

Chapter 5

The Technology of Fertility Change: Present Methods and Future Prospects

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The Technology of Fertility Change: Present Methods and Future Prospects

Abstract

Of the technologies that change birth rates, contraceptive technologies are the most important. Current contraceptive methods, in the order of their use effectiveness, are sterilization, the various forms of steroid hormones, IUDs, barrier devices, vaginal spermicides, coitus interruptus, periodic abstinence (rhythm, natural family planning), and postcoital douches. Contraceptives are judged by the degree to which they are effective; safe; reversible; easy to produce, provide, and use; inexpensive; and acceptable to governments, cultures, religions, and individuals. The "ideal" contraceptive neither exists nor is expected to be developed. A realistic goal is for each country to have enough technologies that are appropriate for local conditions and standards so that each individual has access to at least one that meets current needs. Method risks of contraceptive use are largely confined to oral contraceptives and IUDs. Circulatory system diseases associated with oral contraceptives have caused the most concern and could theoretically cause a fivefold increase in deaths. But nearly three-quarters of the cardiovascular disease deaths occurring annually in the United States to women of reproductive age would be attributable to oral contraceptive use if the increased risk were indeed fivefold. This has not been reflected in vital statistics trends. In extending comparisons of relative risks to women in less developed countries (LDCs), all methods are found safer than no method at all because of high maternal mortality rates in these countries.

New or improved technologies likely to be available by 1990 include safer oral contraceptives, improved IUDs, improved barrier contraceptives for women, improved long-acting steroid injections, improved ovulation-detection methods for use with periodic abstinence, steroid implants, steroid vaginal rings, LRF-analog contraceptives for women, and prostaglandin analogs for induction of menses. Methods that could emerge by 1990 include a monthly steroid-based contraceptive pill, improved monthly steroid injections, new types of drug-releasing IUDs, minidose vaginal rings, an antipregnancy vaccine for women, improved barrier contraceptives for men, sperm suppression contraceptives for men, reversible female sterilization, simplified male and female sterilization, and LRF analogs for self-administered induction of menses. Methods that could be available by 2000 include an antifertility vaccine for men, antisperm drugs for men, lactation-linked oral contraceptives for women, ovulation prediction techniques for use with periodic abstinence, new types of antiovarian contraceptive drugs for women, drugs for women that disrupt ovum transport, reversible male sterilization, pharmacologic or immunological sterilization for men and women, and agents other than LRF analogs for self-administered induction of menses. Limitations of contraceptive technologies and lack of access to their use cause women in all parts of the world to seek induced abortions to terminate unwanted pregnancies; their large numbers are an index of contraceptive need rather than preference for abortion. Technological innovations that could have a major impact on capacity to diagnose the causes of infertility include development of simple techniques to predict and confirm ovulation, tests to determine level of functioning of male seminiferous tubules, and further development of ovulation-inducing drugs. LRF-agonists for inducing ovulation and LRF-agonists and other possible releasing-factor analogs for increasing sperm production are likely to be useful in inducing fertility. Although sex preference is strong in LDCs, present technologies for sex selection are highly ineffective and there is little likelihood of a product for general use becoming available by 2000. All current fertility planning methods have one or more serious shortcomings. Although existing methods have considerable unused potential for lowering LDC birth rates in the next two decades, the need for most couples to use contraception for up to 25 years points to the disparity between existing technologies and both current and future requirements for contraceptive use.

Introduction

Technologies modify each of the three components—birth, death, and migration—of population growth. Medical, agricultural, and sanitation technologies are essential to the reduction of death rates. Communication and transportation technologies play key roles in all aspects of population change. This report, as stated earlier, focuses on the technologies that help to change birth rates, and this chapter deals with the specific fertility planning technologies that human beings use to affect the numbers and characteristics of births.

The most common and most important of these technologies are those used to prevent un-

wanted pregnancy: contraceptive technologies. Less common but important at present are those used for early termination of unwanted pregnancy. Still less common but very important in some societies are technologies used to prevent or correct unwanted infertility, uncommon and little developed are the sex selection technologies used to determine an infant's sex at conception. Techniques to detect pregnancy or important abnormalities of pregnancy or to pre-select genetic characteristics are not included in this study.

The human reproductive process

Sperm are produced continuously in the testes from puberty throughout most of the male's life. The process begins with division of germ cells (spermatogonia) which, in combination with supporting (Sertoli) cells, make up the long seminiferous tubules that take up most of the testes. Interspersed Leydig cells produce male hormones (androgens), notably testosterone, which affect both sperm production and male sex characteristics. Sperm production takes about 72 days. The final stages of sperm maturation take place in the small ducts and long epididymis at the back of the testes. The sperm are ejaculated by a muscular tube, the vas deferens, which enters the urethra as it traverses the prostate gland.

The female menstrual cycle is approximately 28 days, normally ending with menstrual flow unless pregnancy occurs. The germ cells are in the two ovaries and number several million in the fetal stage, are fewer than 1 million at birth, and gradually decrease throughout life. One matures each month in a follicle on the ovary's surface that also produces the hormone, estrogen. The follicle ruptures, and the ovum travels down the fallopian tube to the uterus. The ruptured follicle then changes to a yellowish pro-

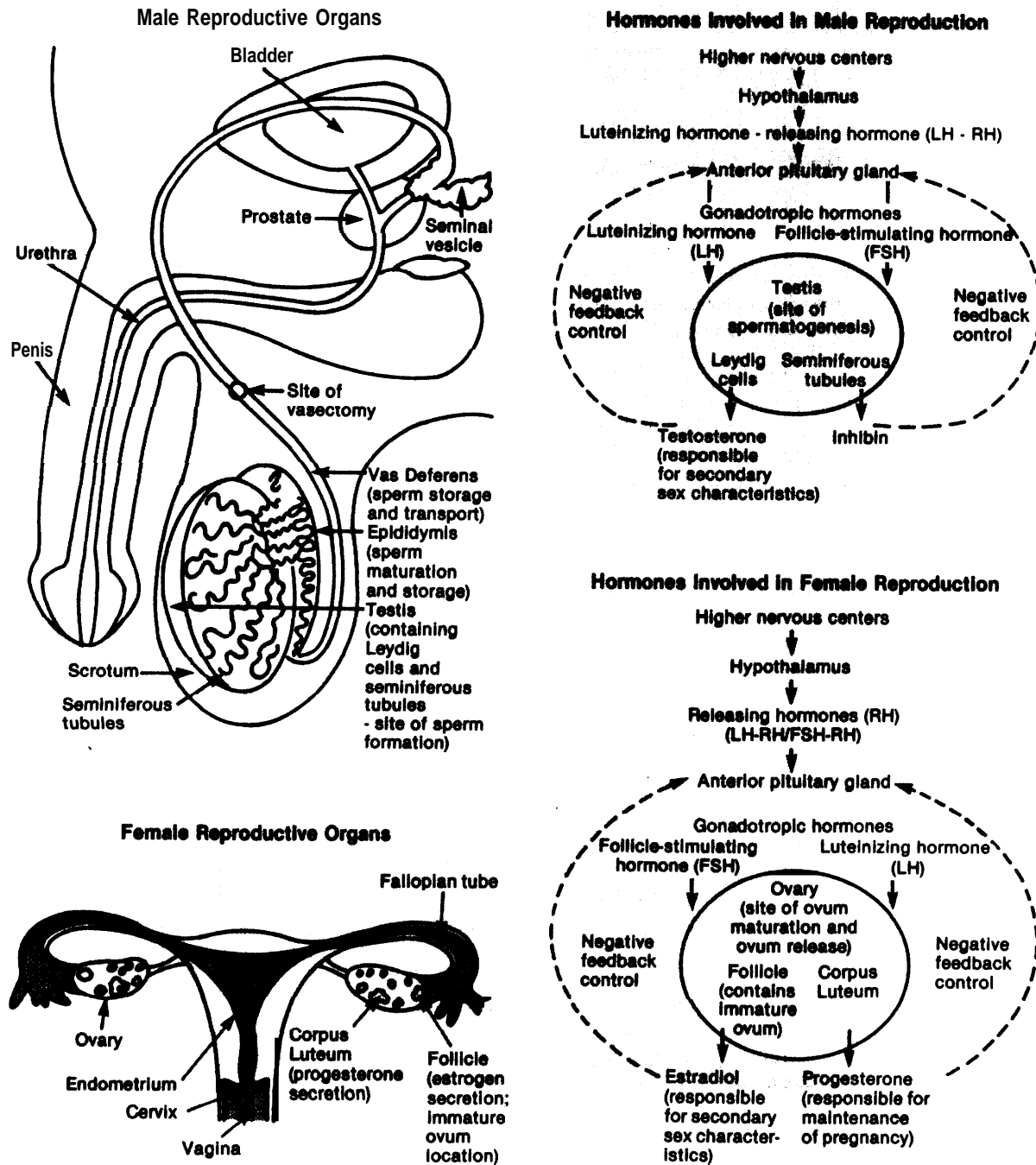
trusion on the ovary called the corpus luteum, which begins to produce another hormone, progesterone, in addition to continued estrogen production. The corpus luteum regresses if pregnancy does not occur. These hormonal changes also prepare the uterus for a possible pregnancy, but if pregnancy does not occur, the uterine lining is sloughed off, producing the menstrual flow.

