HUMAN REPRODUCTION: THREE ISSUES FOR THE MORAL THEOLOGIAN

The rapidly expanding science of reproductive biology poses new and difficult problems for the philosopher, moral theologian, and scientist interested in developing principles of moral behavior. For the Christian, there is an imperative to search for truth; but today that search is complicated by the new and complex technological dimensions created by the rapid growth in scientific knowledge. It is apparent that moral theologians[1] are attempting to cope with this difficult task, as are some men of science.[2] It is the purpose of this paper to look carefully at three issues in human reproduction which have caused recent concern.

It has been stated that "There is an undeniable relationship between the frequency of spontaneous abortion and the overripeness of spermatozoa and especially of the ova. Does this not mean that the rhythm method acts frequently rather as a means of 'birth control' and not simply as contraception, whenever it allows fertilization with aging gametes?"[3] In addition, it has been written that "It seems that the rhythm method as used up to now causes a considerable waste of zygotes, as the I.U.D. is alleged to do and the 'morning after' pill does."[4] This is not a particularly new issue, but it does require considerable clarification.

Diamond claims that "It is now widely recognized that anywhere from one third to one half of all fertilized ova never survive to implant or differentiate to any advanced degree."[5] Others have apparently accepted as near fact the statement that "no more than 22% of all the fertilized eggs are destined for a normal birth."[6] If, in fact, the early human wastage approaches such high levels, it may have an impact on our moral reasoning. This must be further discussed.

Finally, since 1970, the idea has been advanced that once twinning has occurred, the cellular material from the two may recombine to form one individual.[7] This is the concept of twinning and recombination. It

[1] Cf. B. Häring, "New Dimensions of Responsible Parenthood," THEOLOGICAL STUDIES 37 (1976) 120-32; J. F. Dedek, *Human Life: Some Moral Issues* (New York: Sheed and Ward, 1972) pp. 59–90; R. A. McCormick, Talk and discussion before the Denver Clergy Education Conference and the Denver Archdiocesan Pro-Life Convocation, Denver, Colo., Nov. 13, 1974.

[2] Cf. J. J. Diamond, "Abortion, Animation and Biological Hominization," THEOLOGICAL STUDIES 36 (1975) 305-24; A. E. Hellegers, "Fetal Development," *ibid.* 31 (1970) 3–9.

[3] Häring, *art. cit.*, p. 121.

[4] *Ibid.*

[5] Diamond, *art. cit.*, p. 312.

[6] Cf. Häring, *art. cit.*, p. 129, n. 21.

[7] Cf. Hellegers, *art. cit.*, pp. 4–5.

has been put forward by a number of scholars[8] since 1970 as establishing the fact that "final irreversible individuality"[9] does not occur until sometime after implantation of the blastocyst. Thus, Häring could query: "What is the status of the zygote before implantation?"[10] This question needs to be asked, and it demands an answer from both the theological and the scientific community.

The above three aspects of human reproduction will be dealt with in this paper. However, since there is apparently some confusion regarding the various methods of natural family planning[11] and since natural family planning has been central to a number of these issues, the discussion will begin with a brief explanation of those methods.

METHODS OF NATURAL FAMILY PLANNING

All methods of natural family planning are based on the concept that, while men are always fertile, women are at most times infertile. The couple's combined fertility, then, is dependent primarily upon the identification of the fertile and infertile phases of the woman's cycle. But since the couple's combined fertility is never "activated" by the isolation one from the other, the methods require the co-operation of both man and woman when implemented. Its implementation may be either to achieve or to avoid pregnancy.

The primary differences between the different natural methods lie in the means by which they define the fertile and infertile phases of the woman's menstrual cycle. These differences also account for their different efficacies and ease of use.

The Calendar Method. This method is traditionally called the "rhythm" method. It defines the fertile and infertile phases based upon the following assumptions. Ovulation occurs 14 ± 2 days before the onset of the next menstrual period; sperm survival is 3 days and ovum survival 2 days. In addition to these assumptions, the exact lengths of the previous 6 to 12 menstrual cycles must be known. By subtracting 19 (16 + 3) from the length of the shortest previous cycle, one obtains the first day of fertility. By subtracting 10 (12−2) from the longest previous cycle, the last day of the fertile phase is determined. The remaining days are infertile. This method is the original natural method but, since it is not very effective, it is no longer recommended for use. It is not

[8] Cf. *ibid.*; Häring, *art. cit.*, p. 126; Dedek, *op. cit.*, p. 61; McCormick, in the discussion following his talk at the Denver meeting (n. 1 above); Diamond, *art. cit.*, p. 312.

[9] Hellegers, *art. cit.*, p. 5.

[10] Häring, *art. cit.*, p. 121.

[11] *Ibid.* Häring repeatedly refers to either "rhythm" or the "rhythm method," and both terms connote calendar rhythm, a method no longer recommended by the medical community because of its relative ineffectiveness.

highly effective because it does not clearly distinguish the true biological periods of fertility and infertility.

