

Current Medical Research

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Natural Family Planning

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SUPPLEMENT

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NFP Utilization US 1990 - Update. Linda Peterson, National Center for Health Statistics, Hyattsville, Maryland, Personal Communication.

Total contraceptive usage as shown in the 1990 interviews for women aged 15-44 was 59.2%. Of these, Natural Family Planning users actually comprised 2.7%: 2.3% calendar rhythm, 0.37% OM-ST. Other components of the universe included 17.5% women who were sterilized, 5% who were sterile after surgery for non-contraceptive indications, 9% virgins, 8% sexually active but using no contraception. The rest were either pregnant, seeking pregnancy or shortly post-partum. We look forward to the publication of the report in a future issue of *Advance Data*.

Prospective European Multi-center Study of Natural Family Planning (1989-1992): Interim Results. [Part of the results were presented at the VIII Annual Meeting of the Society for the Advancement of Contraception, Barcelona, Spain, October 28-31, 1992]. The European Natural Family Planning Study Center, G. Freundl. *Advances in Contraception* 9 (December 1993):269-283.

A European multi-center prospective study of Natural Family Planning was begun in 1989. Sympto-thermal method providers from 14 centers in Austria, Belgium, Netherlands, France, Germany, Great Britain, Ireland, Italy, Spain, and Switzerland participated. Different clinical indicators and combinations were used: basal body temperature, cervical mucus calculations, cyclical cervical changes in various combinations. Group I used NFP only for

4,277 cycles to avoid pregnancy, while Group II - Fertility Awareness/Mix used 5,007 cycles. Barrier methods or coitus interruptus methods were used at least in some cycles.

Table of Results

Key: UIP = Unintended Pregnancies

PI = Pearl Index

Group/Method	UIP	Cycles	PI
A: Sympto-thermal, double check	15	7,404	2.4
B: muco-thermal	12	1,352	10.6
C: muco-thermal	1	434	*
D: mucus method only	1	70	1*

* Number too small to calculate Pearl Index.

Group B used the mucus to indicate the beginning of the fertile phase and the BBT shift for the ending, while Group C used mucus to detect the beginning of the fertile phase and mucus and BBT changes to determine the end of the fertile phase.

[Groups C & D will probably be dropped from the final report. Personal communication, G. Freundl. Ed.]

A New Diagnostic Aid for Natural Family Planning. M. Barbato, et al. *Advances in Contraception* 9 (December 1993): 335-340.

An interim report of the use effectiveness of ferning of saliva as a diagnostic aide for natural family planning found that 28 of 32 cycles had good correlation between salivary ferning, cervical mucus, and BBT. The PB/53 device was used, which consists of a slide and a pocket microscope. Saliva is placed on the slide, allowed to dry, and

inspected for the presence or absence of ferning. Analysis of a total of 102 cycles awaits completion. [88% correlation is a long way from the 98.6% method effectiveness of cervical mucus. Ed.]

Nontraumatic Tubal Occlusion As a New Technique For Female Voluntary Sterilization. I. Manuaba. *Advances in Contraception* 9 (December 1993): 303-311.

Sixteen percent (16%) of fertile couples worldwide have been sterilized by female sterilization - 138 million. The program is heavily promoted, but hampered by the recognized late complications of psychosomatic psychosexual problems and changes in the menstrual cycle. Some of the complications are thought to be due to interference with the blood supply to the ovary which many times produces menstrual irregularity and premature menopause. A technique of isolating the tube, dissecting it carefully so as to avoid the ovarian arteries is described. It is hoped that this technique will reduce the complications and enhance the popularity of the operation. [This is one of the few acknowledgements that there are complications following tubal ligation. Ed.]

Clinical Pharmacology of RU 486 — an Anti-progestin and Antiglucocorticoid. I.M. Spitz & C.W. Bardin. *Contraception* 48:5 (November 1993): 403-444.

RU486 - A comprehensive review of the biological and clinical aspects of mifepristone (RU486) is summarized: 1) RU486 blocks progesterone recep-

