

CONTRACEPTION AND SEXUAL FUNCTION

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DISCLOSURES

- o Speaker/consultant
 - Shionogi
 - Novo Nordisk
 - Neogyn
 - Intone
 - Lelo


OBJECTIVES

- o Describe the positive and negative impact of contraceptive options on female sexual function
- o Identify appropriate birth control options for patients reporting sexual complaints or at high risk for sexual dysfunction

ACKNOWLEDGEMENTS

Thanks to Drs. Irwin Goldstein, Andrew Goldstein, Brooke Faught and Crista Johnson for the use of some of their content in this presentation


- Contraceptive pills were first approved for use in 1960 (>50 years ago)
- They are currently used by more than 100 million women worldwide and by almost 12 million women in the United States



BIOCHEMICAL CHANGES IN 100% OF HORMONAL CONTRACEPTIVE USERS

Hormonal contraceptives cause:

1. Significant increase in sex hormone binding globulin
2. Significant decrease in calculated free testosterone



Int J Impot Res, 2004 Apr;16(2):112-20.

Serum androgen levels in healthy premenopausal women with and without sexual dysfunction: Part A. Serum androgen levels in women aged 20-49 years with no complaints of sexual dysfunction.

Guay A, Murantiz R, Jacobson J, Takakoub L, Traish A, Quirk F, Goldstein I, Spark R.
Center for Sexual Function, Lahey Clinic Northshore, One Essex Center Drive, Peabody, MA 01960, USA. andre.t.guay@lahay.org

Abstract
Androgen insufficiency is a recognized cause of sexual dysfunction in men and women. Age-related decrements in adrenal and gonadal androgen levels also occur naturally in both sexes. At present, it is unclear if a woman's low serum androgen level is a reflection of the expected normal age-related decline or indicative of an underlying androgen-deficient state. We studied premenopausal women with no complaints of sexual dysfunction to help define a normal female androgen profile. In all, 60 healthy, normally menstruating women, ages 20-49 y, were studied. The Abbreviated Sexual Function Questionnaire was administered along with a detailed interview. Radioimmunoassay measurements of morning serum testosterone (T), free testosterone (FT), dehydroepiandrosterone-sulfate (DHEAS), sex hormone-binding globulin (SHBG), and free androgen index (FAI) were measured during days 8-15 of the menstrual cycle. In women 20-49 y old without complaints of sexual dysfunction, serum androgen levels exhibit a progressive stepwise decline. Comparing values obtained in women age 20-29 y to those obtained in women 40-49 y, specific hormone decrements were DHEAS 195.6-140.4 microg/dl, serum T 51.5-33.7 ng/dl, FT 1.51-1.03 pg/ml. SHBG did not change significantly in women in this age group. The FAI reflected the age-related decrease in female androgen levels. The framework for the development of a female androgen profile in women with no complaints of sexual dysfunction has been established, and an age-related decrease in testosterone and its adrenal precursor, DHEAS, has been demonstrated. The FAI mirrors these decreases and its usefulness in clinical practice is confirmed. A precipitous decline in all androgens occurs after the decade of the 20s, yet SHBG does not show a significant change throughout the premenopausal years.

HORMONAL LEVELS IN HEALTHY PREMENOPAUSAL WOMEN

Age	20-29 (n=17)	30-39 (n=23)	40-49 (n=20)
DHEAS ug/dL	176.9-214.3	139.0-170.8	124.7-156.1
SHBG nmol/L	43.6-58.6	44.6-52.4	47.0-58.4
Total T ng/dL	45.5-57.5	27.6-39.8	27.0-38.6
Free Androgen Index (FAI)	3.72-4.96	2.04-2.96	1.98-2.94
Calculated Free T picomol/L	21.5-27.2	13.4-19.5	12.4-17.8
Calculated Free T ng/dl	0.6 - 0.8	0.4 - 0.6	0.4 - 0.6

Int J Impot Res, 2004 Apr;16(2):112-20.

Serum androgen levels in healthy premenopausal women with and without sexual dysfunction: Part A. Serum androgen levels in women aged 20-49 years with no complaints of sexual dysfunction.

Guay A, Murantiz R, Jacobson J, Takakoub L, Traish A, Quirk F, Goldstein I, Spark R.

