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How to Meet the Needs of Women in Search of "Safe" (No Harm) Contraception and Birth Control

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Abstract

On the background of harm associated with a device for permanent contraception, which had been declared as "safe" by the US Food and Drug Administration (FDA) but had caused severe threats to the health of thousands of women worldwide, the paper discusses the problem of trustworthiness of information provided by health agencies with regard to safety of contraception. The aim of the research paper is to open new avenues for women in search of suitable contraceptive methods by providing them with information necessary for identifying the safest methods.

1. Introduction

As recent clinical experience shows, a growing number of women considers safety as the most important parameter when they choose a personally suitable method for contraception and birth control. Even those women who place highest priority on efficacy consider safety as equally important [1].

The quest for safety seems understandable if one keeps in mind not only the ancient principle of medical practice advocating avoidance of harm ("nil nocere") but also recent events that have shaken the arguments of those health agencies and researchers who pleaded that methods of contraception are safe, including the methods of Long-Acting Reversible Contraception (ARC), ie, implants and diaphragms: "All adolescent and adult women should be informed about the availability of LARC methods, given their extremely high effectiveness, safety, and high rate of continuation" [2].

Despite these affirmations underlining the safety of contraceptive methods, published in 2017, the clinical reality of subsequent years presented a different scenario. The damage done to tens of thousands of women worldwide has convinced researchers as

well as practitioners that contraception is far less safe than commonly assumed. The following discussion describes first, how the US FDA failed to accomplish its mission as an instrument of pharmacovigilance; second, the arguments in favor of natural methods, which are commonly regarded as the safest methods; third the futile attempts of the most influential health agencies to provide accurate information in the form of ratings and rankings.

2. Method and Material

The method implemented is a critical analysis which analyses documents published by the FDA, by the World Health Organization (WHO), by other influential health agencies, and by market-leading pharmaceutical companies.

3. Results

The primordial result of the research article is the finding that information on contraception and birth control provided by pharmaceutical companies and by the most influential health agencies is unreliable. Documents provided by manufacturers for the users of their products frequently are inadequate, and adverse events caused by them are not reported to agents of pharmacovigilance. Moreover, documents disseminated by health agencies fail to furnish accurate information and are at times adulterated by misleading data. Women should be enabled therefore to gain access to publications that contain reliable and accurate information on the most salient parameters of contraceptive methods, namely, safety, efficacy, mechanism of action, satisfaction, and convenience. This information should be subjected to ongoing revisions so that new insight is conveyed instantaneously to the consumers. The most appropriate way of presenting this information are succinct synoptic overviews in the form of ratings and rankings. This author proposes the Contraception Safety-Efficacy-Satisfaction-Convenience Ranking (TABLE 1) which should prove helpful not only for the clinical practice but also for women implementing autodidactic strategies.

TABLE 1. **Contraception Safety - Efficacy - Satisfaction - Convenience Ranking.**

Method	**Efficacy (% of pregnancies per 100 women per year) Optimal use/Negligent use**	**Safety (no harm)** **Adverse events, possible risks and complications**	**Satisfaction/ Convenience**	**Mechanism of action**
SAFEST (no harm) METHODS OF CONTRACEPTION				
Symptothermal	0.4%/24% (CT Failure table)	High safety. No adverse events, risks, or complications. No protection from sexually transmitted diseases.	47%/ High	1. Measuring of body temperature, 2. Observation of cervical mucus (clear texture) 3. Palpation of cervix (soft consistency and opening). 4. Observatons of symptoms such as

				breast tenderness and mittelschmerz.
Lactational Amenorrhea (LAM)	0.9%/2% (WHO 2020)	High safety. No adverse events, risks, or complications. No protection from sexually transmitted diseases.	?/ High	Effective as long as monthly bleeding has not yet returned. Requires exclusive breastfeeding day and night of infant less than 6 months old.
Basal Body Temperature (BBT)	1%/25% (WHO 2017)	High safety. No adverse events, risks, or complications. No protection from sexually transmitted diseases.	? High convenience	Fertile phase has passed when body temperature has risen (0.2°C-0.5°C) and remained such for 3 days. Conception is unlikely from 4th day following rise of temperature until next menstruation.
Male condoms	2%/18%	Modest safety. Possibility of allergic reaction due to material (latex, polyurethane, polyisoprene, or lamb intestine).	43% Moderate	Protects against sexually transmitted diseases (STD) including HIV.
TwoDay	4%/14% (WHO 2017)	High safety. No adverse events, risks, or complications. No protection from sexually transmitted diseases.	47%/ High	Coitus is avoided during fertile days. Fertile phase is tracked by observing presence of cervical mucus (color and consistency). Unprotected coitus may resume after 2 consecutive dry days or absence of secretion.
Standard Days (SDM)	5%/24% (CT Failure table)	High safety. No adverse events, risks, or complications.	47% High	Fertile period is tracked and coitus avoided (usually