In both male and female, sex hormone production is regulated by gonadotropins—hormones from the pituitary gland located just below the brain. The gonadotropins are controlled in turn by the luteinizing hormone releasing factor (LRF) from the hypothalamus, an adjacent section of the brain. In the female, the gonadotropins include the follicle stimulating hormone (FSH), which stimulates follicle growth, and luteinizing hormone (LH), which stimulates estrogen production by the follicle, promotes rupture of the follicle, and, after rupture of the follicle, also stimulates progesterone production from the resulting corpus luteum. Estrogen and progesterone levels act as feedback mechanisms on the hormones released from the hypothalamus and anterior pituitary. The central nervous system also can influence the menstrual cycle. In the male, FSH acts on the

Sertoli cells and is necessary for the initiation of spermatogenesis. LH regulates the secretion of testosterone by the Leydig cells. Testosterone

and other male hormones act as the feedback mechanisms. Figure 18 summarizes the human reproductive cycle.

Figure 18.—Human Reproductive Cycle



SOURCE: C. Djerassi, *The Politics of Contraception*, Norton, 1980

Human reproduction, as for other mammals, is characterized by relatively long intervals of natural infertility in the female. Fertilization can only take place within a few days after ovulation. Pregnancy occurs following fertilization of the ovum by the sperm, usually in the fallopian tube, and implantation of the embryo in the uterus. When pregnancy occurs, the corpus luteum is maintained by another hormone,

human chorionic gonadotropin (HCG), secreted by the implanted embryo, and estrogen and progesterone continue to be produced. Once delivery has taken place, further ovulation is temporarily blocked by the hormonal changes induced by the infant's suckling, including a rise in the level of another pituitary hormone, prolactin.

Contraception

Methods

The major methods of contraception currently in use, listed in order of their use effectiveness in preventing pregnancy, are:

- Sterilization—vasectomy in the male, and tubal ligation/occlusion in the female.
- Steroid hormones—combined (estrogen and progestin) or low dose progestin oral pills, or intramuscular, long-acting progestin injections. These synthetic steroids are given in different combinations and different doses, depending on the commercial product, but they act primarily by inhibiting ovulation through suppression of the hypothalamic hormones that stimulate the release of FSH and LH from the anterior pituitary. The synthetic steroids also cause endometrial changes that make the uterus inappropriate for implantation should breakthrough ovulation and fertilization occur. Other changes that contribute to the contraceptive effect include scant and thick cervical mucus, reduced sperm transport and penetration into the uterus, and altered sperm and ovum transport capabilities within the fallopian tubes.
- Intrauterine devices (IUDs)—the insertion of a foreign body, made either of an inert substance or impregnated with other materials (copper, progesterone). Although the IUD prevents implantation in mammals, its mode of action is unknown in the human being. There are several possible modes of action, from interference with sperm transport, to interference with ovum transport,

to interference with implantation in the uterus. There is also some evidence that IUDs lead to increased sperm damage and affect the motility of the ovum in the fallopian tube.

- Barrier devices—the condom for the male and the diaphragm and cervical cap for the female.
- Vaginal spermicides—high viscosity fluids that both kill sperm and block them from entering the cervical canal.
- Coitus interruptus—male withdrawal prior to ejaculation.
- Periodic abstinence (rhythm, natural family planning) —timed to avoid coitus near the day of ovulation. *
- Postcoital douches—water or spermicidal solutions that flush out and kill sperm in the vagina.

*The basalbody temperature (BBT) method of periodic coital abstinence uses daily temperature-taking to identify the temperature shift that occurs at or shortly after ovulation to determine the "safe" days of the menstrual cycle. By the evening of the third day of sustained high temperature readings following the shift, which may be abrupt or gradual, the postovulatory infertile phase is assumed to be under way. Intercourse must be limited to this phase for highest effectiveness. Cycles during which ovulation does not occur and there is no temperature shift can be a problem during postpartum and premenopausal periods. In the Ovulation—or Billings—method, a woman is taught to identify the precise characteristics of the cervical mucus produced at various stages of her menstrual cycle and their relationship to her fertile and infertile days. In the Sympto-Thermal method, which charts both temperature changes and changes in volume and viscosity of cervical mucus, women are also taught to recognize such subjective symptoms of ovulation as intermenstrual pain.

Characteristics

The potentials of present contraceptive technologies and the limitations that future technologies will need to overcome depend upon how well their characteristics meet the requirements of such diverse groups as users, providers, program administrators, physicians, scientists, theologians, and politicians in various countries and cultures.

Contraceptive technologies are judged by the degree to which they are:

- effective—prevent pregnancy;
- safe—are free of deleterious side effects;
- reversible—permit subsequent pregnancies upon discontinuation of use;
- easy to produce—do not require complex industrial processes;
- easy to provide—do not require frequent resupply or specialized personnel;
- easy to use—do not require periodic application or interfere with coitus;
- inexpensive—have low economic costs to user or society;
- acceptable to governments—are permitted or encouraged by laws and regulations;
- acceptable to cultures—are consonant with local beliefs and customs;
- acceptable to religions—are consonant with religious beliefs; and
- acceptable to individuals—promote general well-being, enhance sexual enjoyment, fit lifecycle, and protect privacy.

How well any characteristic of a contraceptive technology meets individual and societal requirements depends not only on the technology, but on the views and actions of the society in which it is used and of the individuals who use it.

The myth of the ultimate, "ideal" contraceptive is precisely that. The perfect contraceptive would be completely effective in preventing pregnancy, have no harmful effects, be fully reversible, simple and inexpensive to produce and use, need no supplies, specialized personnel, or repetitive use, be acceptable to all governments, cultures, and religions, and fit the needs of all potential users at all stages of their reproductive

lives. No such method exists or is expected to be developed. A realistic goal is for each country to have enough technologies that are appropriate for local conditions and standards so that each individual has access to at least one that meets current needs.

Effectiveness

Contraceptive failure rates are usually quantified according to theoretical v. use effectiveness, because contraceptive failure under average conditions of use can be significantly higher than when methods are used correctly and consistently. The effectiveness of the contraceptive methods listed above is summarized in table 18, where they are listed in descending order of effectiveness under ideal and actual conditions of use. The failure rates represent the number of pregnancies among 100 nonsterile women using the method for 1 year in the United States. If they were to use no contraceptive method, about 90 percent of these women would become pregnant within a year.

Sterilization is the most effective contraceptive method. Use effectiveness equals theoret-

Table 18.—Theoretical and Use Effectiveness of Various Means of Contraception (by pregnancies per 100 woman-years in MDCs)

Method	Theoretical effectiveness	Use effectiveness Range	Average
Sterilization:			
Tubal	—	—	0.06
Vasectomy	—	—	0.15
Steroidal contraceptives:			
Injectable progestins (3-month regimen of medroxyprogesterone acetate)	0.24	—	0.24
Orals	0.1	0.2-4.5	0.7
IUDs:			
Lippes loop	1.9	—	2.7
Copper T	—	—	2.2
Diaphragm and jelly	3	3.3-33.6	12
Condom	3	6-30	12
Aerosol foam	3	3.0-35	14
Jelly or cream	4	2.0-45	20
Coitus interruptus	8	10-38	18
Periodic abstinence	2.5	5-40	20
Suppositories	14	17-27	22
Douche	18	21-40.8	35

SOURCES: R. G. Wheeler, G. W. Duncan, and J. Speidel, *Intrauterine Devices—Development, Evaluation, and Program Implementation*, Academic Press, 1974; and L. Liskin, "Periodic Abstinence: How Well Do New Approaches Work?" Population Information Program, The Johns Hopkins University, Baltimore, Md., September 1981.

ical effectiveness because the procedure is usually performed adequately in the United States and there is no need for additional contraceptive practice once the surgical procedure is performed. The obvious drawback of sterilization is its permanence. For female sterilization, although individual surgeons have reported reversal rates as high as 60 percent, it is estimated that only about one-fifth of all women sterilized by current techniques could have their sterilizations reversed (8). For reversal of male sterilization, the rate of anatomical success as determined by the reappearance of sperm is in the range of 40 to 90 percent, but functional success as determined by the pregnancy rate is much lower, on the order of 18 to 60 percent (3); new microsurgery techniques are reported to have increased the upper range to 70 percent (21).

The steroid hormones and IUDs are very effective in preventing pregnancy, but the degree of prevention depends on how correctly and consistently they are used. Barrier devices (condoms, diaphragms) approach the IUD in theoretical effectiveness but have three to four times the failure rate of the IUD in use effectiveness. The use of vaginal spermicides, coitus interruptus) and periodic abstinence also significantly lower pregnancy rates, but about 20 percent of users will still become pregnant within a year. Postcoital douching also has a preventive effect but will protect only about 35 percent of users.