Impact of Oral Contraceptives on Sex Hormone-Binding Globulin and Androgen Levels: A Retrospective Study in Women with Sexual Dysfunction
J Sex Med 2006;3:104-113

Claudia Panzer, MD,* Sarah Wise, MS,¹ Gemma Fantini, MD,¹ Dongwook Kang, MD,¹ Ricardo Munariz, MD,² Andre Guay, MD, FACP, FACE,² and Irwin Goldstein, MD³

	Continued users	Discontinued users	Never users	
Total testosterone (ng/dl)	31.7	34.6	37.5	P = 0.086
SHBG nmol/L	149	89.7	35	P = 0.0001
Calculated free testosterone (ng/dl)	0.19	0.31	0.65	P = 0.0001

THE EFFECTS OF ORAL CONTRACEPTIVES ON ANDROGEN LEVELS AND THEIR RELEVANCE TO PREMENSTRUAL MOOD AND SEXUAL INTEREST: A COMPARISON OF TWO TRIPHASIC FORMULATIONS CONTAINING NORGESTIMATE AND EITHER 35 OR 25 MCG OF ETHINYL ESTRADIOL.

Both OCs produced reductions in mean Testosterone
 -N/EE35: from 1.33 to 0.60 nmol/L, p<.001;
 -N/EE25: from 1.12 to 1.02 nmol/L; nonsig (NS)

Free Testosterone
 -N/EE35: from 41.3 to 4.4 pmol/L, p<.001
 -N/EE25: from 25.4 to 7.9 pmol/L, p<.01)

Reduction in T / FT was significantly greater with the higher EE dose
 -(N/EE35) (p=.05 and p=.03, respectively).

Greco T, Graham CA, Bancroft J, Tanner A, Doll HA. Contraception. 2007 Jul;76(1):8-17

DOES ORAL CONTRACEPTIVE-INDUCED REDUCTION IN FREE TESTOSTERONE ADVERSELY AFFECT THE SEXUALITY OR MOOD OF WOMEN?

- Aim to examine whether changes in plasma androgen levels (total testosterone (T), free testosterone (FT), and dehydroepiandrosterone-sulfate (DHEA-S)), induced by oral contraceptive (OC) use were related to changes in sexual interest or response or in mood.
- Sixty-one women provided blood samples and were assessed using interviews and standardized questionnaires prior to starting and after 3 months on OCs (Ortho-Tricyclen, Ortho-Tricyclen-Lo, or Ortho-Cyclen), all containing norgestimate.

Graham CA, et al. Psychoneuroendocrinology.2007 Apr;32(3):246-55.

DOES ORAL CONTRACEPTIVE-INDUCED REDUCTION IN FREE TESTOSTERONE ADVERSELY AFFECT THE SEXUALITY OR MOOD OF WOMEN?

- Significant decreased in T, FT, and DHEA-S were found after 3 months, although extent of reduction was variable across women
- Some support for relationship between degree of reduction in total T and FT and frequency of sexual interest after 3 months on OCs.
- **Some women** had NO loss of sexual interest in spite of substantial reduction in FT and there was overall no evidence that reduction in FT affected enjoyment of sexual activity with a partner
- Findings consistent with idea that some women may be more sensitive to changes in T than others
- No relationship was found between negative mood, as assessed by the Beck Depression Inventory, and changes in T, FT and DHEA-S.

Graham CA, et al. Psychoneuroendocrinology.2007 Apr;32(3):246-55.

COMPARISON OF ANDROGENS IN WOMEN WITH HYPOACTIVE SEXUAL DESIRE DISORDER: THOSE ON COMBINED ORAL CONTRACEPTIVES (COCs) VS THOSE NOT ON COCs.

The patients were healthy premenopausal women with HSDD, aged 22-50 years. The 106 patients were divided into two groups: those on COCs (N = 43) and those not on COCs (N = 63). A two-tailed t-test comparison was made between the two groups comparing free and total testosterone and sex hormone-binding globulin (SHBG).

These patients with HSDD on COCs had significantly lower free and total testosterone levels compared with those who were not on COCs. The SHBG was significantly higher in the group on COCs compared with those who were not on COCs.