		No protection from sexually transmitted diseases.		days 8-19 of each 26-32 day cycle).
Withdrawal	4%/22% (CT Failure table)	Moderate safety. No protection from sexually transmitted diseases	46% High	The withdrawal method of contraception (coitus interruptus) is the practice of withdrawing the penis from the vagina and away from a woman's external genitals before ejaculation to prevent pregnancy. Timing of withdrawal is difficult. Risk of ejaculation inside vagina. Possibility of sperms entering the vagina. Pre-ejaculation fluid may contain sperms. “Pull out” may be incorrectly timed.
Calendar (rhythm)	9%/25% (WHO 2017)	High safety. No adverse events, risks, or complications. No protection from sexually transmitted diseases.	?/ High	Monitor pattern of menstrual cycle over at least 6 months. Subtract 18 from shortest cycle (this is the estimated first fertile day) and 11 from longest (this is the estimated last fertile day). Caution when drugs are used (anxiolytic, antidepressant, NSAID, or certain antibiotics).

Female condom	5%/21% (CT Failure table)	Modest safety. Possibility of allergic reaction due to material (polyurethane, natural rubber, or synthetic rubber). Difficult placement in case of vaginal prolapse or other pelvic floor dysfunctions.	41%/ Moderate	Female condom is a soft, loosely fitting pouch inserted into vagina before coitus. It forms a barrier to prevent contact between sperm and egg. Protects against sexually transmitted diseases (STD) including HIV.
MOST EFFECTIVE METHODS OF CONTRACEPTION				
Implants	0.05%/ 0,05% (CT Failure table)	Modest safety. Menstrual changes, mood swings or depressed mood, weight gain, headache, acne. (FDA 2021) Irregular vaginal bleeding. Possibility of breakage and/or migration to pulmonary artery. Contains hormone (progestogen)	84% Modest convenience. Necessity of intervention by physician	Implants are small, flexible rods or capsules placed under the skin of the upper arm; contain progestogen hormone. Inhibit ovulation. Progestogens (progestagens or gestagens) are a class of steroid hormones which bind to the progesterone receptor. Progestogens inhibit ovulation. Progestogens, are a class of steroid hormones that bind to and activate the progesterone receptor.
Male sterilization (Vasectomy)	0.10%/ 0.15% (CT Failure table) >1 after 3-months semen evaluation. 2-3% without semen evaluation. (WHO 2016)	Low safety. Necessity of surgical intervention.	100%/ Low	Permanent contraception by cutting vas deferens. Two main methods: 1. Incisional (one or two incisions of 1-2 cm length) 2.

				No-scalpel technique (encircling and securing the vas using special fixation clamps).
Female sterilization (Tubal ligation)	0.5%/ 0.5% (CT Failure table) >99%	Low safety. Risk of major surgical complications (injury to bladder, bowels, or blood vessels) is low. Risk of death with laparoscopy is 1 in 12,000. The risk of bowel damage is 0.4 in 1000 cases and major blood vessel damage is 0.2 in 1000 cases necessitating laparotomy. Risk of death with laparoscopy is 1 in 12,000. Risk of complications is increased by previous abdominal pelvic surgery, or previous pelvic inflammatory disease or obesity. Long-term complications: post-tubal ligation syndrome, regret and reversal.	100%/ Low (surgical intervention)	Surgical intervention or chemical treatment (Quinacrine is the best studied chemical agent) The technique involves blind intrauterine insertion of Quinacrine pellets through a modified intrauterine inserter.
Combined oral contraceptives (COCs) “the pill”	0.3%/ 9% (CT Failure table)	Moderate safety. Risk of thromboembolism. Spotting/, bleeding between periods. Nausea. Breast tenderness. Headache.	67% Moderate convenience.	Prevent ovulation (release of egg from the ovaries). Contain estrogen and progestogen.
Emergency Contraception (ulipristal acetate 30 mg or	<1 for ulipristal acetate Emergency Contraceptive Pills (ECPs)	Modest safety. Ulipristal acetate: Headache, nausea, abdominal pain, tiredness, dizziness (FDA 2021) Levonorgestrel: menstrual changes, headache, nausea,	?/ High convenience	Pills to be taken twice to prevent pregnancy up to 5 days after coitus.

