Journal Review

Vaginal yeast colonization in non-pregnant women: a longitudinal study. Beigi RH, Meyn LA, Moore DM, Krohn MA, Hillier SL. *Obstet Gynecol* 2004; **104**: 926–930

The relationship between yeast colonisation, symptoms and antifungal self-medication remains poorly understood. Previous studies have involved pregnant women or women using hormonal contraception, and many have been underpowered.

This American cohort study aimed to determine the prevalence of yeast colonisation over a 1-year period in 18–30-year-old, sexually active, non-pregnant women. A total of 1248 women were recruited and more than 80% of the scheduled visits at baseline, 4, 8 and 12 months were attended. At each visit a questionnaire was used to enquire about symptoms, antifungal use, sexual/personal behaviour and contraception in the preceding 4 months. A swab of vaginal fluid was transferred to candida-selective culture media.

Some 70% of women were colonised by vaginal yeast at one or more visits, but only 4% were colonised at all four visits. Factors associated with yeast colonisation included marijuana use [odds ratio (OR) 1.3, 95% CI 1.1–1.5], depot medroxyprogesterone acetate (DMPA) use (OR 1.4, 95% CI 1.1–1.7), sexual activity in past 5 days (OR 1.5, 95% CI 1.2–1.8) and concurrent colonisation with lactobacillus and group B streptococcus. Symptoms of pruritis and vulvovaginal burning were associated with yeast colonisation but antifungal use was not.

The results support the concept that *Candida albicans* exists as part of the normal vaginal flora in many healthy asymptomatic women, and that host factors influence the development of symptoms. The authors suggest that the lack of an association with antifungal use casts doubt on the reliability of self-diagnosis and self-treatment of thrush symptoms. However, the study was limited by possible recall bias and the fact that most women were not examined at the time they had symptoms or used antifungal treatment. Moreover, the study population was relatively young (80% under 25 years) and from similar socioeconomic backgrounds, so may not be representative of the wider female population.

The finding of an association with DMPA conflicts with previous studies showing a protective effect against yeast colonisation. Further research is therefore required to confirm an association between yeast colonisation and injectable progestogen-only contraceptives.

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Effects of estrogen with and without progestin on urinary incontinence. Hendrix SL, Cochrane BB, Nygaard IE, Handa VL, Barnabei VM, Iglesia C, *et al*. *JAMA* 2005; **293**: 935–948

It has been assumed until recently that hormone replacement therapy (HRT) improves urinary symptoms, an assumption based largely on biological, observational and anecdotal evidence. This paper reports more findings from the Women's Health Initiative Study, which has already caused a sea change in HRT prescribing.

A total of 27 347 postmenopausal women were recruited from 40 US centres and randomised to placebo or HRT [either 0.625 mg conjugated equine oestrogen (CEE) and 2.5 mg medroxyprogesterone acetate (MPA) or 0.625 mg CEE alone]. Urinary incontinence and quality of life measures were assessed by questionnaire.

Contrary to expectations, women who were continent at baseline were more likely to develop stress, mixed and urge incontinence at 1 year if taking HRT. The risk was highest for stress incontinence [CEE + MPA relative risk (RR) 1.87; CEE alone RR 2.15]. Urge incontinence was significantly increased only in the CEE alone group (RR 1.32).

Among women who complained of urinary incontinence at baseline, those in the HRT arm reported worse incontinence, more restriction of daily activities and were more bothered by symptoms at 1 year than those taking placebo. Similar trends were seen in a subgroup of women followed up for 3 years.

The study population ranged in age from 50 to 79 years and contained higher numbers of older women compared with typical HRT users in the UK. Subgroup analysis showed that adverse effects were only statistically significant in women over 60 years of age.

In summary, the study failed to show any urological benefits of HRT and indicated deleterious effects on urinary incontinence symptoms, particularly in older women. Has yet another HRT myth been laid to rest? The evidence is certainly unfavourable and is likely to discourage the use of systemic HRT primarily for urinary symptoms.

