IUDs are Contraceptives, Not Abortifacients: A Comment on Research and Belief

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A prevalent social myth holds that IUDs are abortifacients. Even US Supreme Court Justice Paul Stevens, in dissent from the majority opinion in *Webster versus Reproductive Health Services,* subscribed to this belief. Scientists, including developers of IUDs, have believed it. The key element underlying the myth is that IUDs act only at the uterine level, either to prevent implantation or to destroy developing embryos in the uterus before implantation. Today, however, the weight of scientific evidence indicates that IUDs act as contraceptives. They prevent fertilization, diminishing the number of sperm that reach the oviduct and incapacitating them. IUDs, particularly copper devices, decrease the likelihood that ova can be found in the Fallopian tube shortly after ovulation.

All IUDs, inert or medicated, profoundly alter the composition of uterine fluid and the morphology of the human endometrium. After IUD insertion, a foreign body reaction occurs, which is most intense in the space and tissues immediately surrounding the IUD. Leukocytes, the white blood cells, are mobilized, both in the endometrium and in the uterine fluid. Protein levels are elevated, a likely reflection of decay products of macrophages and other leukocytes. Leukocytes and their degradation products are thought to contribute to a cytotoxic anti-fertility effect.

The critical elements in the concept that IUDs are abortifacients operating only at the uterine level are that the fertilized egg, after a brief embryonic development in the human oviduct, passes into a hostile uterine (endometrial) cavity, where it is phagocytized, destroyed by toxic products, or withers because it is unable to implant in the markedly altered endometrium.

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This view implies an ability to find frequent traces of fertilization in IUD users, traces that would be found with similar and high frequency in very early pregnancy among women who are not using contraceptives. One such trace would be a marker of early pregnancy released by the developing embryo. This marker would be detected by a sensitive assay of the woman's blood or urine. No unequivocal, well characterized biochemical marker of pregnancy in the first week following fertilization is available.

Findings from Assays of Early Pregnancy

Human chorionic gonadotropin (hCG) can be detected by sensitive assays approximately seven to eight days after ovulation, when the developing embryo has already reached the uterus. In normal pregnancies, hCG rises sharply and is sustained at high levels. Elevations of hCG followed by declines below the limits of assay sensitivity are interpreted as losses of developing embryos. Among groups of women not using contraceptives, embryonic loss, measured by the transient appearance of hCG, has ranged, over an order of magnitude, from 6 to 57 percent. Similarly wide estimates of embryonic loss have been made for IUD users. The specificity of several of the assays in early studies has been questioned, however. It is now believed that when women, whether IUD users or not, were deemed to experience quite high proportions of embryonic loss, based on determination of serum or urinary hCG, the assays were cross-reacting with another hormone, the luteinizing hormone, LH, which is secreted by the pituitary gland but not produced by a developing embryo. Segal et al. (1985) designed a study that used sensitive assays and had both positive controls (women seeking pregnancy) and negative controls (sterilized women) along with

IUD users. After ovulation, hCG was found only in the group seeking pregnancy. There was no indication of embryonic loss in the IUD group. This study is statistically consistent with an upper limit of not more than 10 percent of IUD users experiencing embryonic loss.

Wilcox et al. (1985) used newer immunoradiometric assays, deemed to be highly sensitive and specific, with sample sizes of about 100 cycles each for IUD users and for controls. They found apparently higher proportions of transient hCG rise in controls (5 percent) than in IUD users (1 percent). The study suggests that an upper limit of 3-4 percent of ovulatory matings might show transitory rises in the presence of an IUD. In a later study, Wilcox et al. (1988) found the incidence of early pregnancy loss to be 6.1 percent in 707 cycles among 221 women who had stopped using contraceptives. Of the 707 menstrual cycles, clinically recognized pregnancies occurred in 21.9 percent of the cycles.

Because of uncertainties about the specificity of many of the assays, the detection of chemical markers of early pregnancy has not pointed to a distinctive IUD mode of action. The assays of Segal et al. (1985) and Wilcox et al. (1985) appear to set a low upper limit on embryonic loss associated with IUD use, and suggest that women who are not using contraceptives experience the same or perhaps higher rates of embryonic loss.