levonorgestrel 1.5 mg)	1 for progestin only ECPs 2 for combined estrogen and Progestin ECPs (WHO 2020) <1 for ulipristal acetate ECPs 1 for progestin only ECPs 2 for combined estrogen and progestin ECPs	dizziness, vomiting, breast pain, tiredness, lower stomach (abdominal) pain. (FDA 2021)		
Contraceptive transdermal patch	0.3%/ 9%% (CT Failure table)	Moderate safety. Spotting/ bleeding between periods Nausea Breast tenderness Headache.	67%/ Moderate. Transdermal patch to be placed on the skin contains the hormones estrogen and progestin.	New patch should be used for 3 weeks (total of 21 days) weeks. Do not use a patch during the 4th week. Prevents ovulation. Releases both estrogen and progestin. (Progestin is a synthetic progestogen. Progestogens are commonly used in hormonal contraception and in menopausal therapy) Pharmacokinetic profile comparable to combined orla contraeptives (COCs).
Contraceptive vaginal ring (CVR)	0.3%/9% (CT Failure table)	Moderate safety. Vaginal discharge Discomfort in the vagina and	67% Moderate convenience. Contains the hormones estrogen and progesterone which are	Vaginal ring is a flexible latex-free plastic ring to be inserted into the vagina. Ring should be kept in vagina for 3 weeks and then taken out for

		irritation. Headache. Mood changes. Nausea. Breast tenderness. .	released over a period of three weeks.	one week Ring can be placed into the vagina without assistance. Put the ring into the vagina yourself. Keep the ring in your vagina for 3 weeks and then take it out for one week.
Progestogen-only pills (POPs) or "the minipill" (Norethindrone)	0.3%/ 7% (WHO 2020)	Moderate safety. Spotting/, bleeding between periods. Nausea. Breast tenderness. Headache.	67% Low convenience. The dose in a minipill is lower than the progestin dose in a combination pill To be taken daily at the same time.	Contains only progestogen, no estrogen. Thickens cervical mucus to block sperms. Prevents ovulation.
Monthly injectables or combined injectable contraceptives (CIC)	0.05%/ 3% (WHO 2020)	Moderate safety.	? Moderate	Monthly injection of combined formulations containing both an estrogen and a progestin Prevents ovulation (release of egg form the ovaries).
Progestogen-only injectables containing medroxyprogesterone acetate (Depo-Provera) Or norethisterone enantate	0.2%/ 4% (WHO 2020)	Moderate Loss of bone density, irregular bleeding, bleeding between periods, headache, weight gain, nervousness, dizziness, abdominal discomfort (FDA 2021) Irregular vaginal bleeding; delayed return to fertility after use.	?/ Moderate Contains hormone progestine (medroxyprogesterone acetate). Injection is given every 3 months	Injections containing only progestogen (depot medroxyprogesterone acetate or norethisterone enantate) are given once every two to three months (Instead of once a month as in case of

				combined injectables). Contraceptive injection contains the hormone progestin (medroxyprogesterone acetate in Depoprovera) Suppresses ovulation.
Intrauterine contraceptives (IUD) – levonorgestrel (Mirena)	0.2% 0.2% (CT Failure table)	Low safety. Irregular bleeding, no periods (amenorrhea), abdominal, /pelvic pain. (FDA 2021) Risk of pelvic inflammatory disease (PID) and expulsion. Pelvic inflammatory disease (PID)	80%/ Low	T-shaped device inserted into uterus. Release of levonorgestrel. Thickens cervical mucus and prevents contact between sperm and egg. .
Intrauterine device (IUD) containing copper (ParaGard)	0.6%/ 0.8% (CT Failure table)	Low safety. Heavier, longer periods Spotting between periods (FDA 2021).	78%/ Low (Amenorrhea)	Copper containing intrauterine device is known also as intrauterine coil. Can be used also as emergency contraception within five days of coitus. Can be left in place for up to 12 years. Copper component damages sperms