The Temperature Method. It has long been known that a woman's basal body temperature rises following ovulation. This shift in the temperature is due to the thermogenic action of the hormone progesterone which is produced by the corpus luteum following ovulation. If one defines the infertile phase to begin on the evening of the third day of the temperature shift, one has a natural method which is based on sound scientific principle and is highly effective. While this method is currently serving many people quite well, its main disadvantage is that it is strictly a postovulatory method and thereby somewhat restrictive.

The Symptothermic Method. This method is widely in use today. It combines the information obtained by the shift in the basal temperature for detecting the postovulatory infertile period with calendar calculations and other symptoms of impending fertility (such as cervical mucus discharge, mid-cycle "ovulatory" pain, changes in the texture and configuration of the cervix and mid-cycle spotting) for the definition of a preovulatory infertile phase. This method, too, is very effective when used to avoid pregnancy.

The Ovulation Method. This is the newest of the natural methods; it relies upon the identification of a characteristic mid-cycle vaginal discharge of cervical mucus to determine the fertile phase of the cycle. This discharge is apparent to women at the opening of the vagina and requires no internal examinations. In this method the menstrual period is considered fertile. Following menstruation, a woman will experience a positive absence of mucus discharge (a dryness) and these days are infertile. The dry days are succeeded by the development of the mucus symptom. The discharge begins as a sticky, cloudy, tacky mucus and progresses to become clear, slippery, stretchy, and lubricative. The last day of the latter mucus is called the Peak. Ovulation occurs, on the average, one day after the Peak. The fertile period extends from the beginning of the mucus discharge through three full days past the Peak. From the evening of the fourth day past Peak until the beginning of the next period is infertile. This method, too, is very effective and its existence has created a renewed interest in natural family plannig.

All methods of natural family planning are best learned from well-trained teachers. Success in their use depends upon the co-operation of the couple combined with a good understanding of the method in use.

AGED SPERM AND AGED OVA AS A CAUSE OF EARLY HUMAN WASTAGE

A number of authors have suggested that the use of the "rhythm method" gives rise to a high incidence of human wastage, since its use produces an environment which is conducive to the fertilization of normal ova with "aged" sperms and/or the fertilization of "aged" ova

with normal sperms.[12] There are a number of studies in animals and a few in humans which may shed light on this controversy. In addition, certain mechanisms which act to protect the human from such occurrences need to be presented.

Aging of sperm is said to occur within the male tract prior to ejaculation or within the female tract after ejaculation. Aging of the female ova is said to occur prior to ovulation, so-called "intrafollicular overripeness," or following ovulation when the egg is lying free waiting to be fertilized—"postovulatory overripeness."

Both the stem spermatogonia and the primary oöcytes, the precursors to viable sperm and ova, are essentially dormant during the prepubertal age of the young male or female. With the onset of puberty, the maturation of germ cells begins. In the female, certain of the primary oöcytes are "selected" each month for further maturation and development culminating in the occurrence of ovulation. The process by which one or two oöcytes are "selected" each month out of the potential 500,000 candidates is presently unknown. Those primary oöcytes which are not selected for ovulation continue to wait their turn and are thus aged along with the age of the woman. Unlike females, when the male process of spermatogenesis begins, the new sperms are continuously replenished from renewing stem cells and thus are always relatively young in comparison to the age of the male.

Aging of Sperm in the Male Tract. It is thought that sperm aged in the male tract will produce a decrease in the ability of the sperm to fertilize the egg, and when fertilization does occur, an increase in the rate of resorbed and aborted fetuses has been observed. Young reported both of these changes in guinea pigs;[13] however, in order to obtain "aged" sperm, it was necessary to artificially ligate the epididymis and vas deferens in three different places. Some 20–25 days following this ligation procedure, he killed the animals, retrieved the "aged" sperm, and then artificially inseminated the female animals by placing the sperm directly into the body of the uterus. In rabbits, Hammond and Asdell used a similar methodology and found that sperm aged in this fashion were reduced in their ability to fertilize.[14] They did not study early developmental abnormalities. More recently, Tesh and Glover

[12] Cf. L. Iffy and M. B. Wingate, "Risks of Rhythm Method of Birth Control," *Journal of Reproductive Medicine* 5 (1970) 96–102; M. Orgebin-Crist, "Sperm Age: Effects on Zygote Development," in W. A. Uricchio, ed., *Proceedings of a Research Conference on Natural Family Planning* (Washington, D.C.: Human Life Foundation, c1973) p. 90; Häring, *art. cit.*

[13] W. C. Young, "A Study of the Function of the Epididymis, III: Functional Changes Undergone by Spermatozoa during Their Passage through the Epididymis and Vas Deferens in the Guinea Pig," *Journal of Experimental Biology* 8 (1931) 151–62.

[14] J. Hammond and S. A. Asdell, "The Vitality of the Spermatozoa in the Male and Female Reproductive Tracts," *British Journal of Experimental Biology* 4 (1926) 155–85.

found that by artificially aging spermatozoa in much the same fashion as these previous investigators, the fertilizing ability of the sperm was reduced and preimplantation and postimplantation loss was increased as the age of the sperm increased.[15] None of these studies even begins to tell what happens in the natural setting.

