OBJECTION OF CONSCIENCE, TESTIMONY IN MEDICAL HEALTH PRACTICE: THE CASE OF EMERGENCY CONTRACEPTION (EC)

1. The debate on the abortive effect of levonogestrel used for EC and objection of conscience

I will discuss the scientific and ethical problems of EC, specifically its use for such purpose of Levonogestrel (LNG) also known as the Morning-After Pill (MAP), to exemplify the issue of the objection of conscience in the medical health field. In Chile, the Ministry of Health has decreed that LNG be supplied free of charge at public outpatient clinics to anyone who requests it, including adolescents between the age of 14 and 18, with no permission from, or information to, the parents being required. Women asking for LNG are told that it does not interfere with implantation. Several local governments have refused to distribute this pill arguing that in principle they cannot knowingly supply a drug that might compromise a human life, much less to minors.

In the ethical debate over EC, in addition to the general objections raised by contraception in general, a major additional point arises: its possibly abortive effect. Public debate has focused on the latter issue, especially in Latin America, where abortion is not legal in many countries. Therefore legal issues arise over the approval of the pill. The ethical problems of contraception and abortion are different and arouse different moral sensitivities, although there is a strong ideological connection between them. [1] In this context, there is also the obligation of the health authorities to provide the population with full and clear information on the above effect.

The debate makes sense to those who acknowledge that modern genetics and embryology have shown that the life of a new human being begins at fertilization and that every human being enjoys an irrevocable right to life regardless of the stage of development or progression of cognitive faculties. Latin American culture retains a major degree of sensitivity concerning such issues, and that is why the debate has been and continues to be focused on the scientific evidence of the abortive effect. We do not refer here to the WHO definition of abortion, which leaves the pre-implantatory embryo

unprotected, but to the real and substantive concept of abortion, i.e. *"no word has the power to change the reality of things: procured abortion is the deliberate and direct killing, by whatever means it is carried out, of a human being in the initial phase of his or her existence, extending from conception to birth."* [2]

Initially in Chile, during the trial before the Supreme Court regarding the legality of marketing LNG**,** Chilean Health authorities admitted that one of the possible effects of the pill was to prevent embryo attachment in the uterus, but acknowledged that LNG was not abortive according to the WHO definition. Marketing LNG was prohibited by the Supreme Court in view of the real definition of abortion.[3] From then on, defenders of LNG focused their arguments on the notion that new available scientific evidence denied any anti-implantatory effect; the Supreme Court reversed the prohibition, finding that the problem should be solved by the scientific community.

2. Purpose of emergency contraception

Research into EC has been designed to find drugs that are highly effective in reducing the likelihood of pregnancy following ´potentially fertilizing sexual intercourse'(PFI), [4] [5] [6] usually known as *unprotected intercourse*. Referring to the administration of drugs in such a case by the name of *emergency contraception* introduces language misleading to the public, who usually understand such a term to mean "*preventing conception or fertilization*"[7], whereas such is not the sole object sought. Researchers themselves admit that for highly effective reduction of the likelihood of pregnancy, it is not enough for an EC pill to have a contraceptive effect by blocking either ovulation or fertilization, but that "it should be capable of interfering with a physiological event that occurs after fertilization, during the early embryonic development prior to implantation" [4] (Figure 1). The following should be stressed: the abortive or interceptive effect[*] was not suggested by people contrary to EC but by the same researchers who were explicitly exploring drugs with such effect. This implies that EC was proposed from an ideological position that –although not explicitly

[*]As the authors worked with the WHO concept of abortion, which excludes intentional elimination of the pre-implantatory embryo, they used the term "interceptive effect" to describe de inhibition of implantation.

declaring as much- in fact denied human beings the right to life in the pre-implantation stage.

EC drugs, in contrast with regular contraceptives, are prescribed following PFI. Use of LNG is recommended soon after PFI, in 2 doses of 0.75 mg with a 12-hour interval, or in a single dose of 1.5 mg.