Microscopic Searches for Embryos and Eggs

Direct evidence on the presence and developmental status of embryos in IUD groups and in controls has been obtained in rhesus monkeys by Hurst et al. (1980) and in humans by Croxatto (1974) and Alvarez et al. (1988). Hurst's group mated 15 rhesus monkeys at ovulation, and searched for embryos or eggs on days 15-20 of the cycle, after performing a laparotomy and flushing the uterus. They detected one-celled eggs and embryos with as few as two cells. In searches of 43 ovulatory cycles, the group recovered 22 embryos (51 percent), of which 5 (12 percent of the base) were classified as degenerating (Table 1). The group also found three unfertilized eggs (7 percent). Searches located neither embryo nor egg 18 times (42 percent). Monkeys were rested for at least one cycle between searches. After the 43 ovulatory control cycles had been completed, the same 15 monkeys were fitted with small plastic IUD coils (of unknown effectiveness). The monkeys were again mated at ovulation and uterine flushing was performed 61 times. All searches for embryos were conducted on days 15-20 of the cycle. Evidence of fertilization was found in only 16 percent of the flushings in cycles in which IUDs were used (Table 1). The

Table 1 Findings from uterine fundal flushings of rhesus monkeys mated in ovulatory cycles

Developmental status	Percent of total	
	Control	IUD
No egg or embryo found	42	82
Unfertilized egg (including degenerating one-celled eggs)	7	2
Fertilization	51	16
Developing embryo	(39)	(5)
Degenerating embryo	(12)	(11)
Total	100	100
Number of ovulatory flushings	43	61

Note: p<.001.
Source: P.R. Hurst, A.D. Wheeler, and P. Eckstein, "A study of uterine embryos recovered from rhesus monkeys fitted with intrauterine devices," *Fertility and Sterility 33* (1980): 69-76.

difference between this 16 percent and the 51 percent fertilization in the control cycles was highly significant statistically (p<.001).

When IUDs were in place, seven (11 percent) of the flushings produced evidence of degenerating embryos, a percentage virtually identical with the 12 percent found in the control cycles. The characteristics of the degenerating embryos in control and in IUD cycles were, however, different. In the IUD group "invasion by leukocytes or macrophages was a consistent feature" (Hurst et al., 1980: 75) not found in the control group. According to the authors, "the results of this experiment... do not, however, determine whether the embryos were rendered abnormal before contact and invasion by leukocytes" (1980: 76).

The Hurst et al. study in nonhuman primates thus demonstrates two points. First, the study shows the comparative rarity of demonstrable fertilization when the IUD is *in situ.* This indicates that the IUD acts as a contraceptive. Second, the study demonstrates that the rate of embryonic loss per mating at mid-cycle of an ovulatory cycle is the same among users of a small plastic IUD as among nonusers of contraception. This indicates that the IUD is no more an abortifacient than is unprotected intercourse at mid-cycle.

In humans, Croxatto (1974) reported findings from transcervical searches for ova or embryos conducted between the second and fifth day after ovulation in IUD users and in controls. Twenty-two percent of the searches for eggs in the control group were successful, but only 1.5 percent of the searches of IUD users found ova in the uterus (p<.01). This study provides evidence that intrauterine devices in humans act before eggs enter the uterus, because in IUD users, normally developing embryos (or eggs) reach the uterus at far lower rates than in controls.

Alvarez et al. (1988) searched for eggs in the uteri and Fallopian tubes of 115 controls and 56 women who used various IUDs. The women were surgically steril-

ized within five-and-a-half days after ovulation, as measured by the LH peak. Since transit through the Fallopian tubes takes three to four days, it is unsurprising that the only eggs found in the uterus were among women who had surgery on the fourth or fifth day after the peak. Four of 37 control subjects (11 percent) and none of the 12 IUD subjects who were sterilized on the fourth or fifth day were found to have ova in the uterus. This difference was not statistically significant, but provides additional evidence in the same direction as the earlier findings of Croxatto (1974) that eggs are rarely found in the uteri of IUD users.

Greater clarity on the fate of eggs in the human reproductive tract is given by Alvarez et al. (1988) by searches for eggs in the Fallopian tube. Excluding four control women whose eggs were found in the uterus, 58 percent of controls, but only 39 percent of IUD users, had one or more eggs discoverable in the Fallopian tubes (p<.05). This significant difference was almost wholly attributable to the paucity of ova found among women who had used the Copper T 200 device, 30 percent. For copper intrauterine devices, the study by Alvarez et al. (1988) provides clear evidence of extrauterine action. In speculating about a mechanism to explain the paucity of eggs in the Fallopian tubes of the IUD group, the authors note that the junction of the uterus and the Fallopian tube does not form a one-way valve. Uterine fluid can intermix with tubal fluid. Investigators have found that copper concentrations in tubular fluid are similar to concentrations found in the uterus, implying a mixture of fluids. Copper, as noted below, is spermicidal and cytotoxic; thus, copper ions as well as leukocytes, or their cytotoxic products, could destroy oviductal eggs prior to fertilization in women using IUDs.