Aging of Sperm in the Female Tract. Developmental defects resulting from sperm aged in the female tract have been observed only in drosophila (fruit flies) and in birds;[16] no such anomalies have been observed in mammals. Soderwall and Blandau observed in rats that, as sperm were aged in the female tract, their ability to fertilize was decreased as they got older; however, no increases in losses during implantation, in developmental anomalies, or in abnormal pregnancies were observed and there was no change in the sex ratio of the offspring.[17] In rabbits, Soderwall and Young observed the same.[18] Regardless of age of the sperm, if fertilization occurred, gestation and development were normal.

Intrafollicular Aging of the Ova. There are two apparent mechanisms whereby ova may be aged prior to ovulation. In the first, the primary oöcyte ages as the woman ages and its "selection" to become a mature ovum is therefore delayed. In the second, in women who have long menstrual cycles, the primary oöcyte that has been "selected" for ovulation is delayed in its development and subsequent ovulation occurs beyond the 14th day of the cycle. Both mechanisms are unrelated to any method of natural fertility control and therefore will not be discussed in this paper. However, since there may be questions related to the second mechanism, it will be discussed in greater detail in the section entitled "Protective Mechanisms in the Human."

Postovulatory Aging of the Ova. In postovulatory aging of the ova, ovulation occurs but fertilization is delayed because of a delay in insemination; as a result, the ovum is aged following ovulation but prior to fertilization and an increase in developmental anomalies is alleged to occur. However, a close evaluation of studies done in mammals indicates that this does not appear to be a major problem in nature. Braden observed both normally mated rats and rats that were artificially de-

[15] J. M. Tesh and T. D. Glover, "The Influence of Aging of Rabbit Spermatozoa on Fertilization and Prenatal Development," *Journal of Reproduction and Fertility* 12 (1966) 414–15.

[16] J. T. Lanman, "Delays during Reproduction and Their Effects on the Embryo and Fetus, I: Aging of Sperm," *New England Journal of Medicine* 278 (1968) 993–99.

[17] A. L. Soderwall and R. J. Blandau, "Duration of Fertilizing Capacity of Spermatozoa in Female Genital Tract of Rat," *Journal of Experimental Zoology* 88 (1941) 55–64.

[18] A. L. Soderwall and W. C. Young, "Effect of Aging in Female Genital Tract on Fertilizing Capacity of Guinea Pig Spermatozoa," *Anatomical Record* 78 (1940) 19–29.

layed in their mating until after ovulation.[19] In the females mated at the normal time, the proportion of ovulated eggs that were lost before the end of gestation was 16.7%, of which 7.1% was due to nonfertilization of the eggs, 1.4% was attributable to abnormal fertilization, 1.1% were lost between fertilization and implantation, and 7.1% were lost after implantation. Corresponding figures for the late-mated females were 68% (total): 27.1%, 14.6%, 7.5%, and 18.8% respectively. Hunter studied pigs that were artificially induced to ovulate and then artificially inseminated via the intracervical approach.[20] In his control animals he found that 3.5% of fertilized eggs were developing abnormally and 5.7% went unfertilized. In those animals in which the ova were aged for an estimated 20 hours, the respective figures were 25.2% and 23.9%. No increase in abnormalities in the experimental group was seen until the ova were at least 12 hours of age. Blandau and Young studied guinea pigs that were artificially inseminated at the normal time preovulatory and at other times postovulatory with sperm obtained from recently killed males.[21] In the control group there was an 83% impregnation rate and a 12% "abnormal pregnancy" rate, but if ovulation was delayed 20 hours, the corresponding figures were 31% and 90%. Marston and Chang studied mice that were artificially induced to ovulate and then artificially inseminated over time periods relating to ovulation.[22] Of the mature mice that were inseminated within 4 hours of estimated ovulation, 100% of the early divisions were considered normal, whereas 20 hours after suspected ovulation only 5.9% were normal. Postimplantation abnormality occurred in 13.0% of the first group and 70.9% of the latter group. A similar trend was observed by Fugo and Butcher when they artificially delayed ovulation in rats by giving them pentobarbital sodium.[23]

These studies clearly indicate that when the mammals under study were placed in an artificial environment whereby the time of insemination was delayed past the time of ovulation, the ability of the ova to be fertilized was reduced and the incidence of developmental abnormalities was increased. However, of greater importance to this discussion is the

[19] A. W. H. Braden, "Are Nongenetic Defects of Gametes Important in the Etiology of Prenatal Mortality?" *Fertility and Sterility* 10 (1959) 285–98.

[20] R. H. F. Hunter, "The Effects of Delayed Insemination on Fertilization and Early Cleavage in the Pig," *Journal of Reproduction and Fertility* 13 (1967) 133–47.

[21] R. J. Blandau and W. C. Young, "The Effects of Delayed Fertilization on the Development of the Guinea Pig Ovum," *American Journal of Anatomy* 64 (1939) 303–29.

[22] J. H. Marston and M. C. Chang, "The Fertilizable Life of Ova and Their Morphology Following Delayed Insemination in Mature and Immature Mice," *Journal of Experimental Zoology* 155 (1964) 237–52.