Wamock JK, et al. J Sex Med. 2006 Sep;3(5):878-82

RELATION OF ANDROGEN RECEPTOR SENSITIVITY AND MOOD TO SEXUAL DESIRE IN HORMONAL CONTRACEPTION USERS

- Study aims to assess role of psychosexual, relationship, hormonal and genetic measures in the sexual desire of users of three hormonal contraceptive products [low-dose combined oral contraceptive (20 mcg ethinylestradiol/150 mcg desogestrel), progestin-only pill (75 mcg desogestrel) and vaginal ring (daily dose of 15 mcg ethinylestradiol/120 mcg etonogestrel)]
- Fifty-five couples were randomized over three groups in which women consecutively used each product during 3 months
- Both partners repeatedly filled out questionnaires on solitary and dyadic sexual desire (desire to behave sexually by oneself or towards a partner)
- Total and free testosterone, sex hormone binding globulin and a genetic marker of androgen receptor sensitivity [cytosine-adenine-guanine (CAG) repeat length] were assessed on blood samples of the female partners

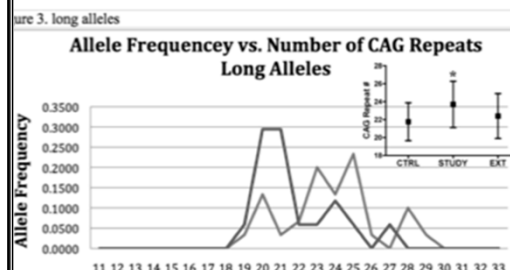
Elaut E, et al. Contraception. 2012 May;85(5):470-9.

RELATION OF ANDROGEN RECEPTOR SENSITIVITY AND MOOD TO SEXUAL DESIRE IN HORMONAL CONTRACEPTION USERS (CONT.)

- Sexual desire was higher in women with short CAG repeat lengths AND LOWER IN WOMEN WITH LONG CAG REPEAT LENGTHS
- Evidence exists for a role of androgen receptor sensitivity and sexual desire of hormonal contraceptive users

Elaut E, et al. Contraception. 2012 May;85(5):470-9.

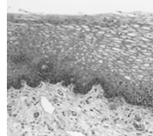
VARIABLE SENSITIVITY TO ANDROGEN CHANGES CAUSED BY CAG REPEAT PATTERNS- WHICH ARE UNIQUE TO THE INDIVIDUAL WOMAN



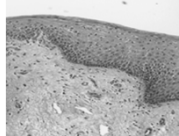
SEXUAL PAIN

VESTIBULODYNIA-OCP INDUCED

- Women who use OCPs before 17 yo have a RR of 9.2 of developing vestibulodynia. Women who start later have a RR 4.6.¹ More common with anti-androgenic and low doses OCPs. As the vestibule is rich in androgen receptors, low free testosterone may cause atrophy or glandular dysfunction.
- Women on OCP have altered morphological pattern with low and sparse dermal papillae. Might affect interlocking function of dermal papillae making epithelium more sensitive to stress (i.e., mechanical strain)²



Normal Vestibular Epithelium²


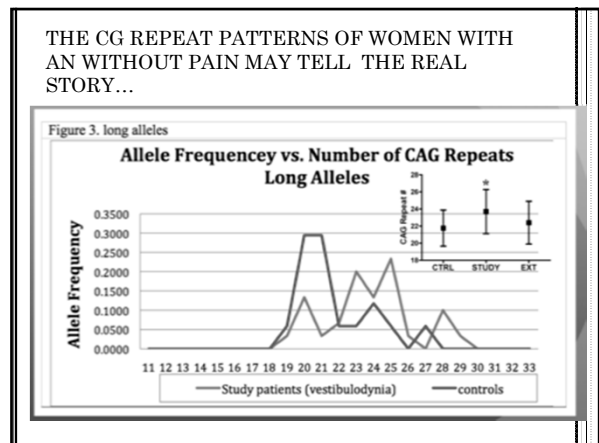


Vestibular Epithelium of Women on OCPs²

1. Bazin S, Bouchard C, Brisson J et al. *Obstet Gynecol* 1994; 83(1):47-50
2. Johannesson U et al. *Br J Dermatol*. 2007; 157: 487-493

HORMONALLY MEDIATED PVD

? ALL women on CHCs destined to develop pain syndromes?