tors in the endometrium. 2) RU486 blocks glucocorticoid receptors. 3) Mifepristone analogs, lilopristone, and onapristone are among 300 compounds now researched to isolate progesterone block from glucocorticoid (cortisol) block. This results in an increase to ACTH production. With short-term or single doses, no clinical affects have been noted, but long-term use has led to signs of cortisol deficiency - weakness, nausea, vomiting, and other signs of adrenocortical deficiency. 4) Besides its well-publicized use as an abortifacient (progesterone block in the endometrium) RU486 softens and dilates the cervix and has been found more useful to prepare for surgical abortion than prostaglandins; it also has fewer side effects. 5) RU486 also blocks progesterone receptors in the ovary and in the pituitary, but to a lesser extent than in the uterus. 6) As an inducer of menses, RU486 was unsatisfactory, even when it blocked ovulation, because it did not induce bleeding. 7) RU486 has been used in small trials as a post-coital agent and compared favorably with standard treatment. 8) RU486 produced subjective improvement of pelvic pain in endometriosis patients, but did not affect the extent of their disease. The women became anovulatory and amenorrheic, but ovarian suppression was incomplete. 9) Uterine fibroids of 10 women decreased to half their size after 12 weeks of treatment. 10) Breast cancer. Some breast cancers contain progesterone receptors. In rats, RU486, combined with antiestrogen or LHRH agonists, breast tumor remission rates were higher than without RU486. However, a pilot trial with 22 post-menopausal or oophorectomized women whose tumors were already resistant to chemotherapy found only 4 women with measurable tumor regression. Another study of 11 post-menopausal women found only 1 with an objective response; 6 were stabilized for a short time, and 4 progressed. 11) Meningiomas. Some meningiomas contain progesterone receptors. While nude mice had some positive responses, the majority of patients did not. 12)

Cushing's Syndrome. The anti-glucocorticoid effect benefitted 7/11 patients with Cushing's Syndrome but was useless in Cushing's Disease. 13) Anti-glucocorticoid effects on preventing muscle atrophy and the growth cycle of herpes and Maloney viruses are being explored. 14) Teratogenic affects so far: Three women whose attempted abortions with RU486 failed, delivered normal babies. One pregnancy was terminated at 18 weeks for ultrasonically demonstrated anomalies which did not necessarily correlate with RU486. Teratogenic effects have been reported after Misoprostol administration which the authors of the review mentioned as a possible alternative to mifepristone. [See abstract on Misoprostol in Brazil. Ed.]

Misoprostol: The Experience of Women in Fortaleza, Brazil. H.L. Coelho, et al. *Contraception* 49 (February 1994): 101-110.

Even though abortion is illegal in Brazil, poor control of drug marketing has led to widespread use of Misoprostol, a prostaglandin indicated for ulcer treatment, which was introduced in 1986 and had spread throughout the country as an abortifacient by 1990. While the drug is a weak abortifacient, the induced bleeding justifies seeking medical assistance to complete the incomplete abortion by curettage at public hospitals. In 1989, 16.4 million tablets of Misoprostol were sold in Brazil, including 4.7 million in the Northeast Region, whose population of 42 million includes 11 million women in the fertile age. Their contraceptive prevalence is 59%, including 38% female sterilization. Because of the epidemic of curettage, Misoprostol sales were prohibited in July 1991. A hundred and two (102) women from Fortaleza were interviewed about their experience of Misoprostol abortion: 57% were 20-29 years old, 46% were never married, had less than 8 years education or were of low socio-economic level; 81% were Roman Catholic; 22% were heads of the family; 39% were wives; 26% were

daughters; 12% lived with friends, and 2% were live-in housemaids. For two-thirds of the group, the use of Misoprostol was their first attempt. Most had heard about the drug from neighbors. Eighty-two percent (82%) experienced bleeding, which led to abortion. More than half of these women required a D&C to complete the abortion. Two-thirds of the women reported intense pelvic pain; more than a third hemorrhaged, and one-fourth complained of headache, while 10% had diarrhea, nausea or vomiting. Thirteen percent (13%) became infected and 4% suffered uterine perforation [Presumably from the D&C. Ed.]. While the majority of women favored legalizing abortion, nearly as many favored prohibiting Misoprostol sales. Two-thirds said they would never repeat the experience and more than half said they would not suggest it for a friend.

Comparative In Vitro Study of Contraceptive Agents With Anti-HIV Activity: Gramicidin, Nonoxynol-9, and Gossypol. A.S. Bourinbaier & S. Lee-Huang. *Contraception* 49 (February 1994): 131-137.

While the spermicide nonoxynol-9 has been alleged to have virucidal activity in vitro, its efficiency is not as high as was previously believed. Gramicidin, an antibiotic produced by the *Bacillus brevis* soil bacteria was compared with nonoxynol-9 in vitro and shown to be effective at a 1000-fold lower dose than that for either nonoxynol-9 or gossypol, which interferes with spermatozoal metabolism and has been used to some extent in China as a male contraceptive. [Its median effective dose was so close to the minimum lethal dose that no Western country would consider using it. Ed.] Gramicidin was used as a spermicide in the former Soviet Union. It is used in the U.S. as a topical non-irritating antibiotic, especially in eye infections, and has shown anti-fungal and anti-protozoan activity also. Further studies are recommended.