[23] N. W. Fugo and R. L. Butcher, "Overripeness and the Mammalian Ova, I: Overripeness and Early Embryonic Development," *Fertility and Sterility* 17 (1966) 804–14.

relatively low incidence of developmental anomalies seen in those laboratory animals that were inseminated under near normal conditions, albeit still artificial and removed from the natural setting.

The Effects of Aging Gametes in the Human. As one would imagine, it is extremely difficult to obtain information regarding the effects of aging gametes on early human development. Nonetheless, a number of investigators have made the attempt. Without exception, all studies so far conducted in human beings have been so methodologically unsound that they prove nothing. Iffy has suggested that ectopic pregnancy,[24] placenta previa and hydatidiform mole,[25] and early spontaneous abortion[26] are all etiologically related to postmid-cycle conception and therefore preovulatory overripeness. However, Iffy's data was gleaned from medical reports published in the medical literature for essentially unrelated reasons. Iffy had no personal contact with any of the cases discussed save one possible exception. When attempting to establish as fine a point as the time of ovulation, such methodology is totally inadequate. Lanman has called his data "untenable both in their interpretation and statistically."[27]

The work of Jongbloet is equally untenable.[28] In a retrospective analysis of 131 institutionalized mentally-retarded children, he suggested that their condition was significantly correlated with aging of the gametes at the time of conception. This methodology is similar to that used by Gregg, in 1941, when he found that the incidence of fetal defect in rubella-infected pregnancies was an extraordinarily high 75%.[29] Such retrospective analyses are usually in great error.

Marshall studied the effects of aging of spermatozoa on the incidence of congenital defects of born infants and the incidence of spontaneous abortion in individuals using the basal-temperature method of fertility control, and found no correlation with the age of spermatozoa and the

[24] L. Iffy, "Contribution to the Aetiology of Ectopic Pregnancy," *Journal of Obstetrics and Gynaecology of the British Commonwealth* 68 (1961) 441–50; L. Iffy, "The Role of Premenstrual, Post Mid-Cycle Conception in the Aetiology of Ectopic Gestation," *ibid.* 70 (1963) 996–1000.

[25] L. Iffy, "The Time of Conception in Pathologic Gestations," *Proceedings of the Royal Society of Medicine* 56 (1963) 48–50.

[26] L. Iffy, "Embryologic Studies of Time of Conception in Ectopic Pregnancy and First-Trimester Abortion," *Obstetrics and Gynecology* 26 (1965) 490–98; L. Iffy, "The Aetiology of Early Abortion," *Journal of Obstetrics and Gynaecology of the British Commonwealth* 69 (1962) 598–605.

[27] J. T. Lanman, "Delays during Reproduction and Their Effects on the Embryo and Fetus, II: Aging of Eggs," *New England Journal of Medicine* 278 (1968) 1047–54.

[28] P. H. A. L. M. Jongbloet, *Mental and Physical Handicaps in Connection with Overripeness Ovopathy* (University of Amsterdam thesis, 1971).

[29] N. M. Gregg, *Transactions of the Ophthalmological Society of Australia* 3 (1941) 35.

incidence of defects or spontaneous abortions.[30] However, his series was small, retrospective, and has as its prime methodological defect the use of the temperature shift as the tool used to identify the time of ovulation. Guerrero and Rojas, using a similar methodology, recently reported a much larger series relating the incidence of spontaneous abortion to both the age of the sperm and the age of the ova.[31] They found that as both the sperm and ova aged, the incidence of spontaneous abortion increased. In order for these investigators (including Marshall) to age the gametes, they had to find a convenient and yet reliable marker for pinpointing the day of ovulation. For this, they used the shift in the basal body temperature. However, it has been shown that the time of ovulation may occur from at least four days prior to to two days following the shift in temperature.[32] This six-day variation in the ability of the basal-temperature shift to pinpoint the day of ovulation is far too excessive to reach conclusions regarding the age of gametes and the role this may play in spontaneous abortion or neonatal abnormalities.

There are other deficiencies in this study. It is primarily a retrospective study of conception cycles from people who were taking their basal temperatures daily. It is unlikely that *all* conception cycles would be collected from the several centers from which data was obtained unless each of the several centers had excellent prospective follow-up procedures. More unlikely than this, however, is the accuracy of the recorded acts of intercourse which were relied upon to date the responsible insemination and therefore the age of the gametes. It is well known that this kind of information is often not very accurately kept, in spite of urging by the people involved in the data collection. Only with very carefully conducted personal interviews occurring shortly after the time of the responsible insemination can any reliance be placed on this type

[30] J. Marshall, "Congenital Defects and the Age of Spermatozoa," *International Journal of Fertility* 13 (1968) 110–20.

[31] R. Guerrero and O. I. Rojas, "Spontaneous Abortion and Aging of Human Ova and Spermatozoa," *New England Journal of Medicine* 293 (1975) 573–75. See also R. Guerrero and C. A. Lanctot, "Aging of Fertilizing Gametes and Spontaneous Abortion," *American Journal of Obstetrics and Gynecology* 107 (1970) 263–67.