3. Effectiveness of LNG

LNG effectiveness in reducing the probability of pregnancy is higher the earlier it is taken. It is calculated to be about 85% if ingested in the first 72 hours after a PFI, and 60% between 72 and 120 hours. To understand the method used to measure the effectiveness of EC it should be recalled that a woman becomes pregnant only if she has had sexual intercourse during the fertile days of her menstrual period, i.e. five days before and one day after ovulation. Wilcox calculated the probability of pregnancy based on the day of sexual intercourse in relation to ovulation (Figure 2).[8] Others, like Trussell, have made similar calculations.[9] It is thus possible to estimate the expected pregnancies for a specific group of women by multiplying the number of women who had sexual intercourse on a certain fertile day in relation to ovulation, by the estimated probability of pregnancy for that day. EC effectiveness has been calculated by comparing the number of pregnancies observed in groups of women who took LNG with the number of pregnancies expected in the absence of the drug. Effectiveness is equal to 1-O/E, where O = observed pregnancies and E = expected pregnancies. By way of illustration, in one of the studies where LNG was given to 976 women, observed pregnancies totaled 11, whereas calculated expected pregnancies were 75.3. Effectiveness is equal to 1- 11/75.3 = 85%. This means that the probability of clinical pregnancy has diminished by 85% with the use of LNG.

Two important biases affect the above method for calculating effectiveness and have been pointed out in a number of publications:

a. expected pregnancies are calculated in a group of women whose characteristics differ from those of the group that received LNG; and

b. the day of ovulation is estimated from the menstrual cycle. Although only women with regular cycles were accepted in all studies, this form of estimation is known to be inaccurate.

Such methodological limitations for calculating LNG effectiveness preclude having a consistent estimate, and reported figures are deemed to be approximations only.[10] [11] The issue is admitted by researchers: *"Although there is general agreement that emergency contraception protects against unwanted pregnancy, the magnitude of the protective effect continue to be a matter of debate. This debate may well never be concluded because, to settle the question, a randomized trial would have to be conducted comparing pregnancy rates in treated and placebo groups, and this would be unethical"*.[10] Here the term *unethical* does not refer to the possibility of the drug being abortive, but to the fact that a placebo could not be given to women seeking to avoid unwanted pregnancy.

The five major randomized studies, four of them under the direction of, or with the assistance of the *"research group on post-ovulatory methods of fertility regulation,"* of the WHO[12] [13] [14] [15] [16] comparing LNG with other EC drugs, have employed the foregoing method to assess LNG effectiveness.

4. LNG mechanism of action

Three possible mechanisms of action to explain the effectiveness of any EC are recognized by all researchers: inhibiting or disrupting ovulation, interfering with fertilization and inhibiting implantation." [17] [18]

For many years the mechanism of action of EC and especially of LNG was studied very little. Researcher interest focused mainly on improving effectiveness. Interest in studying its effect on implantation emerged because many women rejected its use owing to ethical concerns. WHO mentions the issue: *"Although the treatment regimens used in emergency contraception may simply consist of altered doses of widely available contraceptive pills, women may hesitate to use them because of religious, cultural or other reasons. It is important, therefore, to clarify just how emergency*

contraceptives work so that women can decide if these methods are acceptable to them and can choose between the methods in case their modes of action are different." [18] WHO appears to assume that respect for the life of the pre-implantatory embryo is due primary to cultural or religious reasons.

More is known today concerning the possible mechanisms of action involved, although "the precise mode of action is still indeterminate."[19]

a. **Effect on ovulation.** A number of studies show that LNG administered in the pre-follicular (pre-ovulatory) period may interfere with ovulation. Its effectiveness will depend on proximity in time with the peak of the luteinizing hormone (LH) preceding ovulation. Prior to the LH peak, its effectiveness in causing ovular dysfunction would be about 79%-85%. [20] Various authors have reached similar conclusions.[21] [22] [23] No studies have assessed ovulation blockage in the real life situation where LNG is taken, i.e. after PFSI. The foregoing may be important in actual assessment of blocked ovulation, for sexual activity can influence ovulation[24] and also the circumstances in which it takes places, for instance, in a case of rape.
b. **Effect on spermatozoa.** This mechanism is difficult to study and there are few studies on the subject. [25] [26] [27] There is evidence that the administration of LNG 3 to 10 hours post intercourse increased the viscosity of the cervical mucus, beginning at 9 hours after ingestion, preventing further passage of sperm into the uterus. In vitro, LNG failed to show any effect on the motility of spermatozoa or on their acrosomic reaction. The fact that sperm reaches the tubes a few minutes after sexual intercourse[28] makes it unlikely that this mechanism should play a major role in LNG effectiveness.[4] [29]

5 Effect of LNG on implantation

This has been the most widely debated issue. The studies have different level**s** of evidence that must be clearly distinguished

Preliminary and indirect evidence.