In the Alvarez et al. (1988) study, 20 controls and 14 IUD subjects had had intercourse in the periovulatory period preceding surgery. They determined the fertilization status in the tube by examining ova for development. Normal development-that is, fertilization-was found in 50 percent of the control group, but in none of the IUD users (Table 2). No development, a marker of the lack of fertilization, was found in 15 percent of

Table 2 Developmental status of eggs in fallopian tubes, following intercourse in the periovulatory period

Group	Developmental status of ova (%)			
	No develop-ment	Abnormal/Uncertain	Normal	Total
Control (N=20)	15	35	50	100
IUD (N=14)	64	36	0	100

Note: p<.01.

Source: F. Alvarez et al., "New insights on the mode of action of intrauterine contraceptive devices in women," *Fertility and Sterility* 49 (1988): 768-773.

controls and in 64 percent of the IUD users. The large and statistically significant differences in the developmental or fertilization status of eggs in oviducts of IUD users again indicate that sperm rarely fertilize eggs in the presence of IUDs.

The relative rarity of detected fertilizations in IUD users in the rhesus monkey study by Hurst et al. (1980) and in the human studies by Alvarez et al. (1988) requires an examination of what happens to spermatozoa after coitus in women using IUDs.

The IUD's Effects on Spermatozoa

Several studies have reported reduced sperm penetration through cervical mucus in the presence of copper, but other investigators have reported only minimal effects of copper on cervical mucus. Inhibition of sperm transport through cervical mucus is also indicated in the case of some steroid-releasing IUDs, but no effect on cervical mucus is considered likely for plastic or stainless steel IUDs.

All types of IUDs increase the number of uterine leukocytes and the amount of degradation products. Sperm may be destroyed through phagocytosis and through cytotoxic effects. Sperm motility and capacitation may be altered by the fluid medium of uterine cavities containing IUDs. In the case of copper IUDs, many studies have shown copper to be spermicidal or cytotoxic (Holland and White, 1988).

Searches for human spermatozoa after coitus have found that they reach the Fallopian tubes well within two hours of insemination, 15 to 30 minutes often sufficing. Phagocytosis of sperm has been observed in a study of the uterine cavity of women using Lippes loops (Sagiroglu, 1971). In that study, sperm were present in the uterus of all IUD subjects observed within 16 hours of insemination, but were not found in IUD subjects observed at any later interval. Searches for the presence of sperm in the oviduct of IUD users have found them absent or, when present, in diminished numbers. The extent to which the diminished number of sperm retain full capacity to fertilize is not known. In women with Copper T IUDs, a large proportion of oviductal sperm had undergone head-tail separation (Ortiz and Croxatto, 1987).

Two studies reported observations on oviductal sperm following tubal surgery within eight hours of insemination (Table 3). Tredway et al. (1975) found no sperm in four IUD users 15-30 minutes post-insemination (study A). In contrast, sperm were detected in the tubes of all six control subjects (p<.005). Aref et al. (1983) performed tubal surgery four to seven hours after

Table 3 Presence or absence of spermatozoa, two studies

Method	Sperm Present (%)	Sperm Absent (%)	N
Study A*			
Control	100	0	6
IUD'	0	100	4
Study B**			
Control	73	23	15
Nonmedicated IUD	40	60	10
Copper IUD	0	100	10

'p<.005, by Fisher's exact test.   **p<.001.

[a] *One copper and three nonmedicated.*
Sources: Study A: D.R. Tredway et al., "Effect of intrauterine devices on sperm transport in the human being: Preliminary report," *American Journal of Obstetrics and Gynecology 123 (1975): 734-735. Study B: I. Aref et al., "Effects of* nonmedicated and copper IUDs on sperm migration," *Contraceptive Delivery Systems 4* (1983): 203-206

coitus. Table 3 (study B) shows a clear gradient in the percentage of women with detectable sperm in the oviducts, from 73 percent in the control group to 40 percent in the nonmedicated IUD group, to zero in the copper IUD group (p<.001). The significant reduction in the number of sperm found in the tubes of IUD users clearly points to a time of IUD action that precedes the entry of the egg, fertilized or not, into the uterus. The data suggest that sperm rarely fertilize ova in IUD users and that the unfertilized ova of Copper T users are destroyed.