[32] W. W. Greulich, "The Reliability of 'Basal' Body Temperature Changes as an Index of Ovulation in Women," *Transactions of the American Society for the Study of Sterility* 1 (1946) 76–97; C. L. Buxton and E. T. Engle, "Time of Ovulation: A Correlation between Basal Temperature, the Appearance of the Endometrium, and the Appearance of the Ovary," *American Journal of Obstetrics and Gynecology* 60 (1950) 539–50; A. R. Abarbanel, "Transvaginal Pelvioscopy: Further Studies in Infertility," in *Proceedings of the 2nd World Congress on Fertility and Sterility* 1 (1956) 1140–59; N. M. Morris, L. E. Underwood, and W. Easterling, "Temporal Relationship between Basal Body Temperature Nadir and Luteinizing Hormone Surge in Normal Women," *Fertility and Sterility* 27 (1976) 780–83.

of data, and then there will continue to be some error. Such close evaluation was not done in this study.

Protective Mechanisms in the Human. For most farm animals, the female is receptive to the male only during a relatively short period of heat, at the end of which ovulation occurs. In other animals, such as rabbits, ovulation occurs only in response to copulation. In both situations nature has a built-in protective mechanism whereby fresh sperm and fresh ova are assured. In the human, however, a number of authors have voiced concern that no such protective mechanisms exist.[33] Since human females have a menstrual rather than an estrous cycle, and since they do not ovulate in response to sexual stimulation, there is, so it is often stated, no protective mechanism. In addition, prolonged sexual rest in the male may needlessly age spermatozoa, with subsequent adverse effects.

With regard to the male, it has been shown that the fertilizing capability of sperm is retained considerably longer with the sperm in the male tract as opposed to the female tract. The time from the division of a stem spermatogonia to the liberation into the lumen of the seminiferous tubules of spermatozoa is certainly longer than 30 days in human males, and the transit time from the testis through the efferent ducts into the epididymis is from 1–12 days.[34] So, within these time elements a few days or a few weeks of sexual rest should be of no consequence. But, in addition, it is highly probable that older sperm are regularly eliminated from the body. It is known that males "leak" sperms into the urethra more or less continuously, for sperms are usually found in the urine of fertile men.[35] Finally, the natural occurrence of "nocturnal emissions" in males starting at the time of puberty serves to regularly flush the entire male system.

As to intrafollicular overripeness, which is alleged to occur in women with long menstrual cycles, Brown has described the basic mechanisms involved.[36] It is the follicle-stimulating hormone (FSH) that stimulates the growth and development of the follicle. The preovulatory output of FSH from the pituitary gland "hunts" upwards, seeking the "threshold" level at which a group of follicles is stimulated into active growth. Within five days these follicles are secreting estradiol. There is an

[33] Lanman, *art. cit.* (n. 6 above) p. 996; Iffy, *art. cit.* (n. 12 above); "Critical Viability of Human Sperms and Oocytes," Editorial, *New England Journal of Medicine* 278 (1968) 1121–22.

[34] Orgebin-Crist, *art. cit.* (n. 12 above) p. 86.

[35] C. G. Hartman, *Science and the Safe Period* (Baltimore: Williams and Wilkins, 1962) p. 43.

[36] J. B. Brown, "Time Intervals during the Menstrual Cycle with Special Reference to the Long Follicular Phase," *Bulletin of the Natural Family Planning Council of Victoria* 3 (1976) 5–6.

intermediate or subthreshold level of FSH production which must be exceeded before a follicle is stimulated sufficiently from its initial growth phase to progress to ovulation. As the dominant follicle is being boosted to ovulation, it is producing increasing amounts of estradiol which feed back to the pituitary and suppress FSH production to below the threshold value; this suppression is important, as it prevents the FSH production from exceeding the desired limit, removes stimulation from lesser follicles which are competing in the race to ovulation, and turns on a maturing mechanism within the dominant follicle which renders it receptive to the second pituitary hormone, luteinizing hormone (LH). The high estradiol levels also activate a positive feedback stimulus to the pituitary, to cause the mid-cycle LH surge which initiates follicular rupture (ovulation). All the above processes require time. The "hunting" phase, where the pituitary is searching for the "threshold" level of FSH production, is one of the variable time sequences of the cycle and may take a week in cycles of normal length or several months in women with infrequent periods. No follicular development occurs until the "threshold" is reached. In prolonged cycles the rise in FSH levels is arrested and it stays within the intermediate or subthreshold phase. Once an ovulatory course is embarked upon, the timing of the subsequent events is highly predictable. As a result, even in long cycles the essential preovulatory age of the ovum-in-development is the same as in normal cycles. The age of the primary oöcyte may be a few days or a few months older in any given cycle, but the process of maturation to an ovulated ovum readying for impregnation is nearly identical. In fact, it is in the last few hours prior to ovulation that the major maturation events occur.[37]

However, the major protective mechanism in the human is the cervical mucus. Odeblad has described two basic types of cervical mucus, Type E (estrogenic) and Type G (gestagenic).[38] Type E mucus is seen at mid-cycle and is produced in response to the hormone estrogen which is being produced in the developing follicle. Type E mucus is characterized by the arrangement of the strands of mucus (micelles) in parallel fashion, allowing, as such, sperm penetration. On the other hand, Type G mucus is seen either in the absence of estrogen hormone or in the presence of progesterone, the dominant postovulatory hormone. Therefore it is seen during the early preovulatory stages of the menstrual cycle and from shortly after ovulation until the beginning of the next cycle. It is characterized by the strands of the mucus being arranged in a

[37] Hartman, *op. cit.* (n. 35 above) pp. 83–85.