New techniques are now being employed to evaluate pregnancies that occur during use of periodic abstinence methods. Unintended pregnancies are analyzed in terms of when in the woman's cycle they occurred and whether the couple proceeded with a particular act of intercourse despite advance knowledge of the reasonable likelihood of conception; which of these pregnancies can be attributed to the methods themselves; and which pregnancies are likely to have resulted from difficulties in teaching or learning the various methods (10).

Most determinants of effectiveness are inherent in the technology, but variations occur depending on the conditions and behavior of the user. The closer a couple are to the number of children they want, the more effective is

their use of barrier methods or periodic abstinence. Couples who are using contraception to prevent any future births achieve much higher effectiveness than couples merely spacing the next birth. Highly motivated and experienced couples can prevent pregnancy much more effectively than less motivated couples.

Risks

Risk estimates attempt to compare the relative risks of each contraceptive method not only against other methods but also against the risk of using no contraceptive method. The latter risk is in becoming pregnant and the morbidity and mortality associated with pregnancy and childbirth. The risks of each contraceptive method are the morbidity and mortality associated with use of the method and with those pregnancies that the particular method does not prevent. For these comparative estimates, the measure of risk used is the death rate, comprised of method-associated (use of a particular contraceptive method or failure of a contraceptive method) and birth-associated (use of no contraceptive method) deaths.

A further distinction must be made between absolute and relative risks. For example, relative incidence in the population is important.

If the incidence of a disease is 1 per million among non-exposed persons, and the use of a particular drug increases the relative risk of disease tenfold, then one would anticipate 10 cases per million users of the drug. On the other hand, if the incidence of another disease is 100 per million, and drug exposure increases the risk only twofold, then one would anticipate 200 cases per million among users of the drug. The latter situation would clearly entail a much greater public health problem, even though the relative risk is much smaller (24).

Language is also important when studies of risk are discussed. For example, the conclusion that oral contraceptive users have a five times greater risk of dying from circulatory disease than nonusers can be rephrased to point out that pill users decrease their chances of survival during a year from 99,995 per 100,000 to 99,974 per 100,000—a reduction of only two-hundredths of a percent (0.02 percent) (12).

The method-related risks of contraceptive use are largely confined to oral contraceptives and IUDs. Some morbidity and mortality are also associated with sterilization procedures, but these are limited to the time at which the procedure is performed. Barrier devices and spermicides are relatively risk-free except for the risks associated with pregnancy from the higher degree of contraceptive failure with these methods.

Barrier devices, principally those used by the woman, have been associated only with minor side effects—allergic reactions, vaginal irritation, and infections (26).

Spermicides, apart from local reactions such as tissue irritation to either partner, have been considered very safe insofar as method-related risks are concerned. Such risks might be incurred from: 1) systemic effects on the woman resulting from absorption of the spermicide through the vagina; 2) damage to a developing fetus from spermicide components or metabolites in the woman's circulation; and 3) genetic damage to conceptions involving sperm damaged by spermicides (5). A recent study has shown a positive correlation between spermicide use in the 10 months prior to conception and the prevalence of certain major congenital anomalies (9). The prevalence of such abnormalities as limb-reduction deformities, neoplasms, and syndromes associated with chromosomal abnormalities was 2.2 percent, compared to an incidence of 1 percent in infants born to mothers who had not used spermicides in the 10 months prior to conception. The rate of spontaneous abortion requiring hospitalization was also 1.8 times more common. The investigators considered these findings tentative, as these abnormalities were diverse and did not appear as a well-defined syndrome. This area clearly warrants further investigation.

The basic risks of IUDs are: 1) increased menstrual bleeding or spotting; 2) perforation of the uterus; 3) increased frequency of pelvic infection; and 4) unwanted pregnancies that are more likely to be ectopic (implanted outside the uterus in the fallopian tube or abdominal cavity) or to result in septic midtrimester abortion than pregnancies in nonusers (17). Method-related mortality from IUDs stems principally from ec-

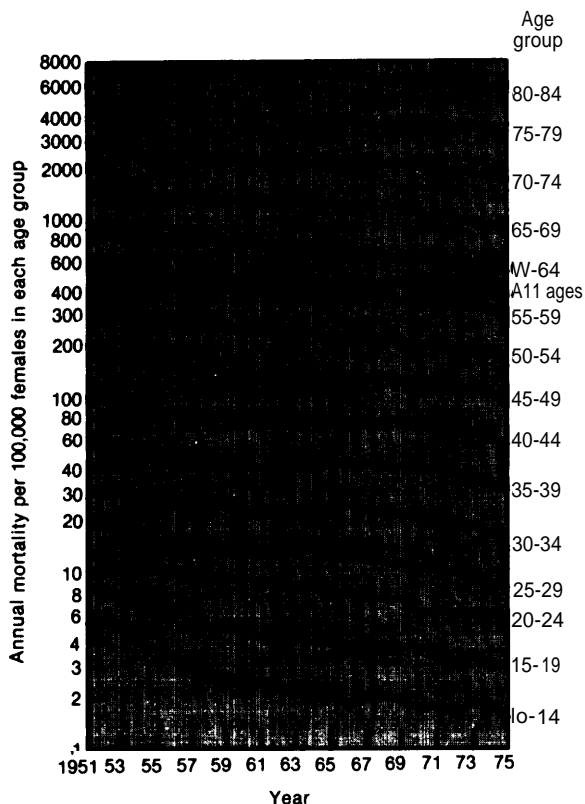
topic pregnancies—a life-threatening emergency—and septic abortions.

Circulatory system diseases associated with oral contraceptives have caused the most concern. Venous thromboembolic disease—principally of the legs—was the first recognized circulatory system risk associated with oral contraceptive use. Excess mortality has been estimated at 2 to 3 per 100,000 women annually, with no increase of risk associated with duration of use. Heart attacks and subarachnoid hemorrhage—a type of stroke probably from rupture of congenitally weak cerebral blood vessels—are the other circulatory system risks. The risk of heart attack depends on other predisposing factors, e.g., cigarette smoking, hypertension, diabetes. The chances of heart attack thus increase with age, smoking, and other predisposing factors. The risk of subarachnoid hemorrhage increases with smoking and duration of use (17).

Together, these circulatory system diseases would theoretically account for a fivefold increase in deaths, but questions have arisen as to why such an increase has not been reflected in vital statistics trends. A researcher at the U.S. Center for Disease Control estimates that nearly three-quarters of the cardiovascular disease deaths occurring annually in the United States to women of reproductive age would be attributable to oral contraceptive use if the increased risk was indeed fivefold. Such a high proportion of cardiovascular deaths attributable in oral contraceptive use should have been reflected in dramatically increased rates of cardiovascular deaths in women of reproductive age since the onset of oral contraceptive use, but such increased rates have not appeared. In addition, instead of the death rate from these diseases diverging for men and women as would be expected, U.S. cardiovascular disease death rates have been falling nearly equally and steadily for men and women of reproductive ages since 1950 (13). (See fig. 19 for circulatory system death rates for U.S. women.)

Research on long-term risks of oral contraceptives has found no statistically significant increase in the cancer rate. A rare type of benign liver tumor does occur, especially with the older

Figure 19.—Mortality From All Circulatory System Diseases,^a Females, Aged 10-84, by 5-Year Age Groups, United States, 1951-75



^aICD 390-458 (1968-75); ICD 330-334 (1951-67)

SOURCE: R. T. Ravenholt and Ward Rinehart, "Age Specific Mortality Trends in the United States Relative to Use of Oral Contraceptives," from *Risks, Benefits and Controversies in Fertility Control*, Sciarra, Zatuchni, and Speidel (eds.), PARFR series on fertility regulation, 1978, Harper & Row.

high-dose oral contraceptives, and the risk increases with duration of use, but the disease is still rare (1). Oral contraceptives appear to have a protective effect against benign breast tumors, and there have been recent indications that they may also have a protective effect against ovarian cancer, perhaps from the interruption of ovulation (17).

Using what is known about the effectiveness and risks of the different contraceptive methods, researchers have developed models that compare their relative risks. This comparison for MDCs is summarized in table 19. Sterilization is not included but the use of induced abortion (which is here assumed to be legal and per-

formed in medically approved settings)) either alone or in conjunction with barrier methods, is included.

In MDCs, between ages 25 to 35, the risk for oral contraceptive users who smoke is about the same as for those using no method, but is 50 percent higher between ages 35 to 39 and about three times higher after age 40. For nonsmoking oral contraceptive users, the risk is much less under age 40. Barrier methods in combination with access to legal abortion in the event of contraceptive failure are the safest, but induced abortion is a controversial method which is morally unacceptable to many, or, if acceptable, may not be readily available. IUDs have low risk rates throughout the reproductive years.