A major portion of the information supplied to the public assuring that LNG does not alter implantation comes from this type of evidence.

a. **Animal studies.** Preclinical studies are an important reference for clinical studies, but cannot be considered evidence. In some cases the effect on humans is not the same as on other species and there is also the difficulty of making the dosage comparable. Indeed, out of five drugs that pass the screen of preclinical tests, only one wins approval for use on humans[30] [31].

b. **Studies of some post fertilization events that could alter implantation.** Possible post- fertilization processes that could be altered by the use of LNG include transport of the zygote through the Fallopian tubes; preimplantation development; endometrial receptivity; sufficiency of the *corpus luteum*; and uterine ability to retain the embryo.[6] Of these physiological events, "*the sole post-fertilization mechanism investigated in women is alteration of endometrial receptivity, an indirect mechanism.*"[6] Initially, several authors found endometrial alterations upon administering LNG before and after ovulation. [32] [33] [34]. Recent studies, using the recommended doses for EC and techniques thought to be more accurate, have found no such alterations.[35] [36] One author has found alterations with higher doses of LNG used for EC and suggests that: "*the surface alterations seen with high doses may not be detected under the influence of recommended doses, but the underlying molecular changes, caused by levonorgestrel, may correspond to the contraceptive effect*".[37] A recent study showed that when LNG was given before the LH peak in women whose ovulation was not inhibited, there was a drop in Glicodeline A, which "*might reflect a reduction of the immuno-suppressive environment at the time of implantation*" and might be an element to alter implantation.[38] Most researchers, however, consider that to date there is no consistent evidence to support alteration of endometrial receptivity. In any event, whether or not alterations are found in the endometrium and its receptivity markers is not decisive evidence in determining the possible effect of LNG on implantation. It must be pointed out also that there are other post-fertilization physiological events that have not been studied.

We believe that the debate has often erroneously focused on expert physiological opinions, animal studies, and indirect studies of endometrial morphology and receptivity. This information is important, but it cannot give a final and precise answer to the question regarding the effect of LNG on implantation in humans. The answer to this question requires an epidemiological study that should compare the probability of pregnancy in randomized clinical trials (RCT) where LNG is administered on certain days of the menstrual cycle when it cannot act on ovulation or sperm. This is the only way to definitively prove an effect of any drug universally accepted.[39] The approval of any drug includes a set of sequential trials to assess the information about effectiveness and safety that is needed to weigh the overall benefit-risk relationship of the drug[40]. It must be said that all the studies in EC have focused on the assessment of the benefit-risk relationship for the women, but not on the safety of the embryo, who derives no benefit from these drugs.

Direct epidemiological evidence.

To date no reliable test for fertilization can detect the presence of a new human being under gestation. This can be done only after the implantation process has begun.[†] As a result, it is not possible to check directly whether LNG reduces the number of embryos implanted. However, substantive information may be acquired by examining LNG effectiveness relative to the day of the cycle when it is taken. Researchers agree that the mechanism of action of LNG is dependent on the period of the cycle when the drug is taken.[4 5 6] If the drug only acts to block ovulation, it would not be effective when taken on days following ovulation. Therefore, to answer the question concerning the effect of LNG on implantation (abortive effect), it is necessary to ***assess the effectiveness of LNG taken on days of the cycle when it is not possible for it to inhibit ovulation***, that is, from 1 day before to 4 or 5 days after ovulation (Figure 1). One way to estimate such effectiveness would be to separate out all the women, from the five studies mentioned above, who received the drug on the day of ovulation or on the days following it, and then estimate the effectiveness of the drug in reducing the probability

[†] Initially, this is done by chemical methods based on chorionic gonadotropin levels, later by clinical signs of pregnancy.

of pregnancy. Information on the day of the cycle when the women received the drug exists, though it is not available through the publications. If these data were made known, such a study might be performed and more powerful and precise information regarding this effect could be obtained. These results will have the methodological limitations discussed above: the lack of a control group and inaccuracy of the day of ovulation. Some authors claim that for those very reasons such a study would be worthless. However, for the same reasons such authors should conclude that the estimations of the effectiveness of LNG would also be worthless, because in all the studies the expected pregnancies were calculated according to the day when sexual intercourse took place in relation to the day of ovulation.