[38] E. Odeblad, "Biophysical Techniques of Assessing Cervical Mucus and Microstructure of Cervical Epithelium," in WHO Colloquium, Geneva, 1972: *Cervical Mucus in Human Reproduction* (Copenhagen: Scriptor, 1973) pp. 58–74.

tight-knit, dense meshwork which is impenetrable to spermatozoa. Recently this structure has been clearly identified with the use of the scanning electron microscope.[39] In addition, Moghissi has shown that sperm do not penetrate the cervical mucus during the early follicular phase of the cycle and during the postovulatory phase of the cycle, both corresponding to the presence of Type G mucus.[40] He found sperm penetrability of the cervical mucus to begin about 5–6 days prior to ovulation, reaching a peak the day before ovulation and rapidly decreasing after ovulation so that no sperm penetration was seen two days after ovulation.

The work of the last fifteen years related to the cervical mucus has clearly shown that this mucus acts like a biological valve. At certain times during the menstrual cycle the valve is open and at other times the valve is closed. When the valve is open, sperm can penetrate; when it is closed, there is no penetration. Work in our own laboratory confirms this finding. The biological valve is open for only a short period of time before ovulation and it closes shortly after ovulation. Type E mucus is produced in response to the hormone estrogen which is produced in the follicle that is being boosted to ovulation, so that the biological valve opens in response to the developing follicle for the 5–6 days prior to ovulation.

Because of this valvular action, both fresh sperm and fresh ova are assured in human conception. If sperm are deposited when the valve is closed, they die in a few hours, because they cannot escape the hostile, acidic environment of the vagina. In addition, old eggs are prevented from being fertilized, because the valve closes very quickly after ovulation; in fact, in many women it may close prior to actual ovulation.

In 51 menstrual cycles which have currently been studied of the ovulation method, 96% of ovulations have been judged to occur (via LH radioimmunoassay) from the day of the Peak mucus secretion (day of greatest Type E secretion) through three days past the Peak and 80.3% were from 1–3 days after the Peak.[41] This would indicate that in the overwhelming majority of cases the biological valve is either closed or in the process of being closed prior to the time of ovulation.

The opening of the biological valve always accompanies ovulation,

[39] F. C. Chretien, J. Cohen, V. Borg, and A. Psychoyos, "Human Cervical Mucus during the Menstrual Cycle and Pregnancy in Normal and Pathological Conditions," *Journal of Reproductive Medicine* 14 (1975) 192–96.

[40] K. S. Moghissi, "Sperm Migration through the Human Cervix," *op. cit.* (n. 38 above) pp. 128–52.

[41] E. L. Billings, J. J. Billings, J. B. Brown, and H. G. Burger, "Symptoms and Hormonal Changes Accompanying Ovulation," *Lancet*, Feb. 5, 1972, pp. 282–84; A. M. Flynn and S. S. Lynch, "Cervical Mucus and Identification of the Fertile Phase of the Menstrual Cycle" (in press).

except in a few rare cases in which ovulation occurred but the valve was closed. These women did not achieve pregnancy as one would expect.[42]

In addition to this phenomenon, when the valve is closed, there are also a large number of white blood cells present in the mucus which assist in the destruction of sperm.[43] It has also been theorized that the Type E mucus, because of its arrangement in parallel strands, also acts as a filter whereby morphologically abnormal sperm are kept from penetrating the cervix and reaching the ova.[44]

The valvular mechanism of cervical mucus is operative independent of whatever method of natural family planning is being used; therefore, whatever method is used, this protection is offered. However, a method such as calendar rhythm, which operates independent of the valve, is therefore less effective than other methods. The ovulation method of natural family planning is the only method which functions solely on this principle. As a result, it can also teach couples the ideal time to achieve pregnancy. This has been done with great success.[45]

WHAT IS THE NATURAL HUMAN WASTAGE?

When one reads that 30–50% of all fertilized ova die sometime prior to birth, one is constantly referred to the research of Hertig and Rock. These investigators studied 34 human "ova" within the first 17 days of development that were obtained by examining 211 patients who had had hysterectomies. Depending upon which of their papers you believe, 13,[46] 10,[47] or 11[48] of the "ova" were abnormal. Their work is essentially one of a kind, since it has never been repeated. Medicine has looked upon their work as a classic, and while this work can legitimately be viewed as such, exorbitant claims regarding early human wastage cannot be deduced from the results of this study, since the methodology of the study does not lend itself to such conclusions.

First, the study is *very* small. On the basis of 34 recovered "ova" one

[42] J. J. Billings, personal communication.

[43] Moghissi, *art. cit.*

[44] V. Davajan, R. Nakamura, and K. Kharma, "Spermatozoa Transport in Cervical Mucus," *Obstetrical and Gynecological Survey* 25 (1970) 1–43.