This model has been extended to the LDCs and is summarized in table 20. The principal assumptions are: 1) the ability to become pregnant is the same in more developed countries (MDCs) and LDCs but lactational amenorrhea following childbirth is 8 months longer in LDCs because of the higher prevalence of breastfeeding; 2) maternal mortality in Korea and Taiwan is representative of rates for middle-income LDCs and maternal mortality in Bangladesh is representative of rates in poorer LDCs; 3) maternal mortality due to induced abortion is twice as high in middle-income LDCs and five times as high in low-income LDCs as in the United States; 4) use-effectiveness of all methods except IUDs is slightly lower in LDCs; 5) method-related risks from IUDs and sterilization are two to five times higher in LDCs; and 6) risks of circulatory disease are lower in all LDCs. Oral contraceptive users are separated into those with and without predisposing conditions, and sterilization in women—tubectomy—is also included.

Because of the higher maternal mortality rates in LDCs, all methods are safer than no method at all except for some methods for older women. In middle-income LDCs, oral contraceptive users with predisposing conditions and over age 40 have a higher risk of death than those who use no method, but in poorer countries, oral contraceptive use is safer. As in the MDCs, barrier methods in combination with access to

Table 19.—U.S. Birth-Related, Method-Related, and Total Deaths per 100,000 Women per Year, by Contraceptive Method and Age of Woman, 1972-78

Regimen	Age in years					
	15-19	20-24	25-29	30-34	35-39	40-44
No control:						
Birth-related	4.7	5.3	6.5	10.7	19.3	23.2
Oral contraceptives only/nonsmokers:						
Birth-related	0.1	0.2	0.2	0.3	0.6	0.5
Method-related	0.6	1.1	1.6	3.0	9.1	17.7
Total deaths	0.7	1.3	1.8	3.3	9.7	18.2
Oral contraceptives only/smokers:						
Birth-related	0.1	0.2	0.2	0.3	0.6	0.5
Method-related	2.1	4.2	6.1	11.8	31.3	60.9
Total deaths	2.2	4.4	6.3	12.1	31.9	61.4
IUDs only:						
Birth-related	0.1	0.2	0.2	0.3	0.6	0.5
Method-related	0.8	0.8	1.0	1.0	1.4	1.4
Total deaths	0.9	1.0	1.2	1.3	2.0	1.9
Barrier methods only:						
Birth-related	1.1	1.5	1.9	3.3	5.0	4.0
Abortion only:						
Method-related	0.5	1.1	1.3	2.0	1.9	1.2
Barrier methods plus abortion:						
Method-related	0.1	0.2	0.2	0.3	0.3	0.2

SOURCE: C. Tietze, *Induced Abortion—A World Review*, 1981, Population Council Fact Book, 4th ed.

legal abortion provided under adequate medical supervision in the event of contraceptive failure are the safest, but the higher maternal mortality rates make all methods—with the exceptions noted above—safer than no method at all. Thus, in LDCs, the risks of the different methods are relatively less significant than in MDCs because of much higher maternal mortality rates, and the choice of methods depends more on different legal and medical circumstances, kinds of methods available, and the convenience and acceptability of particular methods.

Future technologies

The following forecasts are based on four major elements. The first is the past rate of innovation in reproductive and contraceptive research. Between 1960 and 1970 a revolution in contraceptive technology occurred, and more than a dozen new technologies—oral contraceptives, IUDs, and new sterilization and abortion techniques—reached the public. This rapid pace of innovation continued through the 1970's, which saw the widespread introduction and adoption of new types of vaginal spermicides,

contraceptive injections, drug-releasing IUDs, outpatient sterilization methods, and low-dose oral contraceptives.

A second element is the present base of knowledge available to researchers. As early as 1974, it was evident that the field of reproductive biology was benefiting from the explosion of basic research in biology and especially from fundamental new discoveries in biochemistry and genetics made during the 1960's (2). The consolidation of knowledge about these new discoveries that took place during the 1970's has been extensively applied in the areas of scientific methodology, medicine, and fertility.

A third element is the magnitude of current applied research and development efforts. A worldwide network of facilities is engaged in the development of fertility planning agents with government and private foundation support. Private companies are also working to develop new methods.

The fourth basis for these forecasts is expert opinion on both the overall likelihood of innovation in this field, and on the likelihood of devel-

Table 20.—Annual Number of Birth-Related and Method-Related Deaths per 100,000 Nonsterile Women, by Fertility Planning Method, Age, and Development of Country

Regimen	Age group/country type								
	15-19			20-24			25-29		
	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II
No method:									
Birth-related	5.6	8.3	290.0	6.1	9.2	183.8	7.4	10.8	215.9
Oral contraceptives (no pre-disposing conditions):									
Birth-related	0.1	0.3	11.1	0.2	0.5	10.6	0.2	0.7	13.0
Method-related	1.2	0.8	0.8	1.2	0.8	0.8	1.2	0.8	0.8
Total deaths	1.3	1.1	11.9	1.4	1.3	11.4	1.4	1.5	13.8
Oral contraceptives (with pre-disposing conditions):									
Birth-related	0.1	0.3	11.1	0.2	0.5	10.6	0.2	0.7	13.0
Method-related	1.4	1.0	1.0	1.4	1.0	1.0	1.4	1.0	1.0
Total deaths	1.5	1.3	12.1	1.6	1.5	11.6	1.6	1.7	14.0
IUDs:									
Birth-related	0.1	0.2	8.0	0.2	0.4	7.7	0.2	0.5	9.5
Method-related	0.5	1.0	1.5	0.5	1.0	1.5	0.5	1.0	1.5
Total deaths	0.6	1.2	9.5	0.7	1.4	9.2	0.7	1.5	11.0
Tubectomy:									
Birth-associated	0			0		0.4	0	0	0.5
Method-associated ^a				0.5	0.9	2.3	0.6	1.2	3.0
Total deaths				0.5	0.9	2.7	0.6	1.2	3.5

Regimen	Age group/country type								
	30-34			35-39			40-44		
	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II
No method:									
Birth-related	13.8	20.0	199.7	21.0	34.2	171.0	22.6	35.9	191.5
Oral contraceptives (no pre-disposing conditions)									
Birth-related	0.4	1.2	12.0	0.6	1.8	9.2	0.5	1.3	7.1
Method-related	1.9	1.3	1.3	4.0	3.0	3.0	7.3	5.5	5.5
Total deaths	2.3	2.5	13.3	4.6	4.8	12.2	7.8	6.8	12.6
Oral contraceptives (with pre-disposing conditions)									
Birth-related	0.4	1.2	12.0	0.6	1.8	9.2	0.5	1.3	
Method-related	11.4	6.0	6.0	28.8	13.0	13.0	103.8	63.0	63.0
Total deaths	11.8	7.2	18.0	29.4	14.8	22.2	104.3	64.3	70.1
IUDs:									
Birth-related	0.4	0.9	8.7	0.6	1.3	6.6	0.5	1.0	5.1
Method-related	0.8	1.5	2.3	1.0	2.0	2.0	1.0	2.0	3.0
Total deaths	1.2	2.4	11.0	1.6	3.3	8.6	1.5	3.0	8.1
Tubectomy:									
Birth-associated	0	0	0.4	0	0	0.4	0	0	0.2
Method-associated ^a	0.9	1.7	4.4	2.3	4.6	11.5	13.3	26.7	66.7
Total deaths	0.9	1.7	4.8	2.3	4.6	11.9	13.3	26.7	66.9

Regimen	Age group/country type								
	15-19			20-24			25-29		
	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II
Traditional contraception ^b :									
Birth-related	0.6	1.5	53.0	0.9	2.3	46.6	1.2	2.8	56.5
Abortion:									
Method-related	1.2	2.4	6.0	1.6	3.2	8.0	1.6	3.2	7.9

Table 20.—Annual Number of Birth-Related and Method-Related Deaths per 100,000 Nonsterile Women, by Fertility Planning Method, Age, and Development of Country—Continued

Regimen	Age group/country type								
	15-19			20-24			25-29		
	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II
Traditional contraception and abortion:									
Method-related	0.1	0.2	0.6	0.1	0.4	0.9	0.1	0.4	0.9
Regimen	Age group/country type								
	30-34			35-39			40-44		
	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II	MDC	LDC-I	LDC-II
Traditional contraception?									
Birth-related	2.2	5.2	52.3	2.9	8.1	40.8	2.4	6.3	33.7
Abortion:									
Method-related	2.0	4.0	10.1	1.7	3.4	8.5	1.5	3.0	7.4
Traditional contraception and abortion:									
Method-related	0.2	0.5	1.2	0.1	0.4	0.9	0.1	0.3	0.7

^aMortality during the year of procedure divided by remaining years of fertility.

^bOther methods not listed; e.g., barriers, spermicides, rhythm, and douches.

LDC-I—Middle income LDCs where maternal mortality is relatively high; e.g., South Korea and Taiwan.

LDC-II—Lower income LDCs where maternal mortality is very high; e.g., Bangladesh and Ethiopia.