Evidence from Studies of Extrauterine Pregnancy

The studies adduced above have been biological or biochemical in nature, dealing for the most part with events or states detectable only by electron microscopy or by highly sensitive assays. One may fruitfully address the question of whether IUDs produce an antifertility effect beyond the uterine level by availing oneself of clues provided in large-scale epidemiological studies of extrauterine (ectopic) pregnancy. The two most comprehensive epidemiological investigations of ectopic pregnancy are the Woman's Health Study in the US (Ory and The Woman's Health Study, 1981) and a World Health Organization (WHO) international case-control study (WHO, 1985). Each study found that IUDs significantly reduce a woman's risk of extrauterine pregnancy as compared with risks to nonusers of contraceptives. The reduction in ectopic pregnancy in the IUD group was of the order of 50 percent in the WHO study and was 60 percent in the US study. The IUDs in these two studies were generally far less effective in reducing the incidence of ectopic pregnancy than are more recent intrauterine devices like the Copper T 380. The Copper T 380 has an incidence of ectopic pregnancy one-third that of the Copper T 200 or Lippes loop, and hence reduces the incidence of ectopic pregnancy by 80 percent or more as compared with nonusers of

contraception. The highly significant findings of the epidemiological studies and the low absolute incidence of ectopic pregnancy in IUD users in cohort studies (Vessey et al., 1976; Sivin and Stern, 1979) leave room for no other interpretation than that IUDs have effects outside the uterus. These effects are not rare, as the sperm and ova studies demonstrate, and constitute the primary mechanisms of action. In surveying the evidence from such studies, the World Health Organization stated: "It is unlikely that the contraceptive efficacy of IUDs results, mainly or exclusively, from their capacity to interfere with implantation; it is more probable that they exert their antifertility effects beyond the uterus and interfere with steps in the reproductive process that take place before the ova reach the uterine cavity" (WHO, 1987:16).

To be sure, if an IUD is left *in situ* after a woman recognizes she is pregnant, the chances that the recognized pregnancy will end in a spontaneous abortion are about 50 percent (Vessey et al., 1976), which are higher than in normal pregnancies (20-27 percent) (Roman and Stevenson, 1983; Casterline, 1989). Even so, the absolute level of observable spontaneous abortion would be about 10 per 1,000 woman-years of IUD use (assuming an average annual failure rate of 2 per 100), well below the comparable figures for women who use no contraceptives, a figure that would vary by age between 40 and 100 per 1,000 woman-years. Twenty percent or more of clinically observable pregnancies in normal women who are not practicing contraception end in spontaneous abortion (Roman and Stevenson, 1983; Casterline, 1989). The IUD-abortion debate, however, has not generally focused on this set of considerations. Rather, it has been confined to events that antedate a woman's recognition of pregnancy.

Summary and Conclusion

No studies show that IUDs destroy developing embryos at rates higher than those found in women who are not using contraceptives. Studies of early pregnancy factors have not shown statistically significant differences in transient levels of hCG between IUD and control groups, a sign of early abortion. The small, careful study by Segal et al. (1985) found no transient rise of hCG in the IUD group. The highly sensitive assay in a larger sample of IUD users, by Wilcox et al. (1985), suggests that an upper limit of only 3 or 4 percent of ovulatory matings with an IUD *in situ* might show transient rises of hCG.

The electron microscopy of Hurst et al. (1980) demonstrated the existence of leukocyte-ridden degenerating embryos in rhesus monkeys fitted with IUDs, but found the same percentage of degenerating embryos in the control group. In this respect, IUDs do no more than nature. The work of Hurst et al. also demonstrates the comparative rarity of fertilized ova in rhesus monkeys fitted with IUDs. Croxatto (1974) and Alvarez et al. (1988) showed that this was also true for humans.

A variety of studies demonstrate that IUD use diminishes both the number of sperm reaching the oviduct and their capacity to fertilize ova. Depending on the type of IUD and the drug dose, sperm are hindered from penetrating cervical mucus, are phagocytized by leukocytes, are incapacitated, with head-tail separation in the presence of copper, and suffer other cytotoxic effects in the IUD-altered uterine fluid. In the oviducts of copper-IUD users, ova are found significantly less frequently than in controls. Ova, similar to sperm, are affected, apparently, by the altered uterine fluid. After insemination in mid-cycle, no eggs of IUD users have shown traces of fertilization in carefully conducted searches of the oviducts. Finally, cohort and case-control studies demonstrate that IUD use reduces the incidence of extrauterine pregnancy. In all these studies, the primary mode of IUD action appears to be interference with fertilization rather than with implantation. The studies thus show that the mechanism of action by which IUDs prevent pregnancy is contraceptive; IUDs are not abortifacients.

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