outcomes. Physicians could also be concerned about being caught up in the abortion debate. For whatever reasons, they appear until now to have been reluctant providers of emergency contraception. For example, two surveys, one of 300 obstetric-gynecologists (18) and another of 167 doctors who practice adolescent medicine (14), found that although 70% (18) to 80% (14) prescribed hormonal emergency contraception, most of them had done so only a few times per year (14, 18). These physicians also reported that they seldom discussed emergency contraception as an option during routine visits by their patients (14, 18). It will be interesting to see what changes come about now that ACOG has started its informational campaign (21).

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References