[45] J. B. Brown, "The Ovulation Method in the Subfertile Couple," Paper presented before the Natural Family Planning Council of Victoria, Mercy Maternity Hospital, Melbourne, Australia, June 26, 1976.

[46] A. T. Hertig, J. Rock, and E. C. Adams, "A Description of 34 Human Ova within the First 17 Days of Development," *American Journal of Anatomy* 98 (1956) 435–93.

[47] A. T. Hertig, J. Rock, E. C. Adams, and M. C. Menkin, "Thirty-four Fertilized Ova, Good, Bad and Indifferent, Recovered from 210 Women of Known Fertility," *Pediatrics* 23 (1959) 202–11.

[48] A. T. Hertig, "Human Trophoblast: Normal and Abnormal," *American Journal of Clinical Pathology* 47 (1967) 249–68.

cannot legitimately make statistical claims. This becomes even more vital when it is realized that only a small subsection of the study is used as the basis for the claim that 50% of early embryos are lost. In the Hertig–Rock study, 4 of 8 (50%) of "ova" recovered prior to implantation were abnormal. This small subseries is where the claims emanate.

Second, the study suffers drastically from the lack of any comparable material by which the specimens could be compared. As a result, there is serious question as to whether or not the "ova" that were recovered free-lying in the uterus and tubes were even really fertilized to begin with. It is now well known that cleavage alone is not enough to establish the occurrence of fertilization, since unfertilized mammalian (including human) ova often exhibit degenerative changes which resemble cleavage (parthogenetic cleavage).[49] Shettles has aspirated unfertilized ova from perfectly intact ovarian follicles that have cleaved to the morula and early blastocyst stages.[50]

Third, the Hertig–Rock study suffers from a myriad of other methodological defects which make statistical claims inappropriate. The "ova" were obtained from women who had uterine and tubal pathology. The patients were definitely older than average and were nearly all multiparous. A good case could be made that these factors could also influence the incidence of abnormalities observed.

Roberts' and Lowe's claim that there is an estimated 78% prenatal loss is totally untenable.[51] One is simply referred to their list of assumptions with subsequent mathematical analysis for your own evaluation.

What is the natural human wastage? We know that approximately 10–15% of all pregnancies will spontaneously abort in such a fashion as to be clinically noticeable. Many of these spontaneous abortions are due to early genetic defects, and while it is tempting to say that this is due to aging of gametes,[52] there is only tangential evidence to support that concept. While aging of the gametes may explain some of the early chromosomal abnormalities, one must be very hesitant in claiming it as the only cause. The mechanisms are far too complex, with too little known, to jump to such conclusions. Perhaps the ovum or sperm are abnormal to begin with; perhaps the tubal and uterine environment is abnormal in some way; perhaps there is an abnormality in the protective mechanisms. All these and others could theoretically lead to chro-

[49] L. Mastroianni and C. Noriega, "Observations on Human Ova and the Fertilization Process," *American Journal of Obstetrics and Gynecology* 107 (1970) 682–90.

[50] L. B. Shettles, personal communication, September 1976.

[51] C. J. Roberts and C. R. Lowe, "Where Have All the Conceptions Gone?" *Lancet* March 1, 1975, pp. 498–99.

[52] K. Mikamo, "Anatomic and Chromosomal Anomalies in Spontaneous Abortion," *American Journal of Obstetrics and Gynecology* 106 (1970) 243–54.

mosomal aberrations, and all would be unrelated to aging and unrelated to the use of any natural method of family planning.

Unfortunately, the answer is not yet known. The best data available, however, comes from a number of investigations which have been previously cited regarding work with aging gametes.[53] In all of these studies there were controls which approximated the natural state (albeit artificially), and in these mammals the spontaneous fetal loss was consistently less than 15% and the preimplantation loss 1–3%. This data certainly dictates a new look at the over-all question. The question will never be solved until good prospective surveys in human females, with accurate sexual histories and sophisticated early-pregnancy tests, like the baro-receptor assay for the HCG beta-subunit, are performed.

TWINNING AND RECOMBINATION

It should first be emphasized that there is a great deal more that we do not know about the twinning process in the human than that which we do know. Dizygotic or fraternal twins arise from the fertilization of two separate ova ovulated at approximately the same time. Monozygotic twins are thought to arise from the fertilization of one ovum which subsequently divides into two independent individuals. There are several theoretical mechanisms by which this might occur.

Twins occur in 1 out of 90 births, and 2 out of 3 sets of twins are fraternal. Therefore, approximately 1 in 270 births results in identical or monozygotic twins. This figure may be even smaller, since it is at least possible that some sets of "identical" twins arise from the fertilization of one ovum and its polar body.[54] These twins could develop normally if there was an equal distribution of cytoplasm between the ovum and the polar body. Since both cells would have identical genetic material, these twins would conceivably be more identical than fraternal twins but less identical than identical twins.

The work of Mintz has led some to believe that fusion of two fertilized ova and/or recombination of twins once divided may occur in the human.[55] Mintz fused early mouse embryos that were in the 2-cell stage to the blastocyst stage. Up to 16 cleaved eggs have been fused to form one large blastocyst. Some of the newly-formed aggregates have developed normally where birth of a mouse occurred with the genetic components of the aggregate present. For this to be accomplished, however, it was

[53] Cf. articles by Braden, Hunter, Blandau and Young, Marston and Chang, and Fugo and Butcher (nn. 19–23 above).