Diaphragm (with spermicide)	6%/12% (CT Failure table)	Moderate Irritation, allergic reaction, urinary tract infection. (FDA 2021)	57% Moderate	Prevents sperms from entering the uterus. Small, reusable rubber or silicone cup with a flexible rim that covers the cervix. Before coitus the diaphragm is inserted deep into the vagina so that part of the rim fits snugly behind the pubic bone. The diaphragm is effective at preventing pregnancy only when used with spermicide. (Mayo Clinic)

4. Discussion

4.1 Failure by the US FDA to accomplish its mission with respect to Pharmacovigilance

Recently, a "safe" device for permanent contraception, -- a nickel coil to be implanted into the fallopian tubes – proved to be a threat to the health of thousands of women worldwide. Approved by the FDA as safe in 2002, it was withdrawn from the market by the manufacturer in 2020. According to press reports the manufacturer went so far as to pay $ 1,6 billion alone in the US for settling claims due to health complications caused by its product: "Bayer said it will pay $ 1,6 billion to settle claims that its birth control device Essure causes serious health complications, the latest in a string of settlements by the German company" [3].

One of the most alarming aspects in the history of this troublesome device was the failure of the US FDA to accomplish its mission as an agent of pharmacovigilance. When the FDA -- after a long period of inactivity -- finally restricted the sale of the device, thousands of women worldwide had already experienced harm and the Australian equivalent of the US FDA, the Australian Therapeutic Goods Agency (TGA) had already withdrawn the device from the market [4]. On August 13, 2018, the Australian Guardian reported about adverse events such as nickel poisoning and about the reaction of the Therapeutic Goods Administration (TGA): "The Australian Register of Therapeutic Goods entry will be cancelled and there will be no further implantations of Essure in Australia, the TGA said" [4]. According to press reports, the device was the subject of about 16000 lawsuits in the US, and Australian women had been urged to join a class action against the manufacturer of the device "that left tens of thousands of patients worldwide with perforations, nickel poisoning and chronic pain" [4].

If an attempt is made to identify those who are responsible for the harm caused by the device, the manufacturer of the product appears as the primary culprit, followed by the US FDA. According to press reports, the manufacturer failed to report complaints lodged by women who had experienced harm after using the device: “Bayer failed to report thousands of complaints of injuries allegedly caused by its Essure contraception device, according to newly unsealed documents” [5]. In an attempt to excuse the FDA the unconvincing argument had been formulated that the FDA was not in a position to recognize the need for updating warnings, so that the entire blame could be put on the manufacturer: “It was Bayer’s failure to comply with its reporting obligations that made it impossible for FDA to know that updates to Essure’s warnings were needed, the attorney, Fidelma Fitzpatrick, said in the filing” [5].

Besides the damages to the health of women, the economic drawbacks for the manufacturer were a topic of press reports. The most tragic blame concerned fetal deaths: “The U.S. Food and Drug Administration may have greatly underestimated the number of fetal deaths among women who became pregnant after using Bayer AG’s Essure contraceptive device” [6]. In 2018 the press reported that the manufacturer was required to implement the restrictions imposed by the FDA and drew attention to the significant drop in sales subsequent to the FDA’s order to conduct a post-marketing study. The actions taken by the FDA appear particularly inefficient if one bears in mind that the US was the last country where the sales of Essure were halted. “The United States is the last country where Essure is being sold. Last September, citing "commercial reasons,” Bayer announced it was ending sales outside the United States” [7].

An additional criticism emphasized that an inadequate study was the basis for the FDA’ s decision to approve the device and blamed the FDA for procrastinating: “Some Essure opponents have long been critical of the FDA, saying it approved the device based on an inadequate study and should have moved more aggressively as safety concerns emerged” [7]. In light of the FDA’s failure as an agent of pharmacovigilance, it is understandable that specific criticism had been voiced concerning the inappropriate and delayed action by the FDA: "The FDA should have required a moratorium on sales and requested that new data be submitted in a much timelier fashion," said Diana Zuckerman, president of the National Center for Health Research, a nonprofit think tank” [7].