SOURCE: M. Potts, P. Diggory, and J. Peel, *Abortion*, (Cambridge, England, Cambridge University Press, 1977), p. 575.

opment of specific versions of new technology (4,7). These views, from personal consultations, mail surveys, and reviews of literature, were brought together in a comprehensive assessment of prospective technologies by a senior scientist as a working paper for this study, which was in turn submitted for critique by external reviewers. The paper reviews each major category of fertility planning technology and examines its current level of development, nature of action, mode of administration, probable effectiveness, probable side effects and safety, delivery requirements, probable cost, probable extent of use, likely time frame for development, and obstacles to development (7).

The predictive power of these forecasts depends on the assumption that current trends continue. Such unforeseen developments as funding changes, toxicity findings, or alterations in cost factors could intervene to retard or even curtail the development of particular technologies. It is also impossible to foresee the scientific discoveries that almost certainly will emerge during the next two decades, giving rise to entirely new opportunities for technology de-

velopment or to greatly accelerated development of methods now under study.

Developments arising from one category of methods—folk methods—deserve special mention. They are not treated further in the discussion to follow because the methods are diverse, and their bases poorly understood. The World Health Organization (WHO) is conducting a collaborative global effort to identify and develop the potential antifertility agents present in plants believed (and used) in numerous LDCs to prevent pregnancy. Among the compounds thus far isolated are extracts from the plant *Montanoa tomentosa*, which has been used as an early abortifacient in Mexican folk medicine for centuries, and from the roots of *Trichosanthis kirilowii maxim*, which has long been used in Chinese medicine to induce menstruation. The likelihood of developing new fertility planning techniques from these sources is unknown, but the potential is unquestionably present. Gossypol, a derivative of the cottonseed plant, induces male infertility and is currently under clinical investigation in China as a male contraceptive, but significant side effects, including potassium

depletion and delayed return to fertility, have been encountered in studies of the extract.

Between now and the end of the century, more than 20 new or significantly improved technologies for contraception could become available. They have been classified in table 21 in three categories: 1) technologies highly likely to become available by 1990; 2) technologies that could become available by 1990, but for which prospects are in doubt; and 3) technologies that are unlikely to become available by 1990, but which could emerge by 2000 (19,7).

Table 21.—Future Fertility Planning Technologies

Highly likely before 1890	
1. Safer oral contraceptives	
2. Improved IUDs	
3. Improved barrier contraceptives for women	
4. Improved long-acting steroid injections	
5. Improved ovulation-detection methods for use with periodic abstinence	
6. Steroid implants	
7. Steroid vaginal rings	
8. LRF-analog contraceptives for women	
9. Prostaglandin analogs for self-administered induction of menses	
Possible by 1990 but prospects doubtful	
1. Monthly steroid-based contraceptive pill	
2. Improved monthly steroid injection	
3. New types of drug releasing IUDs	
4. Minidose vaginal rings	
5. Antipregnancy vaccine for women	
6. Improved barrier contraceptives for men	
7. Sperm suppression contraceptives for men	
8. Reversible female sterilization	
9. Simplified female sterilization techniques	
10. Simplified male sterilization techniques	
11. LRF analogs for self-administered induction of menses	
Unlikely by 1990 but possible by 2000	
1. Antifertility vaccine for men	
2. Antisperm drugs for men	
3. Antisperm maturation drugs for men	
4. Lactation-linked oral contraceptives for women	
5. Ovulation prediction methods for use with periodic abstinence	
6. New types of antioviuation contraceptive drugs for women	
7. Contraceptive drugs for women that disrupt ovum transport	
8. Reversible male sterilization	
9. Pharmacologic or immunologic sterilization for women	
10. Pharmacologic or immunologic sterilization for men	
11. Agents other than LRF analogs for self-administered induction of menses	

SOURCE: Office of Technology Assessment survey; S. B. Schearer and M. K. Harper, 1980.

METHODS HIGHLY LIKELY TO BE AVAILABLE BY 1990

All of the technologies listed below meet two conditions. They are already in advanced stages of research and development, and the scientific and technical knowledge required to complete their development and to permit their manufacture and distribution appears either to be in hand or easily attainable.

Safer Oral Contraceptives.—New versions of the contraceptive pill are being tested that will cause fewer changes in the body metabolism, either because they utilize a smaller amount of contraceptive drug (e.g., the triphasic pill), because they avoid the peak blood levels of drug that occur following ingestion of current pills, or because the effect of the drug is more focused on a specific target or end point. It is assumed that this will reduce the incidence of circulatory system disease, liver hepatomas, and other rare long-term side effects shown to be associated with current formulations of oral contraceptives.

Improved IUDs.—Three improved types of IUDs are anticipated before 1990. The first are advanced versions of the copper-releasing IUDs introduced in the mid-1970's. The improved versions will be effective longer than current IUDs and will not require replacement during the lifetime of the user. The second are advanced versions of the progestin-releasing IUD introduced in the late 1970's. By employing different, more potent contraceptive steroids, the new versions will be much more effective—possibly equaling the pill—and will not require replacement more often than every 5 to 10 years. These new IUDs may cause much less bleeding than existing models, but questions of long-term safety will be present because they release drugs. The third new types are postpartum IUDs—devices that can be safely inserted immediately following delivery without excessively high expulsion and pregnancy rates. They would enable intrauterine contraception to be made available to large numbers of women in LDCs who otherwise might not have access to the medical personnel needed for insertion of other types of IUDs.

Improved Barrier Contraceptives for women.—Improvements center on two areas: increases in convenience of use and increases in contraceptive efficacy. Among the former are one-size-fits-all diaphragms, disposable diaphragms, spermicide-impregnated diaphragms, vaginal films, vaginal sponges, vaginal rings that release spermicides, and cervical caps that can be left in place for weeks or months. Increases in contraceptive efficacy include new formulations of existing spermicides and new types of spermicides. Which of these are likely to survive the R&D process and become new products is uncertain. Because the level of resources being devoted to this work is very low, progress is likely to be slow, and major improvements are unlikely. A substantially increased level of effort would be required to develop highly effective new spermicides or radically improved barrier devices by 1990.

Improved Long-Acting Steroid Injections.—A wide variety of improved injections under development make use of controlled release of contraceptive steroids from biodegradable polymers. Which polymer systems will prove most useful is not certain, but prospects are excellent that one or more will provide the basis for a new form of contraceptive injection. Effectiveness should be extremely high, and duration of action is likely to be between 1 and 6 months, depending on the properties of the polymer system eventually selected. Side effects are expected to be moderately reduced over existing long-acting injections because of a more stable, controlled release of contraceptive steroid. However, the nature of side effects, including alterations in menstrual bleeding patterns in many users, is expected to be similar to those of existing products.

Improved Ovulation-Detection Procedures for Use With Periodic Abstinence Methods.—Although R&D investments continue to be small, technological prospects for development of a routinized, simple test for ovulation appear good. A wide variety of biological and biochemical parameters are altered when a woman ovulates, and researchers are endeavoring to improve or simplify the physical tests that a woman can use herself to determine when she

ovulates. Improved methods that provide clear-cut evaluation of, for example, changes in cervical mucus, hormones in urine and saliva, and basal body temperature would enable larger numbers of users of periodic abstinence to know with certainty when they could safely engage in sexual intercourse during the second half of the menstrual cycle without risk of pregnancy, although the *prediction* of ovulation is likely to remain problematic. Such techniques would also free users of barrier contraceptives, withdrawal, or coitus reservatus from the need to employ these methods during the second half of the cycle. The excretion pattern of urinary metabolites of estrogen and progesterone has been identified and has been successfully used to determine when ovulation has occurred, according to studies conducted by the WHO Special Programme of Research, Development and Research Training in Human Reproduction, which reports that the measurement of these substances in early morning urine was indicative of ovulation in 90 percent of women tested. A number of firms are working to develop a kit for women to use at home, and at least one of the methods is expected to be ready for testing when final analysis of the studies is completed later this year (10).

Steroid Implants.—This new, reversible contraceptive method is likely to undergo several rounds of technological innovation between now and 1990. The first generation product—six steroid-releasing capsules implanted in the forearm providing extremely effective contraception over 5 years—is likely to be either supplemented or supplanted by second generation products employing fewer and smaller capsules that are biodegradable. The first generation product is now being introduced in LDCs and will offer an alternative to sterilization for women who wish to terminate births, as well as a new contraceptive option for long-term spacing between births. While the second generation implants will not require removal, thus eliminating a major drawback of the silicone rubber implants, they will probably need to be replaced at much more frequent intervals than the six-capsule silicone-rubber method. It is likely that a variety of products lasting from 6

months to 2 years will be available. All of these methods are expected to be at least as effective as oral contraceptives and to have a similar incidence and range of side effects. They are expected to have the disadvantage of causing irregular patterns of menstrual bleeding in most users, much the same as do the injectable.