Long-term Contraceptive Effects of Intrauterine Neem Treatment (IUNT) in Bonnet Monkeys: An Alternate To Intrauterine Contraceptive Devices (IUCD). S. Upadhyay, et al. *Contraception* 49 (February 1994): 161-169.

Experimental treatment of female bonnet monkeys with an application of 1 ml of neem oil inserted into the uterine cavity with a catheter blocked fertility for 7-12 months. The effect was reversible as all the animals later became pregnant and delivered normal babies. The neem oil treatment did not affect menstrual cyclicity or ovarian function and microscopic studies of the uterus showed no morphologic change. However, immunohistochemical studies found an increase in the number of MCH-II antigen positive cells following the treatment, showing that the ability of the uterus to produce antigens was increased. This is presumed to be due to the anti-fertility effect of neem oil. Phase I studies on human subjects are now in progress to evaluate the potential of this method as an alternative to intrauterine devices.

Task Force Report on The Outcome of Pregnancies and Children Conceived by In Vitro Fertilization (France: 1987 to 1989). P. Ruffat, et al. *Fertility and Sterility* 61:2 (February 1994): 324-335.

Eleven ART (assisted reproduction) centers cooperated in a study of all pregnancies conceived by IVF-ET, (in vitro fertilization - embryo transfer) Zygote Intrafallopian Transfer (ZIFT) or frozen embryo transfer (ET) performed between January 1, 1987 and June 30, 1989. Only clinical pregnancies were surveyed while chemical pregnancies, those with only a transiently elevated HCG level, were excluded. Of 1,637 pregnancies, there were 1,263 deliveries. Of 1,616 liveborn or still born children, 1,011 were alive after one year. (Several pregnancies resulted in multiple births.) Compared with the general population, the pre-term birth rate for ART was 22.7% for all deliveries, 12.2% for Singleton deliveries, com-

pared with 5.6% in the general population; 34.7% of ART babies weighed less than 2500g compared with 5.2% (in France). The perinatal, neonatal, and infant mortality rates were higher than the national average, while the rate of congenital malformation - 2.86% was comparable with the national rate of 2.08%. Two percent (2%) of the children were diseased during the whole follow-up year. This is considered close to a normal outcome.

Optic Neuropathy Associated With Clomiphene Citrate Therapy. A.W. Lawton. *Fertility and Sterility* 61:2 (February 1994): 390-391.

A 31-year old woman with primary infertility developed loss of vision in her right eye following a 5-day course of 50mg clomiphene citrate per day. Two weeks later, her visual acuity in the affected eye was 20/200. There were vascular changes, including splinter hemorrhages in the eye grounds with marked swelling of the optic disk. Her vision in the right eye gradually improved to 20/60. The diagnosis was anterior ischemic optic neuropathy.

Clomiphene citrate treatment is followed by visual complaints in 5-10% of patients. This is usually confined to blurring or "spots" in their vision. A close chemical relative of clomiphene citrate, tamoxifen, has been linked with bilateral optic neuritis. Optic nerve injury is possible with the use of hormonal agents, particularly when these increase the tendency towards thrombosis. The manufacturer warns that visual symptoms require prompt cessation of treatment and immediate ophthalmologic assessment.

The Use of a Shared Donor Oocyte Program to Evaluate the Effect of Uterine Senescence. J.H. Check, et al. *Fertility and Sterility* 61:2 (February 1994): 252-256.

"Shared donor oocyte program" is a term applied to using ova from one woman for in vitro fertilization and embryo transfer (IVF-ET) to women

who have uteri and non-functioning ovaries, usually due to failure. IVF-ET outcomes were studied in women over and under the age of 40. Clinical pregnancy rate per transfer was 29.2% for younger women and 25.4% for the older women, live birth rate was 29.6% for the younger women and 22.4% for the older recipients. These differences were not significant statistically. When there is a decline in uterine receptivity for embryo implantation due to advancing age, it is at least remediable with hormonal adjustments.

Experiences of Legal Sterilization in Scandinavia. B.E. Ehn & J. Lijestrand. *Contraception* 48:2 (August 1993): 157-167.

Male and female sterilization has been legal in Scandinavia since 1970. Its utilization is low, compared to many other countries.