The harm afflicted to women worldwide and the economic damages experienced by the manufacturer make it clear that safety of contraception and birth control is an ongoing issue -- contrary to the claims advanced by some researchers and by health agencies. Women should therefore be continuously assisted in their quest for safe birth control methods, and these methods should be the object of intensified research.

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4.2 The safest methods of contraception and their endocrinological foundation

Originally designated as “natural family planning” [8] or “periodic abstinence” [9] four methods, (calendar, temperature, cervical mucus or Billings, and symptothermal) have been subsumed under a new taxonomy and are now known as Fertility Awareness-Based Methods, encompassing the symptothermal, the cervical mucus, the Two-day method, and the Standard Days method. These methods can be classified more appropriately under the heading “natural methods of contraception,” as they contain no hormones or copper in contrast to hormonal methods or copper-containing diaphragms. They are commonly regarded as the safest of all methods causing no adverse events, risk or complications.

Proponents of these methods emphasize the absence of any interference with the physiologically occurring hormonal changes during the menstrual cycle [10]. The terminology used by most proponents is “natural conception monitoring” (natürliche Empfängnisregelung = NER). In the European medical popularizing literature, an increasing number of women enthusiastically recommend these methods. Their recommendations are based on the authors’ own sufferings of many years from hormonal contraception [11]. In fact, proponents of the natural methods are able to prove that these methods are based on physiological processes and do not interfere with the secretion of the two main hormones of the female cycle, i.e., estrogens and progesterone. The two principal biologically active estrogens in non-pregnant women are estradiol (E2) and estrone (E1), while the third bioactive estrogen is estriol (E3) which plays no major role in non-pregnant women or in men [12]. Progesterone (P4) is an endogenous steroid and belongs to a group of steroid hormones called progestogens [FIG. 1.] Progestogens play a role in the menstrual cycle, pregnancy, and embryogenesis [13].

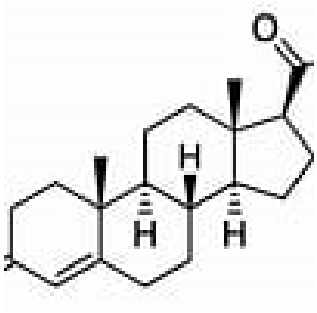

FIG. 1. **Progsterone Structural Formular**.

Chemical formula: $C_{21}H_{30}O_2$, log P: 4.04; Melting point: 126; Molar mass: 314.469 g/mol [13].

Serum progesterone indicates whether ovulation has occurred. It is used to assess infertility, to evaluate abnormal uterine bleeding, or to determine the placental health in high-risk pregnancies [14]. Secretion of progesterone and estradiol is of fundamental importance for the natural methods whose primary target is the identification of the fertile days during which sexual intercourse should be avoided - or a barrier method used. The organs affected by the hormonal changes are the ovaries, the uterus, the cervix, and breast tissue.

The central event in the female cycle is process of ovulation. Ovulation occurs around the 14th day of the cycle and initiates the fertile phase. At this point in time, the serum estradiol reaches as maximal concentration of 150 to 500 pg/ml and leads to a massive release of Luteinizing Hormone (LH) by the adenohypophysis, the so-called LH-peak [8]. “At about the 14th day of the cycle, the distended follicle ruptures, and the ovum is extruded into the abdominal cavity. This is the process of ovulation” [15]. The endocrinological processes during ovulation are at the heart of research on ovulation induction, as for example in fertility treatments for women with polycystic ovary syndrome [16]. The processes following ovulation seem to be well understood after rupturing the follicle is filled with blood and is therefore designated as corpus rubrum [8] or as corpus hemorrhagicum [15].