Steroid Vaginal Rings.—As for the implants, this new reversible contraceptive method employs a previously unused system to administer steroid hormones. A one-size-fits-all silicone rubber ring that releases an ovulation-suppressing dose of contraceptive steroids is left inside the vagina for 3 weeks, then removed for 1 week, during which time menstruation occurs. Because this is a monthly schedule and estrogens as well as progestins are used, menstrual bleeding patterns are not greatly altered. This new method offers an alternative to the pill: it is self-administered, highly effective, potentially available over-the-counter, and has the advantage of simplified administration in comparison with daily pill-taking. The method is likely to have at least some of the rare long-term side effects of pills. As with implants, this method is in advanced development, and second generation products are therefore also likely to emerge before 1990. Second generation vaginal rings are likely to have improved administration schedules, such as continuous wearing of the ring for long periods, and new ring designs that offer advantages in price and convenience.

LRF-Analog Contraceptives for Women.—Although this prospective new contraceptive method has only recently entered clinical testing, relatively extensive R&D investments and a high level of technological promise may make it available during the next 10 years. Many modes of antifertility action for new chemical analogs of LRF are being investigated. The one that stands out as most clearly feasible is reversible inhibition of ovulation using chemically synthesized agonists or antagonists of the naturally occurring LRF. It is not yet clear whether these drugs will be given by injection, nasal spray, suppository, buccal insert, or oral capsule, nor is the duration or frequency of administration that will be required yet known. It is anticipated, however, that these new contraceptives

will offer a major new alternative to the pill, with the advantages of many fewer short-term side effects and, at least potentially, many fewer long-term health hazards. Depending on which chemical analogs are employed and their precise mode of action, the new contraceptives could also offer the advantage of monthly in place of daily administration.

prostaglandin Analogs for Induction of Menses.—After more than a decade of R&D, the first prostaglandin analogs for inducing menstruation are now being introduced in clinical trials. These drugs, which are administered as vaginal suppositories, successfully induce abortion during the first 8 weeks of pregnancy in about 90 percent of cases. Side effects—transient fever, nausea, vomiting, and cramping—are generally manageable, although disagreeable. Second and third generation products are likely to emerge over the course of the next decade: new uterotonic prostaglandin analogs and formulations that are effective in bringing about a complete abortion in over 95 percent of cases and that cause fewer side effects. However, it is doubtful that these agents, which depend on uterine muscle contraction for their action, will ever be 100 percent effective or completely free of gastrointestinal side effects. These drugs can be used in place of surgical abortion during early pregnancy if surgical facilities are available to treat severe complications and to surgically complete the abortion procedure in cases where the medication fails to do so.

METHODS THAT COULD EMERGE BY 1990, BUT FOR WHICH PROSPECTS APPEAR DOUBTFUL

The following technologies are possibilities currently being investigated or seriously considered by R&D groups. Some of them are in advanced stages of development.

It is likely that the majority will be eliminated as realistic prospects during the next 10 years as new information and R&D findings become available. A number will survive as continuing prospects and be carried forward into the following decade for additional R&D to complete their development. A few might meet with greater success and emerge as new technologies during the course of the next decade.

Monthly Steroid-Based Contraceptive Pill.—New developments in technology for formulating sustained-release preparations of contraceptive steroids may be put to use to develop a pill that need only be taken monthly. Effectiveness would be expected to be about equivalent to daily oral contraceptives. Short-term side effects would be similar, although a somewhat greater incidence of altered menstrual patterns might occur. Long-term effects would also be similar. The primary advantage of this new pill would be the added convenience offered by monthly use.

Improved Monthly Steroid Injection.—As for the pill, a monthly injection would use new sustained-release formulation techniques to deliver a monthly dose of estrogen and progestin sufficient to block ovulation and produce a hormonally induced menstrual bleeding at the end of the month. Such new monthly injections might be superior to existing ones in their much lower incidence of menstrual bleeding alterations, in their use of steroids compatible with U.S. Food and Drug Administration toxicity standards, and perhaps in a slightly reduced incidence of such short-term side effects as headaches and weight gain. Effectiveness and the general spectrum of short- and long-term side effects would be similar to those associated with daily oral contraceptives. Costs would likely be somewhat higher.

New Types of Drug-Releasing IUDs.—Several current R&D projects are testing drugs that reduce menstrual bleeding and uterine cramping associated with the IUD. It is likely that one or several of these drugs will eventually be incorporated into a drug-releasing IUD that will cause significantly less bleeding and discomfort than existing IUDs. Another type of drug that may be incorporated into IUDs is antibiotics. Low doses of such agents released locally into the uterus would reduce the incidence of pelvic infection associated with IUDs, thus overcoming one of the major drawbacks of this contraceptive method, especially for young women. None of the new varieties of drug-releasing IUDs is likely to incorporate the improvements in effectiveness anticipated for the new copper-releasing and steroid-releasing IUDs.

Minidose Vaginal Rings.—Minidose rings, while similar to the steroid-releasing vaginal rings that inhibit ovulation described earlier, would employ much lower doses of progestational steroid and no estrogen. Like the minipill, they would exert their contraceptive action primarily through effects on cervical mucus instead of on ovulation. Minidose vaginal rings would offer the advantage of reduced short- and long-term side effects except with respect to menstrual bleeding patterns, which would probably be significantly changed in most users. Another major advantage of this method over the ovulation-suppressing rings would be its continuous use by a woman, avoiding the complexities of a 3-week in, 1-week out schedule. A major drawback would be lower effectiveness, probably in the range of the present-day minipill or inert-IUD contraceptives.

Antipregnancy Vaccine for Women.—This prospective, reversible contraceptive method uses a vaccine to immunize women against the hormone in a specific component of the fertilized egg, such as the zona pellucida. Initially, a series of injections would probably be needed over a period of several weeks or months to establish immunity. Immunity might last from 1 to several years and then disappear unless a booster injection were given. Effectiveness of a vaccine contraceptive is theoretically very high. A number of different antigens are being investigated for use in developing such a vaccine, and tests in monkeys and women have shown the feasibility of several of these. This is one of the prospective future methods that could benefit from greatly expanded R&D efforts, since feasibility appears good, but a wide range of technical problems needs to be overcome to realize this potential.

Improved Barrier Contraceptives for Men.—Although very little R&D is currently under way in this area, a growing market for barrier contraceptives could stimulate significant innovation over the course of the next decade. Present R&D centers on biodegradable condoms, spermicide-impregnated condoms (already marketed in Great Britain), and penile films. The goal is to overcome the drawbacks of decreased sensation, problems of disposal, and

variable effectiveness associated with existing condoms. The scale of this effort is very small, however, as condoms are already an acceptable and effective method. But it is possible for radically improved condoms to be available by 1990 if private sector companies respond to the new market demand by investing in R&D using new synthetic materials.

Sperm Suppression Contraceptives for Men.—For almost a decade, different drugs have been tested for their capacity to suppress sperm production in men. At least two types of drugs—steroids and LRF analogs—are currently under clinical study, and other agents are being investigated in the laboratory. A future sperm-suppressing contraceptive based on one of these agents would for the first time offer men a means of contraception similar to the pill for women. Depending on the type of drug used, it could take the form of a daily, weekly, or monthly pill or, possibly, a long-acting injection or implant. Concerns about possible rare or long-term safety hazards (e.g., teratological effects in any offspring) associated with such a new form of treatment will be important and difficult to overcome.

Reversible Female Sterilization.—Short of extremely expensive and highly uncertain tubal reconstruction surgery, female sterilization is rarely reversible. This major limitation could be overcome if current R&D efforts using fimbrial hoods, tubal plugs, or other methods that permit easy reversal of sterilization are successful. Numerous technical problems remain to be solved, however, before a highly effective, safe, and reversible means of female sterilization is developed.

Simplified Female Sterilization Techniques.—At least three major lines of R&D work are being undertaken in hopes of developing an outpatient method for female sterilization that could be performed by ancillary medical personnel. All of the methods require entry into the uterus via the vagina and cervix in order to apply sclerosing (scarring) chemicals or to use freezing temperatures to destroy a portion of the fallopian tubes. Technical problems in assuring high effectiveness, safety, and freedom from subse-

quent ectopic pregnancies stand in the way of successful development of these methods. These methods could make sterilization much more widely available to women in LDCs at lower cost and in a manner not requiring hospital stays or surgery.

Simplified Male Sterilization Techniques.—Vasectomy is already performed as a simple outpatient technique with very low rates of morbidity or medical complications. One modest improvement being studied entails the injection of a sclerosing chemical into the vas deferens, thus eliminating the need for opening the scrotum and cutting and tying off the vas.

LRF Analogs for Self-Administered Induction of Menses.—A pill that can be taken each month at the expected time of menstruation to ensure that bleeding will occur whether or not a pregnancy has been established is under study. Such a self-administered, menses-inducing agent might also be effective as an abortifacient if taken up to a week or two after a missed period. New uterotonic prostaglandin analogs are likely to offer some but not all of these features. For complete effectiveness, a luteolytic agent (one that destroys the corpus luteum) will probably be needed, and current research findings point to LRF analogs as the most likely future candidates.