% of Sterilized Contraceptive Couples

Country	Male	Female
Sweden	2	4
Norway	4	12
Denmark	NA	NA
USA	17	13
UK	12	11
Thailand	6	23
China	8	28
India	16	22
Australia	10	28
S. Korea	14	45
Worldwide	41.5 m	140 m

Sterilization Male/female ratio/year

Sweden	20/80
Denmark	40/60
Norway	25/75

Ninety-five percent (95%) of men and women are satisfied with the procedure at follow-up. Bleeding disturbances are reported by 9-17% of sterilized women, dysmenorrhea by 15%, 4-9% have abdominal pains which began after the procedure. Pregnancies - 0.54-1.16% after female sterilization, 0.5% after vasectomy.

What We Have Learned From Recent IUD Studies: A Researcher's Perspective. I-C Chi. *Contraception* 48:2 (August 1993): 81-108.

The literature documents that: 1) IUDs are not abortifacients. 2) Newly developed IUDs are highly effective and last for a long time. 3) IUDs may be used by most nursing mothers. 4) Immediate post-placental insertion reduces the risk of expulsion. 5) Medicated IUDs are not associated with an increased risk of pelvic inflammatory disease, nor of ectopic pregnancy or subsequent infertility. The author finds insufficiently addressed issues to be: 1) the effect of the inserter's skill on IUD performance; 2) their use by nulliparous or older women; 3) relationship to chlamydia infection; 4) long-term safety, including actinomyces infections; 5) massive country-wide programs; and 6) removals and replacement. [The review of the literature fails to address the obvious connection between IUDs and sexual promiscuity, hence the potential for STDs as well as the general degradation of the sexual act. Ed.]

Lactation and a Reduced Risk of Premenopausal Breast Cancer. P.A. Newcomb, et al. *New England Journal of Medicine* 330:2 (January 13, 1994): 81-87.

The reduction of the risk of breast cancer among women who have lactated has been assumed but not well studied. A multi-center population based case-control study of 5,878 case subjects and 8,216 controls was analyzed. After adjusting for parity, age at first delivery, and other risk factors for breast cancer, lactation was associated

with a slight reduction of risk of breast cancer among pre-menopausal women, compared to women who had had children and had not lactated (RR = 0.78) while RR among post-menopausal women who had lactated, compared to those who had not, was 1.04. With increasing cumulative length of lactation, the reduced risk of breast cancer among pre-menopausal women was evident. If first lactation began before the age of 20 and total breastfeeding was at least 6 months, RR = 0.54. This risk reduction did not continue into the post menopause, suggesting that other factors are also operating. Since lactation can be modified by behavior, increasing the period of lactation would theoretically reduce the risk of pre-menopausal breast cancer. If women who do not breastfeed or feed for less than 3 months were to increase that to 4-12 months, breast cancer among parous pre-menopausal women could be reduced by 11%; if all women with children lactated for 24 months or longer, the incidence might be reduced by nearly 25%. These figures are speculative.

Finasteride. R.S. Rittmaster. *New England Journal of Medicine* 330:2 (January 13, 1994): 120-125.

Testosterone acts directly on many tissues, including the prostate and skin. It requires conversion by the enzyme 5 α reductase before it can become biologically active as dihydrotestosterone. Recently Finasteride, an inhibitor of 5 α reductase has been used to block dihydrotestosterone production and androgen reaction in the prostate and skin. The drug is used

to treat men with benign prostatic hyperplasia as an alternative to surgery. It is also very expensive. When used in animal experiments, it has led to Leydig cell hyperplasia and adenomas, probably because it causes an increase in LH. However, the decrease in serum dihydrotestosterone concentration with finasteride treatment did not affect LH or FSH in young male volunteer subjects. The administration of 5mg finasteride daily for 12 weeks reduced semen volume by 25%, but had no effect on total sperm counts, sperm motility or morphology. The drug is effective in the treatment of benign prostatic hyperplasia, but reduces libido slightly (5.4%); 4.3% of men reported impotence. Trials with prostate cancer are in progress. Men with natural 5 α reductase deficiency have sparse facial and body hair and male pattern baldness does not develop. Analogous findings were found in patients who took finasteride. No studies in women with hirsutism have been published. No significant effect on acne has been reported.

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Current Medical Research, a supplement of the **NFP Diocesan Activity Report**, is published quarterly. Hanna Klaus, M.D. is the editor. The purpose of the supplement is to serve the Roman Catholic diocesan NFP programs of the United States through providing them with up-to-date information on research within the field of fertility, family planning, and related issues. The Diocesan NFP teacher should be equipped to understand the various methods of contraception and be able to explain their incompatibility with the practice of the natural methods of family planning.

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