What is important for natural methods of contraception is the phenomenon of peritoneal irritation and fleeting pain felt in the lower abdominal cavity: “Minor bleeding from the follicle into the abdominal cavity may cause peritoneal irritation and fleeting

lower abdominal pain ("mittelschmerz")" [15]. The German word "Mittelschmerz" is explained as an "irritation" of the peritoneum, but the details of this irritation have not yet been described adequately [17]. This sensation of pain is an important signal for women indicating that ovulation has occurred, and that the ovum is prepared to undergo fertilization. For one of the non-hormonal options, the so-called symptothermal method, the abdominal pain is considered an important symptom -- similar to breast tenderness -- that should be closely observed by women and the observation documented in a so-called cycle-sheet [8]. Women experiencing the fleeting pain in the lower abdominal cavity can infer that they enter the luteal phase of the menstrual cycle, during which estrogens and progesterone are secreted. This is due to proliferation of the granulosa and theca cells and replacement of the clotted blood with yellowish luteal cells rich in lipid designated as corpus luteum [15]. The gradual disappearance of blood leads to a white coloured structure, the corpus albicans [8]. According to the processes during the first phase of the menstrual cycle, commonly used nomenclatures are "proliferative," "preovulatory" or "follicular."

The pivotal processes leading to ovulation in the ovaries are paralleled by processes in other organs. Thus, the uterus is undergoing a steady increase in thickness due to estrogens and a concomitant lengthening of the uterine glands: "Under the influence of estrogens from the developing follicle, the endometrium increases rapidly in thickness from the 5^{th} to the 14^{th} days of the menstrual cycle. As the thickness increases, the uterine glands are drawn out so that they lengthen" [15]. Changes in the endometrium during the second phase, the secretory or luteal phase, include vascularization and secretion of the glands which now appear coiled and tortuous. Cyclic changes in the uterine cervix affect primarily the cervical mucus, and these changes have become the object of intensified research. The most notable changes concern the amount, the consistency, and the elasticity, called "spinnbarkeit" of the cervical mucus caused either by estrogen or by progesterone: "The mucosa of the uterine cervix does not undergo cyclic desquamation, but there are regular changes in the cervical mucus. Estrogen makes the mucus thinner and more alkaline, changes that promote the survival and transport of sperm. Progesterone makes it thick, tenacious, and cellular. The mucus is thinnest at the time of ovulation, and its elasticity, or spinnbarkeit, increases so that by mid-cycle, a drop can be stretched into a long, thin thread" [15]. Besides the "spinnbarkeit," the fern pattern due to high levels of estrogen just before ovulation, are an important symptom. Ferning is due to the presence of sodium chloride in mucus. "Just before ovulation, the cervical mucus forms fern-like patterns due to crystallization of sodium chloride on mucus fibers" [18].

Changes in cervical mucus have become not only the object of extensive research but they are still pivotal in one of the natural non-hormonal methods, the so-called Billings ovulation method (BOM), which has been characterized also as "a medical model of a natural procreation education method" [19]. While changes in cervical mucus have been investigated extensively, changes in the vaginal cycle seemed of minor importance.

These changes concern the epithelium, which appears as "cornified" under the influence of estrogen and infiltrated with leukocytes under the influence of progesterone. "Under the influence of estrogen, the vaginal epithelium becomes cornified, and cornified epithelial cells can be identified in the vaginal smear. Under the influence of progesterone, a thick mucus is secreted, and the epithelium proliferates and becomes infiltrated with leukocytes" [15].

Cyclic changes in the breasts are characterized by proliferation of the mammary ducts due to estrogens and growth of lobules as well as alveoli due to progesterone. It is important for contraceptive purposes to note that these changes -- felt as swelling, tenderness and pain-- occur during the 10 days preceding ovulation. "The breast swelling, tenderness, and pain experienced by

many women during the 10 days preceding menstruation are probably due to distention of the ducts, hyperemia, and edema of the interstitial tissue of the breast. All these changes regress, along with the symptoms, during menstruation" [15].

In describing the menstrual cycle endocrinological research has also highlighted indicators of ovulation, namely endometrial changes and cellular cervical mucus. The most important of these indicators seem to be the rise in basal body temperature. "A convenient and reasonably reliable indicator of the time of ovulation is a change -- usually a rise -- in the basal body temperature" [15].

As can be seen from the description of endocrinological processes, ovulation in the ovaries and concomitant changes in other organs are the focus of research. In addition, the phenomenon of fluctuations in basal body temperature deserves special attention because it is due to the thermogenic effect of progesterone. As regards the effects of progesterone it is important to bear in mind that it has also a stimulatory effect on respiration. The former effect is the basis for the so-called "Two-day" method of contraception [20]; the latter effect is at the heart of research considering respiratory changes as indicators for fertility [21].