METHODS UNLIKELY TO EMERGE BY 1990, BUT WHICH COULD BE AVAILABLE BY 2000

The following methods are either in the early stages of development or still the subject of mission-oriented research. All appear unlikely to emerge as new fertility planning methods earlier than 1990, but could become available over the course of the following decade. For several, greatly expanded R&D programs could accelerate their development. For several others, it is likely that substantial additions of knowledge from basic research will be needed as a precondition for successful R&D efforts.

Antifertility Vaccine for Men.—Although little R&D has yet been conducted on a male contraceptive vaccine, this area could benefit very substantially from work on a vaccine for women. In men, immunity would be established

against sperm or sperm production in a manner that would render the man infertile. Suitable antigens for such a vaccine have not yet been identified. Whether such a vaccine would be a reversible contraceptive or a permanent sterilization technique is not known.

Antisperm Drugs for Men.—A moderate amount of goal-oriented research has been conducted to identify enzymes essential to the metabolism of sperm, and research for inhibitors of these enzymes has been undertaken. It is possible that specific metabolic processes in sperm could be halted by certain drugs that men could take on a regular basis. A reversible male contraceptive agent in the form of a daily or weekly pill might be developed using this principle.

Antisperm Maturation Contraceptive Drugs for Men.—Such drugs would act on maturing sperm rather than on fully active sperm. If specific steps in the maturation process can be identified that could be blocked by specific drugs, a reversible contraceptive could be developed. Administration would need to be on a daily or weekly basis or by means of a sustained-release formulation such as an implant or injection.

Lactation-Linked Oral Contraceptives for Women.—Efforts to develop a drug regimen that could be administered to breastfeeding women to extend both the duration and ovulation-suppressing intensity of their lactation after childbirth have been unsuccessful. In view of the great health benefits of breastfeeding and the very widespread reliance on this as a means of birth spacing by women in LDCs, this remains a high priority technological goal. Recent findings about LRF and other gonadotropin-releasing factors may make it feasible.

Ovulation Prediction Methods for Use With Periodic Abstinence.—The development of simple techniques for predicting when ovulation will occur would permit the rhythm or natural family planning methods to be practiced with full effectiveness. The development of such techniques is beyond the capacities of current scientific knowledge, but prospects a decade from now should be much better.

New Types of Antiovu/ation Contraceptive Drugs for Women.—Intensive basic and goal-oriented research is under way on factors required for maturation of the ovum in the ovary. If maturation could be prevented, either through direct action or via inhibition of FSH release by the pituitary gland, ovulation would not occur. Prospects that future contraceptives employing a synthetic “inhibin” or chemical analog of an ovum maturation factor will eventually emerge from this research appear good. If such efforts are successful, a new type of nonsteroidal monthly pill or injection for women could result.

Contraceptive Drugs for Women That Disrupt Ovum Transport.—It is known that the transport of the newly fertilized egg and its implantation in the uterus can be disrupted by high doses of estrogens, and this is believed to be the mode of action of the current postcoital pill. A radically improved postcoital pill that could be taken after every coitus without unpleasant side effects or disruption of the menstrual cycle might be developed in the future, using new drugs that interfere with fertilization, ovum transport, or implantation. Despite considerable research, however, no promising agents have yet been identified, and extensive basic and goal-oriented research will be required to achieve this goal.

Reversible Male Sterilization.—Vasectomy is safe, easy to perform, and highly effective. Easy reversal of this procedure to restore fertility would probably have great impact in making the method more widely used. Unfortunately, numerous R&D projects to develop tubes, valves, plugs, and other devices that could be implanted in the vas deferens and reversibly block sperm from passing have ended in failure, so the biological feasibility of a reversible technique is uncertain. New surgical techniques coupled with new biocompatible synthetic materials are likely to be required for development of such a method.

Pharmacologic or Immunologic Sterilization for Women.—A pill or injection that confers permanent infertility has been part of the folklore

of many cultures. While toxicity concerns would have to be resolved, if sufficient R&D were devoted to a careful selection of proper pharmacologic or immunologic agents, high safety and effectiveness should be attainable. The method could be based on drugs that destroy the capacity of the ovaries to produce viable ova or on an immunization against a body protein that is essential for reproduction. Although the method could be effective following a single administration, it is more likely that a series of administrations of the drug or vaccine would be needed. Such a method would offer a low-cost, noninvasive alternative to surgical sterilization.

pharmacologic or Immunologic Sterilization for Men.—Analogous to the method for women summarized above, this prospective future technology would produce sterility in the male by using drugs that permanently eliminate sperm

production or a vaccine that permanently blocks male fertility. Both types of agents are already known, but no significant R&D program has been established to develop them into a male sterilization technique. As for the female method, considerable research would be needed to assure both safety and effectiveness. Since vasectomy is already a simple technique, the advantages of a pharmacologic or immunologic male sterilization method are less dramatic than those associated with a similar method for women.

Agents Other Than LRF Analogs for Self-Administered Induction of Menses.—A variety of agents are being investigated for this purpose: luteolytic prostaglandin analogs, plant extracts, chemicals that bind to different types of hormone receptors, and antibodies that could be administered by injection as a one-time, passive immunization.

Induced abortion

Natural or spontaneous abortion occurs in about one in five known pregnancies. However, the loss of fertilized ova prior to or immediately following implantation is much higher. The combined total may be as high as 70 percent of all fertilized ova (20). Many of these spontaneous abortions are due to defective fetuses, such as those with chromosomal abnormalities.

Induced abortion is a medically safe procedure when performed early in pregnancy (first trimester) by skilled personnel. Simple suction equipment, such as that developed in rural China, and manual syringe equipment for office use, such as that developed in the United States, have begun to replace the primitive methods traditionally used in less developed regions. But the risks of maternal death or serious complications increase greatly when induced abortion is

performed later in pregnancy, and also when the quality of personnel and facilities is lowered.

Although induced abortion is ubiquitous, its legal use is constrained in some countries by religious beliefs. The limitations of current contraceptive technologies, particularly lack of access to their use, cause many women in all parts of the world to seek induced abortions to terminate unwanted pregnancies. Abortion is not a preferred method of birth control but at times is the only means of preventing an undesired birth. The large numbers of women who seek abortions are more an index of how strongly births are not wanted and contraception is needed than an indication of the preference for abortion.

Sterility prevention or reversal

Unwanted sterility is due to a wide range of etiological factors; e.g., infection of the fallopian

tubes with venereal disease; lack of ovulation; defective sperm production; developmental ab-

normalities of the uterus; the effects of repeated or improperly conducted abortions, such as injury to the cervix; etc.

Except for a few congenital defects, the principal criterion for the diagnosis of sterility is failure of a couple to achieve pregnancy after a significant period (e.g., 2 years) of cohabitation without practicing contraception. Worldwide infertility has been estimated as involving 5 to 10 percent of couples (25). The prevalence of sterility rises from a low of 3 to 4 percent among young couples, to 20 percent among couples in their early 30's, and rapidly to 100 percent (menopause) during the woman's 40's. In some areas, as in parts of sub-Saharan Africa, sterility from infectious diseases is common enough to lower birth rates and to be a major reason for seeking medical care. In Zaire, for example, the high prevalence of sterility caused by venereal infections was documented in the 1950's in association with lower than expected birth rates. Following effective efforts to reduce venereal diseases, the occurrence of sterility was markedly reduced and birth rates rose (18).

Several technological innovations could have a major impact on the capacity to diagnose the causes of infertility. These include development of reliable, simple techniques for predicting as well as for confirming ovulation; development of similar tests for determining the level of functioning of the male seminiferous tubules; and further development of ovulation-inducing

drugs to verify the woman's capacity for ovulating.

In women, the major preventable cause of infertility is infection leading to damage of the fallopian tubes. A variety of public health measures can reduce the incidence of such infections, including control over the transmission of venereal disease and, in some countries, prevention of tuberculosis. Two technological developments could be significant: the development of IUDs associated with a lower risk of pelvic inflammatory disease, and the development of vaccines against venereal diseases.

New technologies likely to be extremely useful for inducing fertility in couples are LRF agonists for inducing ovulation and LRF agonists and other possible releasing-factor analogs for increasing sperm production. For some couples, infertility in one partner cannot be treated, and assistance will only be possible in the form of adoption, use of another person's sperm via artificial insemination, or use of in vitro fertilization followed by embryo transfer to the uterus. These technologies now exist but are expected to benefit from improvements in sperm banking and techniques for artificial insemination, and from new developments in ovum extraction, in vitro fertilization, and embryo implantation. These techniques, however, are expected to have little global impact on the treatment of infertility.

Sex selection ———

Sex selection is included as a fertility planning technology in this study because a strong preference for sons persists in many LDCs, scientists are working on new technologies, and the probable impacts of effective technologies could be highly disruptive and contrary to rising expectations of sexual equality.

The evidence for sex preferences in different parts of the world is well documented in descriptions of the divisions of power and labor between men and women and in such practices

as female infanticide (see ch. 7). Despite political actions of a few countries like China to eliminate preference for males by raising the status of women, it seems likely that a simple, effective technology for sex selection would be widely used.