[54] Shettles (cf. n. 50 above).

[55] B. Mintz, "Experimental Genetic Mosaicism in the Mouse," in *Preimplantation Stages of Pregnancy* (Ciba Foundation Symposium, 1965) pp. 194–216.

necessary to enzymatically lyse the zona pellucida, a protective membrane normally present until just prior to implantation.

Normally, the zona pellucida surrounds the early human life, like the shell of an egg, and just prior to implantation the blastocyst "hatches" or breaks out of the zona in order to accomplish implantation. Mintz has herself recognized that one of the normal functions of the zona is to preserve the normal cleavage pattern and *prevent* fusion of the early zygotes. If accidental loss of the zona occurs, then cell fusion could potentially occur.[56]

Those involved with human in vitro fertilization have either never observed the process of recombination[57] or know of no evidence that recombination occurs.[58] Lejeune, the outstanding French geneticist, has stated: "There is *no* evidence in man of recombination between two eggs to form one individual."[59]

While fusion of early cellular material is theoretically possible, it is highly unlikely, since it will not occur with the zona pellucida still intact. For two fertilized ova to fuse, both zonae pellucidae would have to be shed in some freak accident of nature. If this were to occur, it would have to be classified as an abnormality or diseased deviation from the normal process. It would be extremely unlikely for two blastocysts to fuse after the zona has normally been shed just prior to implantation, since the embryonal cells are then contained in the inner-cell mass surrounded and protected by nonspecific chorionic elements. The *extreme* rarity of such potential occurrences has previously been pointed out.[60]

COMMENT

Häring claims that "those who feel that there is still a jump between the data gathered about the fertility of animals and the conclusion reached about humans may not have sufficiently worked through the whole literature and all the arguments," and that "No scientist thinks that we are faced with arbitrary hypotheses or false alarms."[61] Well, this is one scientist, actively involved in the research and study of human reproduction, who feels that the hypotheses are arbitrary and the alarms false, while the reader can be assured that the author has

[56] B. Mintz, "Experimental Study of the Developing Mammalian Egg: Removal of the Zona Pellucida," *Science* 138 (1962) 594–95.

[57] Shettles (cf. n. 50 above).

[58] L. Mastroianni, personal communication, August 1976.

[59] J. Lejeune, personal communication, September 1976.

[60] K. Benirschke, "Spontaneous Chimerism in Mammals: A Critical Review," in K. Benirschke, ed., *Current Topics in Pathology*, 1969, pp. 1–61.

[61] Häring, *art. cit.* (n. 1 above) p. 130.

exhaustively worked through "the whole literature and all the arguments."

Let me work in reverse. The evidence regarding cell fusion and recombination of early zygotic material comes from highly specialized experiments done under carefully controlled and totally artificial laboratory conditions. There is little question that under these conditions such fusion can be accomplished. However, this type of experimental work has essentially no application to the normal, natural process which occurs in early human development. If it does occur, it would occur only extremely rarely, and then only as the result of abnormal, diseased development. Such occurrences should not form the basis of moral decision-making.

With regard to early embryological loss, the references are consistently made to the work of Hertig and Rock. Their work, while of great importance from a histologic and a morphologic point of view, will not, from a statistical point of view, hold up to the claims. While there is undoubtedly some early human loss which is not perceived via ordinary means, whatever reasonably reliable data we have (albeit minimal) would indicate that this loss is very small and its cause still unknown.

Indeed, techniques are currently available which could give a definitive answer to this question in the human. But again, it is clear that whatever those results, abnormalities of growth, development, and function which occur prior to birth should be viewed in the same fashion as those that occur after birth. Certainly, humans can die a natural death from a lethal insult prior to birth, just as they can after birth. It is the challenge of medicine to understand the normal so that the abnormal may be corrected. Suffice it to say that the study of the preborn diagnostically and therapeutically is only just beginning.

Finally, the question of aging gametes and natural family planning. If this paper seems to criticize a great deal of scientific research on the basis of methodology, then you must understand that the results of biomedical research are only as good as the questions asked and the protocol followed. I do not think there is any question that if you artificially age gametes in laboratory animals, a number of structural and functional abnormalities can be seen. But this is a far cry from the natural state of things. Are some early human losses ever secondary to aging gametes? I suspect that the answer to that question is yes, but I also think that this is most likely a rare occurrence, and then only when the normal, regularly occurring events in the female and/or the male reproductive tracts are disturbed for some reason.

With the two most commonly used methods of natural family planning, the symptothermal method and the ovulation method, couples are not only taught how to avoid pregnancy but also how to achieve preg-

nancy. With the implementation of the latter knowledge there should be little debate, regardless of how one interprets the data, that insemination would occur at a time when both fresh sperm and fresh ova are certainly present. For those utilizing the methods to avoid pregnancy, the natural protective mechanisms should, as previously outlined, prohibit the union of aged sperm and aged ova.

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