As can be seen, the natural methods of contraception are based on sound endocrinological research. What is needed for wide-spread use of these methods are reliable studies on the efficacy of each one of them. At this moment there are considerable discrepancies in estimates for perfect (or better "optimal") use as well as for typical (or better "negligent") use.

As a consequence of statistical lacunae, ratings and rankings of these methods remain controversial. However, estimates are a crux also for other methods, as can be seen from the various rating and rankings proposed by high-impact research and by the most influential health organizations.

4.3 Omen misled by ratings and rankings disseminated by the most influential health agencies

Historically, rankings can be traced back to the past century. In 1982 one of the leading medical journals published a ranking entitled "Relative effectiveness of frequently used contraceptive methods" [22]. At the time of this ranking vasectomy was considered the most effective with an estimate of 0.02 (Failures per 100 Woman-Years). Vasectomy was followed by tubal ligation and similar procedures (0.13), by oral contraceptives (0.32 to 1.2), IUDs (Loop D: 1.3 and Copper: 1.5), diaphragm (1.9), Condom (3.6), Withdrawal (6.7), Spermicide (11.9), and rhythm (15.5). The most fatal error in this archetypal ranking was the use of the term "rhythm" which gave rise to numerous misinterpretations, and only few institutions such as the Mayo Clinic clarified the confusion by identifying the "rhythm" method as the "calendar" method [23].

More recently, in 2013 appeared a ranking entitled "Food and Drug Administration (FDA) Approved Methods of Birth Control" [24] which was replaced by a revised version in 2021 entitled "Birth Control Chart" [25] In the ranking of 2013, percentages are indicated for "number of women out of 100 who will not get pregnant", and the usual distinction is made between "perfect" and "typical" use. According to this FDA ranking, several methods achieve more than 99% for both perfect and typical use, namely Sterilization Surgery for Women, Surgical Sterilization Implant for Women, Sterilization Surgery for Men, Implantable Rod, and IUD. These methods are rated as equally effective in both perfect and typical use and are ranked higher than those whose typical use estimates are inferior to their perfect use estimates, namely:

Shot/Injection >99% perfect use (91% typical use)
Oral Contraceptives (Combined pill: “The Pill”) >99% perfect use (91% typical use)
Oral Contraceptives (Progestin-only: “The Pill”) >99% perfect use (91% typical use)
Oral Contraceptives (Extended/Continuous use: “The Pill “) >99% perfect use (91% typical use)
Patch >99 perfect use (91% typical use)
Vaginal Contraceptive Ring >99 perfect use (91% typical use)

Among the less effective methods, according to the FDA, are Male Condom (98% perfect use and 82% typical use); Diaphragm with Spermicide (94% perfect use and 88% typical use); Sponge with Spermicide (80%-91% perfect use and 76%-88% typical use); Cervical Cap with Spermicide (74% perfect use and 60% typical use); Female Condom (95% perfect use and 79% typical use); Spermicide (82% perfect use and 72% typical use). Special attention in the FDA survey is paid to Emergency Contraception (85%) which -- it is warned -- should not be used as a regular form of birth control and which must be implemented within 70 to 120 hours of unprotected coitus.

The warning not to use Emergency Contraception as a regular form of birth control is unjustified in the opinion of this author who claims on grounds of precision medicine that women whose sexual activity is limited to one or even fewer cohabitations per month can implement this method instead of administering a contraceptive pill every day. Rectification of this warning should be applied also to one of the most exhaustive studies on Emergency Contraception published in 2017 [26].

In assessing the accuracy of the FDA publications reference must be made to the publications by the WHO. In 2017 appeared a rating of contraceptive methods entitled “World Health Organization (WHO): Contraceptive Methods” [27]. This publication was followed in 2020 by a rating entitled “Family planning/contraception methods” [28].

In a comparison of the FDA ranking of 2013 with the WHO rating of 2017 noteworthy differences appear. While the WHO rating considers combined patch and vaginal ring as more effective than combined oral contraceptives, the FDA ranking does not mention this combined method but provides data on each one of them separately, namely

Patch >99 perfect use (91% typical use)

Vaginal Contraceptive Ring >99 perfect (91% typical use). Another noteworthy disparity pertains to Emergency Contraception. While the WHO rating considers it as one of the most effective methods with an estimate of 99%, the FDA ranking considers it as one of the least effective, with an estimate of 85% for perfect use.