OTHER CONTRACEPTIVE OPTIONS..LIMITED DATA



RELATION OF ANDROGEN RECEPTOR SENSITIVITY AND MOOD TO SEXUAL DESIRE IN HORMONAL CONTRACEPTION USERS (CONT.)

- Desire levels were higher during vaginal ring use (solitary, $p=.018$; dyadic, $p=.007$)
- Woman's mood was found to impact her dyadic sexual desire ($p<.001$); this scale was also strongly associated with the male partner's sexual desire ($p<.001$)

Elaut E, et al. Contraception. 2012 May;85(5):470-9.

SEXUAL FUNCTION IN FIRST-TIME CONTRACEPTIVE RING AND CONTRACEPTIVE PATCH USERS

To assess sexual function of first-time users of the contraceptive ring and contraceptive patch

Subjects in the ring group had worsening scores in the areas of arousal (score change -0.169 ring vs 0.010 patch), lubrication (score change -0.202 ring vs. 0.031 patch), and pain (score change -0.162 ring vs. 0.182)

Gracia CR, et al. Fertility and Sterility. 2010 Jan;93(1):21-8.

ORAL CONTRACEPTIVES VS INJECTABLE PROGESTIN: THEIR EFFECT ON SEXUAL BEHAVIOR

PRESENTED IN POSTER FORMAT AT THE ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR THE STUDY OF WOMEN'S SEXUAL HEALTH, ST. PETERSBURG, FL, FEB. 18-21, 2010.

ONATHAN A. SCHAFFER, MD, MICHELLE M. ISLEY, MD, MPH, MEGAN WOODWARD, MD

IMPACT OF ETONOGESTREL-RELEASING IMPLANT (Nexplanon) ON QUALITY OF LIFE AND SEXUAL FUNCTIONING

FSFI and SF-36 at baseline, 3mo and 6mo after implantation in Italian women.

No negative effects on libido and sexual functioning

In first 3 mo, users experienced temporary reduction in vitality, mental health, social functioning and emotional role functioning, but disappeared at 6mo

DiCarlo C, et al. Gynecol Endocrinol. 2014 Jan;30(1):53-6.

Devaluation of quality of life and sexual functioning of women using levonorgestrel-releasing intrauterine contraceptive system

- o Coll Antropol. 2008 Dec;32(4):1059-68.
- o Skrzypulec V1, Droszdol A.

Abstract

o The research encompassed 200 women aged between 30 and 45. 52 women using the levonorgestrel-releasing intrauterine system were qualified to the study as the research group (Mirena Group). The control groups consisted of 48 women using a different type of intrauterine device (Control Group I-Other IUD) and 50 women using no contraception (Control Group II). Female Sexual Function Index and Mell-Krat Scale was used as a research tool. A significant beneficial effect of the levonorgestrel-releasing intrauterine system on sexual functioning (sexual desire and arousal) was also revealed in the study. Sexual dysfunctions were diagnosed in 20.8% of Other IUD, 34.7% of Control Group II and 9.6% of Mirena Group. Levonorgestrel-releasing intrauterine system increases female quality of life and sexual functioning parameters

ORIGINAL RESEARCH—WOMEN'S SEXUAL HEALTH

Sexual Functioning in Women Using Levonorgestrel-Releasing Intrauterine Systems as Compared to Copper Intrauterine Devices

- o N= 402 IUD users
- o **Results.** One-third of IUD users (33%) reported a sexual dysfunction (c/w general population data)
- o * 25% a decreased sexual desire
- o * 5% arousal problems,
- o * 8% orgasm problems.
- o OF NOTE: 20% reported an increased sexual desire,
- o Women using a LNG-IUS did not differ significantly in distribution, type, or prevalence of sexual dysfunction, compared to Cu-IUD

Enzlin P, et al. JSM 2012

SUMMARY:

- o CHCs decrease FAI which may be assoc with decreased sexual functioning and vestibulodynia
- o Other birth control options have some impact on sexual functioning
- o IUD = contraceptive option which appears to have few significant sexual side effects and may enhance sexual response.

THANK YOU FOR YOUR KIND ATTENTION!!