Even though this information is lacking, two facts still strongly suggest that LNG may have an anti implantatory effect.

a. One is the information we have from one of the WHO studies on 243 women who had sexual intercourse one day earlier or one day later than expected ovulation[13]. These women took LNG on a day in the cycle when ovulation could not be inhibited. LNG effectiveness was 88%: 4 pregnancies observed, 33 expected (E = 1-4/33) according to data from this study (Table 1, Figure 3). In addition, it must be considered that 46% of the 243 women took the pill in the first 24 hours after intercourse; 36% between 24 and 48 hours. and 19% between 48 and 72 hours. The only possible explanation for the effectiveness of LNG in these women is inhibition of implantation. It could be argued that some of the effect could be due to action on the viscosity of cervical mucus inhibiting further passage of sperm into the uterus. But this would only be possible if LNG is taken before fertilization has taken place and a few hours after intercourse.

b. The other is that the latest studies mentioned above [14 15 16], including a total of 5800 women, show that LNG continues to be effective, though in a lower percentage, even when taken between 72 and 120 hours after. (Table 2) This makes it highly likely that LNG was taken on days when it is impossible to block ovulation, given that a woman's fertile days are up to 5 days before ovulation.

6. Final ethical considerations

a. From an ethical standpoint, the sole fact that EC is intended to have an "interceptive" or abortive effect, and that there are facts showing that such an effect is likely to exist, makes its use inadmissible for all who respect the life of all human beings. This justifies health providers and decision-makers responsible for the pill being distributed or not in refusing to distribute it on the grounds of objection of conscience.

b. According to the principle of bioethics known as the respect for persons or the principle of autonomy, society should protect human beings unable to exercise autonomy[41]. Referring to persons incapable of consent, the recent UNESCO Universal Declaration on Bioethics and Human Rights[42] states that: "*special protection is to be given to persons who do not have the capacity to consent*" and that "*research should only be carried out for his or her direct health benefit*" (Article 7). And it adds, "*Individuals and groups of special vulnerability should be protected and the personal integrity of such individuals respected.*"(Article 8). This is the case of the human being at this stage of life before implantation. Accordingly, irrespective of the level of evidence available on the abortive effect of LNG, what is scientifically and ethically important is that the human embryo derives no benefit from the use of LNG, that inhibiting implantation was the original intent of the promoters of EC, and that existing epidemiological data show that it does so.

c. Based on the same principle, persons are entitled to full and truthful information in order to make autonomous, justifiable, and conscientious decisions. The public are entitled to know that one of the objects of EC, including LNG, is to obtain an "interceptive" or abortive effect; that there is factual evidence showing that LNG can have such an effect when taken on certain days of the menstrual cycle; and that no published study has consistently rejected this. In the editorial of the August 2006 issue of *Contraception*, James Trussell, one of the main researchers and promoters of Emergency Contraception (EC), writes as follows on the subject: "*To make an informed choice, women must know that ECPs … may prevent pregnancy by delaying or inhibiting ovulation, inhibiting*

fertilization, or inhibiting implantation of a fertilized egg in the endometrium" In another recent paper, he states: *"In the absence of absolute proof about Plan B's mechanisms of action, the right to make personal decisions about whether its use is morally acceptable must be respected and for that reason women should continue to be informed, as they are now in the Plan B labeling, that its use may affect post fertilization events."*[43] Although we disagree profoundly with J. Trussell regarding the respect for life that a human being deserves in the initial stages of development and *in* health-care strategies to reduce teenage pregnancies and so-called "unwanted pregnancies", we cannot but agree on the obligation to provide clear and truthful information on the fact that LNG can alter implantation, which means elimination of a human being.

d. Many say that objections to emergency contraception and respect for life arise only among groups of Roman Catholics motivated by religious reasons. This is not so. Respect for the life of an innocent human being is one of the fundamental human rights. What is true is that such respect acquires a new dimension in the perspective of the Sacred Scriptures. As Pope Benedict XVI has said*: "the love of God makes no difference between the newly-conceived infant still in the mother's womb and the child, the youth, the adult, and the elderly. God makes no distinction among them because he sees in each an impression of His image and likeness (Gn 1:26) He makes no distinctions because reflected in all human beings He perceives the traits of his only-begotten Son, in whom He chose us for his children ". . . before the foundation of the world . . . in love he destined us for adoption to himself. . . in accord with the favour of his will" (Eph 1: 4-6)."* [44]

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[2] EV 58

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