The most striking difference pertains to those methods that are described in the WHO rating as Standard Days, Basal Body Temperature (BBT), TwoDay, Symptothermal, Calendar, and Withdrawal. These methods are absent in the FDA ranking. Although one might argue that these methods do not involve drugs and are therefore not a topic for approval by the FDA the bioethical principle of “informed consent“ requires completeness of information to assure self-decision of each women [28]. The omission of several methods in the FDA ranking is the more surprising as it indicates as its source Contraceptive Technology (2011) where these methods are listed and one of them (the symptothermal) considered as one of the most effective

methods due to a perfect use estimate of 0.4%. [20] Despite serious shortcomings in its ranking credit must be given to the FDA for drawing attention to the safest of all methods, namely abstinence.

Concerning the WHO ratings, it should be noted that the latest ratings of 2020 are inferior to the first rating of 2017. While the latter contains at least sporadic information on adverse events, the latest rating of 2020 does not. The only improvement in the latest rating is the elimination of the dichotomy between modern and traditional methods. This distinction seems irrelevant for most women because their interest lies not in historical facts but in safety, efficacy, satisfaction, and convenience.

One of the most deficient classifications are those proposed by the Center for Disease Control in 2017 [29]. In a "Classifications for Fertility Awareness-Based Methods" a dichotomy is made between "symptoms-based" and "calendar-based" methods. Unfortunately, no further information is provided about the methods belonging to each one of these two categories. These "classifications" not only contradict the taxonomies commonly used in the international literature; it also annihilates the results of research on the distinctive features of each one of the methods in question. In fact, there are no methods that are exclusively based on symptoms or on the calendar. All the fertility awareness-based methods rely on both calendar and symptoms. Logically, the fertile days of the menstrual cycle cannot be identified without a calendar or without observing the symptoms appearing as physiological processes during the female cycle. In sum the classifications proposed be the CDC enhance confusion rather than clarity and should be considered as a redundant tautological neologism unsuited for women and practitioners in search of comprehensible information.

The CDC's inability to provide reliable information is conspicuous not only in the 2017 publication but also in a previous one of 2014 [30]. In this publication, entitled "Effectiveness of Family Planning Methods" methods are ranked from the most effective to the least effective, and the fertility awareness-based methods are ranked among the least effective owing to a typical use estimate of 24%. This percentage had been erroneously applied to all of the family planning methods, and no attempt had been made to clearly distinguish each one of the four methods -- as is common in the international literature. Above all, this ranking contradicts some of the most reliable ratings such as the Contraceptive Technology Contraceptive Failure Table (CT Failure table) [20]. The latter indicates a perfect use estimate of 0.4% for one of these methods, is, the symptothermal method, and this estimate is confirmed also by international research which indicates a Pearl- Index of 0.8 [8]. It is incorrect therefore to rank methods with a perfect use estimate of 0.4% or a Pearl Index of 0.8 among the least effective. Rather, such estimates are indicative of the most effective methods.

As can be seen, rankings and ratings proposed hitherto are inadequate for identifying the safest methods and their mechanism of action. The ranking proposed by this author includes this information and heeds insights gained in urogynecological research. It is based on rankings by the WHO, the FDA, Contraceptive Technology, and pertinent research articles [32-34].

5. Conclusions and Implications

As the case of the intratubal implant for permanent contraception shows, the promises of pharmaceutical companies regarding safety are not always trustworthy, and agents of pharmacovigilance, such as the FDA, fail to accomplish their mission. Women are left out in the cold in their search for accurate and reliable information on the safety of contraceptive methods. In this quest,

ratings and rankings proposed by reliable sources, such as the Contraception Safety-Efficacy-Satisfaction-Convenience ranking will prove helpful.

The possibility of identifying safe methods must be seen also from the perspective of the national economy. Methods without adverse events make it possible to avoid costly hospitalizations and medical treatments due to perforations, ectopic pregnancies, thromboembolic events, and other complications causally related to hormonal contraception. It seems desirable therefore to foster studies on natural contraception, in particular on estimates for optimal and negligent use, on satisfaction and -- last but not least-- on appropriate pedagogical strategies to instruct potential users, especially those in developing countries where the cost factor impedes the use of hormonal and other "artificial" methods.

6. Conflict of Interest

The author declares no conflict of interest

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