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Steroid hormones for contraception in men: systematic review of randomized controlled trials. Grimes DA, Gallo MF, Grigorieva V, Nanda K, Schulz KF. *Contraception* 2005; **71**: 89–94

This is a comprehensive review of the progress made so far in the attempts to develop a credible male hormonal contraceptive. The principle behind male hormonal contraception is that it is possible to arrest sperm production by administering exogenous sex steroids that act via the hypothalamo-pituitary axis to suppress luteinising hormone and follicle-stimulating hormone levels. This approach also decreases production of testosterone so 'add-back' androgens are required to maintain physiological levels. Grimes *at al*. conducted a review of only the randomised controlled male hormonal contraceptive trials that used azoospermia as their outcome. They justified their exclusion of studies reporting oligozoospermia as an outcome by two observations. First, that it will be necessary to achieve azoospermia for contraceptive efficacy. However, it has previously been established that severe oligozoospermia (<1 million/ml) would provide efficacy comparable with existing methods of contraception. Their second reason is more robust, stating that the definitions of oligozoospermia varied greatly between trials and made exact comparisons difficult.

There are many different regimens that have been tested as potential male hormonal contraceptives including testosterone alone, and testosterone in conjunction with progestogens or GnRH antagonists. Testosterone is currently available as short- and long-acting injectables, slow-release subcutaneous pellets, transdermal patches, cutaneous gel, oral preparations and a buccal adhesive tablet. Progestogens are available as oral preparations, long-acting injectable and slow-release implants, and GnRH antagonists are currently only available as injectables. There is therefore a very wide range of potential combinations of steroids and delivery methods. They concluded that the abilities of the various regimens analysed varied hugely from 0–100% in the proportion of men who attain azoospermia and that the trial periods used also demonstrated a wide range from 8 weeks to 1 year. The most promising combinations are all progestogen and testosterone regimens but there is not currently any regimen ready for clinical use. They also commented on some of the problems with studies performed in this field to date. Many of the trials are small and underpowered, resulting in fragmented data. There are large numbers of different regimens under investigation making direct comparisons difficult. The next step is for large-scale trials with sufficient participants to be able to confidently assess efficacy. These are currently ongoing; there is a Phase III study in progress in China and a large-scale commercial study underway in Europe.

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Ovarian function with the contraceptive vaginal ring or an oral contraceptive: a randomized study. Duijkers IJ, Klipping C, Verhoeven CH, Dieben TO. *Hum Reprod* 2004; **19**: 2668–2673

There is no doubt about the attractiveness of combined hormonal contraceptives administered in such a way as to avoid hepatic first-pass metabolism and variable efficacy in the presence of gastrointestinal disturbances. This paper from Organon in The Netherlands focuses on the NuvaRing® contraceptive vaginal ring. This ring releases 15 μg ethinylestradiol and 120 μg etonogestrel per day and is inserted for 3 weeks followed by a 1 week ring-free period. Previously it has been demonstrated that this regimen suppresses ovarian function and inhibits ovulation with a predictable cyclical bleeding pattern. The purpose of this study was to compare the effect on ovarian function of the vaginal contraceptive ring with a standard oral contraceptive pill (Microgynon 30®: 30 μg ethinylestradiol and 150 μg levonorgestrel) in healthy volunteers. Women, shown to ovulate in a screening cycle, were randomised to two monitored cycles with the vaginal ring ($n = 21$) or contraceptive pill ($n = 19$). Ovarian function was measured by transvaginal ultrasonography and hormone measurement every 3 days during the study cycles. The study was powered to detect a difference in the ratio of the maximum follicular diameter measured of 1.32. In both cycles ovulation did not occur in any treatment group. However, in the first cycle of treatment there was less follicular suppression in the vaginal ring group [geometric mean follicular diameter 11.8 mm in ring and 8.9 mm in pill groups; ratio 1.32 (1.08–1.62)]. This was not seen in the second cycle [12.7 mm and 11.4 mm, respectively; ratio 1.11 (0.91–1.36)]. The authors suggest that this difference is because the ring is started on Day 5 of the first cycle whereas the pill is started on Day 1. Indeed the endometrial thickness seemed higher in the first cycle of the ring treatment but not in the second. Obviously this was not an efficacy study and the authors claim similar ovarian suppression for the pill and vaginal ring in the second month of the study. However, they also measured serum oestradiol, luteinising hormone and follicle-stimulating hormone concentrations in each cycle. The study was not powered to analyse these and statistical analysis was not done. However, in both cycles it appeared that concentrations of all these hormones tended to be higher for the vaginal ring than for the pill treatment. Although ovulation may not occur, it is still not entirely clear that the biochemical suppression of ovarian function is the same with the vaginal ring and oral contraceptive pill.

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