Current technologies are highly ineffective for sex selection short of performing amniocentesis to ascertain the sex of the developing embryo and then carrying out a second trimester abortion if the embryo is of the unwanted sex.

Noninvasive techniques for sampling cells of early embryos might emerge in the next 20 years, enabling much earlier determination of sex. This would make possible the choice of first trimester abortion if the sex were unwanted, but any such technological advances would face strong social, political, and ethical pressures against the use of induced abortion for what most perceive to be a trivial purpose.

A second approach to sex selection that has been the subject of limited research entails separation of sperm into male-determining sperm (those bearing Y chromosomes), and female-determining sperm (those bearing X chromosomes), followed by artificial insemination with the desired sperm. While this approach might be more acceptable, prospects for developing highly effective sperm separation techniques are limited and even if these existed, the need to employ artificial insemination would

almost certainly prevent this from becoming a generally used procedure.

Claims that certain chemicals present in the vagina at the time of ejaculation or that the timing of intercourse during the menstrual cycle could affect the sex of the offspring have proved largely unfounded. Nonetheless, there exists a remote possibility that a chemical or immunological agent might be discovered that would differentially destroy male- or female-determining sperm. If such a substance were to be developed, a male pill or injection or a vaginal preparation for selecting the sex of the offspring could become a practicable reality. In view of the lack of research aimed at this objective, the serious social questions about the value of sex selection, and uncertainty of an MDC market for sex selection products, it is highly unlikely that a product for general use will become available by 2000 A.D.

The need for better fertility planning technologies

Each existing fertility planning method has one or more serious limitations, such as mode of administration, interference with coitus, need for frequency of use, cost (a significant factor in LDCs), requirements for special personnel and facilities, and conflicts with cultural, religious, and medical norms. Side effects of IUDs and steroids are sufficient to discourage adoption by some women and discontinuation of use by many,

One-year discontinuation rates in LDCs are high for both the pill (60 percent) and the IUD (40 percent) (11). These and other methods can be inappropriate for use in many settings. Pills can be misused by being taken irregularly or in the wrong sequence, resulting in low effectiveness, and because the mode of action of IUDs is not well understood, the devices are sometimes suspected of "migrating" to other parts of the body by women in LDCs. Changes in menstrual duration and flow sometimes cause fears, as do reports of death and injury from various methods. Requirements of vaginal

methods for clean water and a degree of privacy can deter their use in LDCs.

Many methods require medical personnel for delivery and follow-up care, and because their use is not well-researched for LDC groups, relative risks are unknown. A number of methods require logistical support systems that are beyond the capacities of many LDCs, where refrigeration, transport, and storage facilities may be inadequate. The complexities of many methods require high levels of scientific and technical sophistication for their selection, procurement, and delivery. The difficulty of sterilization reversal remains a principal drawback despite improvements in surgical techniques, and no method other than periodic abstinence is acceptable to the Roman Catholic Church.

The failure rate, or inability of the method to accomplish its primary purpose of preventing unwanted pregnancy, is a critical shortcoming. Even in MDCs, where levels of use of the most effective methods are high, contraceptive

failure continues to result in large numbers of unwanted births and large numbers of induced abortions. Some 500,000 babies are born in the United States each year to parents who did not want them, and an approximately equal number of induced abortions are reported for married women (6).

It is clear that although current fertility planning methods are far superior to those of just 20 years ago, they remain inadequate to the needs of MDC users and fall critically short of the needs of couples in LDCs. When the lifetime

needs of both MDC and LDC couples—who will require an effective, safe, reversible, easy-to-use contraceptive method for 20 to 25 years of their lives—are taken into account, the disparity between technology and need is greater still. Current methods have considerable unused potential for lowering LDC birth rates in the next 20 years, but cannot yet adequately meet the needs and desires of people either in MDCs or LDCs. When the urgent desire to reduce the incidence of induced abortion is also taken into account, the magnitude of need for better contraceptive technologies cannot be underestimated.

Chapter 5 references

1. Armed Forces Institute of Pathology, Hepatic Branch, and Center for Disease Control, Bureau of Epidemiology, Family Planning Evaluation Division, "Increased Risk of Hepatocellular Adenoma in Women with Long-Term Use of Oral Contraceptives" *Morbidity and Mortality Weekly Report*, 26(36): 293-294, 1977.
2. Barnes, A. C., Schearer, S. B., and Segal, S. J., "Contraceptive Development," in *Working Papers: The Bellagio Conference on Population* (New York: The Rockefeller Foundation, 1974).
3. Bradshaw, L. E., "Vasectomy Reversibility—A Status Report," *Population Reports*, Series D, No. 3, May 1976. Population Information Program, The Johns Hopkins University, Baltimore.
4. Cain, P., "Future Prospects for the Development of Birth Planning Technology: What the Experts Think," report prepared for OTA, Washington, D. C., 1980.
5. Coleman, S., and Piotrow, P. T., "Spermicides—Simplicity and Safety are Major Assets," *Population Reports*, Series H, No. 5, September 1979, Population Information Program, The Johns Hopkins University, Baltimore.
6. Forrest, J. D., Sullivan, E., and Tietze, C., "Abortion in the United States, 1977-1978," *Family Planning Perspectives*, vol. II, No. 6, November-December 1979, Alan Guttmacher Institute, New York, pp. 329-341.
7. Harper, M. J. K., "Prospects for New or Improved Birth Control Technologies by the Year 2000 A. D.," report prepared for OTA, Washington, D. C., 1980.
8. Henry, A., Rinehart, W., and Piotrow, P. T., "Reversing Female Sterilization," *Population Reports*, Series C, No. 8, September 1980, Population Information Program, The Johns Hopkins University, Baltimore.
9. Jick, H., et al., "Vaginal Spermicides and Congenital Disorders," *Journal of the American Medical Association*, 245(13): 1329-1332, 1981.
10. Kane, L. J., Executive Director, Human Life and Natural Family Planning Foundation, Alexandria, Va., personal communication, 1981.
11. Mauldin, W. P., "Experience With Contraceptive Methods in Developing Countries," in *Contraception: Science, Technology, and Application*, Proceedings of a Symposium, National Academy of Sciences, Washington, D. C., 1979.
12. May, D., "Mortality Associated With the Pill" (letter to the editor), *Lancet*, 2(8044): 921, 1977.
13. Ory, H. W., "The Health Effects of Fertility Control," presented at the Symposium on Contraceptive Technology, National Academy of Sciences, Washington, D. C., May 19, 1978.
14. Piotrow, P. T., Rinehart, W., and Schmidt, J. C., "IUDs—Update on Safety, Effectiveness, and Research," *Population Reports*, Series B, No. 3, May 1979, Population Information Program, The Johns Hopkins University, Baltimore.
15. Potts, M., Speidel, J. J., and Kessel, E., "Relative Risks of Various Means of Fertility Control When Used in Less Developed Countries," in Sciarra, J., Zatuchni, G., and Speidel, J. J. (eds.), *Risks, Benefits, and Controversies in Fertility Control* (Hagerstown, Md.: Harper & Row, 1978).
16. Ravenholt, R. T., and Rinehart, W., "Mortality From Circulatory System Disease in Four Countries," January 1978 (unpublished). Reproduced in: *Population Reports*, "Oral Contraceptives: OCs

- Update on Usage, Safety, and Side Effects." Series A, No. 5, January 1979 (reprinted May 1980).
17. Rinehart, W., and Piotrow, P. T., "Oral Contraceptives—Update on Usage, Safety, and Side Effects," *Population Reports*, Series A, No. 5, May 1980, Population Information Program, The Johns Hopkins University, Baltimore.
 18. Romaniuk, A., "Increases in Natural Fertility During the Early Stages of Modernization: Evidence From an African Case Study, Zaire)" *Population Studies*, 34:293-310, 1980.
 19. Schearer, S. B., "Future Birth Planning Technologies" report prepared for OTA, Washington, D.C. 1980.
 20. Schlesselman, J. J., "How Does One Assess the Risk of Abnormalities From Human In Vitro Fertilization?" *American Journal of Obstetrics and Gynecology*, 135:135-148, 1979.
 21. Silbur, S. J., and Cohen, R. S., "Microsurgical Reversal of Female Sterilization: Techniques and Comparison to Vasectomy Reversal)" in S. J. Silber (cd.), *Microsurgery* (Baltimore: Williams & Wilkins, 1979), p. 185-242.
 22. Tietze, C., *Induced Abortion: A World Review*, 1981 (4th cd.) (New York: The Population Council, 1981).
 23. Wheeler, R. G., Duncan, G. W., and Speidel, J. J. (eds.), *Intrauterine Devices: Development, Evaluation, and Program Implementation* (New York: Academic Press, 1974).
 24. World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, *Seventh Annual Report*, 1978.
 25. World Health Organization, Special Programme of Research Training in Human Reproduction, *Eighth Annual Report*, 1979.
 26. Wortman, J., "The Diaphragm and Other Intra-vaginal Barriers—A Review," *Population Reports*, Series H, No. 4, January 1976, Population Information Program, The Johns Hopkins University, Baltimore.